



STOWERS RESEARCH CONFERENCES:

Ribosome Heterogeneity and Translational Control from Cells to Organisms

#SRCKC26

PROGRAM

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Speaker instructions



Speakers **must upload their presentations to the "Presentation Request Portal" that was shared with them in advance of the meeting OR at the podium** at the designated times listed below, prior to their scheduled sessions.

Speaker file upload times:

Wednesday, October 21

1:00–2:00PM

Thursday, October 22

9:00–9:30 AM

1:30–2:00 PM

Friday, October 23

9:00–9:30 AM

1:30–2:00 PM



Speakers **must get equipped with a microphone at the podium** 15 minutes prior to their scheduled sessions.

Conference Program

All talks will be presented in the Stowers Auditorium
Food and beverages offered are complimentary, please enjoy!

■ 25 min presentation + 10 min Q&A
■ 10 min presentation + 5 min Q&A

WEDNESDAY, OCTOBER 21

12:30 PM TO 2:00 PM | ARRIVAL, CHECK-IN & POSTER SET-UP
Light snacks and refreshments are available outside of the Auditorium

SESSION 1: BIOGENESIS, REGULATION AND FUNCTION

2:00 PM | WELCOME AND INTRODUCTION FROM CHAIRS

2:10 PM TO 2:45 PM | **HOMA GHALEI & LAURYN CURETON, EMORY UNIVERSITY**
Regulation of translation by rRNA modifications

2:50 PM TO 3:05 PM | **SHINO MURAKAMI, YALE UNIVERSITY SCHOOL OF MEDICINE**
m6A alters ribosome dynamics to initiate mRNA degradation

3:10 PM TO 3:45 PM | **XIAO WANG & DANGLIANG LIU, BROAD INSTITUTE**
Deconstruct and reprogram RNA lifecycle

3:45 PM TO 4:05 PM | BREAK – refreshments available outside of the Auditorium

4:10 PM TO 4:45 PM | **SHU-BING QIAN & HAOLUN WU, CORNELL UNIVERSITY**
Ribosome decoding memory acquired from translation of codon repeats

4:50 PM TO 5:05 PM | **SINTHYIA AHMED & SOFIA ORIGANTI, SAINT LOUIS UNIVERSITY**
Structural Basis of Shwachman-Diamond Syndrome

5:10 PM TO 5:45 PM | **ARVIND RASI SUBRAMANIAM & JAMIE YELLAND, FRED HUTCH CANCER CENTER**
Ribosomal Control of the Integrated Stress Response

6:00 PM TO 7:30 PM | WELCOME RECEPTION in the Stowers Library

THURSDAY, OCTOBER 22

9:00 AM TO 9:45 AM | *Coffee and light breakfast options are available outside of the Auditorium*

SESSION 2: TRANSLATION FIDELITY AND CELLULAR ADAPTATION

9:45 AM | OPENING ANNOUNCEMENTS

9:50 AM TO 10:25 AM | **KOTARO FUJII & JACOB BEST, UNIVERSITY OF FLORIDA**
The precision of Mistakes: Dynamic mRNA Translation Fidelity in Development

10:30 AM TO 10:45 AM | **MARIA EUGENIA CORTINA, STOWERS INSTITUTE FOR MEDICAL RESEARCH**
Leaky scanning drives translation of downstream overlapping Open Reading Frames

10:50 AM TO 11:05 AM | **PRAKASH KHAREL, UNIVERSITY OF KANSAS MEDICAL CENTER**
Decoding tRNA Gene Redundancy: Sequence Variation Drives Functional Diversification of tRNA-Derived RNAs

11:05 AM TO 11:25 AM | BREAK – refreshments available outside of the Auditorium

11:25 AM TO 12:00 PM | **SUJATHA JAGANNATHAN & MICHAEL CORTÁZAR OSORIO, UNIVERSITY OF COLORADO ANSCHUTZ**
Decoding the molecular logic of mRNA surveillance

