MOLECULAR PHARMACOLOGY PROGRAM

The Alex Kentsis Lab

Research

Alex Kentsis, MD, PhD
Director of the Tow Center for Developmental Oncology

We study the biology of cancers that affect children and young adults ranging from embryonal tumors in infants, leukemias and brain tumors in children, and sarcomas in young adults. Scientists in our group use inter-disciplinary experimental tools as they work to understand the fundamental causes of cancer and to develop definitive therapies for their control.

With colleagues, we wrote Developmental Oncology: Principles and Therapy of Cancers of Children and Young Adults , a book that redefines them as diseases rooted in specific developmental cell

states and early-life mutational processes, spurring the development of rational and precise clinical therapies targeting this distinct biology.

Detailed information about our research is available at https://alexkentsis.net .

Our current research is focused on developmental cancer biology and developmental therapeutics. Our past research identified molecular mechanisms and therapeutic strategies to interfere with oncogenic kinase signaling, transcriptional and chromatin, and post-transcriptional protein regulation, as well as diagnostic biomarkers of leukemias, solid tumors, and inflammatory conditions. Recently, our group has identified new mechanisms of aberrant gene control and dysregulation of cell death, differentiation and stem cell quiescence in blood cancers, mechanisms of site-specific oncogenic mutations and DNA damage repair signaling in solid tumors, and improved epigenetic, drug delivery and macromolecular therapeutics for cancer. Based on over two decades of research in functional proteomics and genomics, we continue to develop and apply improved proteomic and genomic methods to define oncogenic mechanisms and develop improved therapies, thereby translating laboratory discoveries into rational therapeutic strategies and clinical trials for patients.

1) Leveraging improved methods in functional genomics and proteomics, we revealed developmental mechanisms of site-specific oncogenic mutations in solid tumors that affect children and young adults, molecular and cellular mechanisms, therapeutic targets and rational combination strategies to overcome therapy resistance, and synthetic lethal strategies to pharmacologically target developmental oncogenic mutators in childhood and young-adult human cancers.

2) Our lab has used functional genomic and proteomic approaches to elucidate molecular mechanisms of pathogenesis of acute leukemias with the goal of identifying improved therapeutic strategies, particularly for refractory leukemias of children and young adults. This work led to the development of rational combination strategies to overcome adaptive therapy resistance , mechanisms of leukemia stem cell quiescence , mechanisms, and therapies of signaling-mediated control of oncogenic gene expression , and first-in-class transcriptional coactivator inhibitors .

3) Our research in mass spectrometry proteomics has focused on developing improved methods for quantitative biological proteomics and translational platforms for the discovery of improved biomarkers and therapeutic targets in human disease and cancer in particular. This has enabled comprehensive mapping of cancer proteomes, including methods for detection of chemical modifications and non-canonical proteoforms , and improved approaches for the incorporation of molecular profiling into clinical medicine , as implemented in the Quantitative Cell Proteomics Atlas . More recently, we implemented proteomic barcoding as a platform for macromolecular

screening and delivery, established the scalable ProteomeGenerator framework for integrative proteogenomics, and led the development of a modular platform for therapeutic drug delivery using trifunctional bio-orthogonal macromolecular conjugates (BMC).

4) We continue to apply and advance methods in biophysical theory and computational biology to understand fundamental properties of living systems and develop precisely targeted therapeutic agents. This includes statistical mechanics and molecular dynamics, computational genomics, systems biology, and a project to develop new physics of life to understand biological molecules, development, and disease .

View Lab Overview (https://www.mskcc.org/research/ski/labs/alex-kentsis/overview)

Featured News

ARTICLE

Researchers Discover PGBD5 Guides Normal Brain Development in Addition to Causing Cancers

Read about a discovery that a gene linked to pediatric cancers may play an essential role in normal brain development.

Epigenetic Combination Therapy Could Overcome Treatment Resistance in Epithelioid Sarcomas and Rhabdoid Tumors

Learn about a possible new treatment approach for soft tissue sarcomas.

IN THE LAB

Research Shows How Common Feature of Blood Cancers Can Be Targeted

Research points to the role of a protein called MYB, which has long been known to play a role in cancer.

