Regional Research Collaborations

Merrill Series on
The Research Mission of Public Universities

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Introduction

Mabel Rice

The Fred and Virginia Merrill Distinguished Professor of Advanced Studies and Director, Merrill Advanced Studies Center, The University of Kansas

The following papers each address an aspect of the subject of the thirteenth annual research policy retreat hosted by the Merrill Center: *Regional Research Collaborations*. We are pleased to continue this program that brings together university administrators and researcher-scientists for informal discussions that lead to the identification of pressing issues, understanding of different perspectives, and the creation of plans of action to enhance research productivity within our institutions. This year's focus is on regional collaboration in research: examples of successful collaborations, emerging large-scale regional collaborations and the circumstances contributing to successful collaborations. The 2009 Merrill retreat provided an opportune time to consider the implications of the increase in regional research collaborations, and how these collaborations are managed and fostered.

Benefactors Virginia and Fred Merrill make possible this series of retreats: *The Research Mission of Public Universities*. On behalf of the many participants over more than a decade, I express deep gratitude to the Merrills for their enlightened support. On behalf of the Merrill Advanced Studies Center, I extend my appreciation for the contribution of effort and time of the participants and in particular to the authors of this collection of papers who found time in their busy schedules for the preparation of the materials that follow.

Fifteen senior administrators and faculty from four institutions in Kansas, Missouri, and Nebraska attended the 2009 retreat. Our keynote speaker for the event, Dr. Kevin A. Roth, gave a comprehensive overview of the role of regional collaboration in the success of the University of Alabama's Neuroscience Blueprint Core Center. In addition to those presenters whose remarks are published here, John Colombo served as moderator and contributed a valuable perspective as Director of the Life Span Institute at the University of Kansas.

Though not all discussants' remarks are individually documented, their participation was an essential ingredient in the general discussions that ensued and the preparation of the final papers. The list of all conference attendees is at the end of the publication.

The inaugural event in this series of conferences, in 1997, focused on pressures that hinder the research mission of higher education. In 1998, we turned our attention to competing for new resources and to ways to enhance individual and collective productivity. In 1999, we examined in more depth cross-university alliances. The focus of

the 2000 retreat was on making research a part of the public agenda and championing the cause of research as a valuable state resource. In 2001, the topic was evaluating research productivity, with a focus on the very important National Research Council (NRC) study from 1995. In the wake of 9/11, the topic for 2002 was "Science at a Time of National Emergency"; participants discussed scientists coming to the aid of the country, such as in joint research on preventing and mitigating bioterrorism, while also recognizing the difficulties our universities face because of increased security measures. In 2003 we focused on graduate education and two keynote speakers addressed key issues about retention of students in the doctoral track, efficiency in time to degree, and making the rules of the game transparent. In 2004 we looked at the leadership challenge of a comprehensive public university to accommodate the fluid nature of scientific initiatives to the world of long-term planning for the teaching and service missions of the universities. In 2005 we discussed the interface of science and public policy with an eye toward how to move forward in a way that honors both public trust and scientific integrity. Our retreat in 2006 considered the privatization of public universities and the corresponding shift in research funding and infrastructure. The 2007 retreat focused on the changing climate of research funding, the development of University research resources, and how to calibrate those resources with likely sources of funding, while the 2008 retreat dealt with the many benefits and specific issues of international research collaboration.

Once again, the texts of this year's Merrill white paper reveal various perspectives on only one of the many complex issues faced by research administrators and scientists every day. It is with pleasure that I encourage you to read the papers from the 2009 Merrill policy retreat on *Regional Research Collaborations*.

Executive summary

Regional Neuroscience Research Collaboration: The Alabama Experience

Kevin A. Roth, Robert and Ruth Anderson Professor and Chair, Department of Pathology, University of Alabama at Birmingham

- The Alabama Neuroscience Blueprint Core Center was established in 2006 as one of four Neuroscience Blueprint Interdisciplinary Center Core Grant (P30) Program awardees. The Centers were awarded based on their ability to meet the needs and unique requirements of their local and regional neuroscience research communities.

- The original application included approximately 50 investigators from UAB, Southern Research Institute, Auburn University, University of Alabama, Tulane University, Louisiana State University, and University of South Alabama.

- The P30 program funding our center emphasizes developing effective infrastructure and addressing regional neuroscience needs. The Alabama Neuroscience Center is designed to facilitate interdisciplinary investigation of nervous system function and dysfunction..

- The Alabama Neuroscience Blueprint Core Center rapidly met its original goals and now serves in support of neuroscientists at UAB and participating institutions throughout the Deep South.

- The establishment of this regional neuroscience research center has had a transformative effect on the neuroscience community at UAB and participating institutions and may serve as a model for other regional research efforts. The impact of our award has been felt well beyond the borders of Alabama.

Evolution of Reproductive Sciences at KUMC

Paul Terranova, Vice Chancellor for Research, University of Kansas Medical Center

- The current reproductive research at KUMC emanated from the Department of Obstetrics in 1959 when Kermit Krantz, MD was appointed chairman of the department. Dr. Krantz hired Gilbert Greenwald, Ph.D. who became a world class leader in reproductive biology and led KUMC faculty recruiting to the utmost.

- His involvement in the longest standing (43 years) NIH supported Center (Kansas Intellectual and Developmental Disabilities Research Center) led to the formation of the Center for Reproductive Sciences, Interdisciplinary Center for Male Contraceptive Research and Drug Development, and the Institute for Maternal Fetal Biology.

Collaborations, Scale Invariance, and the Extended Trust

Robert Duncan, Vice Chancellor for Research, University of Missouri

- We collaborate out of our mutual desire to improve our personal performance beyond the level that we can obtain through our efforts in isolation. This is the first and most fundamental criteria for a successful collaboration.

- We look for the collaboration to provide an immediate market for our efforts. We see ourselves as bringing some rare skill or perspective to the larger effort that is valued, and that value will help increase the significance of the entire effort.

- Clearly future collaborations will be required between our major research institutions within the Midwest to build coherently on our strengths in the Animal Health Corridor. As this large-scale collaboration moves more into human health, it will be important for us as a region to develop the infrastructure necessary to become a national powerhouse in translational medicine.

- Business ethics dictates that no one institution will be able to perform their own performance trials that are necessary to bring their own medical products and drugs to market through FDA approval, so this alone will drive a much stronger regional collaboration between our institutions. Great advantages will be realized by those regions of the United States that learn how to collaborate gainfully over a vast range of scales. We look forward to being a critical part of this essential process.

The NBAF is Coming: How did it happen and why Manhattan?

Jerry Jaax, Associate Vice President for Research Compliance and University Veterinarian, Kansas State University

- In January of 2009 the Department of Homeland Security announced that Manhattan Kansas would be the site for the new National Bio and Agrodefense Facility. The winning strategy for the Heartland BioAgro Consortium is a study in planning, cooperation, and regional collaboration. The key element of the winning formula was the quality, breadth and depth of its many active partners.

- An early strategic decision was to create the "NBAF in Kansas Task Force," a strong coalition committed to promoting the importance of research to protect the American food supply and agriculture economy.

- The Kansas Bioscience Authority was created by the Kansas Economic Growth Act of 2004 with the sole purpose of advancing Kansas' leadership in bioscience. The KBA has been a driving force in the planning and execution of the successful bid to land the NBAF in the State.

- The Animal Health Corridor, a conglomeration of animal health industries greatly strengthened the case that Manhattan was ideally located for collaboration and exploitation of research products developed by the new federal laboratory.

- The Kansas City Life Sciences Institute provided an essential element in regional and bi-state cooperation and collaboration during the entire proposal process. Their involvement provided leadership and a coordinating presence in putting together the impressive and diverse regional consortium responsible for the winning proposal.

- In the late 1990s, K-State's commitment to build a major agricultural biocontainment facility, and the overwhelming community acceptance of the BRI was perhaps the biggest discriminator for DHS in their deliberation about a site for the NBAF.

- The formation of the Heartland BioAgro Consortium was a key strategic move in the formulation of the winning bid. The depth and breadth of regional collaboration and support is evident in the diverse makeup of the consortium.

- The Heartland BioAgro Consortium believed that co-location with Kansas State University, a major land grant university with a college of veterinary medicine; and strong programs in agriculture would have strong appeal to planners for the new NBAF. This was in fact borne out in DHS decision matrix documents.

The University of Minnesota Biocontainment Laboratory: What It Is and the Emphasis on Regional

George Stewart, McKee Professor of Microbial Pathogenesis and Chair, Department of Veterinary Pathobiology, University of Missouri

- The RBL network can become a major resource to universities and provide the necessary research environment to advance our knowledge of biothreat and emerging infectious disease agents.

- With the large number of diseases arising naturally in the past twenty years, these facilities will play a vital role in protecting American public health in the years to come.

- To effectively utilize these facilities, researchers must learn to establish research ties with these specialized facilities and the RBL host university must establish effective lines of communication with regional universities and private sector companies to facilitate cooperative research agreements.

- Regional biocontainment laboratories should be truly regional and universities must learn to be less territorial in dealing with their sister institutions. The biocontainment facilities should be a source of new opportunities and if managed correctly, not a fiscal drain on the host university.

Roles of a Center and Institute in Promoting Regional Research Collaborations

Peter Smith, Director, Kansas Intellectual and Developmental Disabilities Research Center, University of Kansas Medical Center

- The role of collaboration in research has become more dominant with the passage of time, as it has become difficult to find individuals whose breadth of technical skills could address the full range of emerging medical questions.

- Logistical issues to be overcome in order to successfully develop collaborative research are as follows: Identifying target areas of research, growing the investigator base, creating group cohesion and a common cause, and thinking regionally.

- A significant challenge in promoting translational research programs is developing communication among individuals with convergent interests. Weekly Translational Discovery Forums (TDFs) provide a vehicle that brings together established scientists and trainees, clinicians and basic researchers, to share interests and ideas in a setting that encourages interactions.

- Partnerships with existing programs have become increasingly important over the past decade. An economy of scale can be beneficial. Typically, independent programs have common interests and needs, and there is little advantage in duplicating existing resources that may already have the capacity to serve additional purposes.

Contract Staffing Partnerships

Kerry Taylor, Assistant Vice President for Research (Animal Care), Kansas State University

- The recruitment and selection of a highly trained and motivated staff is perhaps one the most difficult tasks facing animal-based research programs today.

- Only those institutes that can successfully optimize the mix of in-house, contract and outsourced individuals into a collective of talented and trusted employees will be able to survive and thrive.

- One key ingredient to building an effective research team is the adoption of a counter-intuitive approach to selection of human resources.

- The most successful programs will ensure that staff possess baseline technical abilities and have the interpersonal skills which are critical for meeting the analytical challenges and productivity requirements of laboratory facilities nationwide.

Forming Successful Unconventional Collaborations

Annie Sobel, Assistant to the Provost and the Vice President, University of Missouri

- Forming and sustaining unconventional collaborations is an opportunity to advance knowledge in unanticipated and sometimes surprising ways.

- The exploration of relationships, ideas, cultures, and the range of scientific disciplines define the edges of innovation and entrepreneurship.

- Navigating the landscape to promote successful collaboration is often challenging. Collaboration requires continued nurturing through resources and institutional support to retain sustainability.

- Many collaborations converge on a challenging set of problems and issues characterized as multi-dimensional or inter-disciplinary, and may be catalyzed by emergencies.

Using Analytical Chemistry to Unravel Disease State Mechanisms: Application to Huntington's Disease

Michael Johnson, Assistant Professor of Chemistry, University of Kansas

- In today's research environment, productive collaborations are essential for maximizing the impact of research efforts. This is especially true in neuroscience, one of the most rapidly advancing scientific fields. Productive collaborations have been a positive force in enhancing our ability to address important problems in neuroscience.

- Provided as an example of a collaborative effort are our studies on Huntington's disease, a fatal, genetic neurological disorder. The mission of our laboratory is to develop and apply analytical methods for the study of biological systems.

- Our mission has been enhanced by several important collaborations. These include a collaboration with a research group in Germany to obtain transgenic Huntington's disease rats, and collaborations at the University of Kansas which have strengthened our experimental approaches by expanding our repertoire of capabilities to collect neurochemical and behavioral measurements separately.

- These types of complementary efforts are expected to become increasingly important for neuroscience research as newer, more specialized techniques are developed.

The Nebraska Center for Molecular Biology of Neurosensory Systems: A Collaborative COBRE Project

Shelley Smith, Professor of Pediatrics, University of Nebraska Medical Center

- The Center for Neurosensory Systems has helped build an interactive group of researchers from 3 independent institutions, providing critical core facilities and bringing them together to produce the critical mass that supports discussion and growth of knowledge.

- The funding of research projects and provision of a mentoring program has resulted in independent funding for junior faculty who previously had not had that level of funding, helping our institutions "grow our own".

- Through additional support from other funding sources such as the INBRE or the University of Nebraska, the core facilities enhance the research infrastructure benefiting researchers at all 3 institutions.

- By networking with regional and national COBRE, INBRE, and SEPA researchers, the investment of the NCRR in IDeA states is leveraged further, so that the level of research quality is increased across the region.

Expanding the Reach of KU Research Through Regional Collaborations

Steve Warren, Vice Provost for Research & Graduate Studies, University of Kansas

- Collaboration brings different knowledge sets and skills to together to solve complex problems. However, it is often difficult and comes at a price. It requires social interaction, trust, and must offer advantages for all involved parties. People collaborate because it is necessary to solve an important problem.

- Local collaborations will continue to be the dominant form as measured by sheer numbers of participants. But if there is a good reason to collaborate with someone across the country or on the other side of the world, it is feasible due to email, Skype, secure websites, relatively cheap and frequent air travel. This has become so common that we think little of it.

- Given the relative ease of communicating and collaborating with great talent anywhere in the world, why limit ourselves to "regional collaborations? Here are three scenarios in which regional collaborations may be exactly the right approach: 1) uniquely regional research problems; 2) the development and maintenance of certain types of expensive research infrastructure; and 3) some regional economic development initiatives.

Regional Neuroscience Research Collaboration: The Alabama Experience

Kevin A. Roth

Robert and Ruth Anderson Professor and Chair, Department of Pathology, University of Alabama at Birmingham; Director, Alabama Neuroscience Blueprint Core Center

The Alabama Neuroscience Blueprint Core Center was established in 2006 as one of four Neuroscience Blueprint Interdisciplinary Center Core Grant (P30) Program awardees. The Centers were awarded based on their ability to meet the needs and unique requirements of their local and regional neuroscience research communities. The Alabama Neuroscience Center, which is housed at the University of Alabama at Birmingham (UAB), is designed to facilitate interdisciplinary investigation of nervous system function and dysfunction through a multi-dimensional analysis of genetically modified rodents and other small animal models. The Alabama Neuroscience Blueprint Core Center has rapidly met its original goals and now serves in support of neuroscientists at UAB and participating institutions throughout the Deep South. The establishment of this regional neuroscience research center has had a transformative effect on the neuroscience community at UAB and participating institutions and may serve as a model for other regional research efforts.

Introduction: Planning for the Alabama Neuroscience Blueprint Core Center began in 2005 shortly after the release of the Neuroscience Interdisciplinary Center Core Grant RFA announcement NS-06-003. Fortuitously, this RFA coincided with the preparation and submission of a strategic plan for neuroscience growth at UAB to the Dean of the School of Medicine in October, 2005. It was immediately apparent that there were many striking parallels between the goals of the RFA and the goals for neuroscience research at UAB. Following a series of small group meetings to define the focus of the P30 application, NIH funded neuroscience investigators throughout Alabama, Mississippi, and Louisiana were contacted by e-mail or phone and encouraged to participate in the application. Based on our review of the needs of the regional neuroscience community, we proposed to establish the Alabama Neuroscience Blueprint Core Center at the University of

Alabama at Birmingham. The original application included approximately 50 investigators from UAB, Southern Research Institute, Auburn University, University of Alabama, Tulane University, Louisiana State University, and University of South Alabama.

Neuroscience Blueprint: The P30 program that funds our center arose as a component of the NIH Blueprint for Neuroscience Research. This program is sponsored by 16 NIH Institutes, Centers, and Offices and is designed to focus on cross-cutting neuroscience activities, communicate best practices, and coordinate the planning and funding of research and development tools as well as neuroscience education, training, and career development. Together, these institutes provide approximately $5 billion in NIH funding for neuroscience research with the two largest participating NIH Institutes being the National Institute of Neurological Diseases and Stroke (NINDS) and the National Institute of Mental Health (NIMH).

The Center Core Grant (P30) Program was designed to create a novel approach for funding core resources that would breach interdisciplinary boundaries and promote a team approach to neuroscience discovery. The program emphasizes developing effective infrastructure and addressing regional neuroscience needs. Budgets were capped at $1.5 million per year in direct costs per application and applicants were encouraged to utilize existing institutional resources to enhance new core development. In addition to the Alabama Neuroscience Blueprint Core Center, three other centers were funded (La Jolla Neuroscience Center Core at the Burnham Institute; Neuroscience Center Core at the University of Minnesota and Mayo Clinic; and the Washington University Neuroscience Blueprint Interdisciplinary Center Core).

The Alabama Neuroscience Blueprint Core Center was awarded $8.6 million and began operations in September, 2006. The over arching goal of our Center is to facilitate interdisciplinary investigation of nervous system function and dysfunction through the use of genetically modified experimental animals. The increasingly sophisticated ability to regulate gene expression levels across cellular and temporal domains and to monitor gene expression at the cellular level in living animals and brain slice preparations *ex vivo* provides an unprecedented opportunity to advance our understanding of the neurosciences. To traverse this spectrum of techniques requires cooperation and talents of numerous scientists and is typically beyond the capabilities of individual laboratories. The Alabama Neuroscience Blueprint Core Center has five scientific cores: Molecular Engineering; Cellular and Molecular Neuropathology; Neuroimaging; *In Vivo* Physiology and Phenotyping; and Cellular and Synaptic Physiology; as well as an Administrative Core (http://www.alneurosciencecenter.uab.edu).

The Center has been remarkably successful and as of May 2009, over 50 manuscripts have acknowledged our assistance, including publications in Science [1], Nature Medicine [2], Nature

Neuroscience [3], and Journal of Neuroscience [4-7]. These publications include authors from greater than ten Southern Universities and approximately thirty United State's and international institutions demonstrating that the impact of our award has been felt well beyond the borders of Alabama.

Metrics of Success: The establishment of the Alabama Neuroscience Blueprint Core Center has been transformative for the neuroscience community at UAB. By providing new interdisciplinary core resources and external "validation" of the exciting neuroscience investigations at UAB and other participating institutions, there has been rapid and compelling growth of neuroscience-related research and educational activities in Alabama. The following is a partial list of direct and indirect consequences of our Blueprint award:

- Between 2005 and 2008, the number of NIH Neuroscience Blueprint affiliated awards increased from approximately 200 to almost 300.
- NIMH funding increased 112%, NINDS funding by 78%, and NIA funding by 33% between 2005 and 2008.
- The Alabama Neuroscience Blueprint Core Center affiliated UAB Comprehensive Neuroscience Center (Dr. Kevin A. Roth served as inaugural Director) was awarded full University-wide Inter-disciplinary Research Center status by the University of Alabama Board of Trustees in 2008.
- A new Undergraduate major in Neuroscience was approved by the University of Alabama Board of Trustees and its first class enrolled in 2009.
- UAB has experienced a net increase of approximately 40 new faculty in neuroscience-related tenure track positions since 2006.

In total, the impact of this award is now being demonstrated by increased number of NIH awards, more manuscripts being published in high impact scientific journals, new neuroscience-related training grants, and submission of interdisciplinary neuroscience grant applications involving investigators from multiple Alabama and regional institutions. The joint development and operation of the Alabama Neuroscience Blueprint Core Center and the UAB Comprehensive Neuroscience Center will hopefully, be a model for now neuroscience-related clinical care, research and education can be organized and maximally facilitated through an interdisciplinary, multi-institutional approach.

Looking Forward: The Alabama Neuroscience Blueprint Core Center and UAB remain committed to the growth of regional neuroscience. To accomplish this goal we must remain focused on effective communication and collaboration. Through these efforts we hope to obtain a better understanding of neurological and psychiatric disease pathogenesis and to use this knowledge to develop new treatments and cures for nervous system disorders.

Acknowledgements: I'd like to thank Dr. Tom Miller (Office of Translational Research, NINDS,

NIH) and the UAB Neuroscience Community for many helpful discussions and their unmatched enthusiasm for neuroscience investigation. The Alabama Neuroscience Blueprint Core Center is supported by NIH Grant NINDS P30 NS57098.

