THE HELIX LOOP HELIX PROTEIN ID4 IS EPIGENETICALLY SILENCED IN PROSTATE CANCER CELLS: ECTOPIC ID4 EXPRESSION INDUCES ANDROGEN RECEPTOR EXPRESSION (AR) AND RESPONSE IN AR NEGATIVE PROSTATE CANCER CELLS.

Jason P. W. Carey¹, Ananthi J. Asirvatham¹, Oliver Galm² and Jaideep Chaudhary¹

¹Department of Biology, Center for Cancer Research and Therapeutics Development, Clark Atlanta University, Atlanta, GA 30314, USA
²Medizinische Klinik IV, Universitätsklinikum Aachen, RWTH Aachen, Pauwelsstrasse 30, 52074 Aachen, Germany

Abstract: Inhibitor of differentiation 4 (Id4), a member of the Id gene family is also a dominant negative regulator of basic helix loop helix (bHLH) transcription factors. Some of the functions of Id4 appear to be unique as compared to its other family members Id1, Id2 and Id3. Loss of Id4 gene expression in many cancers in association with promoter hypermethylation has led to the proposal that Id4 may act as a tumor suppressor. In this study we demonstrate that Id4 itself acts as a tumor suppressor and is part of a cancer associated epigenetic re-programming. Ectopic expression of Id4 in DU145 prostate cancer cells demonstrating native Id4 promoter hypermethylation significantly decreased proliferation and induced an epithelial cell phenotype with increased expression of E-cadherin and p53. This change in phenotype and cell proliferation was also associated with re-expression of androgen receptor and partial demethylation of Id4 promoter itself. An increase in PSA expression following androgen exposure demonstrated a functional androgen receptor axis in DU145-Id4 cells. In conclusion, our results suggest that Id4 acts as a tumor suppressor by influencing a hierarchy of cellular processes that lead to reduced proliferation possibly mediated through induction of previously silenced tumor suppressors. The AR methylation status in DU145-Id4 cells and the effect of ectopic Id4 expression of another AR-ve prostate cancer cell line PC3 are currently being investigated. Results from these studies will also be presented in the meeting.