resistance need to be identified and/or validated in clinical specimens from melanoma patients treated with these agents.

With the goal of creating a unified model of RAF-inhibitor resistance, we are developing a custom, targeted RNA sequencing assay capable of detecting epigenetic alterations and BRAF splice variants implicated as the molecular basis for RAF inhibitor resistance in our preclinical and preliminary clinical studies. Data generated with this assay will be integrated with DNA analyses generated using massively parallel sequencing methods.

Finally, we seek to develop blood-based assays to noninvasively detect the putative resistance mechanisms identified in the tissue-based assay prior to radiographic and/or clinical disease progression. The ultimate goals of these efforts will be to develop mechanism-based combination strategies to prevent or delay the emergence of drug resistance. This work is supported by a Melanoma Research Alliance Team Science Grant (PI: David Solit), R01-CA16935 (PIs: Neal Rosen and David Solit) and P01-CA129243 (Project 2 Co-PIs: Neal Rosen and David Solit).