MEIS-Mediated Suppression of Prostate Cancer Growth and Metastasis Through HOXB13-Dependent Regulation of Proteoglycans

Calvin VanOpstall[1], Hannah Brechka[1], Marc Gillard[2], Baizhen Zhu[2], Ryan Brown[3], Sophia Lamperis[3], Raj Bhanvadia[4], and **Donald J. Vander Griend[3,*]**

[1]The Committee on Cancer Biology; The University of Chicago, Chicago, IL 60637, USA.
[2]Department of Surgery, Section of Urology; The University of Chicago, Chicago, IL 60637, USA.
[3]Department of Pathology; The University of Illinois at Chicago, Chicago, IL 60612, USA.
[4]Department of Urology; UT Southwestern, Dallas, TX 75390, USA.
*Lead Contact/Correspondence: dvanderg@uic.edu

Abstract:
The discovery of germline mutations in the MEIS-interacting domains of HOXB13 associated with increased prostate cancer (PrCa) risk highlights a critical role for MEIS and HOX function in PrCa etiology and progression. MEIS1 and MEIS2 are putative tumor suppressors in PrCa and are frequently silenced throughout disease progression and metastasis. Here we show that expression of MEIS1 or MEIS2 is sufficient to decrease proliferation and metastasis of PrCa cells *in vitro* and *in vivo.* Utilizing CRISPR technology we also demonstrate that the tumor-suppressive activity of MEIS1 is dependent on HOXB13. Further, integration of ChIP-seq and RNA-seq revealed direct and HOXB13-dependent regulation of proteoglycans including decorin (DCN) as one mechanism of MEIS1-driven tumor suppression. These results underscore the importance of MEIS1-HOXB13 transcriptional regulation in PrCa, supports DCN as a potential therapeutic in prostate cancer, and provide a framework for investigation of HOXB13 and other cancer-associated cofactors when *MEIS1*/2 are silenced.

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