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OLFM4 (Olfactomedin-4) Gene Expression and Its Significance in Prostate Cancer Progression: A brief update on clinical implications

Wencong Jiang[1], Nan He[2], Ming Xi[1*] and Benyi Li[2*]

[1]Department of Urology & Huadu Institute of Medical Sciences, Huadu District People's Hospital and the Affiliated Guangzhou Hospital of Jinan University, Guangzhou, Guangdong 510800, China; [2]Department of Urology, the University of Kansas Medical Center, Kansas City, KS 66160, USA
* Corresponding Authors: Ming Xi, MD/PhD, Huadu District People's Hospital, Guangzhou, Email: bulesimon@sina.com
Benyi Li, MD/PhD, KUMC Urology, Email: bli@kumc.edu

ABSTRACT

Background: Prostate cancer (PCa) remains the most frequently diagnosed solid malignancy among men worldwide. While localized disease carries a favorable prognosis, a substantial subset progresses to castration-resistant prostate cancer (CRPC) and metastatic disease. Current biomarkers, most notably prostate-specific antigen (PSA), are insufficient for risk stratification, particularly in intermediate-risk and PSA-gray-zone cases. The OLFM4 (*olfactomedin-4*) gene, encoding a secreted olfactomedin-domain glycoprotein, has emerged as a candidate tumor suppressor in the prostate, though its role remains underrecognized in the urologic oncology literature.

Evidence Synthesis: This review synthesizes findings from human tissue genetics, epigenetic profiling, knockout mouse models, cell-based gain/loss-of-function studies, and public transcriptomic cohort analyses. Convergent lines of evidence establish that OLFM4, located at 13q14.3, a cytogenetic region subject to frequent loss of heterozygosity in PCa, is silenced through complementary genetic deletion and promoter CpG hypermethylation, with loss correlating inversely with Gleason score, biochemical recurrence, and metastatic progression. The Olfm4$^{-/-}$ mouse spontaneously develops prostatic intraepithelial neoplasia (PIN) and adenocarcinoma, and crossing with the TRAMP model accelerates lethal progression. At the molecular level, OLFM4 exerts tumor-suppressive effects by (i) directly binding and inhibiting cathepsin D and blocking the SDF-1/CXCR4-AKT invasive axis; (ii) interacting with Sonic Hedgehog (SHH) and restraining hedgehog signaling; and (iii) maintaining prostate epithelial differentiation such that its loss derepresses WNT/APC/MYC signaling in stem/progenitor-like compartments, creating a therapeutically exploitable MYC-addicted state.

Conclusions: OLFM4 occupies a well-supported position as a 13q14.3 candidate tumor suppressor in prostate cancer, silenced by deletion and methylation, whose loss facilitates EMT, hedgehog/Wnt/Myc pathway activation, and eventual CRPC progression. Incorporating OLFM4 immunostaining or 13q14 FISH/CNV assessment into needle-biopsy risk stratification, as an adjunct to, not replacement for, Gleason grading and genomic classifiers, represents the most actionable near-term translational path.

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1. Introduction

Prostate cancer (PCa) is the most frequently diagnosed non-cutaneous malignancy and the second leading cause of cancer-related death among men in the United States [1]. While organ-confined tumors detected by PSA screening are often indolent, a biologically aggressive subset escapes local control and progresses to castration-resistant prostate cancer (CRPC), bone metastasis, and death [2]. The molecular determinants of this progression are multifactorial, yet efforts to identify clinically actionable biomarkers beyond PSA have yielded limited success in routine practice [3].

The OLFM4 gene (*olfactomedin-4*; aliases: hGC-1, GW112, hOlfD) encodes a ~510-amino-acid secreted glycoprotein characterized by a C-terminal olfactomedin domain, an evolutionarily conserved structural motif implicated in protein-protein interaction, cell adhesion, and extracellular matrix organization [4]. OLFM4 was originally cloned from human myeloid progenitor cells as a G-CSF-responsive transcript and subsequently detected in a restricted set of normal tis-

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sues including bone marrow neutrophils, intestinal Paneth cells, gastric epithelium, and critically, the normal prostate epithelium [5].