12:05 PM TO 12:20 PM	SALEEM BHAT, UNIVERSITY OF PENNSYLVANIA <i>Selective Inhibition of Eukaryotic Release Factor Accommodation Promotes Therapeutic Translational Readthrough of Premature Termination Codons</i>
12:30 PM TO 2:00 PM	LUNCH BREAK – join us in the Stowers Library for lunch

SESSION 3: SPECIALIZED TRANSLATION IN DEVELOPMENT AND PHYSIOLOGY

2:10 PM TO 2:45 PM	MICHAEL BUSZCZAK, UT SOUTHWESTERN <i>Dynamic regulation of ribosome biogenesis and turnover in mammalian cells</i>
2:50 PM TO 3:05 PM	MICHAY DIEZ, STOWERS INSTITUTE FOR MEDICAL RESEARCH <i>A new type of ribosome in the zebrafish germline</i>
3:10 PM TO 3:45 PM	SCOTT LINDNER & ROBBIE KELLY, PENN STATE UNIVERSITY <i>Specialized Ribosomes and Translational Control Promote the Efficient Transmission of Malaria Parasites</i>
3:45 PM TO 4:00 PM	BREAK – refreshments available outside of the Auditorium
4:05 PM TO 4:40 PM	JULIE ASPDEN, UNIVERSITY OF LEEDS <i>Dissecting mechanisms of translational regulation by specialized ribosomes</i>
4:45 PM TO 5:00 PM	CAROLINE MCNINCH, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE <i>HSP-1/HSPA8 directs selective translation towards longevity or immunity</i>
5:00 PM TO 5:15 PM	FLASH TALKS – ROUND 1
5:15 PM TO 6:30 PM	POSTER SESSION 1 – proceed down the staircase to the Stowers Gallery <i>Light snacks and refreshments are available at the base of the stairs.</i>
6:30 PM TO 7:30 PM	DINNER – join us in the Stowers Library for dinner

FRIDAY, OCTOBER 23

9:00 AM TO 9:45 AM	Coffee and light breakfast options are available outside of the Auditorium
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SESSION 4: TRANSLATION IN STEM CELLS AND DISEASE

9:45 AM	OPENING ANNOUNCEMENTS
9:50 AM TO 10:25 AM	WILLIAM FALLER & JOANA SILVA, UNIVERSITY OF BRISTOL <i>RAP regulation of intestinal stem cell identity</i>
10:30 AM TO 10:45 AM	MICHAEL MURPHY, COLUMBIA UNIVERSITY <i>Ribosomal protein paralog switching modulates translation elongation rates and protects against pathological cardiac aging</i>
10:50 AM TO 11:05 AM	DAPHNA ROTHSCCHILD, STANFORD UNIVERSITY <i>Ribosome heterogeneity arising from common and rare rRNA sequence variants affects diverse human phenotypes</i>
11:05 AM TO 11:25 AM	BREAK – refreshments available outside of the Auditorium
11:25 AM TO 12:00 PM	DAVIDE RUGGERO & MACEY SLOTA, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO <i>The Ribosome Epitranscriptome Underlies Heterogeneity in Health and Disease</i>
12:05 PM TO 12:20 PM	MAXWELL SHAPIRO, ST. JUDE CHILDREN'S RESEARCH HOSPITAL <i>From rRNA variants to ribotypes: resolving variant linkage and abundance in translating ribosome populations</i>

12:30 PM TO 2:00 PM	LUNCH BREAK – <i>join us in the Stowers Library for lunch</i>
2:10 PM TO 2:25 PM	FLASH TALKS – ROUND 2
2:30 PM TO 3:30 PM	KEYNOTE LECTURE JEFFREY MACKLIS & JOHN FROBERG, HARVARD UNIVERSITY <i>Building a brain and its cerebral cortex requires subcellular regulation beyond transcription: Neuronal subtype-specific translational regulation, ribosomal complexes, and circuit-specificity in development and degeneration</i>
3:30 PM	CLOSING REMARKS
3:45 PM TO 5:00 PM	POSTER SESSION 2 – <i>proceed down the staircase to the Stowers Gallery</i> <i>Light snacks and refreshments are available at the base of the stairs.</i>
5:30 PM TO 7:30 PM	CLOSING RECEPTION – LINDA HALL LIBRARY <i>A shuttle is available to take you to the Linda Hall Library.</i> <i>Tours of their Rare Books Collection will take place every 20 minutes.</i> <i>Small bites, desserts, and refreshments available.</i>