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Evolution of Reproductive Sciences at KUMC

Paul Terranova
Vice Chancellor for Research, University of Kansas Medical Center

Kermit E. Krantz, MD, was appointed chair of the department of Obstetrics & Gynecology at the University of Kansas Medical Center (KUMC) in 1959. His appointment as chair was central to the establishment of reproductive research at KUMC. Dr. Krantz was a well-known physician and researcher who had trained at Northwestern University in Chicago. He had a solid reputation as an emerging physician-scientist. His goal was to establish a clinical department with an emphasis on research. Two years after his arrival at KUMC, Dr. Krantz hired Gilbert S. Greenwald, Ph.D. as the first endowed chair in human reproductive research. Dr. Greenwald had trained at the University of California at Berkeley where he received his doctorate and was introduced to the female reproductive system, which served as the foundation for the remainder of his scientific career. Dr. Greenwald trained as a postdoctoral student at the Carnegie Institute of Embryology of Johns Hopkins University with a focus on the reproductive system.

After completing his postdoctoral studies at Hopkins in 1956, he moved to Seattle where he assumed the position of Instructor of Anatomy at the University of Washington. At the University of Washington, Dr. Greenwald published his first of many monumental papers on the ovary. In 1960, at a scientific meeting, Greenwald met Krantz, the new chair of Obstetrics and Gynecology at KUMC. Dr. Krantz recognized Gil's talents and enthusiasm for research and in 1961 offered him an Endowed Professorship in Research in Human Reproduction as well as a promotion to Associate Professor. The appointment of Dr. Krantz, who subsequently appointed Dr. Greenwald as a basic research scientist in the Department of Obstetrics & Gynecology, was the origin of a long history of outstanding reproductive research at KUMC. More faculty appointments in Obstetrics & Gynecology occurred. Zeev Dickmann, Ph.D., who had trained at Cambridge University and later at Vanderbilt University, was recruited to KUMC in 1962. His area of research was regulation of early pregnancy and embryo implantation. Almost simultaneously, Donald C. Johnson, Ph.D., a reproductive researcher with interest in ovarian function and pregnancy, was recruited to KUMC from the University of Iowa. These three individuals served as the core from which more than 45 years of reproductive research emanates from KUMC. The primary reasons for the persistence of reproductive research were their ability to garner NIH funding

for the research programs and the high quality of their publications. A few years later, Dr. Greenwald secured a Ford Foundation training grant in reproductive research which provided more than seven hundred thousand dollars over 15 consecutive years. This training grant supported numerous postdoctoral fellows from across the world and thus, enhanced the reputation of reproductive research at KUMC.

The Foundation provided by NIH and the Ralph L. Smith Foundation. In the mid 1960's KU obtained a program project grant entitled "Learning Disorders, Special Education and Speech Perception" from the National Institute of Child Health and Human Development (NICHD) of the NIH with leveraged monetary support from the Ralph L. Smith Foundation. There were three reproductive themes in the program project. A unique underlying principle was that abnormal reproductive processes might lead to abnormal development; at the time, little was known about these areas. Three reproductive themes in the program project grant from NIH were:

- Hormonal Regulation of Ovarian Function/ Reproductive Physiology and Neuroendocrinology led by Gilbert S. Greenwald.
- Control and Functional Relationships of Gonado-trophins led by Donald C. Johnson.
- Control of Preimplantation in Pregnancy led by Zeev Dickmann.

This program project grant was renewed as a NIH P30 grant that supported the Center in Mental Retardation and now is the Kansas Intellectual and Developmental Disabilities Research Center (www2.kumc.edu/kiddrc/). The Center is in its 43rd year of continuous funding and represents the longest continually held NIH grant by the University. The Ralph L. Smith Foundation provided resources to assist in the building of Smith East and West as well as the Miller Building on the KUMC campus in the late 1960's.

In 1975, KU obtained a NICHD T32 postdoctoral training grant in mental retardation. Several postdoctoral fellows in reproductive biology were supported by that grant including the author of this chapter (Paul Terranova, Ph.D., Vice Chancellor for Research at KUMC). From the early 1960's through the mid 1970's, reproductive research at KUMC gained a very solid reputation both nationally and internationally even though the reproductive group had only three faculty.

The next important event in the history of reproductive research at KUMC was the appointment of Gilbert Greenwald as Chairman of the Department of Physiology in 1977. He had negotiated with the Dean to recruit several new faculty. The recruits are listed below with a short description of their reproductive research at KUMC.

Gilbert Greenwald Recruits in the Department of Physiology related to Reproductive Research:

1. James Voogt, Ph.D. was recruited in 1977. His research focused on regulation of prolactin secretion. Dr. Voogt succeeded Dr. Greenwald after his retirement as Chair of Physiology in the mid 1990's.

2. Paul Terranova, Ph.D. was also recruited in 1977. His research focused on regulation of ovarian function. Dr. Terranova was the founding Director of the Center for Reproductive Sciences in 1995.
3. Michael Soares, Ph.D. was recruited in 1984. His research focused on placental trophoblast differentiation. Dr. Soares is the founding Director of the Institute of Maternal Fetal Biology at KUMC.
4. Joseph Tash, Ph.D. was recruited in 1990. His research focused on regulation of sperm motility and male reproductive function. Dr. Tash is the founding Director of the Center for Interdisciplinary Male Contraceptive Research & Drug Development, a NICHD sponsored center at KUMC.
5. Peter Smith, Ph.D. was recruited in 1986. His research focused on neurobiology of the autonomic nervous system but more recently has focused on factors regulating female pelvic pain. He is the Director of the Kansas Intellectual and Developmental Disabilities Research Center (formerly known as the Mental Retardation Research Center), a NICHD sponsored center for 43 years on the KUMC campus.

Because of the growing success of the reproductive group within the Departments of Obstetrics & Gynecology and Physiology, several other key recruits in various departments occurred. Those are listed below.

1. S.K.Dey, Ph.D., trained as a Ford Foundation postdoctoral fellow at KUMC in the laboratory of Zeev Dickmann, Ph.D. Dr. Dey developed his own research program in the Department of Obstetrics & Gynecology and rose to the rank of Professor in the Department of Obstetrics & Gynecology. His research focused on regulation of implantation during early pregnancy. He was a core and project leader in the KUMC Reproductive Center grants from NICHD. Dr. Dey subsequently moved to Vanderbilt University and then to Children's Hospital associated with the University of Cincinnati. Dr. Dey obtained two MERIT awards from NIH (NICHD and NIDA).
2. Joan Hunt, Ph.D., trained as a postdoctoral fellow at KUMC and joined the Department of Anatomy & Cell Biology, where she is a University Distinguished Professor. She studies the immunology of early pregnancy establishment and has held numerous NIH grants, including a program project. She was a core and project leader in the KUMC Reproductive Center grants from NICHD and Associate Director of the Reproductive Center.
3. William Kinsey, Ph.D., was recruited to KUMC from the University of Miami. He is currently a Professor of Anatomy & Cell Biology and Co-Director of the Center for Reproductive Sciences. He is also a core leader in the NICHD supported Interdisciplinary Center for Male Contraceptive Research and Drug Development at KUMC.
4. George Enders, Ph.D., Associate Professor of Anatomy & Cell Biology, trained at Harvard University and was a core leader in the Reproductive Center grants from NICHD. His research focused on testicular development.
5. Glen Andrews, Ph.D., is a University Distinguished Professor in the Department of Biochemistry & Molecular Biology. His research focuses on gene regulation in early development. He was recruited from Baylor College of Medicine and is an active participant in the activities of the Reproductive Center and Institute of Maternal Fetal Biology.
6. Leslie Heckert, Ph.D., is the Marion M. Osborne Professor of Molecular & Integrative Physiology and currently Co-Director of the Center for Reproductive Sciences. She was

also a project leader in the Reproductive Center grant and is currently a project leader in the NICHD supported Interdisciplinary Center for Male Contraceptive Research and Drug Development. She was recruited from Case Western Reserve University. Her research focuses on transcriptional regulation of testicular development.

7. Gustavo Blanco, MD., Ph.D., was recruited from Saint Louis University, is an Associate Professor of Molecular & Integrative Physiology and a Project Leader in the NICHD supported Interdisciplinary Center for Male Contraceptive Research and Drug Development.
8. Michael Wolfe, Ph.D., was recruited from Case Western Reserve University and is an Associate Professor of Molecular & Integrative Physiology. He was a new program development awardee in the original Reproductive Center grant from NICHD.
9. T. Raj Kumar, Ph.D., was recruited from Baylor College of Medicine and is currently an Associate Professor of Molecular & Integrative Physiology. His research focus is on genetic regulation of reproductive development.
10. Lane Christenson, Ph.D., was recruited from the University of Pennsylvania and is currently an Assistant Professor of Molecular & Integrative Physiology at KUMC. His research focuses on factors regulating ovarian function.
11. Katherine Roby, Ph.D., trained at KUMC and is a Research Associate Professor of Anatomy & Cell Biology. She was an Associate core leader in the Reproductive Center grants. Her research focused on factors regulating ovarian function and ovarian cancer.
12. Daudi Langat, Ph.D., is a Research Assistant Professor of Anatomy & Cell Biology. His research focuses on the immunology of placental development.
13. Margaret Petroff, Ph.D., is an Assistant Professor of Anatomy & Cell Biology. She studies the immunology of implantation and early placental development. She is project leader in the program project related to immunobiology of pregnancy.
14. Warren Nothnick, Ph.D., is an Associate Professor of Obstetrics & Gynecology. He studies the role of matrix metalloproteinases in female reproductive function with emphasis on the ovary and uterus.
15. Ajay Nangia, MD., is an Associate Professor of Urology and studies factors regulating fertility and infertility in men. He is an active participant in the NICHD supported Interdisciplinary Center for Male Contraceptive Research and Drug Development.
16. Carl Weiner, MD, is the Kermit E. Krantz Professor and Chair of the Department of Obstetrics & Gynecology. He studies factors regulating interactions between the mother and baby using human and animal models.
17. David Albertini, Ph.D., Hall Professor in the Department of Molecular and Integrative Physiology. He studies ovarian function with emphasis on the egg.
18. Yafeng Dong, MD, Ph.D., Research Assistant Professor of Obstetrics & Gynecology, studies maternal fetal interactions with emphasis on factors that are detrimental to the baby and mother.
19. Jeffrey Holzbeirlein, MD, Associate Professor of Urology, studies prostate cancer.
20. Sam Kim, MD., Associate Professor of Obstetrics & Gynecology, studies factors regulating the development of egg and preservation of ovaries for patients with cancer.
21. Benyi Li, MD, Ph.D., Associate Professor of Urology studies prostate cancer.
22. Linda Nelson, MD., Ph.D., Associate Professor of Obstetrics & Gynecology studies factors

regulating ovarian function with emphasis on fertility and infertility.

23. Brian Petroff, DVM, Ph.D., Associate Professor of Medicine, studies ovarian aging, ovarian toxicology, and breast and ovarian cancer.
24. Gregory Vanden Heuvel, Ph.D., Associate Professor of Anatomy & Cell Biology, studies molecular aspects of growth regulation in the kidney.
25. Xuan Zhang, MD, Ph.D., Research Assistant Professor of Obstetrics & Gynecology, studies ovarian and uterine function.

The Center for Reproductive Sciences (Founding Director, Paul Terranova, Ph.D., 1995; www2.kumc.edu/crs/)

In 1993, the reproductive group of 10 faculty met to determine their mission and future needs of their research programs. The Center's mission is to carry out basic and clinical research in the reproductive sciences. In order to support this mission, the group discussed several grant opportunities through the NICHD, including a core based center grant, postdoctoral training grant, and program project grant. Initially, a P30 (Core-based) Center grant with a new program development component and a training grant application were submitted to NICHD after discussions with the Dean of the School of Medicine, Daniel Hollander, MD and NICHD staff. An agreement was reached with the Dean that a Center for Reproductive Sciences would be established if the NICHD center grant opportunity would be funded. Support would be promised to the Center from the School of Medicine. In addition, the KUMC Research Institute, Inc. provided support for development of the center grant application, including visits from the external advisory board that was critical for enhancing the chances of the Center's success. The grant applications (center and training) were prepared in 1995 and subsequently funded in 1996. Thus, the KUMC Center for Reproductive Sciences opened for business in 1996, thirty-seven years after the arrival of Kermit Krantz, MD, chair of Obstetrics & Gynecology. The reasons for success in obtaining a 5-year NICHD center grant that totaled more than $1 million were multifold. First, even though the original members, Greenwald, Johnson and Dickmann, were at the end of their careers, the junior members that Krantz, Greenwald, and others recruited in the interim (1977-95) had rising academic careers. Each became well established in the reproductive field. Most importantly, each member held at least one NIH grant (10 funded faculty, 16 R01s, and most of them were from NICHD) with exception of the very junior faculty. The junior, mid-level, and senior mix of the faculty in reproductive sciences was also a strength that helped garner funding support for the new program development component of the P30 application. A second reason for success was the "centeredness" that the group exhibited prior to submission of the grant. This was evidenced by regular reproductive group seminars, external review board involvement in the center, joint publications, joint grants and joint students amongst the members, and the need for sharing of resources (cores such as cell culture, DNA sequencing, transgenic/gene targeting and image analysis). The third reason for success was the support provided to the Center from the School of Medicine.

Two years prior to competitive renewal of the Center grant, NICHD decided to end the P30-core based center program and replace it with a U54 Center mechanism that was a cooperative research agreement program. Significant changes in structure that focused on new research projects and fewer cores were required. Cooperative research with other NICHD-supported centers was also required. Thus, 4 research projects (similar to R01s) and 3 open cores (administration, cell culture and image analysis) were designed and integrated. The renewal was submitted and funded for another 5 years.

During the second 5 years, NICHD required a more focused application on a single topic with a substantial clinical component/project that integrated into the basic projects and thus, our next renewal would have to change again. This became very difficult for the large basic group at KUMC and thus, other avenues of Center grants were pursued. Most importantly, and in our favor, was that the group had grown to nearly 30 members so that initiatives could be developed for: a) male fertility regulation and infertility, b) female fertility/infertility and c) pregnancy. The pregnancy component led by Joan Hunt, Ph.D., is supported by a NICHD program project that studies the immunology of early pregnancy establishment. That project involves important collaborations with the University of Chicago as well as other universities throughout the world and is in its second 5-year renewal. The male component, led by Joseph Tash, Ph.D., is now funded as a NICHD supported Interdisciplinary Center for Male Contraceptive Research and Drug Development with research projects and cores. The third component, female, is under development in the area of female fertility/infertility.

The NICHD supported Interdisciplinary Center for Male Contraceptive Research and Drug Development (Founding Director, Joseph Tash, Ph.D., 2007; www.kumc.edu/mc/)

This Center is supported largely by a Cooperative Agreement grant from the Contraceptive Research Branch of NICHD. Three research projects led by Joseph Tash, Gustavo Blanco and Leslie Heckert are the center piece of the grant. The grant focuses on developing novel non-steroidal drugs that block sperm development and assess their mechanism of action. The group collaborates with researchers at the University of California at San Francisco, University of Minnesota, Hauptman-Woodward Medical Research Institute, UMDNJ-RW Johnson Medical School, Vivo Quest, University of Pennsylvania, and Wyeth. In addition, the Center has 3 NICHD supported cores, administration, drug design/synthesis/discovery led by Gunda Georg, Ph.D., at the University of Minnesota and former KU Faculty member, and an imaging core. A $2.8 million NICHD subcontract through the University of Minnesota (Dr. Georg as PI) to test and further develop male contraceptives is also an important component of this Center. This group is heavily involved in drug discovery and development and thus interacts closely with the Institute for Advanced Medical Innovation. Dr. Heckert, a member of

this Center, is also developing another Center grant application focused on male infertility. Dr. Tash has expanded the concept of fertility regulation to pet species (cats and dogs) and is vying for a grant from the Michelson Foundation to further develop this idea.

Institute for Maternal Fetal Biology (Founding Director, Michael Soares, Ph.D., 2002; www.imfb.org)

The mission of the Institute for Maternal Fetal Biology is to improve the health and quality of life for mothers and babies. Currently, there are 13 faculty in the Institute from KU, including Lawrence, Kansas City and one from Children's Mercy Hospital (Kansas City, Missouri) with a NIH grant portfolio of ~$4 million annually. The faculty in the Institute study diseases of pregnancy such as: preeclampsia, early pregnancy loss, intrauterine growth restriction; diseases of the fetus including anemia, thalassemia, sexual development, maternal substance abuse, birth defects, and pulmonary development and lung injury.

Summary

The current reproductive research at KUMC emanated from the Department of Obstetrics in 1959 when Kermit Krantz, MD was appointed chairman of the department. Dr. Krantz hired Gilbert Greenwald, Ph.D. who became a world class leader in reproductive biology and led KUMC faculty recruiting to the utmost. His involvement in the longest standing (43 years) NIH supported Center (Kansas Intellectual and Developmental Disabilities Research Center) led to the formation of the Center for Reproductive Sciences, Interdisciplinary Center for Male Contraceptive Research and Drug Development, and the Institute for Maternal Fetal Biology.

Collaborations, Scale Invariance, and The Extended Trust

Robert Duncan, Vice Chancellor for Research, University of Missouri

Be cautious in your trust of this, or any other document concerning collaborations that is created under single authorship! It should, at first glance, seem as suspect as yet another monotonic lecture on the virtues of interactive teaching.

But there is actually an imbedded message here: We don't collaborate for collaboration sake, but rather we collaborate out of our mutual desire to improve our individual performance, and hence our individual condition, beyond the level that we can obtain through our efforts in isolation. This is the first and most fundamental criteria for a successful collaboration. If it is missing, then the individual's participation in the collaboration will not be sustainable. Secondly, we look for the collaboration to provide an immediate market for our efforts. We see ourselves, and more importantly others see us, as bringing some rare skill or perspective to the larger effort that is valued, and that value will help increase the significance of the entire effort. This second condition must be met as well for a genuine collaboration to be sustained. Remarkably this is 'scale-invariant', since it applies to collaborations where each individual is a person, group of people, corporation, and even nations.

Three Classes of Collaborations

Let me define three basic classes of collaborations: The first class of collaborations is the most common, and hence the class that I used in the lead-in to this essay above. It consists of collaborations between individuals (again, people, corporations, or nations) that depend on each other to accomplish a more complex objective than they could achieve on their own. The second general class of collaborations exists between different disciplines or different schools of thought, generally in an effort to define new approaches to our common problems that defy solution through a single disciplined approach. While certainly individuals will be the vehicles of these disciplines and thoughts, it none-the-less is useful to think more abstractly of these collaborations in a class by themselves, since in this class the point of view or professional approach becomes the generalized 'individual' in this higher-order concept of collaboration. Finally, a third class of collaborations has recently been defined through our ability to participate in mass collaborations without even knowing those with whom we are collaborating. These new mass collaborations are implemented through 'wikis' and other publicly edited documents, and through interactive web

sites that center on a particular theme, concern or topic. This class of mass collaboration has recently been explored brilliantly by Tapscott and Williams in their book entitled Wikinomics. Clearly this third class of collaboration is the most powerful, since it is strictly egalitarian by its very design. It has changed everything, and provided an opportunity for humans to adapt to an entirely new environment where the center is firmly on the question of 'what's right?', and not on the authoritative perspective of 'who's right?'. Now let's define specific concepts that will be important in the communication and evaluation of collaborations quite generally.

Trust, Negotiations, Collaborations, and Scale

Trust is essential in every human interaction, and hence it is manifested in different ways in every general class of collaboration as well. At a personal level, everyone who interacts with another will set their limits of interaction and hence their level of candor based on the level of trust that they have achieved with one another. At this level trust is based on the degree to which each individual is confident that the other will protect their well-being in the interaction. Hence this trust depends strongly on the assessment of each person of the motivations of the other, and on the value that each person perceives in the other to develop and nurture an ongoing relationship through the present interaction. When I interact with a person who I have just met, my level of candidness with this person will be based on what I think that the other person wants out of this interaction. Does this reporter want a fair and balanced story, or is (s)he looking for cheap sensationalism to draw attention to themselves and their press organizations? Secondly, with that considered, do they see their interaction with me as a one-time 'hit and run' encounter, or as something that will build our trust in one another for many years to come? Such considerations are critical in deciding if I am ready to go 'off the record' to help this reporter who I just met to more completely understand the issues surrounding their topic of interest. In our personal interaction we 'test the waters' continuously by offering to be more candid and observing the response of the other. Trust over time is based not only on the other person's candor, but also on their demonstrated integrity to hold to their commitments, both stated and implied, to use the gained information in such a way that does not materially damage us as the source. While we all often interact with many other people than reporters, this example demonstrates effectively those aspects of our interaction that are used to define our level of interpersonal trust.

At the institutional level many of these same principles apply, but now trust is more based upon an aggregate understanding of the position and desires of each collaborating institution or organization. Trust becomes more objective, since it may be based upon an analysis of what each party stands to gain or lose in a given interaction, and on the record of each organization's past adherence to do as they agree to do. While personal trust and friendship between the negotiating parties in a

business deal are critical to the willingness of each individual to sit down around the same table, once the business negotiation starts, it is (and by all rights should be) much more centered on defining how both institutional objectives may be further advanced through the proposed collaboration. In fact, the negotiation itself is simply the process by which the proposed collaboration is better refined to provide assurance of mutual value between the collaborating institutions. The process of negotiating such collaborations critically depends on the ability of the people who are negotiating to think selflessly and act at the higher composite level of the institution's representative, and not merely out of their personal concerns. Those who can do this most effectively are those who become the most valued to lead their respective organizations and institutions.

