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BMS

Judging Dept.

**Fang Liu**

Student

BMS

4

Bruce Herron

Dept or Program Years in program

Mentor

## Defining the role of Stratifin and I-Kappa Kinase alpha in epidermal development

Author (s)

**Fang Liu, Gretchen Kusek, Barbara Beyer, Melissa Behr, John P. Sundberg, Bruce Herron**

Genetics and genomics are powerful approaches to elucidate the molecular mechanisms that control cancer progression. We have used a combination of mouse genetics and global gene expression analysis to better understand how two similar mouse mutations in distinct genes, stratifin (sfn, also called 14-3-3 sigma) and I-Kappa Kinase alpha (IKK alpha) affect skin development. This information will be useful for the determination of genes that contribute to epithelial diseases and cancers that carry mutations in either of these proteins.

Both sfn and IKKalpha deficient mice have profound defects in epidermal development that lead to neonatal lethality. While no heritable mutations in sfn or IKKalpha have been reported in humans, stratifin expression is repressed by hyper-methylation in many human tumors. Recently, reports of IKK alpha mutations in aggressive squamous cell carcinomas have suggested additional biological links between these proteins.

Here, we demonstrate that epidermis from Sfn and IKK alpha deficient mice share abnormalities in terminal differentiation, but IKK alpha epidermis has additional defects in keratinocyte proliferation. Our current working hypothesis is that Sfn and IKK alpha mutations act through a common mechanism to maintain tumor cells in an undifferentiated state while IKK alpha mutations have additional defects in cellular proliferation. Our ongoing work will determine role of the Er form of sfn in cell cycle regulation and keratinocyte differentiation; and identify important pathways that contribute to disease progression.