MIT Industrial Liaison Program Faculty Knowledgebase Report

Health Science Technology

December 8, 2022 11:00 am - 12:35 pm

11:00 AM

Welcome & Introduction
Sheryl Greenberg
Program Director, MIT Industrial Liaison Program

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Sheryl Greenberg initiates and promotes the interactions and development of relationships between academic and industrial entities to facilitate the transfer of new ideas and technologies between MIT and companies, and has created numerous successful partnerships. By understanding the business, technology, and commercial problems within a company, and understanding the technologies and expertise of MIT researchers, Greenberg identifies appropriate resources and expertise to foster new technology applications and collaborative opportunities.

Prior to MIT, Greenberg created and directed the Office of Technology Transfer at Brandeis University. In the process of managing intellectual property protection, marketing, and licensing, she has promoted the successful commercialization of technologies as diverse as new chemicals and manufacturing, biotechnology, food compositions, software, and medical devices. She facilitated the founding and funding of new companies, as well as creating a profitable technology transfer program. She also facilitated the patenting, marketing, and licensing of Massachusetts General Hospital technologies. In addition to her cellular, biochemical, and genetic research experience in academic and corporate environments, she has also created intellectual property for medical uses. Greenberg has been an independent intellectual property and business development consultant, is a U.S. Patent Agent, and has previously served the Juvenile Diabetes Research Foundation as Co-Chair of the Islet Research Program Advisory Committee and grant reviewer. She currently also mentors startup companies and facilitates partnering them with large life science and healthcare companies.

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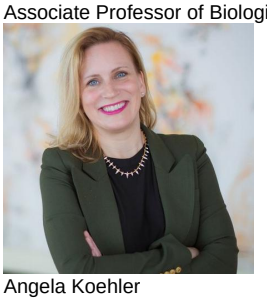
11:03 AM

Expanding the Repertoire of Druggable Targets

Angela Koehler
Intramural Faculty, Koch Institute for Integrative Cancer Research (KIICR)
Associate Member, Broad Institute
Associate Professor of Biological Engineering, MIT Department of Biological Engineering



Angela Koehler
Intramural Faculty, Koch Institute for Integrative Cancer Research (KIICR)
Associate Member, Broad Institute
Associate Professor of Biological Engineering
MIT Department of Biological Engineering

Angela Koehler is the Kathleen and Curtis Marble Professor in Cancer Research, an Associate Professor in the Department of Biological Engineering at MIT, and an Associate Director of the David H. Koch Institute for Integrative Cancer Research at MIT. She is also an Institute Member of the Broad Institute and a Member of the MIT Center for Precision Cancer Medicine. Her research group aims to discover and develop functional small-molecule probes of targets emerging from patient-based genomics, including targets deemed recalcitrant to small molecule drug discovery efforts, such as transcription factors, RNA-binding proteins or cytokines. Selected probes may be developed into imaging agents, diagnostic tools, or therapeutic leads.

Angela received her B.A. in Biochemistry and Molecular Biology from Reed College in 1997. There she worked under the guidance of Professor Arthur Glasfeld on structural and biochemical studies of proteins that recognize tRNA or DNA. In 2003, she received her Ph.D. in Chemistry from Harvard University where she worked with Professor Stuart Schreiber to develop novel technologies for identifying and characterizing interactions between proteins and small molecules. Upon graduation, she became an Institute Fellow in the Chemical Biology Program at the Broad Institute and a Group Leader for the NCI Initiative for Chemical Genetics.

At MIT, Angela serves as the Faculty Director of the High-Throughput Sciences Facility in the Swanson Biotechnology Center. She is a co-Director of the MIT Biomedical Engineering Undergraduate Program and a member of the Committee on Pre-Health Advising. Angela has served on the Chemists in Cancer Research Executive Advisory Board for AACR. Awards include being named a Genome Technology Young Investigator and a Broad Institute Merkin Fellow as well as the Novartis Lectureship in Chemistry, the Ono Pharma Breakthrough Science Award, the AACR-Bayer Innovation and Discovery Award and the MIT Junior Bose Award for Excellence in Teaching. Angela serves as a consultant or scientific advisory board member to several pharmaceutical or biotechnology companies and has founded several biotechnology companies, including Ligon Discovery, Kronos Bio, and 76Bio.

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For decades, transcription factors (TFs) have been identified as key biological players in diseases, including cancer, diabetes, and autoimmune disorders. However, outside of nuclear receptors, this class of proteins has traditionally been considered “undruggable” by small molecules due to significant structural disorder and lack of defined binding pockets. A renewed interest in the field has been ignited by significant advances in chemical biology approaches to ligand discovery and optimization, especially the advent of targeted protein degradation approaches, along with increasing appreciation of the critical role a limited number of collaborators play in the regulation of key TF effector genes. Dr. Koehler will review recent advances in the lab involving successful targeting strategies, including discussion of compounds that modulate MYC-driven transcription via mechanisms involving the MAX partner protein or the transcriptional kinase CDK9. Finally, new directions for cancer target classes beyond transcription factors will be discussed, including RNA-binding proteins and cytokines.

11:23 AM

Discovery of Small Molecule Inhibitors to Cytokines: Video begins at time stamp: 21.52

Sean Quinnell
Postdoctoral Associate
MIT Koch Institute of Integrative Cancer Research

The cytokine family of proteins consists of over 100 proteins involved in the development, inflammation, and immune responses. Dysregulated cytokine signaling is associated with numerous conditions, such as cancer, inflammatory conditions, and autoimmune diseases, making them attractive drug targets. Antibodies and peptides have shown success at targeting cytokine receptors, but there has been a lack of small molecule inhibitors directed to soluble cytokines. We developed a pipeline to identify small molecule inhibitors to cytokines through a combination of high throughput screening, binding-based and cell-based assays.

Using a combination of small molecule microarray and differential scanning fluorimetry, we identified 10 putative to the cytokine IL-4. The lead small molecule, Nico-52, inhibits both type I and type II IL-4 signalling pathways in both human and murine cell lines with micromolar potency. After the successful discovery of the IL-4 inhibitor Nico-52, we sought to expand our discovery pipeline to multiple proteins in the cytokine family. Using small molecule microarray, we have screened 33 cytokines and have begun to build selectivity maps based on chemotypes and the specific cytokines that they target. Preliminary analyses indicate trends in both physicochemical properties and specific scaffolds as putative binders to members of this protein family. This compound mapping strategy may be used as prioritization tool to rapidly advance compounds to validation studies based on their selectivity against cytokine(s) of interest.

11:43 AM

Beyond the Inhibition Paradigm: Design and Characterization of Highly Potent and Selective Heterobifunctional Degraders: Video begins at time stamp: 39.01

Mo Toure
Bioengineering Doctoral Candidate
MIT Koch Institute of Integrative Cancer Research

Targeted protein degradation offers a novel approach for treating disease where conventional small molecules have struggled to have meaningful clinical impact. Degrader molecules harness our cells' natural housekeeping system to selectively remove disease-causing proteins from the body. We will discuss the design and characterization of highly selective and potent degrader molecules against the cyclin-dependent kinase 9 (CDK9). The selective degradation of CDK9 presents an attractive strategy to attenuate transcriptional addiction and provide relief for patients with aggressive cancers.

12:03 PM

MIT Startup Exchange Startups: Delivering Big DNA: "Video begins at time stamp: 58.50 "

Alexander "Xander" Kerman
Director of BD & Partnerships
Syntegra

12:20 PM

Adjournment