Icahn School of Medicine at Mount Sinai

Department of Pharmacological Sciences

3Q
THIRD QUARTER
SEPT.2021

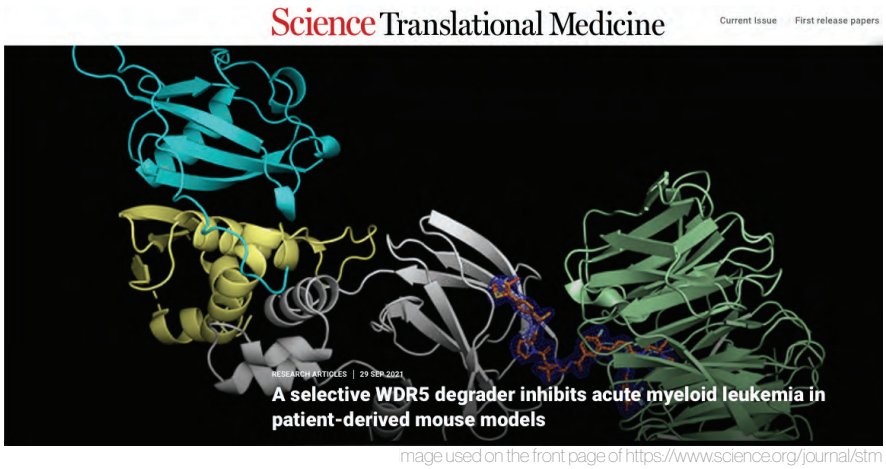
THE JIN LAB AT THE FOREFRONT OF CANCER DRUG DISCOVERY

JIAN JIN, PHD
Professor

XUFEN YU, PHD
Instructor

BRANDON DALE
MD/ PhD Student

Targeted protein degradation (TPD) with heterobifunctional proteolysis targeting chimera (PROTAC) technology is the new frontier of cancer drug discovery. Prof. Jian Jin is widely recognized as a pioneer and leader in this emerging field (Dale, *Nature Reviews Cancer,* 2021). The Jin Lab has made seminal contributions to the TPD field through developing new technologies, including: (1) harnessing the E3 ligase KEAP1 for TPD with a selective small-molecule KEAP1 ligand (Wei, *JACS,* 2021); (2) novel opto-PROTAC and folate-caged PROTAC technologies as precision medicine; and (3) invention of a novel universal strategy for selective degradation of "undruggable" transcription factors (TFs), termed TF-PROTACs (Liu, *JACS,* 2021). These novel TPD technologies have enabled the Jin Lab to create novel small-molecule degraders as new anti-cancer therapies for some of the most challenging onco-proteins. For example, in collaboration with Prof. Ramon Parsons in the Tisch Cancer Institute, the Jin Lab discovered first-in-class degraders for histone lysine methyltransferase EZH2, a key oncogenic driver for triple-negative breast cancer (Ma, *Nature Chemical Biology,* 2020). Recently, together with Prof. Greg Wang at University of North Carolina at Chapel Hill and Prof. Aneel Aggarwal at Mount Sinai, the Jin Lab has developed using rational structure-based design a potent and selective WDR5 PROTAC degrader that shows robust *in vivo* antitumor activity in mice (Yu, *Science Translational Medicine,* 2021). Since 2020, Prof. Jin and his colleagues have published 14 papers in the TPD field, and their research has further resulted in 15 patent applications filed through Mount Sinai Innovation Partners.



