



Friday, April 11, 2008  
2:00 pm – 3:00 pm  
COOK 3118 A&B

## Structure–Activity Relationship Study of MEK–4 & Genistein

Sankar Narayan Krishna – CBB Masters Student

### ABSTRACT:

Dual specificity Mitogen-activated protein kinase kinase 4 (MEK-4) regulates Prostate Cancer (Pca) cell invasion and metastasis. Inhibition of MEK-4 by the indigenously developed lead compound from the Bergan Lab, 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 use the derived structure-activity relationship information for the synthesis of a more effective lead compound. The study will initially use computational approaches, homology modeling of the MEK-4 protein and docking simulation of MEK-4 with Genistein. Additionally, the modeling will be subject to intense scrutiny using validated experimental data and only then be used for prediction purposes. The predicted agents will then be tested and used during the drug synthesis stage.

### Research Advisor:

Raymond Bergan, Department of Medicine, Feinberg School of Medicine

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## Characteristics of Epstein–Barr Virus Envelope Protein gp42: Application of Sequence and Structure Analysis

Pamela Shaw – CBB Masters Student

### ABSTRACT:

Epstein-Barr virus (EBV) is a gamma herpes virus which requires a number of envelope glycoproteins for fusion and entry into host cells. Human EBV gp42 is required for infection of host B-lymphocytes, but it is inhibitory to entry into epithelial cells. EBV gp42's crystalline structure, as bound to its HLA Class II receptor, was determined in 2002. The structure reveals that gp42 contains a canonical natural-killer receptor-like C-type lectin-like domain (NK-receptor-like CTLD). Using features of gp42, we have begun our analysis of gp42 by comparing it to other species viral proteins; investigating its canonical CTLD domains and attempting to predict the structure of the flexible N-terminal region implicated in binding to other EBV envelope glycoproteins. Such an understanding of protein structure and sequence assists future mutational studies which will ultimately lead to improved methods of inhibiting EBV fusion and entry to host cells.

### Research Advisor:

Richard M. Longnecker, Department of Microbiology-Immunology, Feinberg School of Medicine