Poster Sessions

Poster Session

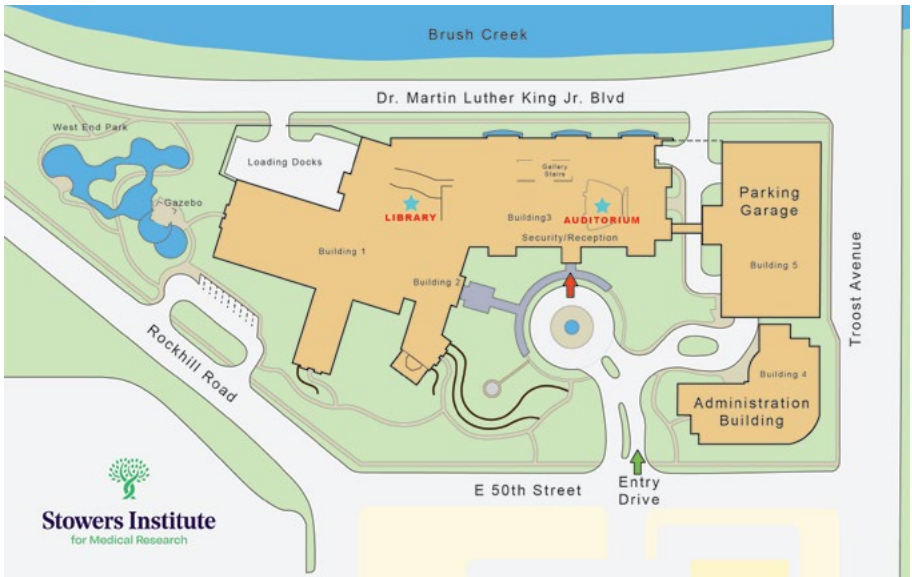
Poster Session 1, odd numbers: Thursday, October 22 | 5:15 PM – 6:30 PM

Poster Session 2, even numbers: Friday, October 23 | 3:45 PM – 5:00 PM

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Campus Map



All **talks** will be presented in the Auditorium.

**Food and beverages are not allowed inside of the auditorium.*

Breaks will be in the hallway outside of the auditorium.

Lunch will be in the Stowers library.

Poster Session will be in the Gallery, down the staircase outside of the auditorium.

Conference Room 114 is reserved as a **workspace**.

** Food and beverages are allowed inside Conference Room 114.*

Shuttle Schedule



A shuttle will run between the [Kansas City Marriott – Country Club Plaza Hotel](#) (4445 Main St, Kansas City, MO 64111) and the Stowers Institute for Medical Research (1000 E. 50th St, Kansas City, MO 64110) at the times listed below:

Wednesday, October 21:

12:30 PM & 1:00 PM Pick up at Marriott Hotel, drop off at Stowers
7:00 PM & 7:30 PM Pick up at Stowers, drop off at Marriott Hotel

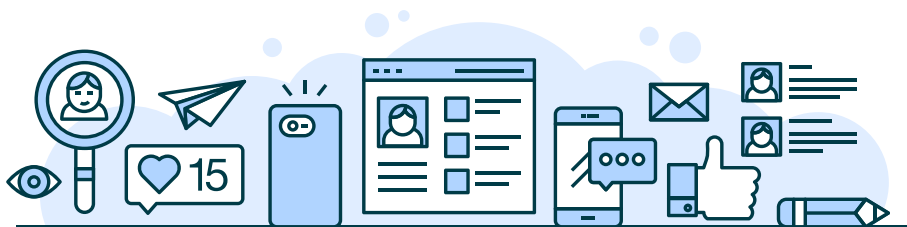
Thursday, October 22:

8:30 AM & 9:00 AM Pick up at Marriott Hotel, drop off at Stowers
7:15 PM & 7:45 PM Pick up at Stowers, drop off at Marriott Hotel

Friday, October 23:

8:30 AM & 9:00 AM Pick up at Marriott Hotel, drop off at Stowers
5:00 PM Pick up at Stowers, drop off at Linda Hall Library
7:30 PM Pick up at Linda Hall, drop off at Marriott Hotel & Stowers

SRC Social Media Guidelines



The Stowers Research Conference organizers **encourage** the use of social media to **share information and network** with other attendees.

We remind you to **remain courteous and respectful** in your comments and posts.

Avoid sharing speaker or poster presentation content that's not your own, copyrighted or trademarked, or material protected by other intellectual property rights.

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@Stowers_SRC on [X \(Twitter\)](#)

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social** on [Bluesky](#)

Use hashtag **#SRCKC26**

Invited Speakers



Jeffrey Macklis (Keynote)

Harvard University

[!\[\]\(65669ef2a9341eca7c5ba6092e766555_img.jpg\) Lab Website](#)



Homa Ghalei

Emory University

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Arvind Rasi Subramaniam

Fred Hutch Cancer Center

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Xiao Wang

Broad Institute

[!\[\]\(af26bfd2c3812732860041a1728b438b_img.jpg\) Lab Website](#)



Shu-Bing Qian

Cornell University

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Davide Ruggero

**University of California
San Francisco**

[!\[\]\(5334afa5a3acb96dca56ae8f5827da09_img.jpg\) Lab Website](#)



Scott Lindner

**Pennsylvania State
University**

[!\[\]\(1f09637acf4b1a7d07a6873de97df7d8_img.jpg\) Lab Website](#)



Sujatha Jagannathan

**University of Colorado
Anschutz**

[!\[\]\(061b2f98a688e3f5d47a49a3b4c1c4f9_img.jpg\) Lab Website](#)



William Faller

University of Bristol

[!\[\]\(fcb2f86e324283489f4f30c15dd97268_img.jpg\) Lab Website](#)



Michael Buszczak

UT Southwestern

[!\[\]\(21fc6be44ad8511f1af3a02d43c85c7f_img.jpg\) Lab Website](#)



Kotaro Fujii

University of Florida

[!\[\]\(4eabcca32659c44935a6b5196a8918a0_img.jpg\) Lab Website](#)



Julie Aspden

University of Leeds

[!\[\]\(4d2abbb132275c6b7d14df9fb3e24ddb_img.jpg\) Lab Website](#)

Conserved Factors, Divergent snoRNAs: Two Ribosome Biogenesis Pathways in One Organism

Jui Feng Lu¹, Madelaine Gogol¹, Huzaifa Hassan¹, Hua Li¹, Kamena Kostova¹

¹Stowers Institute for Medical Research

Ribosomes have long been regarded as uniform machines, but it is now appreciated that cells can assemble structurally distinct ribosomes differing in rRNA sequence, rRNA modification, and protein composition. This ribosome heterogeneity constitutes an important layer of gene regulation, with demonstrated roles in development, cell differentiation, and the stress response. The assembly of a canonical ribosome is itself an extraordinarily regulated process, requiring more than 200 biogenesis factors along with a large complement of small nucleolar RNAs (snoRNAs) that guide site-specific rRNA cleavage and modification. How such a tightly controlled pathway is altered to accommodate the assembly of different types of ribosomes within the same organism remains unclear. Zebrafish, with its distinct maternal and zygotic ribosome types carrying unique rRNA compositions, provides a compelling model for investigating how ribosome heterogeneity is established.

