Kelly Elizabeth Johnson
PhD Candidate

“Direct effects of VEGF on keratinocyte function
during skin carcinogenesis and wound healing”

8/15/2013
137 Hamilton Hall
9:30 AM
VITA

7/22/1980 .......................... Born – Worthington, Ohio
5/8/2002 ............................. B.A., Biology Oberlin College

AWARDS AND HONORS

University Fellowship 2008-2009
The Ohio State University

Systems and Integrative Biology Fellowship 2009-2011
NIH 5T32GM068412-04
The Ohio State University

Ray Travel Award 2011
Council of Graduate Students
The Ohio State University

COMMITTEE MEMBERS

Traci A.Wilgus
Tatiana Oberyszyn
Amanda Toland
Gregory Lesinski

FUTURE PLANS

Kelly is remaining with her current lab for the next few months to complete her research projects and publications while interviewing for postdoc positions. She plans to begin an academic postdoc in the autumn of this year. After completing her postdoc training, she hopes to continue working in academic research and pursue a career as a professor.
Epidermal keratinocytes, the predominant cell type in epidermis, play a crucial role in two processes that can occur in the skin: skin carcinogenesis and cutaneous wound healing. Non-melanoma skin cancer (NMSC) is the most prevalent type of cancer, with 3.5 million cases diagnosed each year in the US. These cancers, including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are primarily caused by chronic exposure to ultraviolet (UV) light from the sun. Wound healing is a key process in many aspects of medicine. In addition to injury and trauma, millions of surgeries are performed each year, all requiring the repair of a wound. Chronic wounds, which do not heal properly, can lead to hospitalizations, amputations and even death. These abnormally healing wounds affect 6.5 million patients every year at an estimated cost of $12 billion dollars. Therefore, it is critical to understand how keratinocytes function in both of these conditions.

Angiogenesis, the growth and expansion of new blood vessels, is a key process during both NMSC and wound healing. Vascular endothelial growth factor (VEGF), a factor that promotes angiogenesis by causing the proliferation, migration and survival of vascular endothelial cells, is produced by the skin in response to UV and is known to promote NMSC indirectly through the induction of angiogenesis. Additionally, wounds contain high levels of VEGF. VEGF receptor 1 (VEGFR-1) has now been identified on epidermal keratinocytes, suggesting that VEGF can affect keratinocytes directly. Therefore, we hypothesize that, in addition to promoting angiogenesis, VEGF may influence wound healing and skin carcinogenesis by directly affecting keratinocytes via VEGFR-1. To examine the direct effects of VEGF on keratinocytes in vivo, we generated a unique strain of conditional knockout mice with VEGFR-1-deficient keratinocytes (cKO) using the cre-lox system. cKO mice were utilized in acute and chronic
UV-induced skin carcinogenesis studies as well as wound healing studies.

Immunohistochemical analysis of human and murine NMSC samples revealed that VEGFR-1 is highly expressed in skin tumors. Furthermore, in vitro studies indicated that keratinocyte VEGF and VEGFR-1 expression is regulated by UV light. To examine the direct effects of VEGF on keratinocytes in skin carcinogenesis, cKO and control mice were exposed to acute and long term UV radiation. Keratinocytes in the epidermis of cKO mice showed a significant increase in apoptosis 24 hours following a single UV exposure compared to controls, suggesting that VEGF may promote the survival of UV-damaged keratinocytes. Additionally, macrophage recruitment to UV damaged skin was reduced in cKO mice. Long term UV-induced skin carcinogenesis studies are ongoing and suggest that cKO mice are resistant to UV-induced skin carcinogenesis compared to controls. Taken together, these results suggest that VEGF promotes skin carcinogenesis via keratinocyte VEGFR-1, in addition to promoting angiogenesis.

To examine the direct role of VEGF on keratinocytes in wound repair, excisional wounds were made on the backs of cKO and control mice and wounds were examined 1, 3, 5, 7, 10 and 14 days following wounding. A significant delay in reepithelialization was observed in cKO mice compared to controls 5 days after wounding. On average, wounds from cKO mice were 68% covered by new keratinocytes compared to 95% for control wounds. Strikingly, only 20% of the cKO wounds showed complete healing while 85.7% of the controls wounds were completely healed. These results suggest that VEGF can stimulate epidermal keratinocytes directly to promote reepithelialization. A significant decrease in the number of macrophages was observed in wounds from cKO mice compared to controls, indicating that VEGF stimulates keratinocytes to recruit macrophages to the wound bed. Overall, these studies have uncovered novel roles of VEGF in two important processes in the skin: wound healing and skin carcinogenesis.

**RECENT ABSTRACTS AND PRESENTATION**