mage used on the front page of https://www.science.org/journal/stm

THE MA'AYAN LAB'S SUMMER RESEARCH CAMP FOR BIOMEDICAL BIG DATA SCIENCE

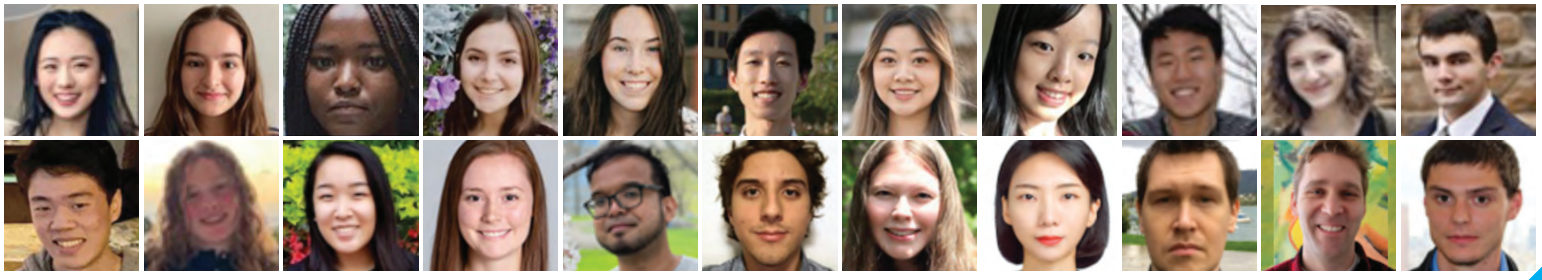
AVI MA'AYAN, PHD
Professor

SHERRY JENKINS
Project Director

The Ma'ayan Lab's Summer Research Training Program in Biomedical Big Data Science, directed by Ms. Sherry Jenkin, is an NIH-funded ten-week training program for undergraduate and graduate students interested in cutting-edge research aimed at solving data-intensive biomedical problems. These summer research trainees are engaged in faculty-mentored independent research projects in data harmonization, artificial intelligence, cloud computing and dynamic data visualization. As part of the Mount Sinai Center for Bioinformatics' community training and outreach efforts, this Program offers an excellent research framework for educating next-generation biomedical data scientists with a focus on perturbation data generated by the NIH Common Fund's Library of Integrated Networks-Based Cellular Signatures (LINCS) Program. These summer trainees who worked on data science research related to LINCS perturbation data carry their experiences to their next training stages, further cultivating the impact of LINCS resources and satisfying the need for the development of a pipeline of diverse Data Scientists in biomedical research.

PROGRAM OUTCOMES AND HIGHLIGHTS

Two program alumni are currently Data Scientists in the Ma'ayan Lab and serve in integral roles on the team's innovative NIH-funded projects aimed at creating useful tools for scientific discovery. Other trainees have entered the PhD programs in computational systems biology at the top-tier academic institutions in the US including the Icahn School of Medicine at Mount Sinai, MIT, Harvard, and the University of Pennsylvania; the MD/PhD program at Albert Einstein College of Medicine; and the MD program at Mount Sinai. Training outcomes also include multiple peer-reviewed publications co-authored by summer research trainees. For example, program research highlight featured on the NIH Common Fund's website includes the lab's recent study on identifying targets for pain medication with artificial intelligence.



HIGHLIGHTS

PROFESSOR IAN MAZE SELECTED AS A HOWARD HUGHES MEDICAL INSTITUTE INVESTIGATOR

The Howard Hughes Medical Institute (HHMI) has selected Ian Maze, PhD, Associate Professor of Neuroscience, and Pharmacological Sciences, at the Icahn School of Medicine at Mount Sinai, as an HHMI Investigator. Prof. Maze's research is centered on the study of the brains of rodents and postmortem humans, as well as human iPSC-derived neurons, to uncover chromatin-based mechanisms of neurological diseases (*Nature* 2019; *Science* 2020). The highly competitive appointment is reserved for outstanding researchers who are known for their scientific discoveries, innovation, and ability to push the bounds of knowledge in biomedical research. Our congratulations to Prof. Maze on this monumental recognition of his exceptional academic achievements!

PAPERS

Sato K, Padgaonkar AA, Baker SJ, Consenza SC, Rechkoblit O, Subbaiah DRC, Domingo-Domenech J, Bartkowski A, Port ER, **Aneel K. Aggarwal**, MV Ramana Reddy, Irie H, **E.Premkumar Reddy**. (2021) ***Nature Commun.*** 12, 4671

Shah RB, Kernan JL, Hoogstraten AV, Ando K, Li Y, Belcher AL, Mininger I, Bussenault AM, Raman R, Ramanagoudr-Bhojappa R, Huang TT, D'Andrea AD, Chandrasekharappa SC, **Aneel K. Aggarwal**, Thompson R, Sidi S. (2021) ***Developmental Cell***, 56(15), 2207-2222.e7

Jatiani SS, Christie S, Leshchenko VV, Jain R, Kapoor A, Bisignano P, Lee C, Kaniskan HÜ, Edwards D, Meng F, Laganà A, Youssef Y, Wiestner A, Alinari L, **Jin J**, **Marta Filizola**, **Aggarwal AK**, Parekh S. (2021) ***Clin Cancer Res.***, 27(16), 4652-4663

Pryce KD, Kang HJ, Sakloth F, Liu Y, Khan S, Toth K, Kapoor A, Nicolais A, Che T, Qin L, Bertherat F, Kaniskan HÜ, Jin J, Cameron MD, Roth BL, Zachariou V, **Marta Filizola**. (2021) ***Neuropharmacology***, 195, 108673

Kuleshov M, Xie Z, London ABK, Yang J, Evangelista JE, Lachmann A, Shu I, Torre D, **Avi Ma'ayan**. (2021) ***Nucleic Acids Res.***, 49(W1), W304–W316

