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> — Chemist Derek Tan

An Interview With **DEREK TAN**

Chemical biology is bringing new analytic techniques, molecular probes, and potential therapeutic leads to biomedical research — and to cancer research in particular. To take advantage of this new vanguard, Memorial Sloan Kettering has created a Chemical Biology Program within the Sloan Kettering Institute under the leadership of chemist Derek Tan. It is the first new SKI program in more than a decade.

"The establishment of this program reflects the growing relevance of chemistry to the field of cancer research," says SKI Director Joan Massagué. "It's one more step in MSK's commitment to fostering this scientific area under Dr. Tan's outstanding leadership."

Here, Dr. Tan talks about the importance of chemical biology to cancer research and how MSK's new program will help advance the field.

What exactly is chemical biology, and how is it essential to understanding and treating cancer and other diseases?

Chemical biology involves the use of chemical tools and principles, such as organic synthesis and drug design, to study and manipulate biological systems in cancer and other areas. Chemists bring the unique ability to synthesize new small molecules that can be used as probes to dissect biological pathways and, ultimately, as drugs.

For example, by inhibiting enzymes or blocking protein–protein interactions selectively, small molecules allow us to gain a full understanding of complex biological processes such as those that drive cancer, neurodegenerative disorders such as Parkinson's and Alzheimer's, and bacterial infections. When promising new therapeutic targets are identified, small molecules are often the most effective means of addressing those targets. In fact, most of the drugs in your medicine cabinet are small molecules synthesized by chemists.

What role has SKI played in the history of chemical biology and how will it continue leading the way forward?

Chemical biology has a long, rich history at SKI dating back to the institute's inception in 1945. Some of the earliest examples of what we today call proteomics and metabolomics — studies of proteins and metabolites — were being done by chemists such as Konrad Dobriner and George Bosworth Brown at SKI some 60 years ago. The recruitment of Samuel Danishefsky in 1991 put SKI on the map in the minds of the chemistry community at large. He was already a giant in organic chemistry, and his move here set the stage for bringing high-level chemical synthesis to the biomedical research enterprise. Later, in the 2000s, David Scheinberg recruited to the then-named Molecular Pharmacology and Chemistry Program a fantastic group of scientists who work at the interface of chemistry and biology.

What constitutes the new Chemical Biology Program, and what is its purpose?

In addition to myself, the program includes Gabriela Chiosis, Yueming Li, Dr. Danishefsky, and Minkui Luo, as well as a new recruit, Daniel Bachovchin, who recently completed a post-doctoral fellowship at the Broad Institute of MIT and Harvard.

As a group, we're a collection of distinct laboratories that have individual interests, but I think what ties us together is a fundamental understanding of chemistry — in particular chemical synthesis — and applying those insights to the study of biological systems. We cover a huge array of disease areas as well as individual biological targets. Dr. Chiosis is doing exciting work targeting a protein called Hsp90, which is known to play an important role in cancer and neurodegenerative diseases, using a compound she developed called PU-H71 that is now in clinical trials. Dr. Danishefsky's program in natural product and carbohydrate synthesis has also led to a number of small molecules and vaccines that have advanced to clinical trials.

Dr. Luo developed novel functional proteomic techniques in his lab to study the role of protein methylation in epigenetics. Dr. Bachovchin is also using a powerful functional proteomic platform that he developed to study the molecular mechanisms of promising new anticancer agents. Dr. Li is studying gamma secretase, an enzyme that is implicated in both signal transduction and Alzheimer's disease, using a variety of chemical and biochemical tools. Meanwhile, a lot of work in my own lab is focused on designing enzyme inhibitors, mainly for antibacterial applications to treat diseases such as tuberculosis and malaria. Collectively, we are well-positioned to take chemical biology to the next level at SKI by continuing to investigate these diseases and find new drug targets.

What lies ahead for this program in the near future? What other lessons has your work taught you?

We plan to recruit more investigators so we can further expand the impact of chemical biology on our biomedical research mission. This new program makes clear the institution's commitment to chemical biology, and as a standalone department it puts SKI more prominently on the radar screens of chemists who are postdocs at top institutions and looking to launch their careers. Now that we have a formal Chemical Biology Program, we hope that it will encourage them to apply here. It's important that we continue bringing in top chemical biologists if we hope to understand cancer and other diseases at a molecular level and to use that knowledge to create new drugs to combat them. ●