Over the past decade, a body of work centered at the intersection of human tumor genetics and targeted mouse modeling has repositioned OLFM4 from an obscure innate-immunity marker to a plausible tumor-suppressor gene on chromosome 13q14.3 in prostate cancer [6, 7]. This stands in apparent contrast to its reported pro-survival/upregulated behavior in gastrointestinal malignancies (gastric, colorectal, pancreatic), underscoring a recurring theme in cancer biology: the same molecule can serve opposing functions depending on tissue context and the underlying micro-environmental niche [8-11].

This review provides a comprehensive synthesis of the evidence, genetic, epigenetic, functional, mechanistic, and clinical, supporting OLFM4's role in prostate cancer progression, and discusses its emerging translational relevance as a tissue-based biomarker and a gatekeeper whose loss reveals druggable pathway vulnerabilities.

2. Genomic Context and Basic Biology of OLFM4

2.1 Chromosomal Localization at 13q14.3

The *OLFM4* gene maps to chromosome 13q14.3, a cytogenetic band that has long intrigued prostate cancer geneticists. Loss of heterozygosity (LOH) spanning 13q has been reported in 32%–85% of prostate carcinomas across series, with the minimal deleted region centering on 13q14 [6]. The locus itself spans ~23 kb, comprises five exons, and sits in proximity to the RB1 gene (13q14.2), another canonical tumor suppressor frequently inactivated in advanced and neuroendocrine PCa [12].

2.2 Protein Architecture and Cellular Localization

OLFM4 contains an N-terminal serine-rich region, a coiled-coil domain, and the signature C-terminal olfactomedin domain that drives oligomerization and secretion [7]. The protein localizes to the secretory pathway and extracellular space, associates with cell-surface lectins and cadherins, and has been detected in prostasomes (seminal fluid extracellular vesicles) [13]. These features are mechanistically important: as a secreted/scaffolding protein, OLFM4 can shape the pericellular microenvironment, binding proteases, chemokines, and morphogens, rather than acting solely through classical intracellular tumor-suppressor pathways [14, 15].

2.3 Normal Expression in the Prostate

In normal prostate epithelium, OLFM4 protein is readily detectable in luminal acinar cells and, as recent single-cell profiling confirms, in a defined subset of stem/progenitor-like epithelial cells (overlapping with *KRT13*$^{+}$/*LY6D*$^{+}$ hillock/basal-transition phenotypes) [16]. This normal-expression baseline makes its loss in cancer all the more informative: OLFM4 is not merely absent because prostate epithelium is replaced by undifferentiated mesenchyme-like tissue; it is actively lost by targeted genetic and epigenetic mechanisms, as detailed below.

3. Genetic Deletion of OLFM4 in Human Prostate Cancer

The strongest early evidence came from Li et al., who applied laser-capture microdissection (LCM) to isolate pure populations of malignant *vs*. adjacent normal epithelial cells from 31 prostatectomy specimens, followed by genomic DNA sequencing across the OLFM4 locus [6]. They found that intragenic deletions within OLFM4 were detected in ~25% of cancer-cell microdissections *vs*. paired normal epithelium. Deletions included OLFM4 exon 5 (the exon encoding the olfactomedin domain) in cancer loci from multiple patients. Fluorescence in situ hybridization (FISH) across 44 independent patient samples revealed 28%–45% hemizygous and 15%–57% homozygous OLFM4 deletion. Notably, homozygous deletion correlated significantly with advanced (high Gleason) disease. IHC across 162 tissue-array cores spanning Gleason 4–10 demonstrated a stepwise reduction/loss of OLFM4 protein in tumor-acinar cells *vs*. adjacent normal acini, with loss enriched in high-Gleason cases.

A truncation mutant lacking the olfactomedin domain lost the ability to suppress PC-3 cell growth, establishing that the same domain deleted in patient cancers is functionally required for OLFM4's growth-inhibitory effect. These data established, for the first time, direct somatic deletion of OLFM4, not merely reduced mRNA, as a recurrent event in human PCa, consistent with a two-hit tumor-suppressor model operating at 13q14.3 [6, 15, 16].

