**2012 JMNMF RSA Photo & Summary**

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*Pictured from Left to Right: Marcus Bosenberg, MD, PhD, Associate Professor Dermatology & Pathology, Yale School of Medicine; Denise Safko, JMNMF Secretary & RSA Committee Member; Nicholas Theodosakis, JMNMF RSA Recipient; and, Greg Safko, JMNMF President.*

## SUMMARY: Determiniation of the Mechanisms of Melanoma Metastasis

The lymphatic system, a system of vessels that work in parallel to the arteries and veins to help maintain fluid pressure and filter out pathogens, has long been known to play a major role in the growth and spread of tumors. In order for a tumor to grow, much like any other tissue, it requires a large supply of nutrients, oxygen, and growth factors that are primarily delivered by the blood. In a process known as "angiogenesis," malignancies secrete a number of different signaling proteins that drive the growth and development of new blood vessels, and at the same time, lymphatic vessels, that penetrate and feed the new tumor. Later, in a process that is still poorly understood, small numbers of cancer cells gain the ability to break off from the original tumor and into these lymphatic vessels, allowing them to travel throughout the body and potentially colonize new organs. These new tumors are called "metastases," and in all forms of cancer, their appearance shows a strong correlation with poor clinical outcomes and shorter average survival time.

Our laboratory is interested in investigating the steps of this process at the cellular level in both the tumor cells and the cells of the lymphatic channels themselves. In concert with collaborators at Yale, we have constructed a mouse model which develops malignant melanoma at a rate of 100% within the timeframe of several months, and whose melanoma cells produce a protein that fluoresces green under ultraviolet light. At the same time, the lymphatic channels of this mouse produce a protein that fluoresces red. These labels allows us to image the tumors and the lymphatics of mice at multiple time points, letting us track the growth and spread of both the original tumor and the individuals tumor cells shed into the lymphatics, dubbed "micrometastases." Once we have obtained a better understanding of the individual steps and the timing of this process, we will then be able to study ways in which it might be possible to prevent micrometasases from spreading, including disrupting angiogenesis, altering vessel permeability, and changing the tumor microenvironment to decrease the shedding of cells, all with the ultimate goal of finding ways to decrease disease spread in patients and increase melanoma survivability.