CHEMICAL BIOLOGY PROGRAM

The Gabriela Chiosis Lab

Research

Gabriela Chiosis, PhD

The goal of my program is to investigate stressor maladaptation mechanisms such as they occur in several diseases. Our approach takes advantage of the way nature has evolved to control such stressors, and that is by a unique usage of the chaperome, referred here as the epichaperome. The epichaperome, which we discovered, is structurally, dynamically and functionally distinct from the housekeeping chaperome, and my lab has pioneered an approach to take advantage of such features. By using innovative methods, we develop small molecule chemical toolsets specifically targeted to the epichaperome; these act as “sensors” of the epichaperome, and in turn, of the chronic stressor-associated proteome-wide malfunctions. By the use of these unique toolsets we aim to understand, diagnose and treat cellular processes associated with chronic stressors. We address multiple mechanistic and biochemical questions less amenable to approaches that treat the chaperome as monolithic entity (*i.e.* the classical biochemical and genetic tools). We investigate in endogenous systems, both at the cellular and the

organismal level, the inherent proteome changes and mechanisms that lead to disease, *i.e.* we can understand. By sensing disease states through the chemical toolsets, we go beyond investigation; we identify, measure and quantify, *i.e.* we can diagnose. By attacking the epichaperome specifically, we perturb the disease-causing proteome, and in turn revert or slow the disease phenotype, *i.e.* we can treat.

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Research Projects

- Protein-protein interaction networks in disease
- Mechanisms of disease
- Epichaperomes in Neurodegenerative Diseases
- Paradigms for Precision Medicine
- Development of Chemical Probes

View All Projects

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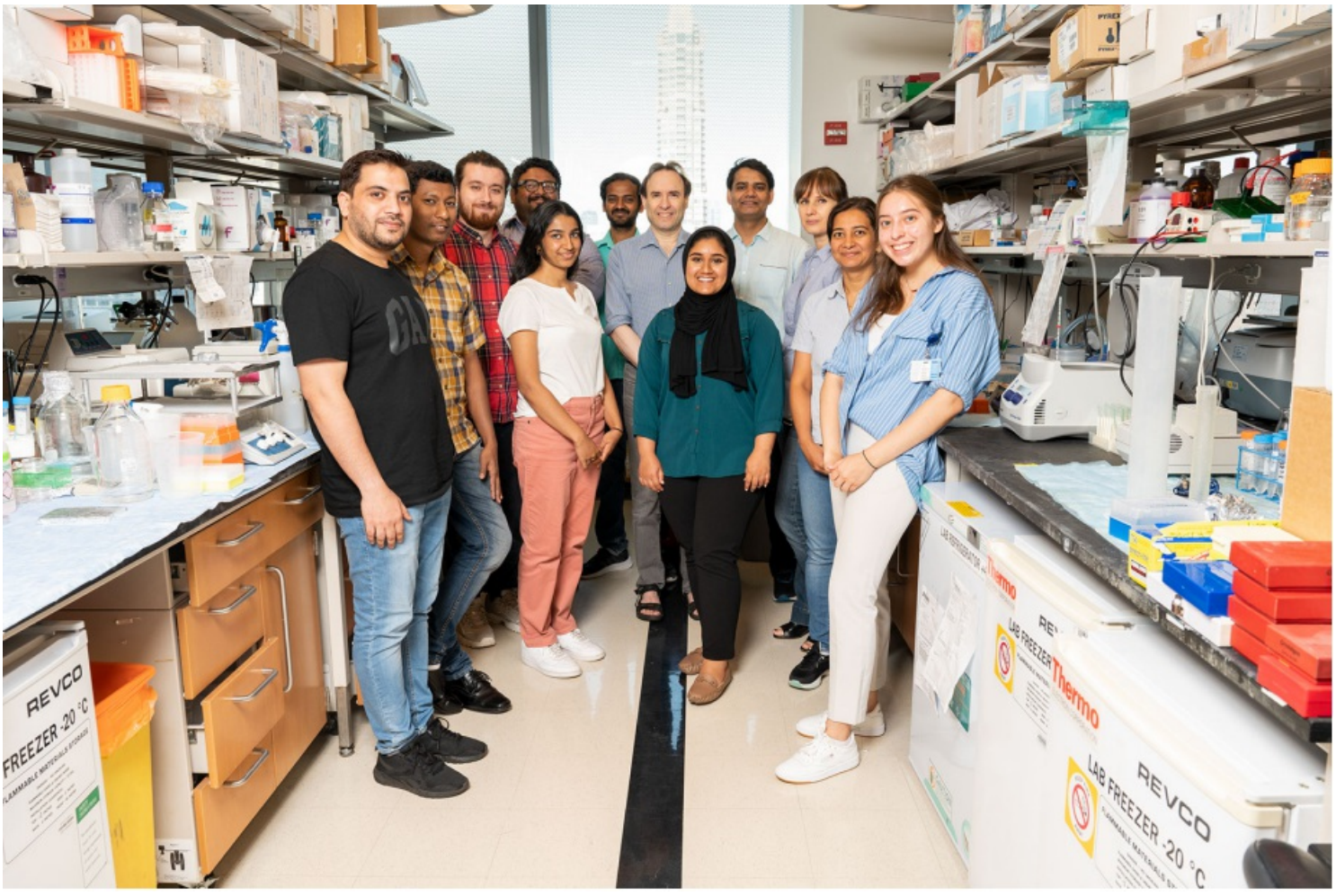