Negotiations that lead to collaborations between sovereign nations are quite similar to those described above between organizations and institutions, with one profound difference: There is no higher authority to police the process and hence to provide restitution in the case where either party proceeds unjustly or dishonestly. Hence the interactions between nations are profoundly influenced by the credible ability of either nation to wage war on the other, and negotiations between non-sovereign entities with sovereign entities are quite dangerous, as most Native Americans can attest. Niccoli Machiavelli recognized this difference clearly when he defined the powers of the sovereign in his book The Prince. The concept that the means justify the ends only holds at the position of the head of state, and never at lower levels. As the head of the State of Israel, what methods would you consider to be ethically off-limits in your efforts to avoid another attempted genocide of your people, as was attempted in the Holocaust? There are many examples throughout history of attempts to define a higher policing authority that nations are obligated to obey, either out of religious conviction, or out of fear of collective economic reprisal by the other nations of the world. Neither of these has proven effective, and neither will likely prevail in the future, in my opinion. The frustration over this fact was discussed eloquently by President Lincoln in his Second Inaugural Address in March, 1865, when he said of the two combatants within the Civil War: "Both read the same Bible, and pray to the same God; and each invokes His aid against the other." In sum, historically sovereign nations collectively respond only to power and the proposed outcome of their actions. This is a critical aspect to consider in any negotiation with, or between, sovereign powers. Attempts such as the League of National and the United Nations to impose global law on the basis of trade retaliation to hostile acts have generally failed, since these consequences for the obnoxious pursuit of a nation's self-interest is generally not of adequate consequence to limit outrageous national behavior.

So as time evolves, will there ever be a method of ensuring a positive global economy through the assurance of trust at the national scale, free of the

treat of mass destruction and global war? Petty wars between superpowers have been effectively outlawed through concerns of escalation to nuclear mass destruction, and this has shifted the possibility of direct warfare between nations to only those nations that cannot retaliate against each other at this extreme level. Ironically, it is the desire for peace and security that has escalated the proliferation of nuclear weapons throughout the world. No one will directly threaten to destroy a nuclear power for fear of nuclear retaliation, yet every nuclear power understands their inability to use nuclear weapons in any aggressive pursuit to better their nation, and this fact alone has made nuclear weapons an absurd route to peace in the 'mutually assured destruction' sense. When the world's first nuclear submarine went underway, the basing of nuclear weapons became impossible to locate, and hence the ability of any country to win a nuclear war against another became clearly and absolutely impossible. Today we are under nuclear threat from groups with no assignable national identity, where no retaliation against a sovereign state is possible.

The future may offer another possibility to establish a peaceful world: As we transition to a true knowledge-based economy, the gainful efforts of the world's most creative people, connected together through the internet, has established a new global market for innovation and commerce, and this situation will likely strengthen indefinitely for the foreseeable time ahead. Image a situation where the United Nations had the power to drop a nation off of the world-wide web if that nation disrespected international law. Today, and more so in the future, such an action would devastate any single economy throughout the world. Such a policy could be enforced, since those nations at the perimeter of the offending state would have the power to physically interrupt land lines and fiber optics, and all but a few nations today could be blocked from satellite signal relay. Once such an action rises to the point that the economic impact would be truly devastating to the offending nation's economy, we will have a chance at securing an assured peace based upon ethical global rule. Once this situation presents we will have achieved a level of integrated global economy in which petty differentiations based upon our country of origin are insignificant compared to the collective value that all of us working together can achieve. At that point the world will be able to turn its full resources toward productive endeavors, and toward battling common threats, such as curing major human diseases. With the current emergence of exceptional power being gained through mass collaborations over the internet, it is not unrealistic to predict that such as day as this may come.

Presentation at the Merrill Retreat

I presented on two major collaborations that I have helped structure and lead over the last twelve years. The first was a fundamental physics collaboration between many universities in preparation for a fundamental physics mission in space, named "Critical Dynamics in Microgravity". This collaboration was sharp and narrow in its intellectual focus, using the capabilities and

expertise at many locations (UNM, Caltech, Stanford, and other less directly involved institutions) to achieve the exceptionally difficult technical objective of understanding out-of-equilibrium.

The second major collaboration was quite different in its focus. It was called the New Mexico Consortium (of Universities), which operated the Institute for Advanced Studies within Los Alamos National Laboratory. This collaboration focused on four different primary research topics, and as such was quite broad intellectually. This collaboration created a close infrastructure for many different universities to work closely with Los Alamos National Laboratory.

Clearly future collaborations will be required between our major research institutions within the Midwest to build coherently on our strengths in the Animal Health Corridor. As this large-scale collaboration moves more into human health, it will be important for us as a region to develop the infrastructure necessary to become a national powerhouse in translational medicine. Business ethics dictates that no one institution will be able to perform their own clinical trials that are necessary to bring their own medical products and drugs to market through FDA approval, so this alone will drive a much stronger regional collaboration between our institutions.

Our institutions have distinct strengths that are far more complementary than they are competitive. As such, possibly we could define a regional task force between all regional institutions that want to participate to define genuinely new ways to address major problems. Teams between peer institutions will naturally self-assemble to take on major challenges that we could not address otherwise. Great advantages will be realized by those regions of the United States that learn how to collaborate gainfully over a vast range of scales. We look forward to being a critical part of this essential process.

The National Bio and Agrodefense Facility is Coming: How did it happen and why Manhattan?

Jerry Jaax

Associate Vice President for Research Compliance and University Veterinarian
Kansas State University

In January of 2009 the Department of Homeland Security (DHS) announced that Manhattan Kansas would be the site for the new National Bio and Agrodefense Facility (NBAF). The NBAF is a major federal procurement initiative to replace the aging Plum Island Animal Disease Center (PIADC) located at the tip of Long Island Yew York. With project costs estimated to exceed $500 million, the NBAF site competition has been at the center of a fierce three year-long competition between almost thirty groups vying for award of this major infectious disease laboratory. The winning strategy for the Heartland BioAgro Consortium, is a study in planning, cooperation, and regional collaboration.

Why do we need NBAF: In the sixties, seventies and eighties, national planners believed that infectious disease had been largely defeated: smallpox had been eradicated; efficacious vaccines and antibiotics had been developed and deployed; public health and nutritional programs improving well-being and quality of life were successful; and serious agricultural diseases like foot and mouth disease and brucellosis had been controlled. This resulted in the shift of research priorities away from infectious disease to other competing health concerns like cancer and heart disease. In the wake of the 9-11 terrorist and the subsequent anthrax attacks, the federal government recognized that there was a looming and plausible threat from infectious diseases. This included dozens of pathogens, most of which were zoonotic – affecting both humans and animals. Additionally, it became clear that many biological agents have properties that make them ideal for potential use as weapons by both state and non-state actors, with compelling evidence of massive offensive bioweapons programs in the old Soviet Union. Additionally, concerns arose about proliferation of biological agents and / or bioweapons technology to rogue nations for possible terrorist use. Most importantly, it became clear that infectious disease and biodefense research infrastructure in the U.S. was inadequate to meet current and future potential threats.

Consequently, major federal programs were imitated to strengthen biocontainment research capabilities and infrastructure. On the agricultural front, the 60 year old Plum Island Animal Disease Center (PIADC) lacked

important operational capabilities to work safely with biosafety-level 4 (BSL-4) agents like Nipah and Hendra virus, and had deteriorated beyond a condition reasonable to repair. Accordingly, national planners made the decision to build a modern research and development facility to address pathogens of consequence to agricultural entities. In 2005, the National Bio and Agrodefense Facility initiative was launched. One of the most important considerations of the DHS and their partner the United States Department of Agriculture (USDA) was where to locate the new laboratory. As a footnote to planning for the NBAF, in 2008 Graham - Talent headed a bipartisan commission studying weapons of mass destruction. In their report (World at Risk), they concluded that there was high probability of a biological or radiological attack in the U.S. by 2013, reinforcing the significant nature of the threat and the need for modern research facilities.

What is NBAF: The National Bio and Agrodefense Facility (NBAF) is the proposed federal infectious disease research, development, test and evaluation (RDTE) laboratory intended to replace the PIADC. Its mission: To protect U.S. agriculture from foreign animal diseases and zoonotic diseases, the latter being transmitted from animals to people. The principal means for accomplishing this mission: threat detection, vulnerability assessment, formulation of mitigation strategies, development of disease countermeasures, and vaccine licensing support. The NBAF is projected to be a 500,000 square foot facility and cost over five hundred million dollars. Permanent professional, technical and support staff will be greater than three hundred, with many hundreds of construction jobs created during construction. The anticipated long-term economic boost to the region and surrounding community is believed to ultimately be in the billions. Diseases currently projected for study in the NBAF: FMD Virus, Classical Swine Fever, African Swine Fever, Rift Valley Fever, Contagious Bovine Pleuropneumonia, Japanese Encephalitis Virus, Nipah Virus and Hendra Virus. Significantly, the NBAF will be built with state-of-the-art capabilities to work with any emerging or remerging pathogens determined to be a threat to U.S. agricultural infrastructure.

How did we win? The anatomy of a successful consortium: There are many factors that contributed to the successful bid of the Heartland BioAgro Consortium for the NBAF site. These would include:

Pre-existing Working Relationships: When the NBAF solicitation appeared in 2005, key state and regional leaders already had established good working relationships and communications on other initiatives. Examples include:

1. the successful effort to build the Biosecurity Research Institute (BRI), a fifty-five million dollar state-funded, state-of-the-art, agricultural biocontainment facility on campus at K-State; and
2. regional efforts to establish the Kansas City Animal Health Corridor (a result of recommendations in the

2002 Brakke Report). Consequently, the backbone of a nascent working consortium was in place to provide early planning and coordination.

Establishment of a Dedicated Task Force: One of the key early strategic decisions was to create the "NBAF in Kansas Task Force," a strong coalition committed to promoting the importance of research to protect the American food supply and agriculture economy.

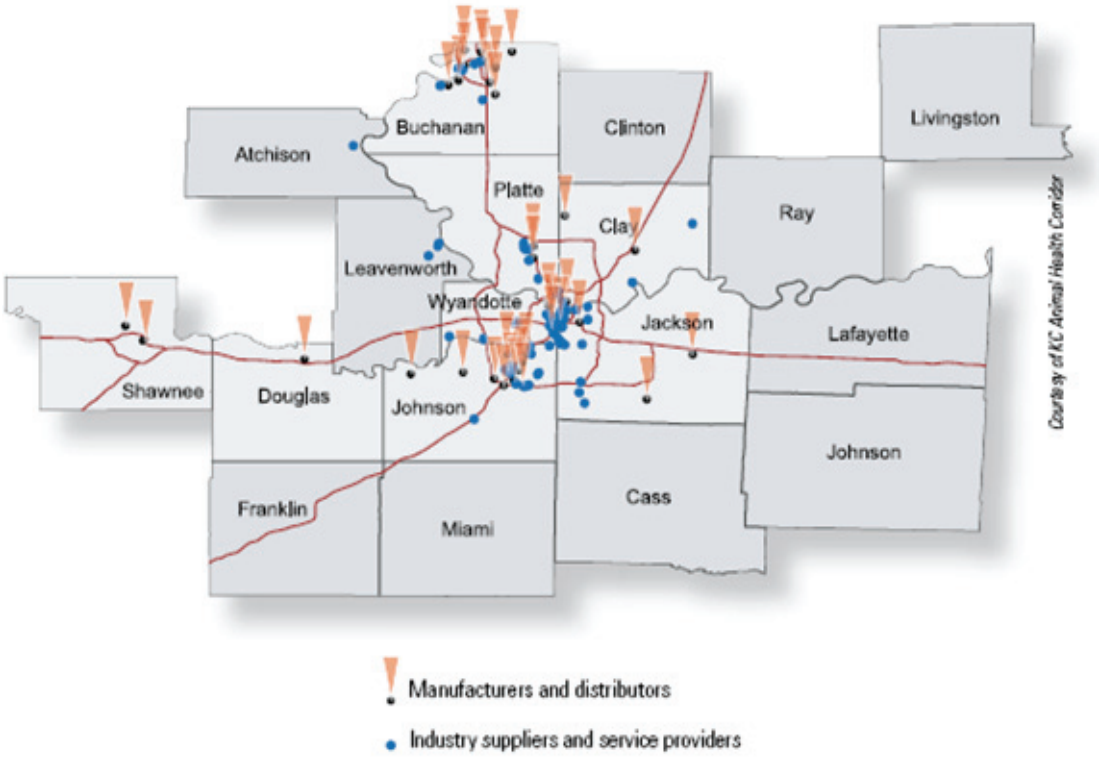
The task force worked to facilitate the NBAF proposal preparation, and to secure the site award for the consortium.

The task force worked on the premise that the state is uniquely prepared and qualified to advance the NBAF research mission. Appointed by executive order, the NBAF in Kansas Task Force included a team of citizens, scientists, civic leaders, elected officials, industry leaders, farmers, and agricultural specialists working closely with the Kansas Bioscience Authority (KBA) to provide seamless support to the federal government throughout the NBAF process.

During the site selection portion of the process, the task force assisted in the development of the site location packages; coordinated with the Kansas congressional delegation; fostered collaboration among state research institutions and industry; provided information to the public; and responded to requests for information from the U.S. Department of Homeland Security (DHS).

Involvement of the Kansas Bioscience Authority (KBA): The KBA was created by the Kansas Economic Growth Act of 2004 with the sole purpose of advancing Kansas' leadership in bioscience. The KBA vision and strategies for the authority: *Kansas is the preeminent bioscience center in the Midwest, serving healthcare, energy, agricultural, animal health, biomaterial, and national-security needs throughout the nation and around the world by virtue of its excellent research, education, and vibrant industry clusters.* The KBA recognizes that "its public, private, and academic partners are often at the forefront of efforts to expand bioscience R&D, foster the formation and growth of startups, and lead corporate expansion and attraction efforts." The KBA has been a driving force in the planning and execution of the successful bid to land the NBAF in the State.

The Animal Health Corridor: In 2002, the consulting firm, Braake, Inc., identified animal health as a notable and unrecognized regional strength, ideal for economic development and leverage within the area. This recognition led to the designation of the Kansas City Animal Health Corridor, a region roughly bounded by an area stretching west to east from Manhattan KS to Columbia MO, and north to south from St Joseph MO to southern Johnson County KS. Remarkably, this relatively compact area contains corporate headquarters for the largest concentration of animal health industries in the world, responsible for one third of the global market for animal health products and services. This conglomeration of animal health industries greatly strengthened the case that Manhattan was ideally located for collaboration and exploitation of



research products developed by the new federal laboratory.

Kansas City Life Sciences Institute (KCLSI): The KCLSI provided an essential element in regional and bi-state cooperation and collaboration during the entire proposal process. Their involvement provided leadership and a coordinating presence in putting together the impressive and diverse regional consortium responsible for the winning proposal.

Pre-existing Agricultural Biocontainment Research Commitment: In the late 1990, K-State identified food safety and security as major programmatic thrust areas for the university. In March 1999, K-State created the "*Homeland Defense Food Safety, Security, and Emergency Preparedness Program*," and proposed the need for a BSL-3Ag facility to confront emerging threats to the food supply. In October 1999, K-State President Wefald testified before the U.S. Senate's Emerging Threats Subcommittee on the "*Agricultural Biological Weapons Threat*" facing America. This forward-thinking decision by university leaders to focus on threats to the nation's agricultural infrastructure eventually resulted in the construction of the Biosecurity Research Institute (BRI) at K-State, a world-class biomedical research facility with capabilities to perform large-scale infectious disease research activities with food animals. The commitment of the university to build a major agricultural biocontainment facility, and the overwhelming community acceptance of the BRI was perhaps the biggest discriminator for DHS in their deliberation about a site for the NBAF.

Fifteen Governors + countless "One Health" collaborators support NBAF in Kansas

Contributions in kind: A major factor in the selection process were the "contributions in kind" pledged in support of the winning bid. These included: donation of nearly 40 acres of K-State campus real estate for the NBAF; millions of dollars for programs to jump-start mission-critical research in the interim period before the NBAF facilities are completed; and favorable agreements for Manhattan city services for the NBAF.

The Heartland BioAgro Consortium: The formation of the Heartland BioAgro Consortium was a key strategic move in the formulation of the winning bid. The depth and breadth of regional collaboration and support is evident in the diverse makeup of the consortium.

Organized and Strong State and Local Political Support: From the initial stages of planning and preparation for the NBAF bid, there was strong bipartisan political and community support for the project. Active participants included: the Kansas Congressional Delegation; Kansas Governor and Legislature; Kansas Governor's NBAF Task Force; Kansas Board of Regents; Riley County Commission; Manhattan City Commission; Manhattan Area Chamber of Commerce; K-State Faculty Senate Leadership; K-State Classified Senate Leadership; K-State Student Governing Association; and Kansas Agricultural Producer Groups

Co-location with Kansas State University: The Heartland BioAgro Consortium believed that co-location with a major land grant university with; a college of veterinary medicine; and strong programs in agriculture would have strong appeal to planners for the new NBAF. This was in fact borne out in DHS decision matrix documents.

In concert with the theme of the Merrill Research Retreat: "Regional Research Collaborations," the selection

of Manhattan Kansas as the site for the National Bio and Agrodefense Facility (NBAF) underscores the importance of vision, strategic planning and perhaps most importantly, collaboration and regional team-building. Without the collective power of a regional collaborative approach involving a broad stratum of partners, collaborators, and stakeholders, the Department of Homeland Security would probably have picked another site for the NBAF. So for the Heartland BioAgro Consortium, the key element of the winning formula was the quality, breadth and depth of its many active partners.

The University of Missouri Regional Biocontainment Laboratory – What It Is and the Emphasis on Regional

George Stewart

McKee Professor of Microbial Pathogenesis and Chairman, Department of Veterinary Pathology, University of Missouri

If you build it, he will come

W. P. Kinsella (Shoeless Joe, Houghton Mifflin, 1982*)*

Concerns over bioterrorism, emerging infectious diseases, and food safety and security led to the creation of a regional network of biosafety level 3 facilities in the United States. These facilities provide safe environments for conducting research on high consequence bacterial and viral pathogens. The facilities were expensive to build and will be expensive to operate. They do, however, provide unique opportunities for researchers throughout the country to conduct research programs that are not possible without the specialized containment laboratories. To be economically viable, the biocontainment labs must be maximally utilized. This necessitates that Universities that host these facilities create an environment that encourages and facilitates collaborative and cooperative research agreements with regional research institutions.

Introduction

Contemporary scientific research often involves the use of expensive equipment and facilities. When universities make a commitment to provide these facilities, the decision not only involves an up-front expenditure of often scarce resources, but programmatically commits the university to very specific research directions. Prior to having the specialized facilities, it is unlikely that a critical mass of faculty will exist who work in that research arena, because of the very lack of those facilities. The newly constructed facilities, or expensive equipment, thus become the "Field of Dreams" with the expectation that researchers who can exploit the resources will be identified. Some may be recruited to the University, other users as collaborators or users of the facilities on a fee-for-service basis.

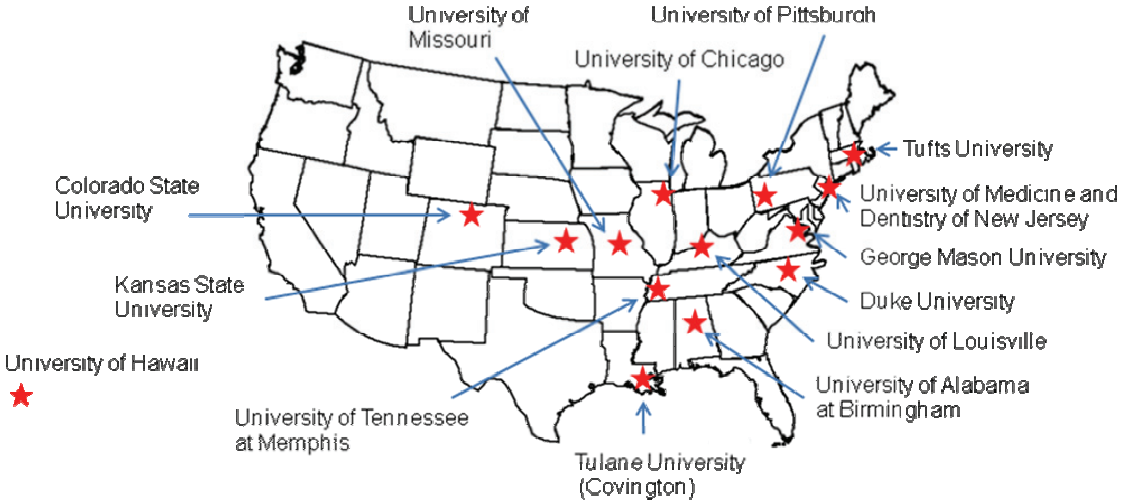
This model has been quite successfully applied in certain scientific disciplines, most notably physics, where the costs of particle colliders, cyclotrons, and nuclear reactors are beyond the scope of most university budgets. Physicists at Universities lacking these facilities book time on these instruments and then spend the bulk of the year analyzing the data back at their home institution. Biologists, as a general rule, tend not to think regionally when it comes to their individual research

programs. For example, Midwestern schools lack research programs in marine biology, despite being ideally situated equidistant from the Pacific and Atlantic Oceans. We do not seek out time-sharing options with institutions which have the ships and equipment to conduct this type of research (i.e. Scripts and Woods Hole Oceanographic Institutions). Modern research in molecular biology is increasingly dependent on the use of expensive equipment and specialized facilities. Will biologists follow the lead of our physicist colleagues and make use of regional or national resources? This will soon be put to the test with the construction of the national network of Regional Biocontainment Laboratories.