4. Epigenetic Silencing: Promoter CpG Hypermethylation

Genetic deletion is not the whole story. Systematic examination was conducted to determine if OLFM4 is also subject to transcriptional silencing *via* promoter CpG-island hypermethylation [16, 17]. Pyrosequenc-

ing of eight CpG sites in the OLFM4 promoter region (microdissected cancerous vs. adjacent normal prostate cells) showed three sites significantly hypermethylated in cancer cells. In the benign RWPE1 and cancer PC-3 lines, the DNA-methyltransferase inhibitor 5-azacytidine restored OLFM4 mRNA, confirming that methylation contributes to reversible silencing [16]. Across clinical cohorts (bioinformatics + TMA), OLFM4 protein loss tracked with both deletion status and methylation, and patients with reduced OLFM4 mRNA showed higher Gleason scores and lower recurrence-free survival. The takeaway is that advanced PCa eliminates OLFM4 through a dual mechanism: hard-coded deletion (partial or homozygous) *plus* epigenetic methylation silencing of any remaining allele, ensuring effective biallelic loss even in cases without homozygous deletion [17].

5. The Olfm4$^{-/-}$ Knockout Mouse: Causal Evidence for Tumor Suppression

5.1 Spontaneous Prostate Neoplasia

The most decisive argument for a tumor-suppressor role is phenocopy by gene ablation *in vivo*. Constitutive Olfm4$^{-/-}$ mice developed prostatic intraepithelial neoplasia (PIN) in 44% of aged males and prostatic adenocarcinoma in 28% (by 18–24 months) [15]. Gene-expression signatures of neoplastic priming were already visible in young (3-month) knockout prostates. In contrast, age-matched wild-type controls showed no such lesions, establishing that Olfm4 loss is rate-limiting for spontaneous prostate epithelial transformation [15].

5.2 Acceleration on the TRAMP Background

Crossing Olfm4$^{-/-}$ onto the TRAMP (transgenic adenocarcinoma of mouse prostate) model produced the clearest phenotype [15, 18]. Advanced prostate cancer incidence jumped from 11.9% (5/42) in Olfm4^{++}/TRAMP to 47.6% (20/42) in Olfm4$^{-/-}$/TRAMP ($p < 0.01$). Histopathology revealed increased heterogeneity, including CK8^{+}/AR^{+} tumor cells, SYN^{+} neuroendocrine-like cells, and VIM^{+}/CK8^{+} EMT-like cells. Both Olfm4^{++} and Olfm4$^{-/-}$ TRAMP tumors initially responded to surgical castration, but Olfm4$^{-/-}$ tumors displayed accelerated outgrowth of resistant, dedifferentiated clones. This experiment demonstrates that OLFM4 loss does not initiate cancer *de novo* in every context, but it removes a critical barrier to progression, lineage plasticity, and therapy resistance, precisely the barrier whose loss distinguishes lethal from indolent disease [15, 18].

6. Loss-Of-Function and Rescue Studies in Cell Models

6.1 Ectopic OLFM4 expression suppresses malignant phenotypes

In prostate cancer PC-3 (OLFM4-negative) and DU145 cells, stable OLFM4 re-expression reduced anchorage-dependent and -independent proliferation, suppressed Matrigel invasiveness and migration, and slowed down tumor growth and bone invasion/metastasis in nude mouse xenografts [17]. OLFM4 overexpression also preserved or restored epithelial markers, such as increased E-cadherin expression but reduced vimentin/N-cadherin expression [19].

6.2 OLFM4 knockdown in benign prostate cells is sufficient to drive premalignancy

In the immortalized benign line RWPE1 (which expresses OLFM4 basally), shRNA-mediated knockdown enhanced anchorage-independent growth and increased EMT marker expression (Snail, Slug, Twist; E-cadherin loss), shifting gene expression toward a less differentiated, more progenitor-like state [16]. Together, these reciprocal experiments satisfy Koch-like criteria: OLFM4 presence constrains the malignant phenotype; its absence enables it.

7. Molecular Mechanisms of Tumor Suppression

7.1 Direct Negative Regulation of Cathepsin D and the SDF-1→AKT Invasion Axis

Chen et al. showed that OLFM4 protein co-immunoprecipitates with cathepsin D and SDF-1 (CXCL12) [14]. OLFM4 reduces cathepsin D protein stability and enzymatic activity, attenuating cathepsin D–driven proliferation. OLFM4 blocks SDF-1–induced AKT phosphorylation, suppressing chemokine-driven invasion. Nude mice receiving OLFM4-expressing PC-3 cells showed not only smaller primary tumors but also reduced bone invasion and metastasis. Functionally, this positions OLFM4 as a pericellular scaffold/inhibitor that neutralizes two classical pro-metastatic effectors, a lysosomal protease and a bone-marrow-homing chemokine, at the same time [14].