Featured News

[MSK Research Highlights, June 29, 2023]

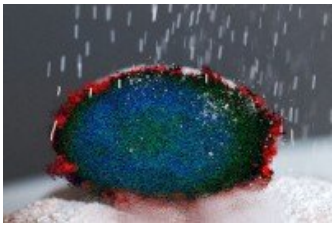
New MSK research discovered ferroptosis regulators that suggest therapeutic opportunities against hormone receptor-positive cancers; examined how tumor-associated macrophages might be turned against cancer; acquired new insights into joint inflammation in rheumatoid arthritis; developed a systems-level platform called epichaperomics to map changes in interactors among thousands of proteins involved in cancer-related processes; and investigated how artificial intelligence could help diagnose an invasive form of breast cancer.

IN THE LAB

[Experimental Drug Targets Misbehaving Proteins in Brain Cancer and Alzheimer's Disease]

Memorial Sloan Kettering researchers are studying how drugs that reverse malfunctioning proteins may treat disease.

IN THE LAB



[Just Add Sugar: How a Protein's Small Change Leads to Big Trouble for Cells]

A study from investigators in the Sloan Kettering Institute uncovers the details of how a key protein called GRP94 becomes disrupted, leading to cancer and other diseases.

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Publications Highlights

The epichaperome is an integrated chaperome network that facilitates tumour survival. Rodina A, Wang T, Yan P, Gomes

ED, Dunphy MP, Pillarsetty N, Koren J, Gerecitano JF, Taldone T, Zong H, Caldas-Lopes E, Alpaugh M, Corben A, Riolo M, Beattie B, Pressl C, Peter RI, Xu C, Trondl R, Patel HJ, Shimizu F, Bolaender A, Yang C, Panchal P, Farooq MF, Kishinevsky S, Modi S, Lin O, Chu F, Patil S, Erdjument-Bromage H, Zanzonico P, Hudis C, Studer L, Roboz GJ, Cesarman E, Cerchietti L, Levine R, Melnick A, Larson SM, Lewis JS, Guzman ML, Chiosis G. Nature. 2016 Oct 5. doi: 10.1038/nature19807.

