CSBC Investigator Highlight

Dr. Sylvia Plevritis Engineers Analytical Approaches to Understand Cancer Metastasis

Sylvia Plevritis, Ph.D., a CSBC Investigator at Stanford University, develops computational tools to analyze genomic and imaging data related to cancer metastasis, the progressive spread of cancer cells from an initial tumor to another part of the body.

She studies cancer because "it's a deadly disease and we need to do everything in our power to prevent cancer-related deaths." Dr. Plevritis is also optimistic and believes that "we are making progress and will eventually win the war against cancer."

In this interview, she discusses her engineering background, views on cancer systems biology, and her CSBC project investigating tumor immunosuppression and the metastatic cascade.

- **How does your training in electrical engineering contribute to your studies of cancer?**

  My training in electrical engineering was in a subspecialty known as information theory. This subspecialty aims to decode a "black box" based on how the black box responds to different stimuli. Today, I am applying the basic principles of information theory to my studies of cancer, where cancer is the black box.

- **What is a major challenge in cancer biology research?**

  The study of cancer progression is a major challenge that is well suited for systems biology research. Since we cannot ethically observe the natural history of cancer in people, we must try to unravel it from "disease snapshots" at different times. We often examine disease characteristics at diagnosis and then during different stages of treatment responses. We also try to understand cancer progression in humans from multi-species analysis, often leveraging mouse models of cancer.

- **What are some computational approaches that have advanced cancer systems biology?**

  I have found concepts in sparse regression, multitask learning, linear programming, and topological network analysis to be very powerful in our cancer systems biology research. Computational methods help us integrate data across multiple scales, determine the significance of findings from high-throughput data, and predict the evolution of cancer. The specific approach we use depends on the biological question we are trying to answer and the available data.

- **What skills do you think are important for trainees in cancer systems biology?**

Fundamental understanding of cancer biology, up-to-date knowledge of the latest experimental technologies, and training in analytical methods that integrate information across different platforms are critical.

Also, the commitment to be a continual learner with a genuine interest in talking to and learning from researchers in different disciplines helps!

- **Can you describe your CSBC-supported research?**

  Our Stanford CSBC aims to understand cancer progression by trying to unravel the metastatic cascade because most cancer patients die of metastatic disease, not their primary tumor.

  We are testing the hypothesis that initial metastasis to the lymph node triggers systemic immunosuppression, which leads to dissemination of the malignant cells from the primary site to other organs.

  If our findings support our hypothesis, our work should lead to a paradigm shift in cancer progression and provide new insights for cancer control.

- **What led to your CSBC collaboration with other investigators at Stanford?**

  The CSBC funding announcement solicited applications that applied systems biology to a focused scientific question. I was confident that we were developing valuable systems biology approaches, but did not settle on the scientific question until I met Ed Engleman, a tumor immunologist at Stanford.

  While Ed and I were waiting for a thesis defense to start, he told me about a new project in his lab examining the role of lymph node metastasis in mouse models. I began to realize that our systems biology approach could be useful in his study of metastases.

  Ed was working with Garry Nolan, who was a longtime colleague of mine too. There was a natural connection between the three of us. Meanwhile, Garry was developing a novel, highly multiplexed *in situ* imaging approach that could be applied to study the spatial cellular architecture of lymph node metastasis.

  These concepts, along with my lab's development of analytical approaches to integrate complex biological data, formed the crux of our CSBC collaboration.

  To ensure the translational significance of the work, we set out to study human samples from primary tumors and lymph nodes. This led us to collaborate with John Sunwoo and Andrew Gentles. John has clinical research expertise that enables us to study lymph node metastases of head and neck cancer, while Andrew's computational expertise helps us generate robust pan-cancer signatures of disease progression.

  Ultimately, I am hopeful that our CSBC collaboration will lead us to better understand the basic mechanisms underlying metastasis, develop new therapies to improve patient outcomes, and identify potential biomarkers for monitoring cancer progression.

Links

Stanford Profile of Sylvia Plevritis

Plevritis Lab Website