7.2 Interaction with Sonic Hedgehog and Hedgehog Pathway Restraint

Li et al. demonstrated that Olfm4$^{-/-}$ mouse prostate shows marked upregulation of hedgehog pathway components (Shh, Gli1/2 targets) [15]. Exogenous OLFM4 significantly inhibits GLI-reporter activity in PC-3 cells. Co-IP confirms OLFM4–Shh protein interaction. Human TMAs show OLFM4 loss / SHH

gain enriched in high-Gleason tumors [15]. Because hedgehog signaling reactivation is linked to prostate cancer stemness, EMT, and therapy resistance, OLFM4's role as an extracellular hedgehog ligand-interacting brake is a mechanistically elegant explanation for why its loss primes the epithelium for dedifferentiation.

7.3 WNT/APC/MYC Hyperactivation and Stem/Progenitor Compartment Expansion

A third, and arguably most translationally exciting, axis is the MYC connection [16]. Analysis of Olfm4-KO RWPE1 cells and Olfm4$^{-/-}$ mouse prostate revealed enrichment for WNT/APC/MYC signatures and MYC direct targets (ribosome biogenesis, metabolism, cell cycle), MYC protein elevation at both mRNA and protein levels, and expansion of the stem/progenitor-like compartment biased toward symmetric self-renewing division. OLFM4-null cells are MYC-addicted and hypersensitive to MYC-axis suppression. This reframes OLFM4 loss not just as "something breaks to cancer grows" but as removal of a differentiation gate, leading to MYC-driven progenitor expansion and a therapeutically exploitable Achilles' heel, a selective vulnerability to BET-bromodomain inhibition (JQ1) [20].

7.4 EMT Suppression as a Unifying Phenotypic Readout

Across all model systems, OLFM4 loss consistently produces the cadherin switch (reduced expression of E-cadherin but increased expression of N-cadherin and vimentin) and upregulates Snail/Slug/Twist, while OLFM4 restoration reverses these changes [17]. Since EMT is the gateway to both invasion and acquisition of a therapy-resistant cancer stem cell phenotype [21], OLFM4's anti-EMT effect is likely the integrative phenotypic consequence of cathepsin D neutralization + hedgehog restraint + MYC-driven dedifferentiation blockade, operating simultaneously.

8. Clinical Correlations: OLFM4 Expression vs. Outcome

8.1 Inverse Correlation with Gleason Score and Tumor Grade

IHC approach with more than 160 prostatectomy TMA cores (Gleason 6–10) showed a stepwise decline in OLFM4 protein intensity with increasing grade [17]. OLFM4 loss tracks with E-cadherin loss but not with PSA level [6]. This independence from PSA is a key asset: PSA fluctuates with BPH and falls in anaplastic/neuroendocrine variants, whereas OLFM4 loss reflects a genetically programmed dedifferentiation event.

8.2 Biochemical Recurrence and Survival

Bioinformatics re-analysis of public datasets (GSE21032, TCGA-PRAD) confirms that patients in the lowest quartile of OLFM4 expression have significantly shorter recurrence-free survival ($p \approx 0.02$) [17]. OLFM4 CNV loss follows a trajectory paralleling other canonical suppressors (PTEN, TP53, RB1). The pattern suggests OLFM4 behaves as a threshold gate: partial reduction may be tolerated, but once expression is fully eliminated (biallelic deletion + methylation), the risk of recurrence accelerates [17].

8.3 Castration Resistance and Metastatic Disease

OLFM4 mRNA is further reduced/lost in CRPC and metastatic samples relative to hormone-naïve primaries. On the TRAMP background, Olfm4$^{-/-}$ tumors not only progress faster but also generate more SYN^{+} neuroendocrine-like and EMT^{+} clonal populations post-castration [18], implicating OLFM4 loss in the lineage plasticity that underlies lethal CRPC-NE transformation.

9. The OLFM4 Paradox: Why Opposite Roles in Different Cancer Types?

A persistent source of confusion in the literature is that OLFM4 is upregulated in well-differentiated gastric and colorectal carcinoma and can mark a LGR5^{+}/OLFM4^{+} crypt stem-like pool (Table 1).

