

EVOLUTION OF THE KIDNEY RESEARCH PROGRAM AT THE UNIVERSITY OF KANSAS MEDICAL CENTER

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Evolution is a “hot” topic in Kansas this year and there is no better place to see the impact of evolutionary pressures on organ development than in the kidneys. It seems appropriate, therefore, to consider kidney evolution in a related context, i.e. the emergence of a comprehensive program in renal research and patient care at the University of Kansas Medical Center.

In the beginning. In 1952, Paul R. Schloerb, M.D. became the first investigator to initiate studies on body fluid and electrolyte metabolism at the University of Kansas Medical Center (KUMC). His coming was the equivalent of the birth of the first living organisms in the ancient seas. Prior to this there was no identifiable renal research program at the University of Kansas although two unwitting contributions to the body of knowledge were made in the first half of the 20th century.

At the turn of the century Marshall Barber, a University of Kansas microbiologist, invented a glass micropipette and micromanipulator that he used to capture a single bacterium from a broth culture. He was the first to unequivocally prove Koch’s postulates underlying the germ theory by injecting a single anthrax bacillus into an animal and reproducing the disease. In the middle of the century Barber’s pipette found even wider application in the study of kidney tubule physiology by A.N. Richards in Philadelphia and a host of others. Today a minor refinement of Barber’s pipette is the major device used to transfer DNA from one cell into another, the cornerstone method for cloning experiments.

In 1939, Homer Smith, a renal physiologist from New York, delivered a series of lectures at the University of Kansas that later became the foundation of his popular book entitled “From Fish to Philosopher.” In this book he elucidated the extraordinary parallels between the evolution of the kidney from protovertebrates to man and the development of the kidney in the embryos of all mammals. Indeed, renal ontogeny recapitulates phylogeny. Smith advocated that the evolution of the kidney was the central development that permitted mammals to live on land rather than in the seas, a hypothesis that has been forcefully supported

through the years by experimental evidence. It is ironic, indeed, that vociferous debate on the role of evolution in the ascent of man has been rekindled in a state with an academic and fossil record used by scientists throughout the world in support of the theory of evolution.

Emergence of Renal Physiology and Nephrology at KUMC. In 1965 Lawrence Sullivan, Ph.D. arrived on the KUMC campus to begin the first modern studies of renal tubular function. He was joined one year later by Darrell Fanestil, M.D. who developed the first dialysis and transplantation program in the State. In 1969 Jared Grantham, M.D., Donald Tucker, M.D. and Dennis Diederich, M.D. were recruited to the Nephrology Division in the Department of Internal Medicine. In 1970 Dr. Fanestil left the university and Dr. Grantham became Director of the Division of Nephrology. In 1974 Billy Hudson, Ph.D. joined the Department of Biochemistry and instituted studies of the renal biomatrix.

Renal research discoveries at KUMC. The diversity of research in the early days led to further differentiation and advancement of the renal research program. In 1972 Dr. Grantham discovered that the renal tubules of mammalian kidneys secreted as well as reabsorbed solutes and water. This finding formed the basis of a series of experiments demonstrating that in patients with polycystic kidney disease, cysts were in fact gigantic, distended renal tubules that secreted fluid into an expanding cavity. In 1983 Doctors Diederich and Weigmann developed a novel method for anticoagulating the blood of patients undergoing hemodialysis. In 1985, Dr. Hudson isolated and determined the chemical composition of the alpha 3 and alpha 4 chains of Type IV collagen from the glomerulus of animal and human kidneys. These proteins were subsequently shown to be instrumental in the pathogenesis of two renal diseases, Goodpasture Disease and Alport Disease. Also in 1985, James Calvet, Ph.D. joined the renal research effort and discovered that polycystic kidneys aberrantly expressed growth regulating genes called proto-oncogenes, thereby placing polycystic kidney disease in the context of a neoplastic disorder. All of these discoveries served as important points of departure for the subsequent understanding of renal biology and disease.

National and international recognition of renal research at KUMC. By 1985 the annual NIH direct costs budget for investigator-initiated research exceeded \$1,000,000 and University of Kansas was recognized nationally as one of the leading renal research centers in the country.

In 1982 Dr. Grantham teamed with Mr. Joseph Bruening to create the Polycystic Kidney Research Foundation, headquartered in Kansas City, Missouri. In 1999, the PKRF was responsible for directly funding nearly \$2,000,000 in national and international grants and in influencing

federal support for PKD research to the extent of an additional \$10,000,000 per year.

In 1989 the Journal of the American Society of Nephrology was founded by Dr. Grantham and Dr. Sullivan. Upon completion of their editorial terms in 1996, the journal had the highest impact factor of over 30 titles in nephrology and urology throughout the world.

In 1998 Doctors Grantham, Hudson and Calvet successfully competed for a five year NIH Program Project Grant for studies of "Chronic Progressive Renal Diseases." This was followed by the recruitment of Dale Abrahamson, Ph.D., an expert in kidney development research, to be the Chair of Anatomy and Cell Biology. In 1999 Doctors Grantham, Calvet, Maser, Peterson, Buechner and Lu were chosen in a stiff competition to be one of the Magnet Centers for Polycystic Kidney Research by the National Institutes of Diabetes, Digestive and Kidney Diseases. In 2000 Tom DuBose, M.D., an authority in disorders of acid-base balance, became the Chair of Internal Medicine.

Research training and clinical care programs in Nephrology. The propagation of species depends upon a healthy reproductive system. Since 1969 KUMC has trained 50 nephrologists, 18 of whom spend significant amounts of their time in renal research in several universities. Seventeen nephrology trainees practice in Kansas, seven in Western Missouri, three in Nebraska, one in Iowa and 18 others elsewhere. The University of Kansas Medical Center has also graduated many renal researchers with Ph.D. degrees and postdoctoral fellowships obtained in the Departments of Biochemistry and Molecular Biology, Anatomy and Cell Biology and Molecular and Integrative Physiology.

KUMC has the highest 3-year success rate for kidney transplant survival among all of the transplanting centers in Kansas, Missouri, Nebraska and Iowa. Four of the KUMC staff nephrologists have been chosen *Outstanding Doctors of America*.

The Kidney Institute at the University of Kansas Medical Center. In 2000 a new order arose on this campus, the Kidney Institute. The Kidney Institute is a magnificent collection of scholars and trainees pursuing research programs in polycystic kidney diseases, progressive renal diseases including diabetic nephropathy and Alport Syndrome, and disorders of kidney development and metabolism. The Institute is comprised of 34 collaborating faculty investigators including 15 clinicians and 19 basic scientists. Over 100 research associates, graduate students, fellows and support staff are directly associated with the Institute. The annual total direct costs budget of the Institute in 2000 is \$4,761,976, the majority of which comes from the National Institutes of Health.

The future of the Kidney Institute. The emergence of the Kidney Institute at the University of Kansas Medical Center exemplifies the survival of the fittest in a challenging environment. The highly differentiated Kidney Institute at the University of Kansas Medical Center is a model of interactive research by talented, imaginative and successful scientists and clinicians who work toward a common goal of high excellence in renal research and patient care. The Kidney Institute is positioned to grow by the addition of exceptionally talented clinicians and researchers who will flourish in this strong growth environment.