MEIS1 and MEIS2 Expression and Prostate Cancer Progression: A Role For HOXB13 Binding Partners in Metastatic Disease

Raj R. Bhanvadia[1,11], Calvin VanOpstall[2,11], Hannah Brechka[2], Nimrod S. Barashi[10], Marc Gillard[10], Erin M. McAuley[4], Juan Manuel Vasquez[9], Gladell Paner[5], Wen-Ching Chan[6], Jorge Andrade[6,7], Angelo M. De Marzo[8], Misop Han[8], Russell Z. Szmulewitz[3], and **Donald J. Vander Griend**[2,10]

[1] The Pritzker School of Medicine; The University of Chicago, Chicago, IL.
[2] The Committee on Cancer Biology; The University of Chicago, Chicago, IL.
[3] Department of Medicine, Section of Hematology and Oncology; The University of Chicago, Chicago, IL.
[4] The Committee on Molecular Pathology and Molecular Medicine; The University of Chicago, Chicago, IL.
[5] The Department of Pathology; The University of Chicago, Chicago, IL.
[6] The Center for Research Informatics; The University of Chicago, Chicago, IL.
[7] The Department of Pediatrics; The University of Chicago, Chicago, IL.
[8] The Brady Urological Institute; The Johns Hopkins School of Medicine, Baltimore, MD.
[9] The Post-Baccalaureate Research Education Program (PREP); The University of Chicago, Chicago, IL
[10] Department of Surgery, Section of Urology; The University of Chicago, Chicago, IL.
[11] These authors contributed equally.

Purpose: Germline mutations within the MEIS-interaction domain of HOXB13 have implicated a critical function for MEIS-HOX interactions in prostate cancer etiology and progression. The functional and predictive role of changes in MEIS expression within prostate tumor progression, however, remain largely unexplored.
Experimental Design: Here we utilize RNA expression datasets, annotated tissue microarrays, and cell-based functional assays to investigate the role of MEIS1 and MEIS2 in prostate cancer and metastatic progression.
Results: These analyses demonstrate a stepwise decrease in the expression of both MEIS1 and MEIS2 from benign epithelia, to primary tumor, to metastatic tissues. Positive expression of MEIS proteins in primary tumors, however, is associated with a lower hazard of clinical metastasis (HR = 0.28) after multivariable analysis. Pathway and gene set enrichment analyses identified MEIS-associated networks involved in cMYC signaling, cellular proliferation, motility, and local tumor environment. Depletion of MEIS1 and MEIS2 resulted in increased tumor growth over time *in vivo*, and decreased MEIS expression in both patient-derived tumors and MEIS-depleted cell lines was associated with increased expression of the pro-tumorigenic genes cMYC and CD142, and decreased expression of AXIN2, FN1, ROCK1, SERPINE2, SNAI2, and TGF▪2.
Conclusions: These data implicate a functional role for MEIS proteins in regulating cancer progression, and support a hypothesis whereby tumor expression of MEIS1 and MEIS2 expression confers a more indolent prostate cancer phenotype, with a decreased propensity for metastatic progression.

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