Northern blot analysis revealed distinct rRNA banding patterns between maternal and zygotic stages, indicating that pre-rRNA is cleaved at different sites and that the two stages employ separate biogenesis pathways. RNA sequencing of ribosome biogenesis factors and snoRNAs showed that biogenesis factors are largely shared between stages, whereas snoRNA expression is highly differentiated, implicating snoRNAs rather than the core biogenesis machinery as the primary source of stage-specific ribosome maturation. This study aims to test this model directly, using CRISPR-Cas13d microinjection to deplete candidate biogenesis factors, predicted to be universally required and therefore lethal in all injected embryos, and to subsequently deplete stage-enriched snoRNAs to determine whether maternal snoRNAs act specifically within the ovary while zygotic snoRNAs act embryo-wide. This research will facilitate our understanding of ribosome biogenesis and its mechanisms. Ultimately, this work may uncover pivotal insights into gene expression regulation, cellular adaptation, and disease mechanisms, contributing to the broader landscape of molecular biology and offering potential avenues for therapeutic interventions.

Structural insights into the SBDS disease variants associated with Shwachman-Diamond Syndrome

Sinthyia Ahmed¹, Rajnandani Kashyap², Edwin Antony², Sofia Origanti¹

¹ Department of Biology, Saint Louis University, MO, USA

² Department of Biochemistry and Molecular Biology, Saint Louis University School of Medicine, MO, USA

Shwachman-Diamond Syndrome (SDS) is a rare autosomal recessive ribosomopathy that is characterized by dysfunction of the large 60S ribosomal subunit. The SDS phenotype entails poor growth and bone marrow dysfunction with an increased predisposition to leukemias. SDS is primarily associated with biallelic mutations in SBDS, a 60S maturation factor. SBDS cooperates with the EFL1-GTPase to release the anti-association factor eIF6 from the 60S subunit. The key maturation defect in SDS is the impaired eviction of eIF6 from the late cytoplasmic 60S subunits due to mutations in SBDS. Inability to release eIF6 prevents the joining of 60S and 40S ribosomal subunits and represses global protein synthesis. The mechanism through which the 60S-binding disease variants of SBDS inhibit release of eIF6 remains to be determined. In this study, by resolving the cryo-EM structures of wild type and pathogenic variants of human SBDS bound to human 60S, we have uncovered allosteric communications across the three domains of SBDS. Remarkably, disease mutations in domains II and III disrupt the key interactions of domain I of SBDS with the P-site loop of RPL10 (uL16) that is essential for the mature conformation of the peptidyl transferase center. The mutants also alter the dynamics of GTPase activating center. Thus, SBDS not only senses the integrity of P-site loop of RPL10 but is actively engaged in stabilizing the RPL10 loop and its interactions with the PTC. These findings provide a structural basis for understanding the SDS pathology.

NAT10 promotes the biogenesis of translationally competent m¹acp³Ψ-deficient ribosomes

Mahmood H Dalhat¹, Sharath Narayan¹, Daniel Arango¹

¹ Northwestern University

The ribosome is a ribonucleoprotein complex responsible for protein synthesis. Although initially considered invariable machines, recent findings show that ribosomes exhibit heterogeneity in protein composition and ribosomal RNA (rRNA) modifications, including the presence or absence of 1-methyl-3-(3-amino-3-carboxypropyl)-pseudouridine (m¹acp³Ψ). TSR3 catalyzes the final step of m¹acp³Ψ formation by transferring the aminocarboxypropyl (acp) group from S-adenosylmethionine to 1-methyl pseudouridine (m¹Ψ) at 18S rRNA. This modification, together with subsequent trimming of a 3'-terminal tail, is the defining feature distinguishing mature 40S from immature pre-40S subunits. Notably, m¹acp³Ψ levels are significantly reduced in the ribosomes of cancer cells, but the mechanism leading to m¹acp³Ψ loss remains poorly understood. Using deep mutational scanning, Nanopore direct RNA sequencing, and eCLIP-seq, we identified NAT10, an rRNA-modifying enzyme and oncogenic factor, as a direct regulator of m¹acp³Ψ deposition. We found that NAT10 enhances global 40S biogenesis while simultaneously preventing m¹acp³Ψ deposition by interfering with TSR3 activity. Remarkably, loss of m¹acp³Ψ has no effect on ribosome biogenesis or trimming of the 3'-terminal tail of pre-40S subunits. Instead, m¹acp³Ψ-deficient ribosomes are loaded into polysomes, and complete loss of m¹acp³Ψ increases translation efficiency and cell proliferation, indicating that m¹acp³Ψ-deficient ribosomes are functionally active and enhance cellular fitness. Given that loss of m¹acp³Ψ is a defining feature of cancer-associated ribosomes, these findings implicate NAT10 in promoting this cancer-specific rRNA signature and provide a mechanistic basis for the selective loss of m¹acp³Ψ in cancer.