The RBL Network

The anthrax postal (Amerithrax) bioterrorism events in the fall of 2001 raised bioterror concerns in the US and worldwide[1]. In February 2002, consultations between the National Institute of Allergy and Infectious Diseases (NIAID) and its Blue Ribbon Panel on Bioterrorism produced several recommendations for NIAID to better protect the American public from the threat of bioterrorism. One recommendation was to create more laboratory space for work with dangerous pathogens. A request for proposals was issued to create a regional network of biosafety level 3 laboratories (Regional Biocontainment Laboratories [RBLs]) and biosafety level 4 facilities (National Biocontainment Laboratories [NBLs][2]. Two NBLs were ultimately created, one in Boston, MA and the other in Galveston, TX. Thirteen RBLs were created in this program (Figure 1). NIH provided 75% of the construction costs for the RBLs and the remainder of the construction costs was provided by the host institution or state. The grantees in turn agreed to operate the biocontainment labs for a period of twenty years. The two NBLs, with the highest level of biocontainment (BSL-4), receive operation support through the NIH awards and are facilities that can handle exceedingly dangerous pathogens for which there is no vaccine or therapy available. The RBLs, are BSL-3 facilities which are designed for work on pathogens that are transmitted by the aerosol route, have significant mortality rates, but for which vaccines or treatments are available. The NIH provided construction costs for the RBLs, but made it clear that operating costs for them was not to be part of this program. The Biosecurity Research Institute (BRI) at Kansas State University was not part of the NIH program, but is included in this discussion because of its unique attributes relative to the other containment facilities.

Microbial pathogens that are of concern as agents of bioterrorism, are part of the federal government's Select Agent program, and research on these agents require BSL-3 containment facilities[3]. The select agent pathogens include a variety of bacterial, viral pathogens that share the property of being transmissible by the aerosol route. Examples include the agent of anthrax (*Bacillus anthracis*), plague (*Yersinia pestis*), tularemia (*Francisella tularensis*), and St. Louis Encephalitis Virus. Prior to 2001, research on virulent strains of *B.*



BSL-3 Facility	Location	Approximate Gross Square Footage	Estimated Cost
Colorado State University RBL	Ft. Collins, CO	33,850	$30 million
George Mason University Biomedical Research Laboratory	Fairfax, VA	53,000	$48 million
Howard T. Ricketts RBL (University of Chicago)	Chicago, IL	35,000	$31 million
Kansas State University Biosecurity Research Institute	Manhattan, KS	113,000	$54 million
New England Regional Biosafety Laboratory (Tufts University)	Boston, MA	41,000	$33.7 million
Pacific RBL University of Hawaii	Honolulu, HI	25,000	$47.5 million
RBL at Duke University	Durham, NC	33,145	$22.4 million
Southeast Biosafety Laboratory (Univ. Alabama at Birmingham)	Birmingham, AL	43,500	$32 million
Tulane University RBL	Covington, LA	38,000	$27.5 million
University of Medicine & Dentistry Of New Jersey RBL	Newark, NJ	34,700	$39 million
University of Louisville Center for Preventive Medicine	Louisville, KY	37,000	$34.6 million
University of Missouri	Columbia, MO	32,500	$18.5 million
University of Pittsburgh RBL	Pittsburgh, PA	20,000	$28.8 million
University of Tennessee Health Science Center RBL	Memphis, TN	30,315	$25 million

anthracis could be conducted at the lower biocontainment level, BSL-2, which is more typical of the level of typical University medical microbiology laboratories. However, with inclusion of *B. anthracis* on the select agent list, research on this pathogen requires the more specialized and expensive BSL-3 containment. Thus reclassification of biosafety conditions, in addition to an increased emphasis on biodefense-related research, created the increased

demand for biocontainment research laboratories.

The RBLs support NIAID-funded biodefense and emerging infectious diseases research and are members of the NIAID Biodefense Network. Additionally, the RBLs serve as regional resources for research institutions in the area, and would be available and prepared to assist national, state, and local public health efforts in the event of a bioterrorism emergency. At the same time as the RBL construction grant program, NIAID held a competition to establish a network of Regional Centers of Excellence for Research in Biodefense and Emerging Infectious Diseases (RCEs)[4]. Although the RBL construction grant program was distinct form the RCE program, the RBLs have in many cases formed an alliance with the RCEs and provide an important source of biocontainment research space for the RCE research projects.

The RBLs are intended to be regional resources, although the majority of them are concentrated in the eastern half of the United States. The Universities hosting the RBLs fall into a spectrum of experience in research programs related to high containment pathogens. At one end of the spectrum was Colorado State University, which had large established biosafety level 3 programs in tuberculosis and arthropod-borne viruses. Construction of the RBL permitted them to expand their heavily utilized facilities and further build these research programs. The existing programs at Colorado State meant that at the time of the RBL construction, investigators and projects going into the new space were already largely identified.

At the other end of the spectrum were Kansas State University, the University of Louisville and the University of Missouri that at the time of the awarding of the RBL grants, had either no biosafety level 3 laboratory space or had small individual laboratories. Existing faculty with need for these facilities were not present at these universities at the time of the RBL grant submissions or were present in too small a number to utilized the newly constructed research space. Without the specialized facilities, no existing projects were in place in these institutions. Thus the RBLs were built with the intention that biocontainment-requiring programs would have to be established *de novo*.

The Kansas State University Biosecurity Research Institute is unique among the biocontainment laboratories in that it is a BSL-3Ag facility, specifically designed to permit research on larger animals, specifically food animals. It is the only facility listed above which can study zoonotic infections involving cattle, sheep, goats, and swine. It is a remarkable facility that can contribute substantially to our understanding of zoonotic diseases and food safety. Although Kansas State had strong research programs in food safety and security, at the time the University completed construction of the BRI, it had no active BSL-3 or BSL-3Ag research programs. However, the facility has already paid dividends for the University as the presence of the BRI has been cited as one factor in the selection of the Manhattan, KS site for the Department of Homeland Security's

National Agro- and Biodefense Facility (NBAF), a biosafety level 3 and 4 facility for research on foreign animal diseases and zoonoses to replace the aging Plum Island Animal Disease Center. Construction of NBAF will create a 500,000 sq ft. facility dedicated to the study of zoonotic and foreign animal diseases and will provide an influx of infectious disease expertise to the Midwest. However, Kansas State, like the other Universities hosting RBLs, must internally build up its research programs in infectious diseases to make optimal use of their new facilities.

Challenges to internally building biocontainment research programs

Biocontainment facilities are expensive to build, especially with the requirement for redundant safety features. They are additionally expensive to operate. Their energy costs are greater than conventional laboratory buildings. They require a special work force of highly trained individuals to provide for the increased security and maintenance aspects of the building. The need for a larger and more highly trained work force for biocontainment facilities drives up personnel costs. Many of these expenses are fixed, and thus operating the facility at 50% capacity is not significantly less expensive than operating it at full capacity. Thus the only way that these facilities will not be an economic drain on the Universities is to have them operating at capacity and the research projects bringing in revenue in the form of grants and contracts to the host institutions. It is critical that Universities, once they commit to operating biocontainment facilities, recruit faculty specifically to the facilities. These faculty could be recruited to different departments at the University (such as Biology, Biochemistry, Microbiology, etc). However, usually it is a specific group or department that was the driving force in the development of the proposal for the RBL, and other departments did not necessarily buy in to this specific research direction for the University. Because of chronically tight budgets, new faculty hires are limited at the Universities. Many departments opt not to recruit with the RBL in mind. This may be due to specific programmatic or teaching needs for the individual department. Another potential concern, however, is economic. With universities committed to operating the RBLs or the BRI, funding sources to operate these facilities will have to come from overly stretched budgets. Adding a faculty member who utilizes the facility might target that department for providing funds for operational costs. At least that is the fear shared by heads of the departments. As a consequence, for many of the RBLs and the BRI, very few faculty researchers have actually been recruited to staff the biocontainment laboratories and to write grants to support operation of the facilities. Most of these facilities will be markedly under-utilized at the time they acquire the requisite certifications to begin BSL-3 and Select Agent Program operations.

The addition of faculty after the facilities become operational, improves the situation but takes time before the newly hired researchers can contribute. The faculty, and whatever postdoctoral, student, and technical staff they hire,

must undergo Department of Justice background checks and extensive training before they can begin working under biosafety level 3 conditions. Research projects must be approved by University Compliance committees (the Institutional Biosafety Committee [IBC] and the Animal Care and Use Committee [ACUC]) as well as obtaining CDC or USDA authorization for select agent-related activities. These are time-consuming processes that can delay the initiation of research projects by many months. Only after all of the compliance approvals are in place and all of the biosafety and agent-specific training have been conducted, will the research projects be initiated. Only then can the preliminary data be generated to support research grant applications to federal agencies. The development of a funding stream to the RBL based on research grants is a very slow and laborious process.

Putting the "regional" in regional biocontainment laboratories

Construction of the BRI is finished and that of the RBLs is largely accomplished (although many have not yet initiated operations until the appropriate federals approvals [i.e. CDC Select Agent]) are in place. It is obvious that as these facilities begin operations, space will be available for researchers outside the host university to conduct infectious disease research. University researchers, as well as those in the private sector, will have opportunities to conduct research or evaluate therapeutics or vaccines that would be either impossible in their home institutions owing to a lack of biocontainment space or difficulties in scheduling space in over-subscribed small individual biocontainment labs. One path for this activity would be to establish a formal collaboration with a faculty member at the RBL host institution. The limited number of biocontainment-related investigators initially at the RBL host institution, however, limits this approach. A more fruitful initial approach would be for the RBL host institutions to contract out the use of its biocontainment facilities and technical expertise to regional universities and biotech or pharmaceutical companies. The RBL would not only provide the facilities and specialized equipment necessary to conduct the studies, but would provide a trained technical staff as well. The advantages to this approach to the outside investigator would be not having to provide the federal regulatory clearances for lab workers, not having to train lab personnel in techniques which may not be totally familiar to the investigator, and not having to secure housing for the researchers during the duration of the experiments.

The biocontainment facility host institutions will have to develop business plans to facilitate these contract services. Fee for service rates would have to be established. Marketing approaches would have to be established and web sites developed to effectively inform researchers from both academic institutions and the private sector about the capabilities of the biocontainment facility and the types of expertise resident in the facility. Development of effective business and marketing strategies is beyond the expertise of the scientists conducting

infectious disease research, so it is imperative that the Universities mobilize the requisite expertise from other sectors of the university. It is also important that university officials of the RBL host institution maintain open lines of communication with the other regional research universities so that when opportunities for research interactions arise, the institutions involved will be able to respond quickly to these.

Impediments to regional cooperation

Time is the biggest concern when establishing cooperative research agreements involving biocontainment facilities. Once an agreement between institutions is reached, a long list of approvals at both the federal and local levels is required. If select agent organisms are involved, approval by the CDC and/or the USDA is required. The RBL would have to gain approval for working with the specific agent, if approval for that particular organism is not in place. Agent-specific standard operating procedures would have to be developed and agent-specific training of the RBL personnel instituted. At the host university level, project applications to the research compliance committees, the IBC and ACUC committees. Getting proposals approved by these federal and university committees can take months to achieve. University research compliance committees will be placed in a relatively unique position of evaluating proposals for projects originating from outside the university. University Research Offices will have to develop policies to effectively handle these occurrences. The establishment of inter-university agreements whereby the institutions would accept the compliance approvals from the other university would greatly streamline this approval process. Institutions lacking containment facilities may not have the requisite biosafety expertise on their research compliance committees. In these cases, a full review by the RBL host university would be necessary.

Another issue which could slow down the agreement process, especially when dealing with private sector companies, is the handling of intellectual property issues. This is especially important when research involving potential therapeutic agents or vaccines is conducted. Again it is imperative that the RBL host university have in place personnel and procedures to act on these issues in a timely manner.

Summary

The RBL network can become a major resource to universities and provide the necessary research environment to advance our knowledge of biothreat and emerging infectious disease agents. With the large number of diseases arising naturally in the past twenty years (Mother Nature being the ultimate bioterrorist), these facilities will play a vital role in protecting American public health in the years to come. However, to effectively utilize these facilities, researchers must learn to establish research ties with these specialized facilities and the RBL host university must establish effective lines of communication with regional universities and private sector companies to facilitate cooperative research agreements. Regional biocontainment laboratories should be truly regional and universities must

learn to be less territorial in dealing with their sister institutions. The biocontainment facilities should be a source of new opportunities and if managed correctly, not a fiscal drain on the host university.

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Roles of a Center and Institute in Promoting Regional Research Collaborations

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The role of collaborations in research has become more dominant with the passage of time. This should not be surprising given the evolution of the study of biomedical problems. If we look back to the middle of the last century, research was very different. Problems were more basic – we had just begun to recognize and understand the genome and molecular biology was yet to be invented; the tools for research were relatively rudimentary – the electron microscope, which ultimately revolutionized cell biology, was just beginning to enjoy widespread use; and the questions investigators asked were very much framed by their discipline; most researchers were trained in a single area, and applied a single technique to just one aspect of a problem. The pressure to pursue an integrated approach was minimal.

This began to change rapidly in the latter part of the 20th century. Problems became more complex, with larger available armamentaria with which to pursue these questions. Of course, with more advanced technologies and a greater desire to incorporate multidisciplinary approaches in attacking biomedical problems, also came challenges. Training began to lag behind technology; it became difficult to find individuals whose breadth of technical skills was suitable to bring to bear upon the full range of emerging medical questions. Clearly, the easiest way to achieve the necessary critical mass of technologies and disciplines was through research collaborations.

While a need for creating research collaborations has been recognized for some time, the magnitude of collaborations necessary for advancing biomedical research has continued to grow with the increasing complexities of the questions at hand. We have seen the norm in academic collaborations grow from simple ad hoc associations that develop in a grass-roots manner, to the creation of research teams in more formal settings. While this model is widely applied in the commercial and government sectors, it has been late in coming to academia, owing to several reasons. In large part, this may be attributed to a number of logistical issues that have to be overcome in order to successfully develop collaborative

research teams. Some of these issues are as follows.

- Identifying target areas. There need to be clearly defined and agreed upon target areas that will provide a framework in which collaborative research programs can develop and grow.
- Growing the investigator base. In order to attain meaningful collaborative teams, it is essential to have sufficient strength to draw upon so that teams with the appropriate expertise are in place. This may involve either identifying existing potential members, or recruiting members to join the sponsoring institution
- Creating group cohesion and a common cause. A collaborative group needs to see a common vision. If the programmatic direction is unclear, if the vision is unshared, or if the outcome of the collaboration is vague or in dispute, collaborative research will suffer. However, mechanisms must also be in place to permit adjustments to programmatic direction that take into account changes in strength due to the addition of new members or the loss of existing members.
- Thinking regionally. Given the range of approaches that can be potentially applied to biomedical research problems, it is becoming more likely that collaborations beyond the walls of any given academic institution become necessary; this is especially true of smaller institutions. These types of collaborations raise a new set of issues; bridging institutional barriers, distribution of resources, and overcoming problems associated with distance between institutions are chief among these.

How can we encourage development of regional collaborative research enterprises? There are probably a large number of potential approaches, and there clearly is no absolute formula that can guarantee success. However, we have been fortunate in having some success in developing collaborative programs, and our model may be instructive to others who may wish to replicate the experience – or perhaps learn from our mistakes!

Role of a Research Center in developing collaborations

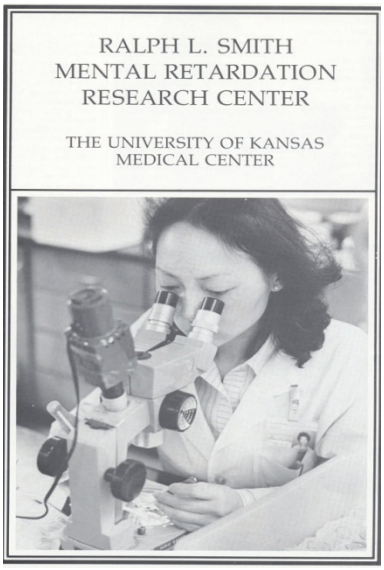
The University of Kansas was fortunate in 1966 to be one of an elite handful of universities to be awarded funds from the newly formed National Institute for Child Health and Human Development (NICHD) to create a Mental Retardation Research Center (MRRC). KU, under the leadership of Richard Schiefelbusch, was one of twelve original host sites for sponsoring these MRRCs. The objective of these centers was to promote research in mental retardation and other disabilities affecting the nervous system and behavior. While the objective of this NIH P30 grant was not to initiate research collaborations per se, the award did a number of important things in easing us along this path. One factor was that it required us to identify and develop research themes. Each center is expected to have areas of research emphasis relevant to mental retardation and developmental disabilities (MRDD). In our case, we began with a substantial number – originally in excess of 8. What is somewhat surprising is that, rather than increasing the numbers of themes over time as might be expected to occur with normal institutional growth, the number actually decreased. It appears that some Darwinian processes may be

at hand, favoring the perpetuation of some themes and the demise of others.

There may be several reasons for this. One is clearly related to leadership. Those themes that had strong leaders remained viable, while those where a clear leader was less obvious did not prove to be durable. A second factor appears to be related to group drift. Stronger groups, while perhaps not intentionally meaning to, often times absorb members of the weaker groups. This may be associated with people gravitating to the stronger leaders, but is also seems that thriving programs may provide greater opportunities – and some of these are in the form of potential collaborations. Because of a need to define themes, the MRRC grant formalized and legitimized potential collaborative areas and identified and empowered group leaders to move these areas forward. So while the major thrust of the MRRC grant was not to develop research collaborations per se, it was probably inevitable that this should have been the case.

These principles seem aptly illustrated with regard to the evolution of the R.L. Smith Research Center, the Kansas City branch of the MRRC (the component with which I am most familiar). A new building constructed for the purpose of housing MRRC programs in common space (although that capacity was rapidly exceeded) opened in 1972. In the initial brochure describing Smith Center, 6 thematic areas were listed.

- » Reproductive physiology & Neuroendocrinology
- » Human Genetics
- » Developmental Physiology
- » Impaired fetal & infant development
- » Neurobiological mechanisms
- » Educational and Pediatric psychology



Through the pressures described above, the fates of these areas changed over the next decade and a half. Thus, by the mid-1980's, the number of thematic research areas had diminished essentially to 2: biology of early development (reproductive biology) and neurobiology of intellectual disabilities.

Why did this occur? One probable reason is that maintaining so many divisions requires considerable effort. Another is that not all areas had the mass necessary to sustain (some likely created to induce participation by catering to territorial wants, thus slicing the pie rather thinly). In some cases, key individuals left for other positions. One factor accounting for the durability of the two surviving themes was that they were inherently more inclusive, ably accommodating many members of the smaller original groupings. And perhaps most importantly, both remaining

divisions were able to identify strong leaders who were able to consolidate groups of researchers. Gilbert Greenwald, chair of physiology, was able to bring together and organize a growing number of reproductive biology researchers and, similarly, Fred Samson, Director of the Smith Center, served in a similar role in promoting neurosciences. Both of these leaders were in positions to effect recruitments in their respective areas, thus increasing numbers of collaborating researcher, as well as in organizing existing faculty.

While our original organizers clearly played critical roles, the importance of continuity in leadership should not be underestimated. In both cases, when the time came to pass the mantle, there were relatively clear lines of ascension, with Paul Terranova (now vice chancellor for research) stepping in to lead the reproductive sciences group, and Paul Cheney (now chair of molecular and integrative physiology) assuming direction of the Smith Center and representing the neurosciences group. Continued group cohesion is highly dependent on having potential incumbent leaders in the wings that are able to step in when conditions dictate.

