M & I
Microbiology
and Immunology
University of North Carolina at Chapel Hill

DISSERTATION SEMINAR

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"The role of hemidesmosomal protein BP180 in skin inflammation and cancer"

Monday, December 18, 2017
1:00 p.m.
6004 Marsico Hall

Dissertation Advisor: Dr. Zhi Liu

Presented in partial fulfillment of the requirements for the degree of
Doctor of Philosophy

ABSTRACT

Bin-Jin Hwang: The role of hemidesmosomal protein BP180 in skin inflammation and cancer
(Under the direction of Dr. Zhi Liu)

BP180, also known as collagen XVII, is a transmembrane glycoprotein located in the hemidesmosome of basal keratinocytes. BP180 is a key cell-matrix adhesion molecule, loss of its function either by autoantibody result in the skin autoimmune disease bullous pemphigoid or mutations in BP180 gene in the genetic disorder junctional epidermolysis bullosa leads to subepidermal blistering. However, its other biological functions and involvement in different pathological conditions are unknown. To uncover new functions of BP180, we generated a novel BP180 dysfunctional mouse strain lacking the NC16A domain of BP180 (termed Δ*NC16A*). We found that Δ*NC16A* mice developed a proinflammatory microenvironment in the skin accompanied with an influx of immune cells, including mast cells and MDSCs. *ΔNC16A* mice show **spontaneous skin inflammation** accompanied by TSLP dependent itch**.** When tested in the B16 mouse melanoma models, Δ*NC16A* mice showed significantly increased melanoma progression. NC16A deletion in the skin or basal keratinocytes was sufficient to promote skin inflammation and tumor progression, demonstrating that BP180 dysfunction in basal keratinocytes is responsible for the proinflammatory microenvironment and increased tumor progression. Mast cell-deficient Δ*NC16A* mice had drastically reduced MDSCs in the skin and developed significantly reduced melanoma. Mast cell reconstitution restored the skin infiltration of MDSCs and increased melanoma progression in mast cell-deficient Δ*NC16A* mice. More importantly, MDSC depletion significantly reduced the tumor progression in mast cell-sufficient Δ*NC16A* mice. These findings provide the first evidence suggesting that BP180 in basal keratinocytes, as a hemidesmosomal cell-cell matrix adhesion protein, plays a vital role in skin inflammation and melanoma progression.