BASIC// DISCOVERY

CAN a PRIMROSE COMPOUND FIGHT UVEAL MELANOMA?

UVEAL MELANOMA IS THE MOST COMMON EYE CANCER IN adults. It metastasizes to the liver in 50 percent of patients, and there are no effective therapies to treat those metastases. Yet.

Jeffrey L. Benovic, PhD, Thomas Eakins Endowed Professor of Biochemistry and Molecular Biology, is globally recognized for research uncovering the mechanisms of G protein-coupled receptor (GPCR) signaling and how GPCR dysregulation contributes to disease. GPCRs regulate a variety of biological functions—from neurotransmission and sensory perception to the movement of cells in response to chemical stimuli. They have also been implicated in diseases ranging from cancer to neurological disorders.

GPCRs are the target of about 35 percent of drugs currently on the market—including those to treat cancer, cardiovascular and airway disease, and neurological and metabolic disorders. Dr. Benovic's broad-ranging work on the regulation of GPCR function is creating opportunities to improve on those therapeutics. He is often a catalyst for translational projects, collaborating with clinician-researchers to create and test new treatments for a variety of diseases.

Dr. Benovic and his colleagues recently identified a compound derived from a type of primrose that could be a potent inhibitor of metastatic growth in uveal melanoma. It works by blocking a particular type of G protein that sits on the cell membrane. In uveal melanoma, a subset of these G proteins are mutated, turning on a molecular pathway that leads the cell to become malignant. When Benovic lab researchers treated uveal melanoma cells with small amounts of the compound, the cells appeared to revert to their normal, non-malignant state. And higher doses killed the cells outright.

The next step: Dr. Benovic will work to confirm the findings in a mouse model of uveal melanoma, collaborating with **Takami Sato, MD, PhD**, K. Hasumi Endowed Professor of Medical Oncology, who directs **Jefferson's Metastatic Uveal Melanoma Program**—one of the nation's only centers dedicated to both research and treatment of the disease. ■