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Publications Highlights

Zapater LJ, Lewis SA, Gutierrez RL, Yamada M, Rodriguez-Fos E, Planas-Felix M, Cameron D, Demarest P, Nabila A, Mueller H, Zhao J, Bergin P, Reed C, Chwat-Edelstein T, Pagnozzi A, Nava C, Bourel-Ponchel E, Cornejo P, Dursun A, Özgül RK, Akar HT, Maroofian R, Houlden H, Cheema HA, Anjum MN, Zifarelli G, Essid M, Ben Hafsa M, Benrhouma H, Montoya CIG, Proekt A, Zhao X, Socci ND, Hayes M, Bigot Y, Rabadan R, Torrents D, Kleinmann CL, Kruer MC, Toth M, Kentsis A. A transposase-derived gene required for human brain development. Science Advances, 2026.

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Kazansky Y, Cameron D, Demarest P, Zaffaroni N, Arrighetti N, Zuco V, Kuwahara Y, Qu R, de Stanchina E, Dela Cruz F, Kung A, Gounder M, Kentsis A. Overcoming clinical resistance to EZH2 inhibition using rational epigenetic combination therapy. Cancer Discovery, 2024.

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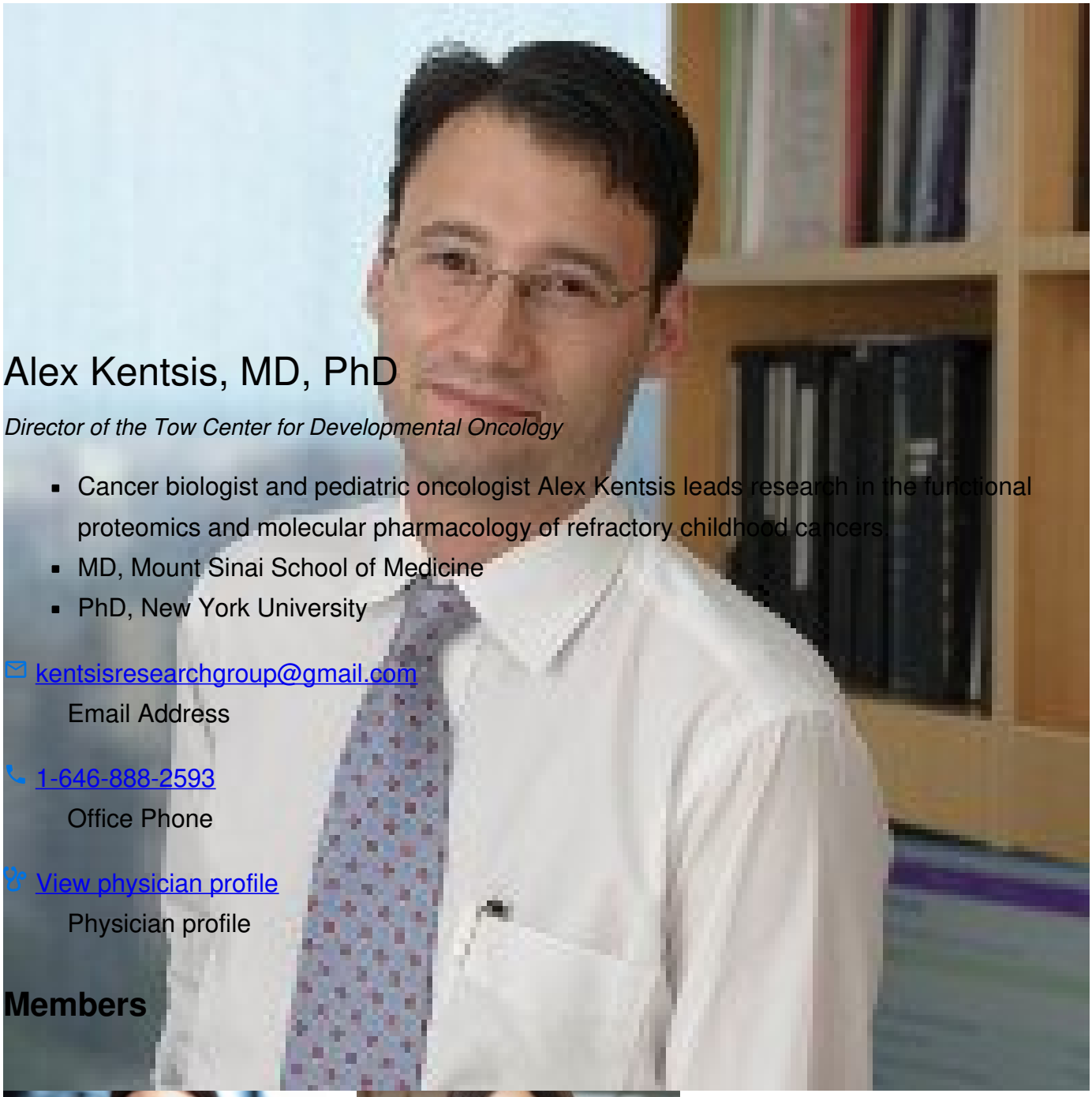
People