As a result of the activities of the MRRC, research on the KUMC campus was impacted very significantly by laying down groundwork for organized research collaborations in 2 areas that have persisted over the years. And indeed, over the years the payoffs have been substantial. These are probably best illustrated in the area of reproductive sciences. In the past decade or so, there have been several program project grants that have come out of the reproductive sciences group. Very significantly, we have seen center grants (initially a P30 and subsequently a U54) in reproductive sciences and now in male contraception come directly from this group, as well as an Institute for Maternal and Fetal Biology. Thus, in the case of reproductive sciences, the MRRC served as an incubator in which a number of newer sub-themes re-emerged, building on the collaborations that were encouraged by the structure of the Mental Retardation Research Center grant **(*see article by Paul Terranova, p. 5*).**

Role of an Institute in developing regional research collaborations

The successes of the MRRC (subsequently renamed the Eunice K. Shriver Kansas Intellectual and Developmental Disabilities Research Center [KIDDRC] in 2007) have been substantial and impressive. However, there were some limitations that, in the evolving environment, are likely to have impeded regional research collaborations. While the NICHD center grant (P30) mechanism was essential in encouraging the establishment of core groups in reproductive biology and neuroscience at KUMC, the ground rules, by their very nature, also limited the evolution of these groups.

Centers funded by the NIH are intended to serve a specific purpose. In the case of the IDDRCs, they are intended to "…advance the diagnosis, prevention, treatment, and amelioration of intellectual and developmental disabilities."(http://grants.nih.gov/grants/guide/rfa-files/RFA-HD-08-016.html). This requirement immediately places constraints on the types of research that

can be included in the IDDRC portfolio. Further, membership within the IDDRC research themes is not open to all investigators. Thus, the purpose of the IDDR center grant is to provide core technical, scientific and administrative support investigators with funded research programs related to forms of intellectual and/or developmental disabilities. Because this is the mission of the NICHD and this Institute is footing the bill, it is totally appropriate that activities be selectively supported. But this also places restrictions on the types of interactions that can occur. Thus, interactions with investigators who have related or complimentary funded research programs, but which are not ostensibly relevant to IDD, are not encouraged by this model. Similarly, those with programs that are relevant but not currently funded are also not supported. Further, because the center is based on a single-institution model, individuals who have relevant programs within the region but outside of the parent institution are not encouraged to participate. And finally, because many clinicians with interests and patient populations relevant to IDDRC thematic areas lack requisite funding, interactions with these clinician-investigators are impeded by the P30 model. While there is a strong rationale for having these guidelines in place, it is also clear that these strictures can impede a research center from evolving to the next level of being a base for regional clinical and basic biomedical research.

How can these limitations be circumvented? The need for alternative strategies to broaden the collaborative research base has been an issue of particular relevance to neuroscientists at the University of Kansas Medical Center. Basic neuroscience research has been a powerhouse at KUMC for some time, owing much of its success to the organizational framework created by the MRRC. In 2008, KUMC had some 40 scientists with programs related to the neurosciences, and with a funding portfolio of approximately $70 M. Perhaps another 80 basic scientists and clinicians were present at KUMC or regionally. Yet the Neurobiology theme of the IDDRC at this time included only 19 members! Clearly, there was a strong need to create an alternative infrastructure that would be more inclusive if we wanted to foster stronger interactions among basic and clinical researchers in the neurosciences. This led to the conceptualization of a regional entity to better accommodate collaborations: the Institute for Neurological Disorders (IND).

The decision to move forward with the IND represented a convergence of multiple factors. An important component was a strategy on the part of KUMC administration to more clearly articulate its priorities and goals for the next 10 years. The result of that effort was a document entitled "The Time is Now"(http://www.kumc.edu/evc/TheTimeIsNow.pdf), in which existent strengths in the neurosciences were acknowledged, making this discipline one of the top priorities. In response to a need to better organize the neuroscience effort, departmental chairs and center directors in programs relevant to the neurosciences convened and formed a plan to create the Institute for Neurological Disorders. Several features

of the IND were put in place to maximize collaborative output.

- A regional entity; no walls. An important aspect of the IND is that, while it is based at KUMC, all regional neuroscientists can be members and participate. This recognizes not only the fact that the Kansas City neuroscience community exists in many relatively small institutions, each lacking desirable critical programmatic mass, but also that in many instances such collaborations had already been established at the grass roots level.
- A place for clinicians as well as basic sciences. In the current atmosphere where the highest value is placed on 'translational' activities, it is essential that the full range of biomedical activities, from discovery to application, be represented. Accordingly, it is important to include members in both the clinical and basic sciences arenas.
- Organization by discipline; finding common threads. Neuroscience is an extremely broad field, and a particular challenge was to identify a finite and manageable number of working groups where essentially all individuals within our broad neuroscience community could belong. We elected to establish 6 divisions within the IND which would be inclusive of members with common interests. Importantly, we wished to encourage further evolution of each of these groups, such that with additional resources and organization, the division may ultimately be elevated to 'Center' status.
- Disorders as a focus. While bench neuroscientists relish the idea of studying mechanisms of axoplasmic flow or neuronal phenotype maintenance for the sake of understanding the basic biology, the reality is that just about everyone else is focused on the disease. In fact, it really is all about improving quality of life and finding preventions and cures for diseases. We have therefore identified specific diseases where we have sufficient expertise to justify the claim that a collaborative research team exists. Accordingly, our efforts are targeted toward some 22 specific disorders where such strengths exist.

With these defining principles in mind, the IND was organized and launched in March 2009, nearly a year after it was first conceived. Our primary

objective was to advance neuroscience translational research programs regionally by coordinating and consolidating basic and clinical research. To do so, we identified 7 specific aims.

1. Provide administrative structure. Very little gets done without significant administrative input. By partnering with existing administrative units, it was possible for the IND to rapidly establish the administrative structure necessary to maintain communication among members and to coordinate events.
2. Promote interactions & communication. As noted above, communication follows directly from having an administrative infrastructure in place. In addition, we've developed mechanisms that seek to promote communication among IND members (see discussion of Translational Discovery Forums below). Arguably, this may be the single most important element necessary for creating cohesion and collaboration.
3. Recruit researchers. The IND is playing a major role in the recruitment of neuroscience researchers. Perhaps the most significant advantage offered by the Institute offers is to bring together multiple partners working toward a common goal. In these days of limited resources, it is increasingly important that departments and centers who share similar needs work together to identify the mean necessary for successfully recruiting the right candidate. The IND has become an integral player in the neuroscience recruitment process, first by helping to identify the appropriate target recruitment area, and then by brokering arrangements whereby multiple departments and centers contribute resources toward the planned recruitment.
4. Promote core technologies. The IND can play a substantive role in promoting technologies within the neuroscience community in two important ways. First, its multi-institutional composition puts it in an excellent position to promote and coordinate core technologies available throughout the Kansas City region. In addition, the IND can play a major role in identifying areas of technological deficiencies, and then mustering resources necessary to incorporate these technologies into existing or new cores.
5. Graduate programs enhancements. The IND, because of its organizational structure, serves as an adjunct to graduate education in the realms of both coursework and training programs. Our organizational structure into divisions is highly conducive to course development, and effectively provides a set of faculty who would be qualified to provide lectures in the related areas. Moreover, the IND with its extensive membership and access to core and individual laboratory technologies, is an attractive partner in formulating a predoctoral training program application and is likely to be viewed as a plus by a peer review committee. Because of its multi-institutional nature and communications web, neuroscientists throughout the region are made aware of new courses originating in

conjunction with the IND and therefore are in a better position to inform their students of educational opportunities available to them, even if they are not currently attending the KUMC program.

6. Commercialization pipelines. The field of neuroscience is fertile ground for development of patents and commercial products. Through enhanced collaborations, multidisciplinary interactions, and close ties with drug development programs and offices of intellectual property, the IND is well positioned to encourage commercialization of neuroscience-related drugs and devices.
7. Integrated space. Because the IND embraces members from 6 different institutions, the probability of ever consolidating all members in a single building is low. Nonetheless, having a single building dedicated to bringing together basic and clinical neuroscientists and that can be identified as the home of the IND would do well to advance the concept of the Institute.

Translational Discovery Forums: A vehicle for clinical-basic conversations

A significant challenge in promoting translational research programs is developing a means of communication among individuals with convergent interests. All too often, clinicians have limited exposure to basic scientists and do not attend common functions. While individuals may have similar interests, often times the clinical or basic researchers are unaware of ongoing related activities across the street. The objective in creating Translational Discovery Forums (TDFs) was to provide a vehicle that would bring together established scientists and trainees, clinicians and basic researchers, to share interests and ideas in a setting that encourages interactions.

Our TDFs consist of interactions centered around a discipline or collaborative approach to a neurological disorder (a few of the topics to date include peripheral neuropathy, fibromyalgia, multiple sclerosis, Alzheimer's disease, and epilepsy). We typically hold these late Friday afternoon, which seems to be a time most compatible with the schedules of both clinicians and basic science faculty. The format is as follows:

- Clinical presentation. An overview of the disorder that forms the basis for the TDF is presented or, alternatively a case history or even patient presentations have formed the basis for this half-hour session. These are presented by a student, fellow or attending physician.
- Basic science journal presentation. This component integrates the established Neuroscience Journal Club. A student in the neurosciences selects a paper relevant to the disorder under discussion and presents this to the audience. The emphasis in this half-hour segment is to stress the relationship of the research to advancing our understanding of the disease.
- Collaborative research presentation. This forms the core of the TDF. Basic scientists and clinicians with common interests in a specific disorder present their research program relevant to the disease. They are strongly encouraged to describe ongoing collaborations and clinical-basic interactions or, if these are not in place, then the areas where

collaborations could occur are described in this one-hour session. Bringing in members from different institutions is strongly encouraged.

These simple monthly forums have received a remarkable level of interest and turned out to be quite effective. Basic scientists frequently work on a disease process without fully understanding the clinical perspective, and therefore especially appreciate the introductory clinical overview. Similarly, clinicians often are not aware of how basic science can be brought to bear in investigating disease mechanisms or treatments, and are often surprised at how revealing some basic science publications may be to disease mechanisms. However, the greatest impact seems to be in the process of organizing the collaborative research presentation. Because these need to represent a coordinated effort, those presenting are encouraged to meet well before the scheduled TDF to discuss their presentations. In some cases where an existing collaboration is in place, there may be few surprises, and a history of how the collaboration evolved is instructive to those groups that are not as far along. However, in a number of cases these meetings have tended to be revelational, where obvious areas of collaboration emerge and light bulbs are turned on. Importantly, TDFs are open to anyone who wants to come, including patients with interest in the disorder. Accordingly, we encourage presenters to take a very basic approach and avoid the technical or jargon-laden *tour de force* approach, thus making these presentations more accessible to all in attendance.

Partnerships with existing programs

One area of collaborative evolution that has become increasingly important over the past decade or so is the extent to which independent programs must now partner with others. The pressures to partner were probably less evident in earlier times of more abundant resources, but it is now clear that an economy of scale can be beneficial. Typically, independent programs have common interests and needs, and there is little advantage in duplicating existing resources that may already have the capacity to serve additional purposes.

Given that the IND in many ways originated from within the Kansas IDDRC, it will not be surprising that these 2 entities are closely aligned and are partnering in areas of intersecting interest. However, the IND has also sought partnerships with other programs as well. These include:

- The Heartland Institute for Clinical and Translational Research. The HICTR serves as the primary regional instrument for advancing translational research in Kansas City, and serves as the organizing force behind an application for a Clinical and Translational Sciences Award. There are clearly a large number of intersecting objectives between the HICTR and IND, and the IND serves to organize neuroscience activities within the HICTR.
- The Kansas IDeA Network for Biomedical Research Excellence. This state-wide program funded by the NIH National Center for Research Resources is intended to promote educational and research programs, with emphasis on cell and developmental biology. There are

several areas where their interests converge with those of the IND, particularly in regard to core services, and areas of common interest continue to evolve.

- Departments with strengths in neurosciences. Several departments have strong programs in the neurosciences and the IND is committed to working closely with these toward common goals. A particularly strong area of convergence pertains to recruitments. Because institutionally all faculty appointments are made through departments, the IND is highly dependent on close interactions in this regard. However, the IND has emerged as a particularly important player in recruitments by serving as a brokerage to bring together multiple players, as larger home for neuroscience recruits, and for providing assistance to clinical departments wishing to expand their research base.
- Center on Aging and the Hoglund Brain Imaging Center. The IND has much in common with other centers that support neuroscience clinical and basic activities. As with the departments, the IND has helped in recruitments and in organizing research programs and the Centers have provided access to programs and core technologies that have served to advance the regional neuroscience effort.
- The KU Endowment Association. Philanthropic support represents an increasingly important mechanism for promoting research programs. Private or foundation donations can support a number of important functions, including research starter funds for generating preliminary data prior to applying for NIH funding, named lectureships, scholarships and fellowships, endowed professorships, and institute or center directorships.

Conclusions

The IND, barely 6 months old at the time of this writing, remains a young and developing entity. Much remains to be done, and many challenges are yet to be overcome. However, the progress to date has been very encouraging. IND membership now exceeds 120 members, with membership in individual Divisions ranging from about 10 to 55. About half of our members are clinicians or clinician-scientists. While the majority is located at KUMC, we have members from all major regional institutions. We have been successful in brokering one major recruitment and are exploring the possibility of a second. Our TDFs continue monthly, and are very highly attended. Clearly, the true metrics for success will come in the form of new collaborations leading to grants, papers, and other evidence of scientific advancement. Such outcomes take time, so we do not yet know the extent of the impact of the IND. Nonetheless, we have seen in several instances new collaborations arise, often unexpectedly and frequently across institutional boundaries. The IND therefore seems to be providing an effective vehicle for moving quickly into a new era of enhanced regional collaborations within the Kansas City area.

Contract Staffing Partnerships

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One of the most critical challenges confronting progressive research institutes is the rapidly growing necessity of a mixed population of employees from several sources in order to meet research objectives. In a perfect world, assuming funding was no object, and that is a giant assumption when one considers the balance required for winning the current economic contest, animal-based research programs would be conducted by willing and cooperative teams of technical professionals squarely focused on the mission. Apart from the adventure of a novel or movie melodrama, putting together a coterie of the finest scientists and support staff doesn't happen as readily as Hollywood or Congress would have us believe. It does not matter what organization we describe, be it academia, the federal government, or emerging biotechnology venture capitalists, recruitment of a highly trained and motivated staff is a continuous struggle.

First and foremost, there is a need for complete and honest appraisal. Despite the hard push for outsourcing the federal research work force, and regardless of whether this is advantageous or less than optimum, we must ask the tough question: is this the correct approach for our research program? Can we get the job done in a tightly controlled biosafety environment using contract personnel? In my opinion, the answer is a resounding yes. But the solution is not about better contracting or outsourcing. From a global perspective, it's about partnership. It's putting together the best and the brightest, regardless of organizational connection, into winning teams. Intelligent individuals placed in the right positions, under the direction of managers who can balance mission with quality of life, can meet the challenge when leadership affords them the opportunities as well as the benefits we seek in a modern capitalistic society.

Outsourcing Options

Why should we venture outside our organizations for staff? In a naive sense, research organization approaches to staffing are somewhat counter-intuitive and sometimes clueless. They often fail to recall that people are not robotic, actuarial automatons, but the cry of "more for less" still reigns. Reality then takes hold after the first thoughts of easy money, and the long forgotten complexities of human endeavor eventually surface. However, that is not to say costs can't be controlled and even reduced, you just have to think long term. Beware of those who offer immediate savings, especially for

personnel involved in biocontainment environments.

There are many reasons for outsourcing staff, as shown in Figure 1 [1]. And experience has demonstrated that improved quality is a very real result. As mentioned, outsourcing has often been presented as an opportunity to reduce overhead costs while simultaneously achieving better service support. However, a survey from the consultant firm Deloitte[2] suggests that not all companies have received what they expected from their outsourcing experience. In fact, most surveyed were actually disappointed – they hadn't managed to cut either costs or complexity.

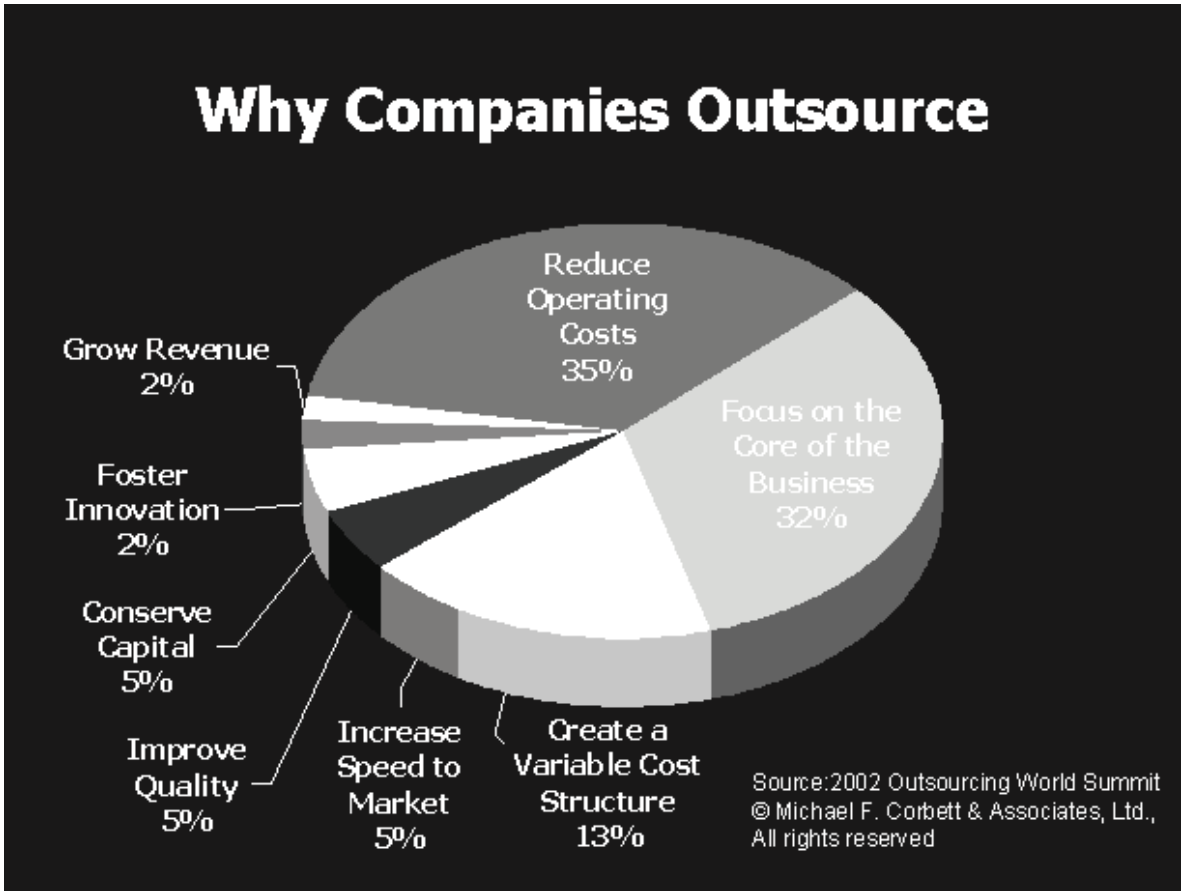

Figure 1. Outsourcing World Summit, © Michael F. Corbett and Associates, Ltd., All Rights Reserved, 2002

So, what's the problem? To reiterate, the effort must be a true partnership. Contract staffing will all but fail if the client does not endorse this concept without hesitation, and believe in an honest, forthright relationship, and the partners will likely not meet the level of trust needed to balance in-house staff with contract employees and outsourced work to get things done efficiently or effectively.

Perhaps it's the realization that just because personnel are contractors or a service is outsourced, it doesn't mean the laboratory can forget everything about personnel oversight– the relationship

has to be managed and modified as the environment changes. If contract staff are hired to service problematic areas the laboratory has previously failed to satisfactorily addressed, you will end up still managing the problem – you just have to manage it at a slightly longer range.

And cost shouldn't be the only motivation – especially if the position or service is vital to your organization and the research enterprise. Would you want the contractor scrimping and cutting corners to make an unrealistic profit margin because you've screwed the contract down tight? It might be attractive at first, but what if this means your service levels start to degrade? Again – think long term!

An important consideration, and often the baseline priority, is reaching a thorough understanding of programmatic needs before you start the process, and then ensure absolute clarity as you move carefully forward to your contractor of choice. Make an honest appraisal of what the work is; be accurate and complete. And understand what your selected contractor can honestly deliver. This is especially important for the laboratories and safety parameters of biocontainment facilities, to ensure contractor managerial staff are both experienced with biosafety parameters and can provide the required training. If you are not completely forthright with what you expect from contract staff, it is inappropriate to demand perfection.

Biosafety and biosecurity are the top issues of concern for many institutes. Therefore, due diligence is an important step before the vendor presents a final staffing proposal. While you, the client, may have selected a vendor on defined criteria based upon institutional requirements such as select agent experience, it is also logical that the contractor will require certain data not contained in a request for proposal. Establishing this back-and-forth information dialogue is a significant piece of the vendor's due diligence, and offers direction to fine tune the final proposal which will become the basis of the relationship. And though the institute may select a seller or contractor on certain predetermined criteria, laboratories requiring the service now must vet the vendor's capabilities through the due diligence process as well. Only when the organization has examined the final proposal from the vendor against the initial scope of work, can the contract staffing project be finalized.

