



Friday, June 6th, 2008
2:00 pm – 3:00 pm
COOK 31 18 A&B

Structure-Activity Relationship Study of MEK 4 with Genistein

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ABSTRACT:

Dual specificity mitogen-activated protein kinase kinase 4 (MEK4) regulates prostate cancer (PCa) cell invasion and metastasis. Inhibition of MEK4, by Genistein, occurs by blocking the P38 Map Kinase pathway in turn leading to inhibition of metastasis in prostate cancer cells. In my study, the goal is to understand the interactions of Genistein with the MEK-4 active site and to be able to use Structure-Activity relationship information derived from the study for the synthesis of a more effective lead compound.

I previously created homology models of MEK4 protein and will use these models to propose *in-silico* docking interactions with Genistein and select modified analogues of the same. The resulting models will be used to study binding site interactions and to predict analogues of Genistein with higher efficacy than the parent molecule.

Research Advisors:

Raymond Bergan, Director, Experimental Therapeutics, Feinberg School of Medicine

Wayne Anderson, Department of Molecular Pharmacology and Biological Chemistry, Feinberg School of Medicine

Motif Discovery in DNase Hypersensitive Sites

Jairav Desai – CBB Master's Student

ABSTRACT:

Cystic fibrosis (CF) is a hereditary disease of complex pathology that primarily affects the lungs and digestive system resulting in a progressive, life shortening disability. The cystic fibrosis transmembrane conductance regulator gene (CFTR), when mutated, causes cystic fibrosis and has thus been highly investigated. The gene shows a tightly regulated pattern of expression; the molecular basis for which is not understood. It is clear that important *cis* regulatory elements are not just restricted to the gene's promoter region. The Harris lab has identified regulatory elements relevant to the CFTR gene and mapped the function of these elements using comparative genomics; in particular, data obtained from the ENCODE (ENcyclopedia of DNA Elements) database was used to identify potential DNA regulatory regions in CFTR using data from multiple experiments in a number of different cell lines. One particularly powerful technique, the DNase CHIP, identifies DNase Hypersensitive Sites (DHS) in DNA which indicate nucleosome-depleted regions of chromatin and thus potential sites for the binding of regulatory elements. The results of DNase CHIP analysis on regions of the CFTR gene identified from the ENCODE database will be used to identify motifs for potential transcription factor binding sites and *de novo* motifs within DHS. Additional cell types have been analyzed which will be discussed in this presentation as well. Another major area of interest is our ongoing attempt to develop a CFTR-centric GBrowse to act as a central repository of information for the Harris Lab.

Research Advisor:

Ann Harris, Department of Pediatrics, Children's Memorial Research Center