Paralog-selective Hsp90 inhibitors define tumor-specific regulation of HER2. Patel PD, Yan P, Seidler PM, Patel HJ, Sun W, Yang C, Que NS, Taldone T, Finotti P, Stephani RA, Gewirth DT, Chiosis G. Nat Chem Biol. 2013 Sep 1. doi: 10.1038/nchembio.1335. [Epub ahead of print]

Identification of an allosteric pocket on human hsp70 reveals a mode of inhibition of this therapeutically important protein. Rodina A, Patel PD, Kang Y, Patel Y, Baaklini I, Wong MJ, Taldone T, Yan P, Yang C, Maharaj R, Gozman A, Patel MR, Patel HJ, Chirico W, Erdjument-Bromage H, Talele TT, Young JC, Chiosis G. Chem Biol. 2013 Dec 19;20(12):1469-80. doi: 10.1016/j.chembiol.2013.10.008. Epub 2013 Nov 14.

Affinity-based proteomics reveal cancer-specific networks coordinated by Hsp90. Moulick K, Ahn JH, Zong H, Rodina A, Cerchietti L, Gomes DaGama EM, Caldas-Lopes E, Beebe K, Perna F, Hatzi K, Vu LP, Zhao X, Zatorska D, Taldone T, Smith-Jones P, Alpaugh M, Gross SS, Pillarsetty N, Ku T, Lewis JS, Larson SM, Levine R, Erdjument-Bromage H, Guzman ML, Nimer SD, Melnick A, Neckers L, Chiosis G. Nat Chem Biol. 2011 Sep 25;7(11):818-26. doi: 10.1038/nchembio.670.

Hsp90 inhibitor PU-H71, a multimodal inhibitor of malignancy, induces complete responses in triple-negative breast cancer models. Caldas-Lopes E, Cerchietti L, Ahn JH, Clement CC, Robles AI, Rodina A, Moulick K, Taldone T, Gozman A, Guo Y, Wu N, de Stanchina E, White J, Gross SS, Ma Y, Varticovski L, Melnick A, Chiosis G. Proc Natl Acad Sci U S A. 2009 May 19;106(20):8368-73. doi: 10.1073/pnas.0903392106. Epub 2009 May 5.

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People

Gabriela Chiosis, PhD

The Chiosis lab uses a unique chemical biology approach to understand, diagnose, and treat cellular processes associated with chronic molecular stress, with the ultimate goal of developing novel therapeutic options for use in the clinic.

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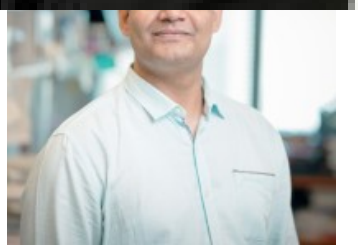

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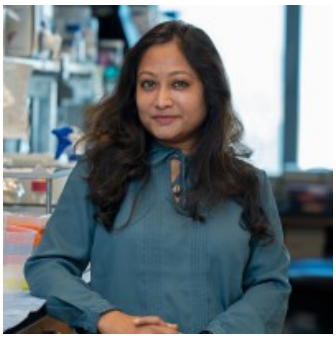

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Lab Affiliations
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Achievements

AACR – Cancer Research and Prevention Career Development Award in Translational Lung Cancer Research, in Memory of Duffy Wall

Susan G. Komen Breast Cancer Translational Research Award

Frederick R. Adler Chair for Junior Faculty

Award for Drug Discovery Research for Frontotemporal Dementia

Top 5 percent cited author in Biology and Biochemistry 2010 (analysis by Thomson Reuters)

Translated from bench-to-bedside the Hsp90 inhibitor PU-H71 and the non-invasive companion diagnostic 124I-PU-H71 PET

assay

Lab News & Events

A new strategy for Alzheimer’s disease treatment targets cell-wide protein malfunction

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MSK requires doctors and faculty members to report (“disclose”) the relationships and financial interests they have with external entities. As a commitment to transparency with our community, we make that information available to the public.

Gabriela Chiosis discloses the following relationships and financial interests:

Samus Therapeutics LLC
Equity; Intellectual Property Rights

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