CSBC Investigator Highlight

Dr. Tim Huang Investigates Epigenomic Mechanisms of Cancer Using Single-Cell Technologies

CSBC investigator, Tim Huang, Ph.D., researches progression and development of hormone-resistance in breast and prostate cancers at the University of Texas Health Science Center at San Antonio (UTHSCSA).

In graduate school, he studied the role of genetics in lung development. This was followed by a post-doctoral fellowship in clinical cytogenetics.

Dr. Huang moved into cancer research during his first job as an assistant professor. His lab was set up in the Ellis Fischel Cancer Center, which allowed him to obtain tissue specimens from patients. He realized that he could apply his knowledge of molecular genetics to investigate the biology of cancer.

In this interview, he shares his career experiences, perspectives on cancer systems biology, and his current work examining epigenomic changes in cancer.

- **What challenges have you overcome during your career journey?**

  I have written so many grant proposals. Nowadays, even if you think you're a seasoned grant writer, you still don't know whether you will be funded. That's been the number one challenge since I was awarded my first grant.

  Then there's the frustrations I, and other scientists, face every day in the lab with the trial and error process of research. You can do an experiment for a long time that doesn't work. It's a risk when you propose a project.

  Another challenge is the publication process. Researchers often spend a lot of time and energy going through the editorial review process to publish their significant results.

- **How do you define cancer systems biology?**

  Cancer systems biology is an exercise in defining a large set of data.

  To start, you collect all the data, which could include the transcriptome, methylome, epigenome, or genome. Then, you integrate these "omic" data sets.

  In the process, you produce an algorithm to generate a computational model. Once you have that, it's a computational exercise to generate a biological hypothesis. Then you go back to the wet lab for validation of the model using experimental approaches. Researchers generally like to model computational findings in animal models or human specimens. The biological findings get sent back to the computational scientists to see if the model can predict real life outcomes. The experimental data will either validate or disprove the computational model.

If the model is not perfect, then you go back to the algorithm and refine it. You perform the "omic" analysis again, generate an improved model, and go back to test the model using experimental approaches.

It's an iterative process to become more accurate and improve the prediction of complex cancer progression or metastatic outcomes. It's an exercise between two sides: computation and wet lab.

- **What systems biology technologies have advanced cancer biology?**

Today, cancer researchers have access to multiple databases, such as [The Cancer Genome Atlas (TCGA)](). Scientists can use algorithms to look at different angles of all this complex data. Mathematical tools have changed how we view cancer biology studies.

- **Can you describe the epigenetic framework studied in your CSBC projects?**

You have a protein complex called an enhancer, which isn't necessarily located close to the promoter. It could be located hundreds of bases away or on a different chromosome. Either way, it increases gene transcription. My lab calls this the first tier of assembly.

For the second-tier of the process, transcription factors, like hormone receptors, bind to the enhancer. This repositions chromatin to bring the enhancer closer to a promoter.

The third tier of the framework relates to long-range promoter-enhancer interactions that affect 3-dimensional chromatin architecture by generating topologically-associated domains (TADs). These regions of chromatin recruit transcription factor complexes and enhancers to the promoters of multiple target genes involved in cancer growth, treatment-resistance, and metastasis.

By understanding these epigenetic mechanisms exploited by cancer cells, we can identify potential therapeutic targets to prevent breast and prostate cancer progression and overcome the persistent challenge of [hormone therapy]()-resistance.

- **How do single-cell technologies of systems biology contribute to your research?**

Using single-cell approaches, we can decipher the complexity of a tumor specimen across different methodologies. Researchers can measure the vast array of genomes, transcriptomes, and epigenomes in thousands of single cells from one sample. However, this research generates a lot of data and you need a high-end computational approach to do simulation analyses.

In a [recent study](), my lab identified a subpopulation of prostate cancer cells based on single-cell RNA sequencing data that had stem cell properties and became resistant to androgen treatment. It's the beauty of single-cell approaches to find a key cell population that likely contributes to cancer progression or metastasis.

Links

[UTHSCSA Profile of Tim Huang]()

[UTHSCSA U54 Center for Cancer Systems Biology Website]()