Table 1. The resolution lies in tissue-specific microenvironments

Context	OLFM4's Predominant Role	Rationale
GI tract (stomach, colon, pancreas)	Pro-survival / colonization-promoting	Co-opted from its normal Paneth-cell antimicrobial / mucosal-integrity function; supports niche retention of adenoma cells
Prostate	Tumor suppressor	Restrains hedgehog/Wnt/MYC-driven progenitor escape; normal prostate does not depend on OLFM4 for mucosal barrier defense, so its loss removes a differentiation brake rather than weakening a protective barrier

As reviewed comprehensively by Liu & Rodgers [5], OLFM4's interactome (GRIM-19, cadherins, NOD1/2, cathepsins C and D, lectins) allows it to modulate very different downstream circuits depending on which epithelial type expresses it and which stromal signals surround it. Recognizing this paradox prevents naive extrapolation across tumor types and clarifies why targeting OLFM4 therapeutically must be context-aware.

10. Translational Prospects: OLFM4 as a Biomarker

10.1 Tissue-Based Detection (Near-Term)

The most immediately viable application is adjunctive tissue assessment at biopsy or TURP, including IHC for OLFM4 protein loss (simple, already validated on TMAs), FISH or NGS-based CNV calling at 13q14.3 combined with E-cadherin or a basal marker panel. OLFM4 status could help up-classify *vs*. de-escalate borderline Gleason 3+4 vs. 4+3 cases. Crucially, OLFM4 loss is driven by hardwired genomic deletion, making it relatively robust against the sampling noise that plagues purely quantitative RNA-based markers.

10.2 Fluid/Blood Approaches (Emerging)

Efforts to capture OLFM4 (or its regulatory signature) in circulation are preliminary, but proof-of-concept exists: Endt et al. [22] developed individual sandwich immunoassays for serum glycoproteins including OLFM4 and showed that, while OLFM4 alone cannot replace PSA, multiplexing CTSD + THBS1 + %fPSA + age improved classification in the PSA 2–10 gray zone (AUC ≈ 0.81). Whether methylated OLFM4 promoter DNA in cfDNA or OLFM4-loss-associated exosomal cargo can be harnessed remains an open experimental question.

11. Therapeutic Implications

11.1 Targeting MYC-Addiction in OLFM4-Deficient Tumors

The most rational lead is BET-bromodomain inhibition (JQ1, OTX015, newer clinical candidates) to suppress MYC transcription [20]. Olfm4$^{-/-}$ tumor organoids and *ex vivo* cultures show selective sensitivity [16]. Patient selection would hinge on demonstrating OLFM4 loss (IHC/FISH) in the tumor, essentially using a tumor-suppressor loss event as a predictive biomarker for pathway-targeted therapy.

11.2 Differentiation-Based Strategies

Since OLFM4 loss drives dedifferentiation, interventions that reinstate epithelial differentiation (e.g., epigenetic reprogramming agents, retinoid-based approaches, noting OLFM4 itself is a retinoic-acid-responsive gene) may synergize with AR-axis or taxane therapy, particularly in OLFM4-null/NE-prone tumors.

11.3 What Not to Do

Because OLFM4 acts as a secreted/scaffolding tumor suppressor, simple "replace the gene" cDNA delivery faces practical hurdles (folding, secretion, correct oligomerization). Small-molecule mimetics that recapitulate OLFM4's cathepsin D– and SHH-binding neutralization are a more plausible long-term pharmaceutical route but remain hypothetical at present.

12. Limitations of the Current Evidence Base (and How to Read it Critically)

Any balanced review must acknowledge that the deepest causal genetics + KO mouse work on OLFM4 in prostate cancer emanates substantially from a single NIH intramural group (Li, Liu, Rodgers *et al.*) [4-7, 14-17, 19]. This is not, in itself, a validity problem; the data are published, peer-reviewed, and reproducible, but it does mean the field would benefit from the following items:

a. an independent replication of the 13q14.3 FISH/CNV frequencies in other pathology cohorts;
b. Conditional prostate-epithelial-specific Olfm4 cKO (vs. the constitutive global KO used to date) to exclude subtle contributions from Olfm4 loss in bone-marrow-derived cells;
c. Larger prospective TMA studies that co-model OLFM4 status against Decipher, Oncotype DX, and PTEN/RB1/TP53 combinatorial genotype
d. Single-cell multi-omics of human OLFM4^{-} vs. OLFM4^{+} tumors to define the exact cellular trajectory from differentiated luminal → OLFM4-loss-driven plastic state.

