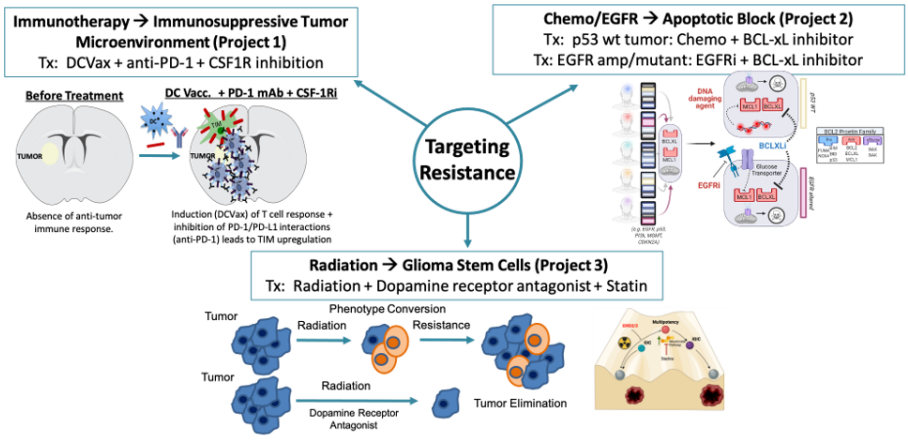
UCLA Health

BRAIN TUMOR CENTER

UCLA SPECIALIZED PROGRAM OF RESEARCH EXCELLENCE (SPORE) IN BRAIN CANCER

PRECISION MEDICINE, COLLABORATION, & PATIENT-CENTERED CARE

Brain cancer is one of the most difficult conditions to effectively treat, and unfortunately ranks among the deadliest of malignancies. Glioblastoma, one of the most common brain tumors in adults, is particularly lethal. Current standard therapies such as surgical resection, radiation, and chemotherapy have not significantly improved survival rates for patients with glioblastoma. However, the Brain Tumor Center at UCLA seeks to challenge these statistics and carve out a more hopeful future for brain cancer patients through significant contribution to the diagnosis, prognosis, and treatment of brain cancer.



Overview schematic of main projects of UCLA SPORE in Brain Cancer. A major focus of research at the UCLA Brain Tumor Center is to target the resistance of brain tumors to current therapies (i.e., resistance to immunotherapy, chemotherapy, and radiation therapy), and to figure out how to overcome treatment resistance, so we can develop new therapies that can lead us to a cure.

The Brain Tumor Center is comprised of a world-class, multidisciplinary team of specialists. Chief among the program's concerns is providing individualized patient care—from personalized brain cancer vaccines to expertly tailored treatment plans, brain cancer patients at UCLA have some of the best survival rates and treatment outcomes in the nation.

The Brain Tumor Center is designated as a Specialized Program of Research Excellence, or SPORE, by the National Cancer Institute (NCI), a distinction that few programs obtain. Dr. Linda Liau, Chair of the Neurosurgery Department and Director of the Brain Tumor Center, describes what makes this designation so impactful. She explains that "[programs] get funded based on the strength of their science, and that is very powerful in terms of showing that our research is scientifically valid and meaningful and hopefully will lead to future treatments." This research excellence contributes to better treatments at the bedside, and continuously pushes the limit to what is believed possible for brain cancer treatments.

The SPORE in Brain Cancer is working to elucidate the genetic underpinnings of brain cancer to more effectively diagnose and treat the condition. In particular, more effective treatments for glioblastoma are desperately needed, a deficiency the program's researchers aim to address. To accomplish these goals, the program supports three diverse research projects that involve mechanistic pre-clinical work and innovative clinical studies. A consistent tenet of these projects is the commitment to addressing knowledge gaps about glioma resistance and developing novel strategies to overcome this treatment resistance, particularly through immunotherapy.

Dr. Linda Liau and Dr. Robert Prins, a research scientist and professor in the neurosurgery department, lead the first of the three SPORE projects. Their research centers on investigating immune evasion following treatment with dendritic cell (DC) vaccines, and developing strategies to overcome the potential immunosuppression that can occur in response to these vaccines.