Piret S, Guo Y, Attallah AA, Horne SJ, Zollman A, Owusu D, Henein J, Sidorenko VS, Revelo MP, Hato T, **Avi Ma'ayan**, He JC, Mallipattu SK. (2021) ***Proc. Natl. Acad. Sci. USA.***, 118(23), e2024414118

Caescu CI, Hansen J, Crockett B, Xiao W, Arnaud P, Spronck B, Weinberg A, Hashimoto T, Murtada SI, Borkar R, Gallo JM, Jondeau G, Boileau C, Humphrey JD, He JC, **Ravi Iyengar, Francesco Ramirez**. (2021) ***ATVB***, 41, 2483–2493

Garibsingh RA, Ndaru E, Garaeva AA, Shi Y, Zielewicz L, Zakrepine P, Bonomi M, Slotboom DJ, Paulino C, Grewer C, **Avner Schlessinger**. (2021) ***Proc. Natl. Acad. Sci. USA***. 118 (37) e2104093118

GRANT HIGHLIGHTS

M. ZAIDI, MD,PHD
Professor

TONY YUEN, PHD
Asst Professor

Profs. Mone Zaidi and Tony Yuen have been leading a cutting-edge research program to gain better understanding of mechanism and function of follicle-stimulating hormone (FSH) in the onset and development of osteoporosis in thyroid disease (*Cell* 2003, 2006), as well as in regulation of body fat and energy balance (*Nature* 2017). They have developed a new humanized FSH antibody that enables their investigation of the clinical potential of targeting FSH as a new treatment for osteoporosis, obesity, hypercholesterolemia, and Alzheimer's disease. Their research is boosted by their two new major research grants received from NIA.

Mone Zaidi (contact), Vahram Haroutunian, **Tony Yuen**, mPIs, "*Elevated FSH - A Driver for Sex Differences in Alzheimer's Disease*", R01, NIA, 09/30/2021-08/31/2026, $6,338,438

Mone Zaidi (contact), **Tony Yuen**, mPIs, "*A Humanized Monoclonal FSH Blocking Antibody for Alzheimer's Disease*", U01, NIA, 09/30/2021-08/31/2026, $8,338,000

EVENTS

THE 14TH JACK PETER GREEN LECTURE

Bryan Roth, MD, PhD
Michael Hooker Distinguished Professor
University of North Carolina, Chapel Hill

"New Chemical and Synthetic Biology Technologies"

Friday, October 14th, 11AM
Goldwurm Auditorium and Virtual
https://mssm.zoom.us/j/88696285044

THE 14TH ANNUAL RESEARCH RETREAT

Dirk Trauner, PhD
Janice Cutler Professor of Chemistry
New York University

"Controlling Protein Degradation and Cytoskeletal Dynamics with Light"

Friday, October 29th , 9AM
Goldwurm Auditorium and Virtual
Registration Coming Soon!

CoDES MOVIE DAY

As part of the CoDES activities, a list of movies/documentaries have been generated with an aim to promote diversity and inclusion in our Department through better understanding of different cultural backgrounds. The CoDES plans to host a "movie day" in conference room where a movie/documentary from the list will be screened followed with discussions. We invite you to nominate your preferred movies/documentaries to CoDES@mssm.edu. See examples here.

DPS MEMBER UPDATE

APPOINTMENT & PROMOTION

Arvin Dar, PhD
Professor

Anna Cantalupo, PhD
Instructor
Ramirez Lab

Carmen Davidson
Financial Analyst
Admin

Mariana L Duarte, PhD
Instructor
Devi Lab

Husnu Kaniskan, PhD
Assoc Professor
Jin Lab

Carole Morel, PhD
Asst Professor
Han Lab

Mustafa Siddiq, PhD
Asst Professor
Iyengar Lab

Xufen Yu, PhD
Instructor
Jin Lab

NEW MEMBERS

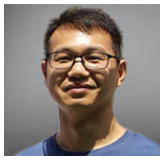
Heather Dahlin, PhD
Postdoctoral Fellow
Lazarus Lab

Pushkar Kumar, MD
Assoc Researcher
Zaidi Lab

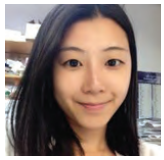
Jiahui Wang
Assoc Researcher
Zhou Lab

NEW ALUMNI

Amy Gutierrez
Asst Rsch Engr
Child Mind Institute



Yulin Han, PhD
Asst Professor
Shuren University



Huen Suk Kim, PhD
Rsch Scientist
Arvinas

Fanye Meng, PhD
Prin Scientist
Insilico Medicine

Renhong Sun, PhD
Head Med Chem
Gluetacs Therap.