Alex Kentsis, MD, PhD

Director of the Tow Center for Developmental Oncology

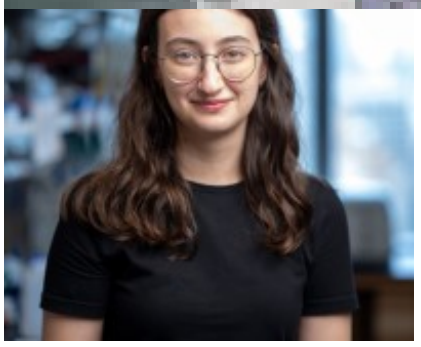
- Cancer biologist and pediatric oncologist Alex Kentsis leads research in the functional proteomics and molecular pharmacology of refractory childhood cancers.
- MD, Mount Sinai School of Medicine
- PhD, New York University

kentsisresearchgroup@gmail.com
Email Address

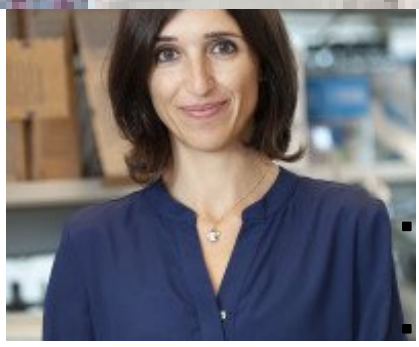
1-646-888-2593
Office Phone

View physician profile
Physician profile

Members



Anna Antonova
Graduate Student



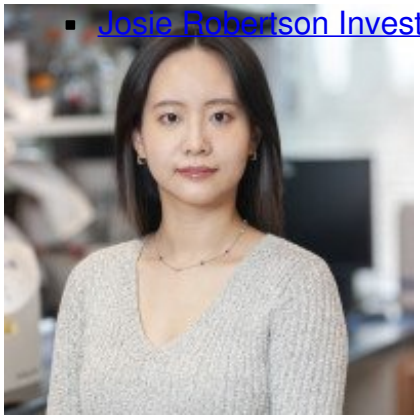
Gabriella Casalena
Scientific Research Manager

Lab Affiliations

Achievements

- Louise and Allston Boyer Award for Clinical Research
- Terry Ann Krulwich Physician-Scientist Alumni Award
- Pershing Square Sohn Prize
- Leukemia & Lymphoma Society Scholar Award

- Josie Robertson Investigator (2013-2018)



Shuyuan Cheng
Graduate Student

Nicole Cruz
Research Fellow

Sara Dolan
Research Technician

Samarah Forbes
Administrative Assistant

Kaisha Garvin
Research Technician

Katarzyna Kulej
Scientific Research Lead

Dinesh Kumar
Research Fellow

Danmeng Luo
Research Fellow

Hannah Major-Monfried
Research Fellow

Helen Mueller
Research Fellow

Laura Schmalbrock
Research Fellow

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Get in Touch

Makiko Yamada
Senior Research Scientist

Jinxin Zhang
Scientific Research Lead

Anna Zychlinsky-Scharff
Research Fellow

kentsisresearchgroup@gmail.com
Lab Head Email

1-646-888-2593
Office Phone

1-646-888-3557
Lab Phone

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Alex Kentsis discloses the following relationships and financial interests:

- Blueprint Medicines
  Professional Services and Activities
- Day One Biopharmaceuticals, Inc.
  Professional Services and Activities
- Novartis
  Professional Services and Activities
- Rgenta Therapeutics Inc.
  Equity; Professional Services and Activities

- Sellas Life Science Group

  Professional Services and Activities
- Syndax

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- U.S. Department of Justice

  Professional Services and Activities

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This page and data include information for a specific MSK annual disclosure period (January 1, 2024 through disclosure submission in spring 2025). This data reflects interests that may or may not still exist. This data is updated annually.

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