

ID4 regulates prostate development and stem cell population in mice prostate

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Inhibitor of differentiation 4 (Id4), a member of the helix-loop-helix family of transcriptional regulators is a novel prostate cancer (PCa) tumor suppressor. Recent studies have shown that Id4 is highly expressed in the normal prostate and decreases in prostate cancer (PCa) due to epigenetic silencing. Genetic ablation of Id (Id4^{-/-}) in mice leads to underdeveloped prostate without the loss of Androgen Receptor (AR) expression but with re-directed activity. In this study, we demonstrate that prostates from the Id4 knockout (Id4^{-/-}) mice show hyperplasia associated with increased stem cell population that was evident by increased Sca-1 and p63 expression. Histological analyses of adult Id4^{-/-} mice prostate shows increased Amacr expression, a biomarker for early prostatic epithelial neoplasia (PIN) but without a clear evidence of PCa. Immuno-histochemical analysis demonstrated undetectable Nkx3.1 and Pten tumor suppressors suggesting lack of epithelial differentiation. Although Pten protein was not present in Id4^{-/-} mice, the presence of the corresponding Pten mRNA suggested intact transcription of the gene with a possible translational or post-translation defect. These results suggested that Id4

plays a role in regulating the translation of the Pten mRNA. The results suggested that Id4^{-/-} results in PIN lesions that may be in part due to a block in Pten translation. These data suggest that loss of Id4 can initiate PIN like lesions through multiple mechanisms such as by maintaining stemness (Sca-1) and down-regulating known tumor suppressors (Pten) and promoters of epithelial differentiation (Nkx3.1) while having no effect on AR expression and function that is reminiscent of castration resistant prostate cancer. We are currently investigating the possible mechanisms by which Id4 regulates cell fate and translational/post-translational mechanisms involved in the regulation Pten.

Speaker Biography

Jaideep Chaudhary has his expertise in Bioinformatics and Molecular Biology. He uses large datasets (microarray and NGS) to develop molecular pathways involved in cell differentiation and diseases, primarily cancer. He is passionate about teaching and mentoring Undergraduate and Graduate students. As a Scientist and an Administrator, he works across the aisle to create educational programs that help developing the new generation of productive scientists and educators.

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