For both the vendor’s and seller’s due diligence process, the set of activities will likely be similar: cross-referencing, personally meeting key staff or physically viewing infrastructure and documentation. However, the outcomes will differ. For the vendor, this exercise will lend comfort to sufficiently outlining performance of the services to be provided. The vendor uses this opportunity to evaluate the proposal and assess the validity of the assumptions, scope and size of the engagement (type of solution offered, at what cost and based on what assumptions, terms and conditions such as regulatory compliance and medical surveillance.) For the buyer, the findings are weighed and linked to the desired outcomes, goals and objectives of the

outsourcing initiative. Regardless, due diligence is an opportunity for fine tuning outsourcing objectives (set by the buyer) as well as the final proposal (proposed by the seller) and this process generates the baseline for evaluating the outsourcing relationship.

The Human Element

Building the human component of research endeavor is the singular most visible and often misunderstood resource allocation exercise in today's dynamic employment market. When choosing to outsource staff, trust in the function of the contractor's human resources department is a critical factor, because it's all about people. The supporting elements for contract staff active in effective recruiting, hiring, benefits and career development, to mention a few, are no different and no less important than the programs offered to in-house employees.

Again, caution is warranted. The low price vendor may save up-front dollars in the short term, but after the budget party is over and services suffer from lack of management oversight and human resource support, the long-term result is the last minute call to the institute for additional funding to avoid mission failure and, particularly, investigative wrath. After all, service is the cornerstone of a long term relationship, and trust in the human resources component of the chosen contract cannot be underestimated.

Contract employees can become your laboratory's sustainable, competitive advantage if they are considered as talent rather than labor. The synergy created from informed and involved contract staff will have an exponential impact on optimization of research productivity. Once again, partnership is the key, because employees organic to the institute or contract are a laboratory's greatest asset. The ultimate goal is trained and qualified staff for the long term.

Based upon economic reality, we now know that a perfect world of institute-only employees does not exist - having been replaced by increased outsourcing of both skilled and unskilled labor, in addition to aggressive downsizing. All you have to do is read the newspaper: reduction in force programs, cuts in health benefits and decreased retirement benefits. The resulting reality, paradoxically, is increased demand for superior service, while levels of employee commitment have dropped dramatically and with a corresponding high rate of turnover.

But the research employment experience can be different. Careful selection of the contractor, based upon depth of support, industry savvy, biocontainment experience, and a commitment to research mission success, is a good start. However, placing a high level of importance on recruitment and staffing coupled to a strongly structured training process is fundamental to continued success and uninterrupted operation of the laboratory. Effective staffing and employee recruitment depends on seeking a winning combination of demonstrated positive behavior, accurate determination of the applicant's past performance and level of commitment, and the willingness to do whatever it takes to attract the best individuals for skilled workforce positions.

Baseline skill sets and credentials are evaluated through the hiring process. But adaptation to a laboratory culture and ensuring competence for research specific tasks frequently requires additional training and continuing education. A solid commitment to internal and external training opportunities and the resources to make it happen are fundamental beliefs of the best contract companies - looked for and demanded. It is important to realize that best fit is accomplished by the application of adult-based learning to a workforce of multi-cultural dimensions. English as a second language is the norm, not the exception. In the end, a balanced approach of realistic expectations, based upon individual development plans, will best meet institute needs. Training is no doubt a critical motive for long term results and an investment well worth supporting, for both in-house and contract employees.

Contract Oversight

Perhaps no other concern is addressed and reinvented more. Whether we address the apparent lack of federal oversight in the development of new drugs, contract overage charges in Iraq, or research consulting; the broad reaching issue of adequate accountability for outsourcing services is a hot topic.

As part of the contract oversight solution, one essential best practice is to recognize the fact that as a partnership, responsibility for contract performance is a shared responsibility. Communication must be the top priority. Hidden agendas, delayed response, and failure of honest self reflection, wastes time and stops solutions cold. Good communicators continue to define precise goals and provide unambiguous plans to carry out research objectives. Only by providing a well-communicated plan of action, which details workforce requirements from beginning to end, will contract employees clearly understand their roles.

Mission motivation is a no brainer. Failure to recognize that contract employees are as qualified as the laboratory personnel they support, and are just as committed to success, places the highest barrier to achieving the research objective desired. Remember, it's all about team. Learning to let go and to accept the fact that not every member of the team can play the same position will go a long way toward establishing realistic benchmarks for measuring performance-based contracts.

Finally, a revisit on why institutes should consider contract staff as members of the research team. Do these questions look familiar? No. 1: Are people hired for their skills and experience only to be burdened with their behavior or attitude? No. 2: Is the program faced with the challenge of program growth with fewer resources for customers who demand more for less? No. 3: Are conflicts within the organization focused on who was involved rather than what is involved? Reports from employers indicate that although science graduates consistently receive stellar marks for their technical knowledge, those same employers often express concern about underlying abilities such as listening, interpersonal

effectiveness, intercultural sensitivity, and teamwork.

What are the answers? For starters, recognize there are strategies to develop and acquire fundamental soft skills to better prepare technical and professional staff for success in the contract staffing arena. There is also an increasing body of hard research on productivity and the impact of soft skills on performance [3, 4, 5]. Productivity differences of those with highly developed soft skills exceed the average new hire by a factor of as much as 10 to 1. So it's important to accept the obvious inference, soft skills are the hard skills. Technical ability and professional credentials, while certainly a baseline requirement, do not necessarily equate to managerial expertise or the gift of leadership. Thus, recognizing that soft skills are vital, and that characterizing and managing the hiring process to capitalize personnel selection based on such skills is a must, institutes can only gain by placement of this task into the hands of a good human resources department and then actively engage in the process to ensure success.

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Forming Successful Unconventional Collaborations

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Forming and sustaining unconventional collaborations is an opportunity to advance knowledge in unanticipated and sometimes surprising ways. Working at the fringes of interdisciplinary work may be exciting and deeply rewarding. The exploration of relationships, ideas, cultures, and the range of scientific disciplines define the edges of innovation and entrepreneurship. This brief paper will describe some emerging unconventional opportunities for collaboration in the life sciences.

The formation of successful unconventional collaborations is often catalyzed through compelling need and a greater understanding of nature, her underlying processes and their complex interactions. The path to collaboration emerges through "self-assembly" of the critical disciplines, and often stresses the "liminal", previously unconsidered areas. For example, in the field of biophysics, natural collaborators have self-organized through a growing understanding of mechanisms of cellular communication, expression of proteins and metabolomes. The dynamic inter-relationships that enable cell signaling and trafficking has emerged as an important discipline in the understanding of living systems.

An important international example of the value of collaborations is the Cooperative Threat Reduction (CTR) program. While intended to facilitate transition of science and technology research from nefarious to legitimate purposes specifically in the fields of biological and chemical engineering, many contributions to global societies have emerged from this program. International cooperation was strengthened, new interdisciplinary research and entrepreneurship opportunities ensued, and previously unrecognized science talent was recognized and funded. In addition, new opportunities for student research and interdisciplinary teaching arose, and scientists began applying resources to a new set of challenges that would play significant roles in advancing medical therapeutics, diagnostics and disease prevention.

Navigating and fertilizing the landscape to promote successful collaboration is often challenging. First, the case for grass roots collaboration is often self-evident and an important initiator for the work, but requires continued nurturing through resources and institutional support to remain sustainability.

Collaboration may sometimes be described as schizophrenic, since the optimal pathway to success often benefits from multiple parallel, and sometime conflicting, initiatives. For example, in the life sciences area, successful programs evolve that address system, cellular and sub-cellular level questions and translational opportunities. The translational opportunities may emerge as entrepreneurial and/or sustainable joint scientific ventures. Success may be defined on many levels, from research publication, to scientific truth, to new opportunities for commercialization, to launching students on a path to a lifetime of scientific discovery.

Collaborations may evolve in a number of ways. The most commonly observed collaborations demonstrate convergence on a challenging set of problems and issues that naturally may be characterized as multi-dimensional or inter-disciplinary; unconventional collaborations may evolve in this way. Other collaborations tend to thrive on fractal formation, with many branch points emerging from the research and entirely new areas for scientific pursuit emerging. In addition, complementarities of purpose, process, and function may emerge from collaboration. Complementarities may be seen in bio-diverse systems and an understanding of how environmental stressors may push evolutionary and adaptation mechanisms.

Alternatively, collaborations may evolve toward divergence; specifically, as understanding of the problem or set of problems evolves, the manifest differences and incongruities become increasingly obvious. Most collaborations adapt to the pressures, both internal and external, that force them to either flourish (successful) or self-extinguish (unsuccessful). Clearly, there are a number of human and cultural factors that drive this process, however, the over-riding factor tends to be the compelling nature of the problem-opportunity.

Unconventional collaborations may be catalyzed by emergencies. For example, climate change and planetary impact has facilitated the cooperation of green chemistry researchers, atmospheric modelers and medical researchers. The increasing prevalence of toxic environmental substances, global urbanization, and overabundant biomass in population dense neighborhoods creates a global melting pot, sort of a genetic soup for transmission and co-evolution of disease.

The significance of furthering our knowledge of an inter-species global health corridor and "collaboratory" of scientists worldwide is gaining traction. The biological sciences community has long understood the importance of tracking avian flight paths, however, only recently has a greater appreciation of opportunities for sentinel disease surveillance employing birds become popularized. Global spread and evolving pathogenicity, are enabled by environmental factors such highly efficient airborne routes of transmission of West Nile Virus, SARS, Avian and Swine influenza. Theses system-level observations emphasize the need for interdisciplinary, adaptive collaboration. Pathogen resistance to preventive

medicine strategies (i.e., anti-viral agents) and the rapid, subtle mutations and genetic shifts underscore the complex system dynamics and are just a few compelling examples of interactions between global communities of animals, humans, and environment.

The expanding body of knowledge and understanding at the system, cellular, and sub cellular-levels of zoonotic diseases, coupled to the complex interactions of humans, animals and plants that express these diseases, renews the scientific community's enthusiasm for collaborations in global health, comparative and translational medicine for generations to come.

Using Analytical Chemistry to Unravel Disease State Mechanisms: Application to Huntington's Disease

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In today's research environment, productive collaborations, either local, regional, or global, are essential for maximizing the impact of research efforts. This sentiment is especially true in many areas of neuroscience, one of the most rapidly advancing scientific fields. Given the inherent complexity of the central nervous system and the analytical advances that are currently being made in order to resolve these intricacies, it is becoming increasingly difficult to maintain of clear grasp of all of the relevant neuroscience concepts and also develop and employ cutting edge technologies important for investigating these concepts. Thus, it is, perhaps, more important than ever for neuroscientists and analytical scientists to establish symbiotic collaborations that will enhance the importance of the research. In this paper, I discuss ongoing research in my laboratory in which we applied sensitive measurement techniques, both in vivo and ex vivo, in order to gain a more complete understanding of Huntington's disease. An important aspect of this discussion is that productive collaborations have been a positive force in enhancing our ability to resolve some of the underlying neurochemical mechanisms of this disorder.

Modeling Huntington's disease in rodents

Huntington's disease is a fatal, genetic neurological disorder caused by an expansion of CAG repeats on the gene encoding huntington (Htt), resulting in an expanded chain of glutamine residues at the N-terminus of the expressed protein (Huntington's Disease Collaborative Research Group, 1993). A sequence of 40 or more CAG repeats results in 100 percent disease penetrance. Moreover, there is a direct correlation between increasing repeat number and decreasing age of onset. HD results in a debilitating behavioral syndrome that includes both psychological and motor disturbances. The hallmark motor feature of HD is chorea, defined recently as "random, abrupt movements superimposed over purposeful acts" (Bates et al. 2002).

The discovery of the HD mutation in 1993 by the Huntington's disease collaborative research group opened the way for the development of genetically-engineered animals that model the neurological and motor phenotype of human HD. The R6 line of transgenic mice was developed in 1996 (Mangiarini et al. 1996) and represents the first genetic rodent model of HD. Within this line the R6/2 mouse, which possess the gene required for the expression of exon I of the human Htt protein

with a CAG repeat length of about 150, is among the most used HD model rodents. This strain develops a motor syndrome at 9 to 11 weeks of age that roughly approximates HD in humans. Since the development of the R6 line, many other mouse lines have been developed, including knock-in and full-length, that are thought by many to more faithfully replicate the neurological phenotype of HD (reviewed in Levine et al. 2004 and Menelled 2005). Additionally, a transgenic HD (HDtg) rat strain that possesses a fragment of the human HD gene with 51 CAG repeats has been developed (von Hörsten et al. 2003). Although the HDtg rat possesses a mutation similar to that of the R6/2 mouse, it has the advantage of developing the disease syndrome over a longer period of time (20-24 months compared to 9-11 weeks), providing a richer array of behavioral abnormalities over the life span of the animal. Additionally, the larger size of the HDtg rat facilitates the conduction more intricate neurochemical and behavioral experiments, including those that involve in vivo microdialysis and fast-scan cyclic voltammetry measurements.

Our collaborative approach toward studying CNS function

Broadly stated, the mission of our laboratory is to develop and apply analytical methods for the study of biological systems. Current methods that we employ include fast-scan cyclic voltammetry at carbon-fiber microelectrodes, microdialysis sampling, and fluorescence microscopy. We currently use these methods to measure dopamine release and uptake in rodents that model HD, including R6/2 mice and HDtg rats. We obtained breeding pairs of these rats through a collaboration with Prof. Stephan von Hörsten, Erlangen University, Germany, and Prof. Olaf Riess, Tubingen University, Germany. Another important aspect of this project is the measurement of behavior. For these studies we are collaborating with Prof. Stephen C. Fowler, Department of Pharmacology and Toxicology, University of Kansas, in order to measure behaviors at millisecond timescales, and also to correlate these behaviors with millisecond timescale voltammetric measurements. Finally, we have entered into a collaboration with Dr. Dave Johnson and Donna Johnson, Pinnacle Technology Inc., Lawrence, KS, to develop a wireless fast-scan cyclic voltammetry system. This technology will enable us to obtain voltammetric measurements in the context of behavioral paradigms of increasing complexity. All of these collaborations have been invaluable in strengthening our experimental approaches by expanding our repertoire of capabilities. For example, we have been able to directly correlate neurochemical signaling events with behaviors in rats by obtaining our fast-scan cyclic voltammetry measurements simultaneously with behavioral measurements collected using a force-plate actometer, developed by S.C. Fowler.

Reserve pool measurements in R6/2 mice

Recent evidence, much of it collected by our laboratory, show that vesicular dopamine release is impaired in the striata of multiple types of HD model rodents. Previous results have indicated that dopamine release is impaired in R6/2 mice compared to WT control mice. Moreover, our data suggest that reserve pool dopamine, which is available for periods of extended synaptic activity, is depleted in R6/2 mice. Therefore, we sought to assess how well dopamine reserve pool vesicles are mobilized. It has been shown recently that cocaine, a powerful psychostimulant that

impairs dopamine uptake by competitively inhibiting the dopamine transporter, also increases dopamine release in mice by mobilizing a synapsin-dependent dopamine reserve pool (Venton et al., 2006). Therefore, we used cocaine as a tool to mobilize dopamine reserve pools in striatal brain slices from R6/2 and WT mice (Fig. 1). This experiment was carried out by treating brain slices with αMPT, which blocks dopamine synthesis, while providing a single electrical stimulus pulse every 5 minutes to deplete releasable vesicles of dopamine. Dopamine release and uptake were measured using FSCV. After dopamine release disappeared during treatment with αMPT, cocaine was applied to the brain slice, in addition to both αMPT treatment and the ongoing application of the stimulus pulses. In both R6/2 and WT brain slices, dopamine release almost immediately reappeared and increased to about 20% of pre-drug release, presumably due to the mobilization of vesicular reserve pools. However, dopamine release from R6/2 brain slices disappeared more quickly than WT (~35 min versus ~105 min). Therefore, these data support a scenario in which vesicles from both R6/2 and WT slices are mobilized effectively; however, it appears that there are less reserve pool vesicles available for mobilization in R6/2 slices.

Behavioral and neurochemical measurements in HDtg rats

A synchronized behavioral /neurochemical approach was employed in which microdialysis sampling was used to measure trends in extracellular dopamine levels while behavior was simultaneously measured at 100 samples/s using the force plate actometer (Fig. 2). Male hmHDtg rats and male WT control rats, 9 months old, were injected with AMPH (5.0 mg/kg, i.p.) and behavior was measured in the actometer for 240 minutes (Fig. 2A). During this time, microdialysis samples were collected from the dorsal lateral striatum every 15 minutes. Dialysates were subsequently analyzed for dopamine concentration using high performance liquid chromatography with electrochemical detection. Our results show that, after injection with AMPH, extracellular dopamine levels increased dramatically and then decreased gradually in both hmHDtg and WT rats (Fig. 2B). During this increase in extracellular dopamine levels, the space used in the actometer, which serves as a measure of focused stereotypy spatial confinement, also was initially elevated. WT rats used significantly less space (more stereotypy) compared to hmHDtg rats 30 to 135 minutes after AMPH injection despite the fact that there was not a difference in extracellular dopamine levels during this time or throughout the entire 240-minute measurement period. Therefore, hmHDtg rats appear to be resistant to AMPH-induced spatial confinement and focused stereotypy, while the WT control rats are not. Additionally, there was no difference in pre-injection dopamine levels or in dopamine levels after injection with saline vehicle (data not shown). Consequently, this experiment is important because it suggests that differences in psychostimulant-induced behavior between HDtg and WT rats do not result from differences in basal extracellular dopamine levels aggregated across 15 min. Thus, we propose an alternate mechanism: behavioral differences between genotypes arise from differences in the characteristics, such as frequency of occurrence, of dopamine transients, which cannot be detected by microdialysis. Our experimental approach, therefore, was to use FSCV to measure striatal dopamine release transients

in ambulatory HDtg rats and WT control rats.

Dopamine transient frequency of occurrence in HDtg rats

We quantified the frequency of occurrence of dopamine release transients in hmHDtg rats and WT control rats (n = 3 hmHDtg and 3 WT; age = 12 months). Shown in Fig. 3 are representative data taken from a 12-month old hmHDtg rat and a 12-month old WT littermate control rat. The release plots (center trace of each picture) for the WT and hmHDtg rats are expressed here in terms of current and show the occurrence of dopamine transients measured at a sampling rate of 10 cycles/s. A CV, corresponding to the peak marked with an asterisk, is shown above the trace and confirms the presence of dopamine. Color plots, constructed by unhinging sequential CVs, stacking them from left to right, and expressing current as color, are also shown. For a given rat, files collected 15 to 21 minutes after attaching the rat to the voltammetry system were analyzed (six 1-minute files per rat). Peaks that represent dopamine transients were identified by inspection of the respective CVs. The frequency of transients was calculated by averaging the number of transients identified by the number of minutes of measurement. The analysis of the data yielded an average of 7.2 ± 2.3 transients/min occurring in the hmHDtg rats and an average of 2.6 ± 0.6 transients/min occurring in the WT rats ($p = 0.084$, t-test). For these analyses, each group consisted of two male rats and one female rat. It is interesting to note that the female rats of both genotypes had a dopamine transient frequency roughly half that of the respective male rats. The recent paper by Bode *et al*. (2008) revealed sex differences present in the HD rats, and the differences seen between male and female rats in our studies may be reflective of these findings. Overall, these data are significant because they suggest that HDtg rats may release dopamine transients at a greater frequency than WT control rats. These increased dopamine signaling events may, therefore, impact MSN neuron firing properties, discussed in the following sub-section.

Simultaneous collection of behavioral and neurochemical data in rats

Collecting neurochemical and behavioral measurements separately allows for behavioral and neurochemical comparisons to be made between age groups and drug treatments. Nevertheless, simultaneous data collection will, due to the close temporal association of the data, allow for even more direct comparisons between behavior and neurochemistry. Additionally, this method also maximizes the use of each rat. To demonstrate feasibility, voltammetry data were collected from a normal male Sprague-Dawley rat behaving on a force plate actometer (Fig. 4). FSCV and actometer measurements were electronically synchronized. The rat received an ip (5 mg/kg) injection of AMPH 60 minutes after the start of data collection. As can be seen from these data, during the last ~24 min, the rat developed focused stereotypy, indicated by the presence of a 10 Hz Z-axis force peak ("Power Spectra"; behavioral data at top of Fig. 4) and by the lack of X-Y movement on the force plate ("Track"). Moreover, naturally occurring dopamine release transients, measured soon after injection, and a longer series of transients, measured 16 minutes after injection, are shown. These data demonstrate the feasibility of simultaneously measuring naturally-occurring dopamine transients and behavioral alterations at near-millisecond temporal resolutions.

Concluding remarks

The data presented here are made available not only by the hard work of personnel in the Johnson laboratory, but also are the product of important collaborations that have been established. These collaborations were necessary to obtain the transgenic HDtg rats (S. von Hörsten and O. Riess, Germany) and also to obtain behavioral measurements (S.C. Fowler). These types of complimentary efforts are expected to become increasingly important for neuroscience research as newer, more specialized techniques are developed.

