2013 JMNMF RSA Summary & Photo
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Pictured Left to Right: Eduardo M. Sotomayor, MD, PhD, Chair in Hematologic Malignancies, Senior Member-Immunology Program, Scientific Director-Personalized Medicine Institute; Andressa S. Laino, JMNMF Award Recipient; and, Jeffrey S. Weber, MD, PhD, Senior Member-H. Lee Moffitt Cancer Center & Research Institute, Director-Donald A. Adam Comprehensive Melanoma Research Center.

Potential Role of HDACs in the Epigenetic Regulation of EOMES: Enhancing Immunotherapeutic Response in Melanoma

The adoptive transfer of antigen-specific T cells is a promising approach in the field of cancer immunotherapy. Isolation and transfer of autologous tumor infiltrating lymphocytes to patients with advanced metastatic melanoma have been shown to significantly reduce tumor burden. However, partial responses and relapse of the disease are related with poor activity and *in vivo* persistence of the transferred T cells. The transcription factor Eomesdermin (EOMES) has been shown to be important to induce a differentiation of T lymphocytes into memory subsets, which may impact in higher proliferation and maintenance of T cells after transfer. Epigenetic changes play a role in the regulation of EOMES, and the differential activity of histone acetyltransferases (HATs) and histone deacetylases (HDACs) seems to be essential to this regulation. Our preliminary data suggests that increased induction of EOMES is associated with positive outcomes in melanoma patients treated with ipilimumab. Therefore, manipulation of EOMES is an attractive therapeutic approach in the sense to generate a population of cytotoxic T cells associated with a favorable clinical outcome in the context of metastatic melanoma. Because it is known that EOMES can be suppressed by histone deacetylation, we propose to inhibit histone deacetylation in order to enhance the therapeutic efficacy of ipilumumab treatment through generation of an enhanced T-cell antitumor response. We also want to elucidate whether distinct HDAC isotypes differentially regulate EOMES expression and thus play a more direct role in its regulation. Our results will contribute to understanding the mechanisms by which cytotoxic T cells exert and maintain their function against melanoma and may have an impact in the current therapeutic protocols.