Benz Lab

As a physician-scientist and medical oncologist for over 40 years, Dr. Benz has focused his lab's research on developmental therapeutics, especially in relation to age-related human cancers. As summarized below, two independent lab projects are currently in progress and await participation by a talented Postbacc/RA candidate looking to make a difference in human health research. One of these projects involves the re-purposing of the lab's originally proposed anti-mitochondrial drug (N-propargylglycine, N-PPG) for cancer treatment into much needed new therapies to protect the brain from neurodegeneration and the kidney from calcium oxalate stone formation.

1. Working with our Buck's Mass Spec/Proteomics group who helped us identify a pivotal role for acetylated p300/CBP chromatin complexes in regulating the half-life of cancer-driving oncogenic transcripts like HER2/ERBB2 mRNA, we are now therapeutically inhibiting the amplified HER2/ERBB2 oncogene's post-transcriptional mechanism using a new class of oral and well tolerated epigenetic drugs that induce accelerated decay of HER2/ERBB2 mRNA and arrest cancer cell growth in our experimental systems modeling the aggressive molecular subtype of cancer arising in 20% of women with newly diagnosed breast cancer. Further mechanistic studies are needed to clarify the mechanism of action and preclinically advance this most promising new anti-cancer treatment strategy.

2. Our lab synthesized and first reported on the anti-cancer potential of a unique suicide inhibitor of the mitochondrial enzyme proline dehydrogenase (PRODH), necessary for cancer growth and metastasis under hypoxic and nutrient stress conditions. Surprisingly, our orally bioavailable PRODH suicide inhibitor (N-PPG) also penetrates the brain and beneficially impacts virtually all normal host tissues by inducing mitohormesis and the mitochondrial unfolded protein response (UPRmt). In close collaboration with the Ellerby lab, we've reported biochemical, behavioral, transcriptomic, and metabolomic mouse data demonstrating the promise of N-PPG in preventing neurodegeneration and, most recently, the formation of calcium oxalate kidney stones leading to renal failure. The latter serendipitous observation was discovered by learning that N-PPG specifically inhibits another structurally related mitochondrial enzyme, PRODH2, that selectively catabolizes hydroxyproline in both liver and kidney organs. As a result, N-PPG inhibition of PRODH2 metabolically impairs liver and kidney synthesis of oxalate, dramatically reducing urinary oxalate secretion and calcium oxalate kidney stone formation. We are now using experimental mouse models to demonstrate that N-PPG treatment protects the kidney by both its metabolic inhibition of oxalate production and its direct mitohormesis effect that increases resiliency of renal tubule cells against progressive calcium-oxalate injury.

Desired Skills or Experience: Background and strong interest in pursuing biological sciences by independent and creative problem solvers. Prior molecular/cellular lab experience preferred.