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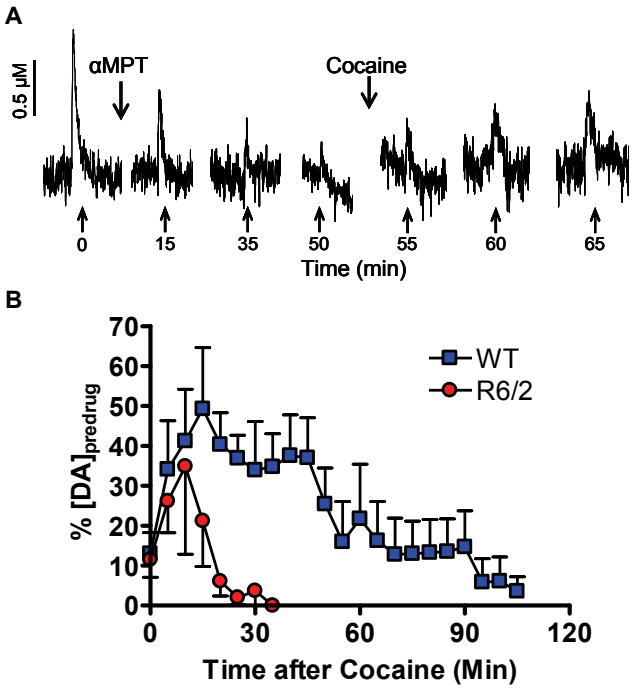

Figure 1. Cocaine-mobilized reserve pools are diminished in R6/2 mice compared to WT mice. Brain slices from 12-week old R6/2 mice and age-matched WT control mice were treated with α-methyl-p-tyrosine (50 μM). When stimulated dopamine release disappeared, cocaine (20 μM) was also added to the perfusion solution. The peak cocaine-induced increase in stimulated dopamine release in R6/2 slices was not significantly less than that observed in WT slices, but was substantially shorter in duration (n = 5 WT and 5 R6/2 mice).

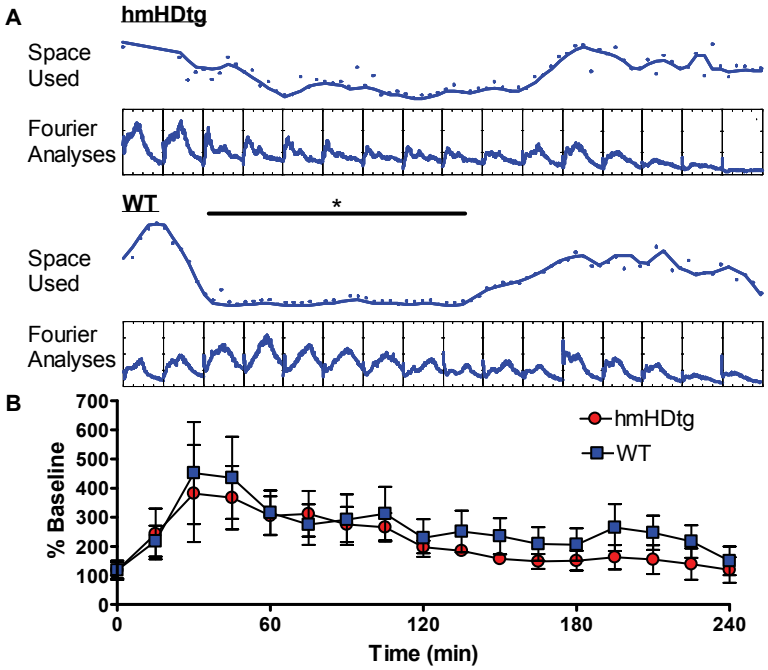

Fig. 2. Transgenic HD rats are less spatially confined than WT rats after AMPH injection even though extracellular dopamine levels are the same. Rats were injected i.p. (5.0 mg/kg) with AMPH at t = 0 min and synchronized behavioral and neurochemical measurements were collected. ***A***, Space used (y-axis) was measured using the force plate actometer. The asterisked bar denotes 15-min time blocks in which the space used was significantly different between WT and hmHDtg rats ($p < 0.01$). Force spectra (arbitrary units), derived from Fourier analyses, are shown below respective plots of Space Used. WT rats develop classic 8 to 10 Hz focused stereotypy, while hmHDtg rats express an altered force response at lower frequencies. Force is normalized to body weight for all force spectra. ***B***, Plot of average (± SEM) extracellular dopamine levels obtained by microdialysis sampling conducted simultaneously with the force plate actometer measurements. Values are normalized against the same rats injected with saline three days prior. Samples were collected from 4 HDtg rats and 5 WT rats while behavior was simultaneously measured using the force-plate actometer. Therefore, the behavioral data directly correspond to the force spectra plots collected within 15 minute time periods between adjacent pairs of data points.

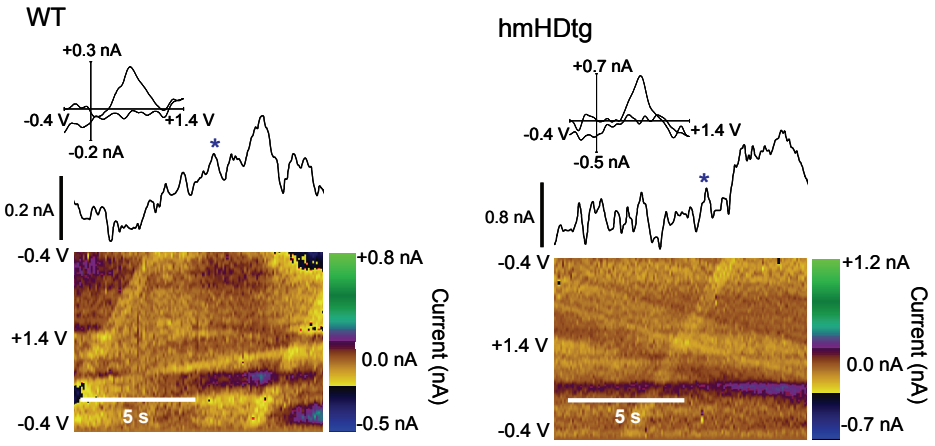

Figure 3. Alterations in dopamine release transients measured from HDtg rats. FSCV was used to measure transient spikes in extracellular dopamine concentration in the dorsolateral caudate of male WT and hmHDtg rats. The release plots of dopamine transients are shown above the color plots. Current was sampled at about +0.6 V for each successive CV. A sample CV corresponding to one of the peaks, denoted by an asterisk, confirms the presence of dopamine. Corresponding color plots of successive CVs, unhinged and stacked, are shown below the release plots. Different currents are expressed as different colors (scale shown on right side of plot). The time scale bar on the color plot also applies to the release plot. Scan rate: 400 V/s, CV update rate: 10 CVs/s.

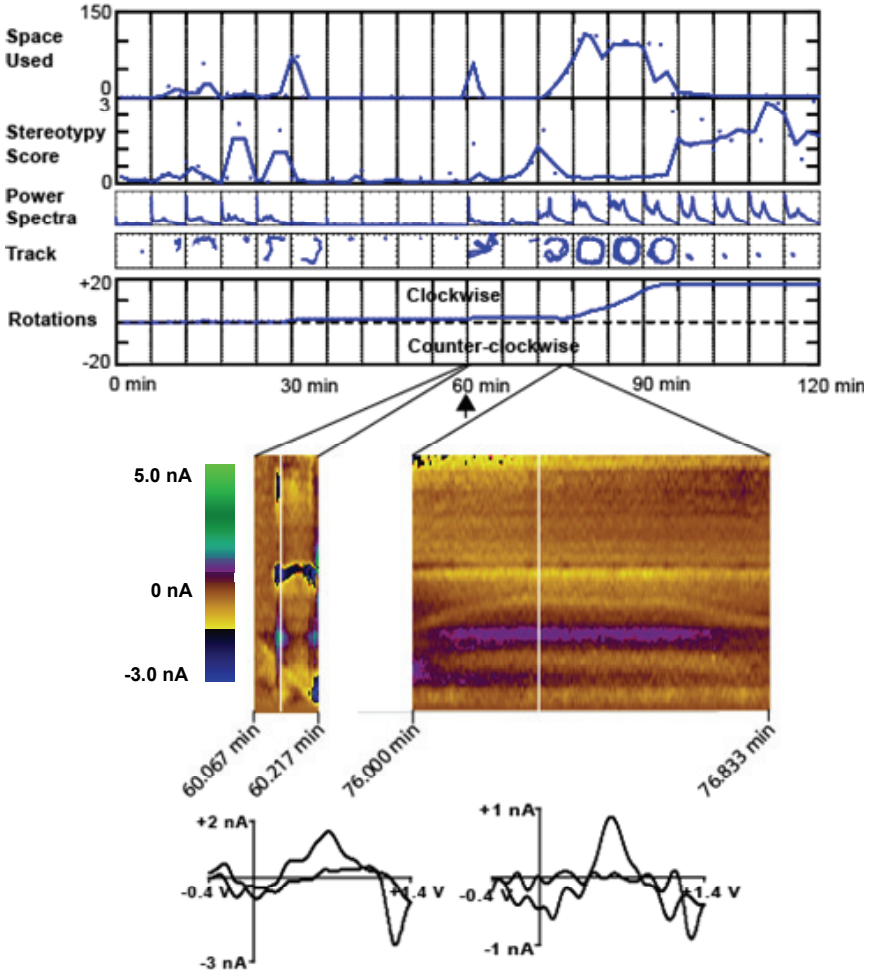

Fig. 4. Simultaneous, near-millisecond measurements of dopamine release transients and behavior. A male Sprague-Dawley rat (weight 500 g) was injected i.p. (5 mg/kg) with AMPH (indicated by arrow) 60 min after initiation of behavioral and voltammetric measurements. The collection of actometer data, including space used, stereotypy score, power spectra, X-Y track, and number of rotations (top panel) was synchronized with the collection of voltammetry files (bottom color plots and CVs). Behavioral data, collected at 100 samples/s, was synchronized to the nearest ms with the voltammetry data, collected at 10 CVs/s. The CVs were sampled from the color plots at the white vertical lines. Voltammetry data sampling ranges are shown beneath the respective color plots.

The Nebraska Center for Molecular Biology of Neurosensory Systems: A Collaborative COBRE Project

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Director, Human Molecular Genetics
Munroe Meyer Institute, University of Nebraska Medical Center

The National Center for Research Resources (NCRR) at the National Institutes of Health has developed the Institutional Development Award (IDeA) program to enhance biomedical research where NIH funding has been in the lower tier. Twenty-three states and Puerto Rico qualify for IDeA programs, including Nebraska, Kansas, and Oklahoma in our region. The Centers for Biomedical Research Excellence (COBRE) program is one of these mechanisms. COBREs are each organized around a central scientific theme, and the growth of research in that area is facilitated in three ways: support of core facilities to serve as resources, support of individual research projects primarily for junior faculty, and development of a mentoring program to ensure that the research projects result in independent NIH funding. In addition to building a network of successful researchers within a COBRE, regional interaction of COBREs and other IDeA programs is encouraged.

In building the research infrastructure of a state, a COBRE program has a particularly unique aspect: the research projects associated with the center are generally junior investigators who have not had previous renewable NIH funding, and their projects are designed to be the basis of grant applications that are funded after 2 -3 years of Center support. When external funding starts, the projects rotate off Center funding and new projects take their place. The mentoring program provides advice to the investigators to help ensure that he projects are successful, and the core facilities provide technical support for the investigators as well as for other researchers in the participating institutions. Thus, the Center can aid junior faculty in establishing an independent research program, and can also help make advanced technologies available to researchers beyond the Center.

The Nebraska Center for the Molecular Biology of Neurosensory Systems is built around the characterization of the molecular mechanisms controlling the development and maintenance of neurosensory functions, particularly vision and hearing. Neurosensory cells of the inner ear and retina are not replaced after damage or degeneration, so understanding of the regulation of

their development and the mechanisms of their loss are important steps to the identification of potential avenues for intervention.

Currently, COBRE projects are funded for 5 years for the first phase, and are eligible to apply for a second 5-year phase. While the focus of the first phase is the support of new investigators, the purpose of the second phase is consolidation and strengthening of the Center, and more senior researchers can be supported in addition to junior investigators. Our Center is currently starting its second phase.

Administration of a multi-institutional center

Our Center for Neurosensory Systems is a collaboration of 3 institutions in Omaha. The University of Nebraska Medical Center is the lead institution and is the primary site for the administrative and scientific cores and has research programs in retinal development and disorders. Creighton University has a long-standing program in the regulation of development of the auditory system, and Boys Town National Research Hospital has strengths in the identification and characterizations of genes causing hearing and vision loss, particularly Usher Syndrome. The administration of the center is handled by co-PIs from each institution and an Administrator who together comprise an Executive Committee (Table 1).

Table 1: Executive Committee for the Center for Neurosensory Systems, Phase I

PI: Shelley D. Smith, Ph.D., University of Nebraska Medical Center
Co-PI: Bernd Fritsch, Ph.D., Creighton University
Co-PI: Edward Walsh, Ph.D., Boys Town National Research Hospital
Administrator: Melanie Schrack, University of Nebraska Medical Center
Advisor: Kirk Beisel, Ph.D., Creighton University

Although a co-PI structure is not the typical structure for a COBRE program, we found this to be very advantageous in coordinating the support of the participating institutions. The Executive Committee manages the overall direction of the Center, overseeing the progress of the investigators on the research projects, reviewing the core facilities, and selecting new projects as the initial projects rotate off COBRE funding. The co-PIs also act as liaisons with the administrations of their institutions, to keep them informed of progress in the Center and ensure their support for the investigators and cores and for recruitment of additional faculty members with interests within the scope of the Center. The potential for pilot funding and mentoring as well as the presence of state-of-the-art core facilities can be effective recruitment tools, and the co-PIs are responsible for keeping administrators and department chairs aware of the strengths of the Center in building research.

COBRE projects also have an External Advisory Committee made up of individuals who have national and international standing in research

related to the Center. Their guidance ensures that the research of the Center is at the forefront of the field, incorporating research questions and technologies that are current and competitive. The EAC for the Neurosensory Center is shown in Table 2. They review Center projects twice a year, in person at an annual 2 ½ day meeting in Omaha, and again in 6 months via e-mail. At the annual meeting, each project investigator presents a 15-minute summary of their project and progress, followed by a 5-minute question period. New projects are also presented for approval for funding.

Table 2: External Advisory Committee, Center for Neurosensory Systems, Phase I

Robb Krumlauf, Ph.D., Stowers Institute for Medical Research, University of Kansas School of Medicine
Cynthia C. Morton, Ph.D., Harvard University and Brigham & Women's Hospital
Suzanne L. Mansour, Ph.D., University of Utah
Kathryn Albers, Ph.D., University of Pittsburg
Guy Richardson, Ph.D., University of Sussex, UK

The next day, the committee meets with the co-PIs and the core directors to discuss the progress of the Center, and then meets with each investigator individually for at least 30 minutes to discuss their projects and give advice. On the third day, the EAC meets again with the co-PIs to present their evaluation of the Center and to start to draft their report. The meeting culminates in a seminar presented by one of the EAC members which is open to the entire research community of the 3 institutions and helps to publicize the interests of the Center. The EAC finalizes its report over the next month and sends it to the PI, who then distributes it to the investigators. The EAC designed a format for progress report from each of the project investigators for submission to them 6 months later. The committee member's evaluations of these reports are shared with each of the investigators, and both of the EAC reports are submitted to the NCRR with the annual progress report.

The structure of the EAC and its evaluations will be unchanged in Phase II of the Center for Neurosensory Systems, with the exception that Dr. Robb Krumlauf will rotate off the committee and will be replaced by Dr. Jane Johnson, University of Texas Southwestern Medical Center, Dallas, TX. One member each year will rotate off and be replaced, thus helping to maintain the continuity of guidance of the center, but also adding new input.

Core Facilities

Similar to other NIH Centers, the COBRE programs have an Administrative Core and several scientific cores. The cores for the Center for Neurosensory Systems are listed in Table 3.

Table 3: Core Facilities

Administration	Director: Shelley D. Smith Administrator: Melanie Schrack
Mouse Genome Engineering	Director: Michael Salbaum (years 1-3), Kay-Uwe Wagner (years 4-5) Supervisor: Judith Stribley
Molecular Phenotyping	Director: Claudia Kappan, (years 1-3); Bernd Fritzsch (year 4-5) Supervisor: Anita Jennings
Gene Expression	Director: James Eudy

The Administrative core is based at UNMC and is responsible for the financial aspects of the Center and its subcontracts to Creighton University and Boys Town National Research Hospital. It also oversees the activities of the Center, including a monthly Journal Club, a seminar series, the annual meetings with the EAC, and a mentoring program.

The mentoring program is a vital part of a COBRE. Each of the junior faculty investigators has a primary mentor to give advice on their research and on their career development. The primary mentor should be a senior researcher who is familiar with the area of research but is not a primary collaborator, thus ensuring the independence of the junior faculty member. Primary mentors are expected to talk with the investigator at least once a month and to review manuscripts and grant proposals. To compensate for the amount of time that is anticipated, a mentor receives salary support from the Center, usually 10% FTE. Several secondary mentors are also designated for each research project, and these individuals have more direct expertise the research project of the investigator. Secondary mentors may change as the requirements of the project progresses.

The co-PIs of the Center also act as mentors, and together with the mentors and scientific core directors, they advise the investigators on publications, presentations at national meetings and the annual EAC meeting, and grant applications. Mock study sections also help the investigators understand the grant review process. The mentor and the EAC members can also identify researchers and potential collaborators outside of Omaha, helping the junior faculty members network in their field of research. Funds from the Center also support travel of each investigator to one national meeting a year to present their research.

The 3 scientific cores provide specialized services that would generally be beyond the expertise and financial resources of an individual lab and cover the basic progression of research of the projects in our center. The Mouse Genome Engineering core provides a variety of mouse models, including transgenic, knock-out, and conditional knock-outs of specific genes, allowing the examination of *in vivo* function of a genetic system in development. The Molecular Phenotyping core supplies an analysis of normal development and the results of genetic changes at the histological level, with techniques such as antibody optimization and immunohistochemistry, *in situ* hybridization, apoptosis assays, competition experiments, double-label studies, and whole mount preparations. The Gene Expression core provides microarray expression analysis using standard or

custom chips. By comparing changes in gene expression at different times in development or as a result of genetic changes, researchers can identify candidate genes and assess their effects on the expression of other genes, thus highlighting genetic regulatory networks.

Research Projects

COBRE programs are designed to support several research projects lasting for 2-3 years. Our Center supported 4-5 projects at about $150,000 per year. We also developed a funding mechanism to allow new investigators to conduct seed projects, generally $15,000-$25,000 per year, to determine the feasibility of a proposal for full project funding. This could be used to construct a mouse model, for example, to determine if the model is viable or has a phenotype that can be analyzed. We also provided bridge funding to lead into or supplement the externally funded project that is expected to result from the Center project. This funding was designed to complement the funded project and to help ensure renewal of the grant. The research projects supported by our Center in Phase I are given in Table 4, and the funding outcomes are shown in Table 5. The research projects in Phase I started out with a slightly broader

Table 4: Research Projects

Investigator	Position and Institution	Title of Research Project
Laura Hansen, Ph.D.	Associate Professor, Biomedical Sciences, Creighton University School of Medicine	Role of *EGFR* and *erbB2* in the regulation of skin innervation
Garrett Soukup, Ph.D.	Associate Professor, Biomedical Sciences, Creighton University School of Medicine	MicroRNA regulation of neurosensory development
Kristen Drescher, Ph.D.	Associate Professor, Medical Microbiology and Immunology , Creighton University	Role of Neuregulins in Myelin Repair in the CNS and PNS
Janee Gelineau-van Waes, D.V.M, Ph.D.	Assistant Professor, Genetics, Cell Biology & Anatomy, UNMC	Role of Microphthalmia-associated Transcription Factor (*Mitf*) in Development of the Retinal Pigment Epithelium (RPE) and Inner Ear (stria vascularis)
Yunxia Lundberg, Ph.D.	Staff Scientist, Boys Town National Research Hospital	Formation and Regulation of Otoconia
Neena Haider, Ph.D.	Assistant Professor, Department of Genetics, Cell Biology & Anatomy, UNMC	Functional characterization of*Nr2e3* in the developing and adult photoreceptor cells
Dr. Sonia Rocha-Sanchez, Ph.D.	Assistant Professor, Oral Biology, Creighton University School of Dentistry	The role of the *E2F2* modulation of *Rb1* in cochlear hair cells and supporting cells to mediate hair cell regeneration
You-Wei Peng, M.D., Ph.D.	Staff Scientist, Boys Town National Research Hospital	Mechanisms of Retinal Degeneration in Usher Syndrome Type IIa
Sumitra Bhattacharya, Ph.D.	Assistant Professor, Ophthalmology and Visual Sciences, UNMC	Characterization of retinal side-population cells

interest on nervous system maintenance and development, including central and peripheral innervations. Subsequently, as the Center grew in numbers, the funded projects became more focused on development of the auditory and visual systems. The projects and a brief summary of their results are as follows:

Laura Hansen, Ph.D., Creighton University School of Medicine

Role of *EGFR* and *erbB2* in the regulation of skin innervation

Epidermal growth factor receptor (*EGFR*) family members *Erbb2*/*HER2*, *Erbb3*/*HER3*, and *Erbb4*/*HER4* are necessary for proper peripheral nervous system development. The role of *EGFR* in peripheral nervous system development, however, has never been investigated in vivo. Dr. Hansen's data demonstrated that *EGFR* is required for development of proper innervation to the dorsal skin in a cell autonomous manner through changes in the cell behavior of the DRG neurons.