These are not reasons to dismiss the OLFM4 tumor-suppressor model; they are the next experiments that will graduate it from "compelling hypothesis" to "clinical standard."

13. Conclusions

The weight of evidence, spanning (i) recurrent somatic deletion at 13q14.3, (ii) promoter hypermethylation silencing, (iii) spontaneous neoplasia in the Olfm4$^{-/-}$ mouse and acceleration on TRAMP, (iv) rescue suppression of invasion and EMT in OLFM4-null lines, and (v) inverse clinical correlation with Gleason and recurrence, supports a coherent conclusion: OLFM4 is a candidate tumor-suppressor gene in prostate cancer whose loss removes a multicomponent brake on cathepsin D/SDF-1 invasive signaling, hedgehog pathway reactivation, and MYC-driven progenitor expansion.

Its independence from PSA, its basis in hardwired genomic deletion, and the druggable liabilities it exposes (particularly MYC addiction) make OLFM4 an attractive addition to the biomarker plus patient-stratification toolkit for prostate cancer, not as a standalone test, but as part of an integrated tissue-genomic profile that finally moves beyond PSA.

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References

1. Collaborators GBDC: **The global, regional, and national burden of cancer, 1990-2023, with forecasts to 2050: a systematic analysis for the Global Burden of Disease Study 2023**. *Lancet* 2025, **406**(10512):1565–1586; doi:10.1016/S0140-6736(25)01635-6; PMC12687902.
2. Spratt DE, Srinivas S, Adra N, Ahmed B, An Y, Bitting R, Chapin B, Cheng HH, Cho SY, D'Amico AV *et al.*: **Prostate Cancer, Version 3.2026, NCCN Clinical Practice Guidelines In Oncology**. *J Natl Compr Canc Netw* 2025, **23**(11):469–493; doi:10.6004/jnccn.2025.0052.
3. Huang F, Li K, Shevach JW, Wang Q: **Emerging therapies to overcome antiandrogen resistance and beyond in lethal prostate cancer**. *J Natl Cancer Cent* 2026, **6**(1):42–57; doi:10.1016/j.jncc.2025.04.004; PMC12925916.
4. Zhang J, Liu WL, Tang DC, Chen L, Wang M, Pack SD, Zhuang Z, Rodgers GP: **Identification and characterization of a novel member of the olfactomedin-related protein family, hGC-1, expressed during myeloid lineage development**. *Gene* 2002, **283**(1-2):83–93; doi:10.1016/s0378-1119(01)00763-6.
5. Liu W, Rodgers GP: **Olfactomedin 4 in cancer development and progression**. *Biochim Biophys Acta Rev Cancer* 2025, **1880**(5):189423; doi:10.1016/j.bbcan.2025.189423; PMC12536507.
6. Li H, Rodriguez-Canales J, Liu W, Zhu J, Hanson JC, Pack S, Zhuang Z, Emmert-Buck MR, Rodgers GP: **Deletion of the olfactomedin 4 gene is associated with progression of human prostate cancer**. *Am J Pathol* 2013, **183**(4):1329–1338; doi:10.1016/j.ajpath.2013.06.028; PMC3791688.
7. Liu W, Rodgers GP: **Olfactomedin 4 expression and functions in innate immunity, inflammation, and cancer**. *Cancer Metastasis Rev* 2016, **35**(2):201–212; doi:10.1007/s10555-016-9624-2.
8. Yu L, Wang L, Chen S: **Olfactomedin 4, a novel marker for the differentiation and progression of gastrointestinal cancers**. *Neoplasma* 2011, **58**(1):9–13; doi:10.4149/neo_2011_01_9.
9. Brzustowicz LM, Kleyn PW, Boyce FM, Lien LL, Monaco AP, Penchaszadeh GK, Das K, Wang CH, Munsat TL, Ott J *et al.*: **Fine-mapping of the spinal muscular atrophy locus to a region flanked by MAP1B and D5S6**. *Genomics* 1992, **13**(4):991–998; doi:10.1016/0888-7543(92)90012-h.
10. Guette C, Valo I, Vetillard A, Coqueret O: **Olfactomedin-4 is a candidate biomarker of solid gastric, colorectal, pancreatic, head and neck, and prostate cancers**. *Proteomics Clin Appl* 2015, **9**(1-2):58–63; doi:10.1002/prca.201400083.
11. Wang XY, Chen SH, Zhang YN, Xu CF: **Olfactomedin-4 in digestive diseases: A mini-review**. *World J Gastroenterol* 2018, **24**(17):1881–1887; doi:10.3748/wjg.v24.i17.1881; PMC5937205.
12. Latil A, Bieche I, Pesche S, Volant A, Valeri A, Fournier G, Cussenot O, Lidereau R: **Loss of heterozygosity at chromosome arm 13q and RB1 status in human prostate cancer**. *Hum Pathol* 1999, **30**(7):809–815; doi:10.1016/s0046-8177(99)90142-9.
13. Block AS, Saraswati S, Lichti CF, Mahadevan M, Diekman AB: **Co-purification of Mac-2 binding protein with galectin-3 and association with prostasomes in human semen**. *Prostate* 2011, **71**(7):711–721; doi:10.1002/pros.21287; PMC3210485.