Selective Inhibition of Eukaryotic Release Factor Accommodation Promotes Therapeutic Translational Readthrough of Premature Termination Codons

Saleem Bhat¹, Hanfei Wang¹, Asuma Janeena¹, Huile Zhu¹, Hong Li¹, David Chenoweth¹, Barry Cooperman¹

¹ Department of Chemistry, University of Pennsylvania

Nonsense mutations constitute ~20% of de novo germline mutations and ~12% of all human disease mutations, giving rise to premature termination codon (PTC) disorders. Currently, no FDA-approved therapies increase PTC readthrough efficiency. The translational readthrough-inducing drug (TRID) ataluren received conditional approval in Europe for Duchenne muscular dystrophy (DMD) from 2014–2025, but approval was withdrawn because of inconsistent clinical efficacy. Nevertheless, Ataluren has demonstrated low toxicity in clinical trials of several PTC disorders. Studies of its mechanism of action (MoA) by us and others show that ataluren selectively inhibits termination at PTCs but not normal termination codons (NTCs) and competitively inhibits binding of the release factor complex (RFC; eRF1-eRF3-GTP) to PTCs without inhibiting binding of aa-tRNA suppressor ternary complexes (TCs; aa-tRNA-eEF1A-GTP). We hypothesize that this selectivity contributes to Ataluren's low toxicity. Although release factors and aa-tRNAs occupy overlapping ribosomal sites, structural analyses reveal distinct molecular interactions with the ribosome, suggesting that selective disruption of release-factor accommodation may preserve aa-tRNA decoding. We identified ribosomal contact sites for eRF1 ("eRF1 pockets") that do not interact with aminoacyl-tRNA and designed peptide analogs targeting these sites. These peptides inhibit termination and promote readthrough in fully reconstituted in vitro eukaryotic translation assays, while mutations of eRF1 residues contacting these pockets markedly reduce termination efficiency, supporting their functional importance.

To identify small-molecule inhibitors of eRF1 binding, we performed structure-based virtual screening of ~17,400 clinically approved drugs using rDock. Three FDA-approved compounds—Telmisartan, Candesartan, and Candesartan cilexetil—selectively inhibited RFC-dependent termination with 5-, 10-, and 80-fold greater potency than Ataluren, respectively. These compounds retain Ataluren's MoA, inhibiting termination while promoting aa-tRNA-dependent readthrough. Our findings establish selective inhibition of RFC-dependent termination as a mechanistically distinct therapeutic strategy for PTC-associated disorders, such as cystic fibrosis, DMD, and many cancers, and highlight opportunities for drug repurposing.