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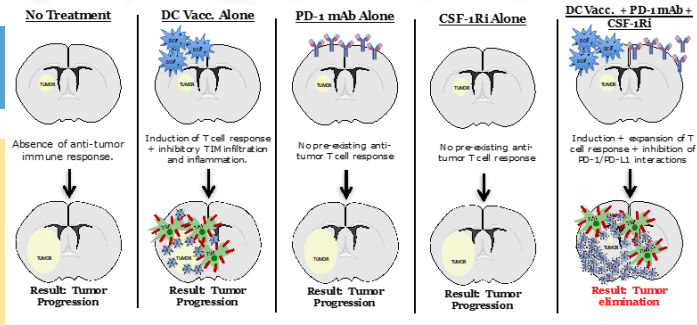
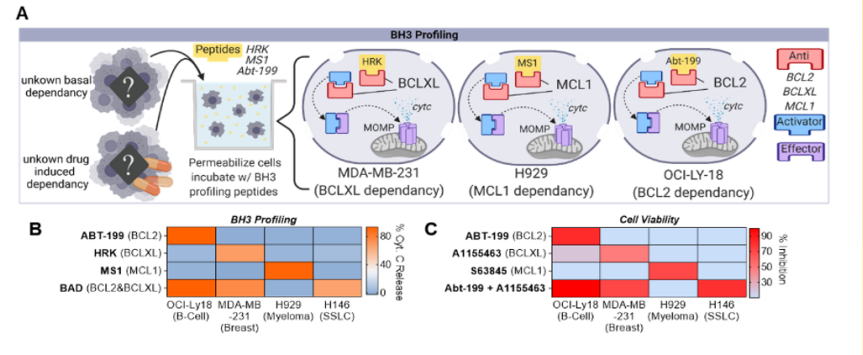


UCLA Brain SPORE Project 1

Dr. Liau and Dr. Prins championed the international study that discovered that DCVax-L—a personalized cancer vaccine for glioblastoma patients—could help patients live longer. The premise of this vaccine is relatively simple, although the underlying mechanisms are complex. "Our brain cancer vaccine is made for the patient," explains Dr. Liau. "We use the patient's tumor cells removed during surgery and immune cells extracted from the patient's blood. In the lab, we train the immune cells to hunt and kill the tumor cells. Those 'killer cells' make up a personalized brain cancer vaccine."

However, a potential downside to this form of therapy is that it can create a pro-inflammatory environment within the tumor that can mitigate the impact of the vaccine by creating an immune tolerance instead of an immune response. Dr. Liau and Dr. Prins are now researching how to address this issue, namely by studying the interactions that occur on a local cellular level. They postulate that these micro-interactions are a critical factor in the efficacy of immunotherapies in glioblastoma patients. Additionally, they hope that their research can provide more insight into impactful ways to induce therapeutic anti-tumor immune responses for glioblastoma.

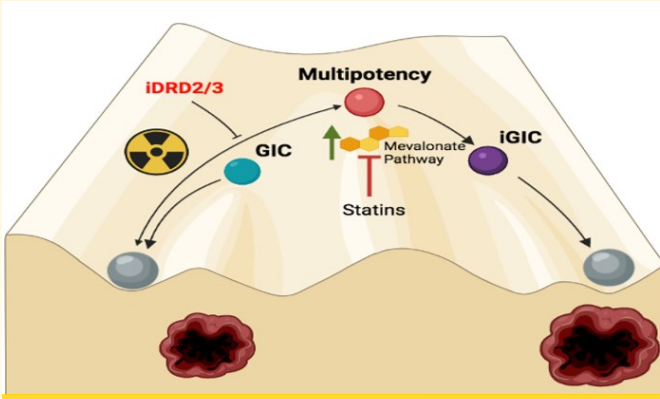


UCLA Brain SPORE Project 2

Despite these potential setbacks, Dr. Prins is optimistic about immunotherapeutic interventions to treat glioblastoma. "Immunotherapy is theoretically one of the best new treatments that can target isolated tumor cells before they metastasize elsewhere," said Dr. Prins. "I think immunotherapies are going to be the next new revolution in this cancer therapy."

The other two SPORE projects target different aspects of brain cancer. For instance, in Project 2, Dr. David Nathanson and Dr. Timothy Cloughesy are researching how apoptosis, or cell death, can be exploited to drive glioblastoma tumor cell death. Past studies have indicated that glioblastoma cells undergo a limited amount of cell death in response to traditional therapies such as chemotherapy or radiation, meaning that glioblastoma are particularly adept at adapting to therapeutic interventions. The researchers hope that they can use the intrinsic cell death pathway within glioblastoma to expose vulnerabilities that can be targeted with novel clinical drugs to induce apoptosis.

Dr. Frank Pajonk and Dr. Leia Nghiemphu direct SPORE Project 3, which homes in on exploring the mechanisms by which radiation therapy fails to treat glioblastoma. Specifically, the researchers are developing strategies to reduce the process by which noncancerous cells become radiation-resistant cancerous cells. Dr. Pajonk and Dr. Nghiemphu posit that by combining radiotherapy with drugs capable of preventing the cells' conversion can improve glioblastoma treatment efficacy.



UCLA Brain SPORE Project 3

The SPORE designation built upon UCLA's already successful brain cancer program and expanded it, allowing the program to have a greater impact on how cancer is treated. The program's interdisciplinary, multi-faceted approach means that observations from the lab can be brought to the clinic quickly. "We now have glioblastoma patients living 15 years beyond their original prognosis of one to two years," says Dr. Liau. "Our team continues to mark and celebrate each year of survival with our patients, which makes our journey to find a cure for brain cancer worthwhile."