14. Chen L, Li H, Liu W, Zhu J, Zhao X, Wright E, Cao L, Ding I, Rodgers GP: **Olfactomedin 4 suppresses prostate cancer cell growth and metastasis via negative interaction with cathepsin D and SDF-1**. *Carcinogenesis* 2011, **32**(7):986–994; doi:10.1093/carcin/bgr065; PMC3128558.
15. Li H, Liu W, Chen W, Zhu J, Deng CX, Rodgers GP: **Olfactomedin 4 deficiency promotes prostate neoplastic progression and is associated with upregulation of the hedgehog-signaling pathway**. *Sci Rep* 2015, **5**:16974; doi:10.1038/srep16974; PMC4652203.
16. Li H, Chaitankar V, Zhu J, Chin K, Liu W, Pirooznia M, Rodgers GP: **Olfactomedin 4 mediation of prostate stem/progenitor-like cell proliferation and differentiation via MYC**. *Sci Rep* 2020, **10**(1):21924; doi:10.1038/s41598-020-78774-5; PMC7736579.
17. Li H, Kim C, Liu W, Zhu J, Chin K, Rodriguez-Canales J, Rodgers GP: **Olfactomedin 4 downregulation is associated with tumor initiation, growth and progression in human prostate cancer**. *Int J Cancer* 2020, **146**(5):1346–1358; doi:10.1002/ijc.32535; PMC7004162.
18. Li H, Liu W, Zhu J, Chin K, Rodgers GP: **Abstract 1548: Olfactomedin 4 deficiency promotes de novo progression of prostate cancer in TRAMP mouse model**. *Cancer Res* 2024, **84**(6_Supplement):1548–1548; doi:10.1158/1538-7445.Am2024-1548.
19. Li H, Chaitankar V, Cui L, Chen W, Chin K, Zhu J, Liu W, Rodgers GP: **Characterization of olfactomedin 4+ cells in prostate and urethral-tube epithelium during murine postnatal development and in adult mice**. *Sci Rep* 2023, **13**(1):10290; doi:10.1038/s41598-023-37320-9; PMC10290983.
20. Ali A, Shafarin J, Unnikannan H, Al-Jabi N, Jabal RA, Bajbouj K, Muhammad JS, Hamad M: **Co-targeting BET bromodomain BRD4 and RAC1 suppresses growth, stemness and tumorigenesis by disrupting the c-MYC-G9a-FTH1axis and downregulating HDAC1 in molecular subtypes of breast cancer**. *Int J Biol Sci* 2021, **17**(15):4474–4492; doi:10.7150/ijbs.62236; PMC8579449.
21. Fontana R, Mestre-Farrera A, Yang J: **Update on Epithelial-Mesenchymal Plasticity in Cancer Progression**. *Annu Rev Pathol* 2024, **19**:133–156; doi:10.1146/annurev-pathmechdis-051222-122423; PMC10872224.
22. Endt K, Goepfert J, Omlin A, Athanasiou A, Tennstedt P, Guenther A, Rainisio M, Engeler DS, Steuber T, Gillessen S *et al.*: **Development and clinical testing of individual immunoassays for the quantification of serum glycoproteins to diagnose prostate cancer**. *PLoS One* 2017, **12**(8):e0181557; doi:10.1371/journal.pone.0181557; PMC5540289.