A. Novel anti-metastatic drugs for cancer therapy

Stephen J. Weiss, M.D.
Research Professor, LSI
Upjohn Professor of Medicine and Oncology
Chief of Molecular Medicine and Genetics, U-M Medical School

- **Problem:** In solid tumors, the hallmark of malignancy is the tumor's ability to penetrate a barrier layer known as the basement membrane, thereby gaining access to blood vessels that carry cancer cells throughout the body.
- **Discovery:** Weiss and his colleagues found that tumor cells use three enzymes that act as "molecular scissors" to cut through the basement membrane.
- **Potential Fund Project:** Develop inhibitors to disrupt these enzymes.
- **Goal:** Within two years, determine the value of using selected enzyme inhibitors as the basis for a spin-off company.

B. A new approach to treating neurodegenerative diseases

Jason Gestwicki, Ph.D.
Research Assistant Professor, LSI
Assistant Professor of Pathology, U-M Medical School

Andrew Lieberman, Ph.D.
Assistant Professor of Pathology, U-M Medical School

- **Problem:** Neurodegenerative diseases, such as Alzheimer's and Huntington's, arise from misfolded proteins that damage brain cells and trigger a progressive decline in cognitive abilities and motor function.
- **Discovery:** Gestwicki and his colleagues found that stimulating a natural protein called Hsp70 protects against protein misfolding in cellular and animal models of neurodegenerative disease.
- **Potential Fund Project:** Find and develop other chemicals that eliminate misfolded proteins.
- **Goal:** Within two years, create the first class of drug-like molecules that directly targets the underlying cause of neurodegenerative diseases.
C. Novel anti-cancer compounds derived from bacteria

David Sherman, PhD.
Research Professor and Director, Center for Chemical Genomics, LSI
Hans W. Vahlteich Professor of Medicinal Chemistry, U-M College of Pharmacy

- **Problem:** Certain cyanobacteria produce a compound called cryptophycin, a potential anti-cancer agent. Despite its promise, high production costs have stymied efforts to commercialize the compound and other, more potent, analogs.
- **Discovery:** Sherman and his colleagues have engineered a series of cryptophycin analogs that possess the compound's anti-cancer properties while clearing the way for practical and economical manufacturing.
- **Potential Fund Project:** Test the engineering techniques to determine if they are scalable for analog development and commercial drug production.
- **Goal:** Within 18 months, determine if new cryptophycin analogs could be used to treat particularly aggressive and lethal cancers, such as pancreatic and gall-bladder cancer.

D. New approach to treating bacterial infections

David Ginsburg, M.D.
Research Professor, LSI
James V. Neel Distinguished University Professor of Internal Medicine and Human Genetics
Investigator, Howard Hughes Medical Institute

- **Problem:** Group A streptococci bacteria cause 700 million infections worldwide each year, including more than 500,000 deaths. The bacteria invade human tissues in part by dissolving protective blood clots.
- **Discovery:** The Ginsburg laboratory has identified several compounds that block the bacteria's ability to dissolve blood clots, thereby preventing the infection from spreading.
- **Potential Fund Project:** Identify additional compounds, optimize the best candidates and test them in mice.
- **Goal:** Within two years, have candidate compounds ready for testing in large animals such as horses (which suffer from a similar infection), with an eye toward eventual human trials.

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