Turnip Crinkle Virus Thrives in a Translation-Repressed Host Environment

Sarah Blachar¹, Alyssa M. Stanfield¹, Jared P. May¹

¹ Division of Biological and Biomedical Systems, School of Science and Engineering, University of Missouri-Kansas City, Kansas City, Missouri, USA

Plant cellular mRNAs typically contain a 5' methyl-guanosine cap and 3' poly(A) tail that promote transcript stability and efficient translation. In contrast, genomic and subgenomic RNAs produced by members of the Tombusviridae lack these canonical features and instead rely on alternative mechanisms to recruit the host translational machinery. Turnip crinkle virus (TCV) encodes a 3' cap-independent translation enhancer (3' CITE) within its 3' untranslated region that forms a tRNA-shaped structure (TSS) capable of directly interacting with the host 60S ribosomal subunit. Here, we investigate whether TCV exploits suppression of host translation to create a cellular environment that preferentially favors 3' CITE-dependent viral translation. TCV accumulated approximately three- to four-fold higher following a 72-h dark treatment, a condition associated with reduced cellular translation, compared with plants maintained under standard light-dark conditions. Consistent with this observation, RNA-seq revealed that TCV infection induces a transcriptional state resembling the dark response and strongly suppresses genes associated with the host translational machinery. Puromycin incorporation further demonstrated reduced global protein synthesis during TCV infection. Together, these findings support a model in which suppression of canonical host translation does not constrain TCV but instead may provide a competitive advantage to viral RNAs capable of 3' CITE-mediated translation. Ongoing translating ribosome affinity purification sequencing (TRAP-seq), using transgenic plants expressing GFP-tagged RPL18, will define changes in ribosome-associated host and viral RNAs during infection and determine whether 3' CITE-containing RNAs exhibit enhanced translational efficiency within this translation-repressed host environment.

MosaiX: Mosaic Sequence Allele Indexing – A Tool to Resolve the Identity and Abundance of Differentially Expressed Ribosomal RNA Alleles

Maxwell Shapiro*¹, Griffin A. Welfer*¹, Jose L. Alejo¹, Melanie Lloyd², Ti-Cheng Chang³, Sebastian Klinge⁴, Roger B. Altman¹, Geoff Neale², Gang Wu³, Scott C. Blanchard^{1,5}

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2 Hartwell Center, St Jude Children's Research Hospital, Memphis, TN, USA

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4 Laboratory of Protein and Nucleic Acid Chemistry, The Rockefeller University, New York, New York 10065, USA

5 Department of Chemical Biology & Therapeutics, St. Jude Children's Research Hospital, Memphis, TN, USA

Background: Physically distinct ribosomes have long been hypothesized to shape gene expression. In *Escherichia coli*, our team has shown that nutrient stress shifts rRNA expression to enrich translating ribosomes from the *rrnH* operon. Enrichment of *rrnH* alters RpoS levels, which reprograms transcription towards a stress-response phenotype (Kurylo Cell Reports 2018). Additionally, our population-scale genomics study revealed pervasive, population-stratified rRNA variation in humans. Variants found at comparable positions in mice 1] map to functional ribosomal centers, 2] exhibit tissue-specific expression, and 3] are present in actively translating ribosomes (Parks Science Advances 2018). While accurately quantifying ribosome subtype expression is critical to experimentally examining their physiological impacts, the complete repertoire of mammalian ribosome subtypes remains unresolved, partly due to nuances associated with specific sequencing platforms, the highly similar nature of rDNA alleles, and limitations of single-molecule variant phasing.

Results: To close this gap, we developed Mosaic sequence allele indexing (MosaiX), an integrated pipeline that resolves full-length rRNA subtypes and quantifies their relative abundance from any source of total RNA or DNA. MosaiX reconstructs the phased variant combinations that define the set of ribosome species in a sample, or "ribotype." Validation against biological controls of defined ribosome composition showed that MosaiX faithfully recovers the identity and relative abundance of ribosome subtypes making up the ribotype, while effectively suppressing technical noise. In the translating pool of human ribosomes, MosaiX identified coexisting 18S and 28S subtypes, revealing substantially greater diversity in the large subunit. Across

organs from isogenic littermate mice, MosaiX uncovered reproducible, tissue-specific ribotypes.

Conclusion: MosaiX provides a quantitative framework for mapping ribotypes across cell types, growth environments, tissues, and time. We are deploying it on public datasets and in independent and collaborative experimental systems to test whether changes in variant allele expression give rise to physically distinct translating ribosomes with programmatic phenotypic consequences.

