**P50 CA261608** (MPIs: M. Herlyn, R. Amaravadi) 09/01/2021-08/31/2026

NIH/NCI

*SPORE in Skin Cancer*

Despite major advances, the death rate from skin cancer remains unacceptably high. Three Projects address the challenges of immunotherapy in melanoma by identifying predictors of response to therapy, novel combinations of drugs designed to enhance response, new approaches to the timing of therapy administration, and the examination of novel tumor microenvironments and their effect on therapy response. This SPORE’s 3 Cores and Developmental Programs are designed to bring together clinical investigators and basic scientists in highly translational efforts to accelerate the pace of therapy for patients suffering from melanoma and other skin cancers, including cutaneous squamous cell carcinoma (cSCC), cutaneous T cell lymphoma (CTCL), or Merkel cell carcinoma.

Roles: Project 3, Co-Leader; Core A, Co-Leader; DRP, Co-Director; CEP, Advisor/Mentor

**U54 CA224070** (MPIs: M. Herlyn [contact], M. Davies) 09/30/2017-08/31/2023\*

NIH/NCI \*Extension

*Rational Approaches to Melanoma Therapy*

The overall objectives of the research projects are to develop effective therapies using inhibitors of the signaling cascades in cells. We expect to develop new combinations of drugs that will reduce not only tumor size but may even be curative.

**P01 CA114046** (MPIs: M. Herlyn [contact], A. Weeraratna) 09/17/2019-08/31/2024

NIH/NCI

*Targeted Therapies in Melanoma*

We will define senescence induced by kinase inhibitors as a potential therapeutic endpoint and will search for new inhibitors that induce either irreversible senescence or overcome reversible senescence.

Roles: Project 1, Co-Project Leader; Core A, Co-Leader; Core B, Core Leader

**Adelson Medical Research Foundation** (PI: M. Herlyn) 10/01/2022-09/30/2025

*Overcoming Resistance to Signaling and Immune Therapies*

The Herlyn lab will generate humanized mouse model mimicking by reconstituting immunodeficient NSG mice with fetal liver derived CD34+ human hematopoietic stem cells and autologous fetal thymus chunks under the renal capsule to promote rapid human T-cell differentiation.

**R01 CA259295-01** (MPIs: J. Celebi [contact], M. Herlyn) 09/01/2021-08/31/2026

*Dissecting Phenotype Switching of Early Stage Melanoma*

The overall aim is to explore the hypothesis that tumor cell intrinsic genetic changes and activation of the STING (Stimulator of Interferon genes) signaling pathway in early-stage non-aggressive melanomas influence tumor-immune cells dynamic interactions in tumor microenvironment (TME) to drive the switch from non-aggressive to aggressive tumor phenotype. The studies in this project are of high significance which may bring new insight into the role of tumor cell intrinsic STING signal pathway and immune TME evolution to aggressive phenotype switch and may identify gene signature biomarkers with clinical utility.

**R01 CA238237-03** (MPIs: A. Raj [contact] and M. Herlyn) 01/13/2019-11/30/2024

NIH/NCI

*Understanding and Overcoming Resistance to BRAF/MEK Kinase Inhibitors in Melanoma*

The overall aim is to develop novel therapeutic strategies that prevent intrinsic resistance and overcome acquired resistance by taking into account the biologic and phenotypic heterogeneity in melanoma.

**1 R01 CA 241148-01A1** (PI:G. Robertson) 04/15/2020-03/31/2025

NIH/NCI

*Targeting Aldehyde Dehydrogenase for Cancer Prevention*

The Herlyn laboratory will help design immunological studies that are used in mouse model. We will help in the processing of tumor, spleen, and lymph node samples for IHC staining and subsequent microscopy and imaging facility. We will also provide help in designing molecular studies including RNAseq experiments and data analysis using our Bioinformatics core.

**1 R01 CA243260-01A1** (PI:P. Poulikakos) 05/15/2020-04/30/2025

NIH/NCI

*Regulation and Adaptive Mechanisms of Oncogneic RAS/ERK*

The Herlyn laboratory will participate in the project by carrying out ex vivo and in vivo assessment of novel, SHP2 inhibitor-based pharmacologic strategies, using our established collection of PDX melanoma models and corresponding primary cultures (including organoid-like reconstructs of human skin). We have >500 PDX available and ~400 melanoma cell lines representing all clinical, genetic, and biological grouping. All tumors resistant to BRAF and MEK inhibitors will be maintained in vitro and in vivo in the presence of the inhibitors. We will also contribute to data analysis and publication of manuscripts resulting from this work.

**1 R01 CA258113** (PI: X. Xu) 12/01/2021-11/31/2026

NIH/NCI

*Gamma delta T cell based melanoma therapies*

The Herlyn lab will generate humanized mouse model mimicking by reconstituting immunodeficient NSG mice with fetal liver derived CD34+ human hematopoietic stem cells and autologous fetal thymus chunks under the renal capsule to promote rapid human T-cell differentiation.