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Project Title: Characterizing the endothelial progenitor cell using a vav-reporter mouse and single cell microfluidics.
Year Awarded: 2013

What can you tell us about the progress made in this area since you completed your Fellowship?
I am currently being funded by the Wound Healing Society's 3M grant for my work in characterizing the adult endothelial progenitor cell. During the first decade of discovery of the endothelial progenitor cell (EPC), these cells generated a lot of interest in the context of generating blood vessels de novo and potential therapeutic utilization. However the very existence of these cells and their importance in neovascularization has since been vastly questioned. These questions we think primarily arise due to inconsistencies in isolation, currently involving intricate in vitro culture techniques of peripheral blood cells rather than a defined surface-marker profile. We used a double transgenic cre-lox based murine model, with hematopoetic cells labeled with GFP and all other cells labeled with RFP for lineage tracing EPCs. This transgenic mouse in parabiosis with a non-fluorescent immunocompromised SCID mouse stimulated with ischemic neovascularization, drew in and homed novel stem cell populations at neovascular sites which we fluorescently sorted and studied. By single cell transciption profiling these cells, we found a small population of stem-like cells expressing established endothelial markers that incorporate into sites of neovascularization. We are currently establishing the importance of these cells in wound healing.

How can this research help patients, clinicians and/or scientists?
Part of the study includes an ability to sort and expand the EPC population so as to use the cells for therapeutic neovacularization. The work is highly focused at improving neovascularization in wounds, especially chronic non-healing wounds commonly seen in diabetes and aging.

Has your work thus far yielded any surprises?
Yes. While we initially expected most stem/ progenitor cells incorporating into ischemic sites in our parabiotic mice to be circulating cells of mesenchymal origin, we found that most of the non-immune cells expressing progenitor markers were in fact hematopoietic in origin.

How did this Fellowship help your career?
The 3M Fellowship currently funds my work. The grant has given me immense support in utilizing novel, currently evolving resources at Stanford that are critical in answering

the questions I am asking.

How did you get interested in wound healing and this area in particular?
I was always fascinated with stem and progenitor cells: questions on their origins, mechanisms of their dormancy, heterogeneity in their populations, migration towards chemokine gradients, homing to wound sites, trophic effects contributing to healing and stem cell death in the presence of inflammation. I started asking these questions as a PhD student at the University of Pittsburgh, in Dr. Alan Well's lab, with close co-mentorship from Dr. Linda Griffith at MIT, working with increasing bone marrow MSC survival for bone regeneration, and continue to do so in Dr. Gurtner's lab at Stanford.

Tell us about some of the outcomes of your research you are most proud of and what it means for patients, clinicians and/or scientists.
Our current work shows that a lot of progenitors being recruited to neovascular sites are hematopoietic in origin, suggesting that a hemangioblast might actually exist in adult tissue and of potential interest to scientists. Similarly the work identifies distinct progenitors that aid in neovascularization. Isolation of these cells in high numbers will strongly aid in therapeutic new blood vessel formation.

What are your future plans for your work in wound healing?
I plan to continue studying the influence of stem cells in wound healing in an academic setting. In parallel I would like this work to contribute towards products that can be used to augment healing.

Who do you consider your mentors and your close associates in this project?
Dr. Geoffrey Gurtner, my postdoctoral mentor has been an immense source of support and an integral part of this work. His lab at Stanford is unique, an amalgamation of surgical skill sets with science, which helps address scientific questions in their actual in vivo setting. Robert Rennert and Michael Januzsyk, senior research fellows in the lab have been invaluable to the work with their expertise in fluorescence sorting and biocomputing respectively.

Can you tell us about your life away from the lab and/or clinic?
I spend my free time biking, hiking and kayaking in the California outdoors. I also enjoy cooking and gardening.