Dr. Hansen also had a project in the COBRE-funded Nebraska Center for Cell Signaling, which was funded at the same time our Center was funded. At the first meeting with our EAC, it was recommended that in the second year her project should incorporate more cell signaling experiments, so funding was transferred entirely to the other COBRE.

Garrett Soukup, Ph.D., Creighton University School of Medicine

MicroRNA regulation of neurosensory development

MicroRNAs have been demonstrated to play fundamental roles in developmental processes including cell proliferation, fate specification and organ morphogenesis. This work established that miRNAs also influence the structural development of the inner ear. By determining the roles of miRNAs in normal ear development and function, the capacity of these genetic regulatory elements to guide specific cell fates and functions might eventually contribute to therapeutic strategies designed to stimulate hair cell regeneration and hearing restoration.

Kristen Drescher, Ph.D., Creighton University School of Medicine

Role of Neuregulins in Myelin Repair in the CNS and PNS

The purpose of this study was to investigate the genetic response to infection to determine which pathways mediate protective responses. To accomplish these studies, TMEV-induced models of demylination were modified to precisely identify where demylination first occurs. Using this model, the effects of conditional knock-outs of the genes *erbB2* and *EGRF* were tested individually and together.

Janee Gelineau-van Waes, D.V.M, Ph.D., University of Nebraska Medical Center

Role of Microphthalmia-associated Transcription Factor (*Mitf*) in Development of the Retinal Pigment Epithelium (RPE) and Inner Ear (stria vascularis)

Although mutations in the Microphthalmia-Associated Transcription Factor (*MITF*) are known to cause retinal disorders and sensorineural hearing loss in humans and mice, the signaling pathways involved have not been characterized. This research demonstrated that *Mift* may regulate iron homeostasis leading to the hypothesis that retinal damage is due in part to oxidative stress. This led

to two tests of therapies; restriction of dietary iron to pregnant dams carrying normal and *Mift*^{vit} embryos, and the ability of transplanted hematopoetic stem cells to replace the damaged RPE. Since excess iron accumulation has been implicated in several neurodegenerative diseases as well as retinal degeneration, this research could have clinical implications beyond the effects of *MITF* mutation.

Yunxia Lundberg, Ph.D., Boys Town National Research Hospital

Formation and Regulation of Otoconia

Over 6 million adults in the United States suffer from disorders of balance and dizziness, disorders which are particularly prevalent in the elderly and a significant cause of morbidity through falling and fractures. A significant cause of balance disorders is the degeneration and dislocation of otoconia, bio-crystals in the vestibular system. We generated a mutant mouse model in which the predominant mammalian otoconial protein, otoconin-90 (Oc90), is absent. The mutant mice had giant otoconia which were not attached to the sensory epithelium, resulting in poor balance and head-tilting. This suggests that perturbed otoconial proteins can lead to loose and dislocated otoconia, which is the cause of benign paroxysomal positional vertigo (BPPV), the most common form of dizziness.

Neena Haider, Ph.D., University of Nebraska Medical Center

Functional characterization of *Nr2e3* in the developing and adult photoreceptor cells

The goal of this project is to understand the mechanisms through which photoreceptors are generated and maintained. The studies utilize the mutant mouse, *rd7*, lacking the retina transcription factor *Nr2e3,* which is a model for the human Enhanced S Cone Syndrome characterized by a retinal degeneration and an increase in the function of blue cone cells. This project demonstrated that Nr2e3 is important in the development of rod and cone cells and in maintaining their function in the adult retina. Dr. Haider also identified 4 potential loci for modifier genes, with strong evidence that one of these is the *Nr1d1* gene. Identification of modifiers will not only pinpoint proteins that interact with *Nr2e3* pathways, but will highlight potential therapies.

Dr. Sonia Rocha-Sanchez, Ph.D., Creighton University School of Dentistry

The role of the *E2F2* modulation of *Rb1* in cochlear hair cells and supporting cells to mediate hair cell regeneration

Rb1 is required for normal hair cell (HC) cell cycle control, including differentiation and mitotic quiescence. Through control of *Rb1* via modulation of the transcription factor *E2F2*, we propose to regulate the proliferation of supporting cells, creating the potential for their trans-differentiation into hair cells. During pilot funding, we produced a conditional knockout of *E2F2* and mice carrying a conditional *E2F2* transgene to allow us to study under- and over-expression of *E2F2*. Analysis of the knockout phenotype showed abnormal number and patterning of cochlear outer hair cells and abnormal innervation. We also performed a microarray analysis to identify potential downstream genes which could be additional targets for regulation.

You-Wei Peng, M.D., Ph.D., Boys Town National Research Hospital

Mechanisms of Retinal Degeneration in Usher Syndrome Type IIa

Usher syndrome type IIa is the most common of the Usher syndromes, making it the single most important genetic cause of combined deafness and blindness in the world. We have evidence that the short isoform of usherin is a basement membrane protein that interacts with $\alpha 1\beta 1$ integrin on retinal pigment epithelial cells, and some human *USH2A* mutations this interaction. We hypothesize that this interaction is essential for the retinal pigment epithelium to function properly, with the resulting dysfunctional cell signaling directly affecting basement membrane metabolism and photoreceptor cell health, culminating in synaptic malformations and photoreceptor apoptosis. We have produced mouse models of integrin and usherin deficiency, and both have progressive retinal degeneration along with delayed translocation of transducin and arrestin in the rod photoreceptors in response to light/dark adaptation. Furthermore, it was demonstrated that increased light exposure produces more rapid photoreceptor degeneration in the mutant retinas.

Table 5: External Funding of Research Projects

Investigator	Years of funding	Grant awards NIH/DOD/NSF	Grant awards Private foundations/other
Hansen	1	R01	Health Futures Foundation, Nebraska LB595
Soukup	3	R01, EPSCOR (NSF)	
Drescher	3	DOD	Multiple Sclerosis Society
Gelineau-van Waes	3	R21	Retina Research Foundation
Lundberg	3	R01, P50 (Deng, PI)	
Haider	3	R01	Hope for Vision
Rocha-Sanchez	1	R03	Deafness Research Foundation
Peng	1		
Bhattacharya	1		Research to Prevent Blindness

Sumitra Bhattacharya, Ph.D., University of Nebraska Medical Center

Characterization of retinal side-population cells

Identification and characterization of retinal progenitor cells offers the possibility to treat degenerative eye diseases using stem cell therapy. However, the success of this approach will largely depend upon the efficiency of enrichment of retinal stem cells and their maintenance ex vivo. Enrichment of neural stem cells is challenging for the lack of specific cell surface markers. We

demonstrated that retinal stem cells can be enriched as a "side population" (SP) by Hoechst dye efflux assay, but this sorted population is still heterogeneous. This project will characterize retinal SP cells in terms of their molecular phenotype and regulation towards providing an approach to reproducibly enrich specific subpopulations of cells and predict the functional outcomes following their transplantation in animal models.

Dr. Rocha-Sanchez, Peng and Bhattacharya will continue their research projects for one more year into Phase II, and we have added two new projects:

David Nichols, Ph.D., Assoc. Professor, Biomedical Sciences, Creighton University School of Medicine

An analysis of the *Lmx1a* (Dreher) mutant inner ear

Our preliminary results show that members of the Dickkopf (Dkk) family of Wnt signaling modulators are altered in mice mutant for the LIM homeobox transcription factor, Lmx1a, suggesting that Lmx1a expression plays a role in the control of Wnt signaling. To verify this, we will compare the spatiotemporal distributions of Wnt's 2b, 4, 5a, b and 7a, plus those of Dkk's 1 and 2 in wildtype and Lmx1a mutant mouse inner ears. These would then be compared with alterations in the pattern of Wnt signaling in Lmx1a//TOPGAL mutant mice, accompanied by a molecular analysis of the genesis of the mutant stria vascularis and endolymphatic duct in the Lmx1a mutant. These studies will determine the role of Lmx1a on the mechanism for endolymphatic homeostatis.

Michael Weston, Ph.D. Asst. Professor, Oral Biology and Biomedical Sciences, Creighton University School of Dentistry

Characterization of a MicroRNA misexpression model of age related deafness

MicroRNAs (miRNAs) are ~22nt noncoding RNAs that inhibit expression of target mRNAs through complementary base pairing. Their functions are similar to transcription factors, but their interactions with know gene regulatory networks is unknown. To study the effects of miRNAs on auditory development, we have generated transgenic miR-183fam misexpression mouse lines, and one of these was found to show progressive loss of auditory hair cells. We hypothesize that this is due to perturbation of specific regulatory, structural and/or metabolic pathways, including the Notch signaling pathway ligand Jagged1 (Jag1) and a downstream effector transcription factor Sox2.

In the second year of Phase II, we anticipate adding two new projects which will be presented to the EAC for their approval. Taken together, the Center projects have common themes in the identification of the regulatory networks in development and maintenance of function of neurosensory systems, and the potential for therapy through regenerative methods, and we have reached a "critical mass" for exchange of ideas and techniques. Most importantly, all of the junior faculty investigators who participated in the COBRE program for more than 2 years have received federal funding.

Regional Integration

The National Center for Research Resources also funds other programs to enhance research in IDeA states. Two major programs serve as a pipeline to research institutions: the Science

Education Partnership Awards (SEPA), which is designed to promote and enhance science education at elementary and secondary school levels, and the IDeA Networks of Biomedical Research Excellence (INBRE), which provides support for students, faculty, and research infrastructure for undergraduate institutions in partnership with research institutions. In Nebraska, a SEPA program headed by Dr. Maurice Godfrey at UNMC provides training for teachers in rural and tribal schools. It also interacts with a SEPA program at the University of Nebraska-Lincoln that is based in the Natural History museum there. These programs are designed to encourage students to go on to college programs in the sciences, and COBRE faculty have assisted in SEPA projects. The INBRE program headed by Dr. James Turpen at UNMC works with small colleges and tribal colleges and connects the faculty with research faculty at UNMC, UN-L, and Creighton University, and supports summer research opportunities for undergraduate students, encouraging them to consider graduate education. The INBRE program has interacted with the COBRE program by contributing to the funding of the Gene Expression Core, and many of the faculty of the COBRE and SEPA programs also participate in INBRE projects.

Regional collaboration between COBRE and INBRE programs is facilitated by meetings of PIs, administrators, and researchers in Nebraska, Kansas, Oklahoma, South Dakota, and North Dakota. The meeting is hosted by an institution from one of the states, giving them the opportunity to present their facility to other researchers in the region. Poster sessions allow all of the researchers to exchange information, and NCRR officials also attend to learn more about the programs and offer guidance. Through these meetings, our Center for Neurosensory Systems has found research goals in common with the Center for Epithelial Function at Kansas State University and the Center for Visual Neuroscience in South Dakota.

On alternate years, a national meeting is held in Bethesda for all COBRE and INBRE programs. This offers the opportunity to create collaborations on a national level, and also provides an opportunity for NCRR and NIH officials to update the PIs on new initiatives and priorities.

Conclusion

The Center for Neurosensory Systems has helped build an interactive group of researchers from 3 independent institutions, providing critical core facilities and bringing them together to produce the critical mass that supports discussion and growth of knowledge. The funding of research projects and provision of a mentoring program has resulted in independent funding for junior faculty who previously had not had that level of funding, helping our institutions "grow our own". Through additional support from other funding sources such as the INBRE or the University of Nebraska, the core facilities enhance the research infrastructure benefiting researchers at all 3 institutions. By networking with regional and national COBRE, INBRE, and SEPA researchers, the investment of the NCRR in IDeA states is leveraged further, so that the level of research quality is increased across the region.

Acknowledgement

This work is funded by NIH-NCRR P20 RR018788.

When Do Regional Research Collaborations Make Sense?

Steven F. Warren

Vice Provost for Research & Graduate Studies, University of Kansas

Collaboration has become the drumbeat of science and innovation. This fact reflects the widespread recognition of the power that comes from bringing different knowledge sets and skills to together to solve complex problems. However, it is also widely recognized that collaboration is often difficult and comes at a price. It requires lots of social interaction, trust, and typically needs to have some obvious advantages for all involved parties. In my experience people do not engage in collaboration because it's fun (although sometimes it is) or it is nice to do. They engage in it because it is necessary to solve an important problem.

The ability to communicate instantly with virtually anyone in the world has also opened the door to collaborations with virtually anyone. Still, it is usually easier and often more satisfying to collaborate with a colleague whose office is down the hall. Thus local collaborations will continue to be the dominant form as measured by sheer numbers of participants. But if there is a good reason to collaborate with someone across the country or on the other side of the world, scientists and innovators think nothing of it these days. Email, Skype, secure websites, relatively cheap and frequent air travel – all of these changes in the basic infrastructure of communication have greatly lowered the cost of collaborations over great distances. For example, I collaborate on research projects with colleagues at several other universities and many of my colleagues carry on collaborations literally all over the globe. This has become so common that we think little of it.

Given the relative ease of communicating and collaborating with great talent anywhere in the world, why would we want to limit ourselves to "regional collaborations"? In fact, such an idea sounds quaint or provincial and more importantly like a poor strategy for competing successfully in an era of globalization. Nevertheless, regional collaborations may still have their place. Thus, I offer for your consideration three scenarios in which regional collaborations may be exactly the right approach. These are 1) uniquely regional research problems; 2) the development and maintenance of certain types of expensive research infrastructure; and 3) some regional economic development initiatives.

Uniquely Regional Research Problems

Some possible topics for regional research collaboration include climate change, energy, and water. Each of these are complex issues is likely to have uniquely regional dimensions. For example, on the Great Plains from Texas north to the Dakotas, water availability and quality is an increasingly critical issue that spans the region. Likewise, the related topic of climate change associated with global warming is likely having some unique regional impacts. Rainfall (already often marginal) is likely to diminish on the western side of the Great Plains while the vast Ogallala Aquifer, the underground sea that runs under the western plains is being rapidly pumped dry in many areas. Thus, both water management and ecological forecasting are good examples of topics for which regional collaboration is potentially critical on many levels. It is not surprising then that a regional climate change research initiative is already underway. This has brought together a consortium of four universities in Kansas and Oklahoma (the University of Kansas, Kansas State University, the University of Oklahoma, and Oklahoma State University). These universities are taking advantage of funding available to them as EPSCoR states by the National Science Foundation to collaborate in the creation of a "cyber commons" – a powerful, integrated cyber environment for knowledge discovery and education across complex environmental phenomena. Specifically, this cyber Commons will integrate two frameworks – the science framework of data, models, analytics, and narratives and the cyber infrastructure framework of hardware, software, and a collaboration and integration environment. Weaving these frameworks together will allow the collaborating scientists at each university to harness the enormous potential of advanced computing for the purpose of dramatically enhancing ecological forecasting across the Great Plains.

Understanding ecological systems and forecasting their responses to global change is one of the great scientific and technological challenges of the 21st century. Addressing this challenge in the context of the Great Plains is critical for the grasslands that are fundamental to the life and economy of the plains. The utter complexity of the forecasting problem makes it a natural project for multi-disciplinary collaboration with a regional focus.

Regional Infrastructure Needs

Research increasingly involves the manipulation and study of vast amounts of information, and thus requires the infrastructure to support this. The Great Plains Network (GPN) is a consortium of universities in Midwestern states dedicated to insuring the provision of advanced networking technology throughout the region. Members include universities in Arkansas, South Dakota, Kansas, Oklahoma, Missouri, Nebraska and Iowa. These universities work together to insure common access to the internet2 and related computing infrastructure that is vital to 21st century science. This is a classic win-win situation for all collaborating partners,

including the respective congressional delegations of each state.

Less formal collaborations occur around highly specialized scientific research cores. For example, some molecular biologists at KU send their DNA samples to the genomic analysis core at Iowa State. This is cost-effective for these KU scientists and at the same time supports the provision of expensive specialized equipment and expertise at Iowa State. Likewise KU looks to scientists from other Midwestern universities help it to use its expensive High Throughput Screening Facility. In reality, these resources can be supported by any university or company, but regional support makes for good neighbors. Nevertheless, this type of regional collaboration remains subject to the relentless rules of globalization – if scientists can get the same service better, faster, and/or cheaper outside the region – then that is probably where they will ultimately send their business.

Regional Economic Development

Certain types of regional economic development may also generate collaboration among scientists, universities, and businesses. For example, the development of high technology economic development initiatives in the greater Boston, San Francisco, and Boston areas have had synergetic effects that have spawned all sorts of opportunities for these regions. Likewise, it can argued that the growth and development of the so-called Animal Health Corridor in Missouri and Kansas has the potential to benefit the biosciences more broadly in general in this region – including biosciences at the University of Kansas – which are focused primarily on human biosciences. These initiatives can bring with them specialized research facilities, talented scientists and innovators, venture capital, and a creative class that can spawn economic growth and development with regional benefits. Indeed, one could argue that any collaborative effort that builds the scientific and technological resources of a region may well lead to increasing collaboration to the benefit of all. Even in a globalized world, regional strengths still matter.

Potential Barriers

There are at least three barriers to regional collaboration. The first is the political constraints associated with state lines. This fact of life can make certain types of collaboration difficult to pull off. For example, if collaboration means that one state is going to "win more than another", why would folks in neighboring states support this? Why for example would folks in Missouri or Iowa support a major economic development in Kansas? The answer is that they won't if they are also competitive for the same prize. However, if they are not, then it may be advantageous for one state to support the other. A case in point is the political support that many states have given to the moving the National Bio and Agro-Defense Facility to Manhattan, Kansas. Much of the direct benefit of this effort may be localized in Kansas. Nevertheless, if it helps the development of agricultural research and business in the Midwest in general, then there are very good reasons to for neighboring states to support this in general – and this has occurred.

A second obvious barrier to regional collaboration is that we live in a relentlessly global marketplace for talent and capital. Globalization can make regional collaboration look like a weak and inefficient development strategy doomed to fail. The potential influence of this dynamic should never be ignored. For example, a state may invest tax revenue into the development of various bioscience companies to help them get started, grow and prosper. But for most investors in such companies, it's simply logical from a global business perspective that once they have proven their value, some larger international company will swoop in and buy them.

The third obvious barrier to regional collaboration is distance. Once the physical distance between any two scientists requires much more than an hour or so to traverse, then if may be just as easy to collaborate with someone hundreds or thousands of miles away as the regional colleague. That is, once the response cost of collaborating with someone in the region grows beyond a rather low time/distance threshold, its regional advantage may be gone. Then the relentless forces of globalization can take hold. Remember, scientists and innovators don't collaborate to be nice; they do it to solve problems efficiently and effectively.

Incentives for Regional Collaboration

What are some potential incentives for regional collaboration? Perhaps the most obvious one is the presence of world class scientific talent in the region itself. This is the edge that the Boston area has in general has with its many world class private universities, as do regions such as the Bay Area in California, and the Research Triangle in North Carolina. We have no such concentrations in the Midwest and instead our great research universities are separated by relatively large distances. These concentrations of talent obviously enable regional collaboration. Fortunately, there are several strategies to overcome the talent concentration challenge. The most obvious one is to simply take advantage of recognized regional strengths. Hence, the recognition in recent years of the large number of companies the make up the so-called animal health corridor in Missouri and Kansas.

Explicit incentives for regional collaboration include the provision of funds to support it and opportunities that require it. Thus, many states are investing substantial funds in various bioenergy initiatives and the biosciences in general through a host of financial incentives. How well these kinds of efforts will work in the long run is yet to be determined. Less expensive incentives can be provided as well. For example, universities could provide modest amounts of direct support for the collaborative efforts of their faculty to work with faculty from neighboring universities. Will that matter in the long run? Again, that remains to be seen. However, I've always been impressed by the large impact that can often be achieved from very small investments that essentially prime the pump to get collaborations going. Supportive administrative policies can also help, as can simply having a history of successful collaboration. Success breeds success. However, in the end it's probably the

case that nothing insures regional collaboration better than a problem that truly requires a regional solution.

Concluding Comments

It's important to recognize that regional collaboration and competition can go hand in hand. How did Wichita, Kansas, become an international force in the commercial aviation industry? Both collaboration, including scientific and technological, and competition were part of the story. And the fundamental story behind the Wichita aircraft industry doesn't differ all that much from the development of Silicon Valley in the Bay Area. The point is - regional collaborations, especially among scientists and businessmen have spawned many extraordinary success stories even in the very recent past, and even in a globalized world.

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