When Neurons Fire, Ribosomes Respond: Capturing the Timing and Location of Activity-Dependent Translation

Kitra Cates, Ph.D1, Jinzhao Wang, Ph.D1, Yuxiang Chen, Ph.D1, Theo Susanto, Ph.D1, Adele Xu, MD, Ph.D1, Marius Wernig, MD, Ph.D1, Maria Barna, Ph.D1

1 Stanford University School of Medicine

How does a brief burst of neuronal activity produce lasting changes in the brain? Landmark studies established that new protein synthesis and ribosome activity are essential for the formation of long-term memories. Yet we do not understand how neuronal activity directs ribosomes to produce the right proteins at the right time and place, often at distant synapses. Because the presence of an RNA does not reveal whether, when, or where it is translated, a fundamental question remains: how are ribosomes remodeled to convert electrical signals into lasting synaptic change? Using RAPIDASH, a tag-free method for identifying ribosome-associated proteins, we discovered LLPH as an activity-responsive component of neuronal ribosomes. LLPH is a small, cell-permeable protein whose Aplysia homolog supports long-term facilitation via transcription-dependent processes unfolding over hours. We found that neuronal excitation causes LLPH to disengage from ribosomes within minutes, a timescale that precedes transcription-dependent facilitation, and that LLPH promotes the translation of unusually long mRNAs encoding proteins important for neural activity. Moreover, neurons expressing truncated LLPH were markedly more excitable than those expressing the normal protein. These findings connect a protein previously implicated in memory-related plasticity to the ribosome and suggest that its regulated ribosome association may help couple neuronal activity to lasting functional change. To capture this spatial dimension in vivo, we generated the RiboBeacon mouse, which incorporates a light-controlled system to label and isolate ribosomes for the first time from selected neuronal compartments during optogenetic stimulation of active neuronal circuits in the mammalian brain. This mouse enables a spatial map that simultaneously demarcates translated transcripts and ribosome remodeling in different parts of the neuron. By revealing how this regulation occurs within intact neural circuits, this work will reframe the ribosome's role in learning and memory and how it may become disrupted in neurological and neurodevelopmental disorders.

Ribo-Tweezer Reveals Ribosomal Proteins as Regulators of Selective Translation and Cell Identity

Yuxiang Chen¹, Ching Pin Cheng¹, Kitra Cates¹, Georgi K Marinov¹, Travis C Lantz¹, Haojun Yang², Isabelle Liu², Naomi R Genuth¹, Christina Andronescu¹, Victoria Hung¹, Abel Bermudez¹, Daphna Rothschild¹, Joseph Georgeson³, Sonia Bustos Barocio¹, Anshul Kundaje¹, Sharon Pitteri¹, Davide Ruggero², Maria Barna¹

¹ Stanford University

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The ribosome is a ribozyme, but it may also act as a dynamic regulator of gene expression. Although ribosomal protein (RP) composition varies, dissecting the functional contributions of individual RPs beyond housekeeping roles has been challenging due to a lack of tools for selective manipulation *in situ*. Here, we developed Ribo-Tweezer, an auxin-inducible degron (AID)-based system enabling rapid, reversible, and selective depletion of individual RPs. Applying Ribo-Tweezer in mouse embryonic stem cells (mESCs), we fused the auxin receptor Tir1 to the late-joining RP RPS26, restricting proteasomal degradation to mature ribosomes and achieving greater specificity and efficiency than conventional AID approaches. Using Ribo-Tweezer to deplete RACK1, we recapitulated its established role in ribosome quality control and uncovered additional functions in translation regulation. We identified a rare subset of cellular mRNAs with poly(A/U)-rich 5'-UTRs whose translation depends on RACK1, paralleling its role in cap-independent translation of poxvirus poly(A)-leader mRNAs—suggesting a conserved determinant of RACK1-selective translation. Among the most prominent RACK1-dependent targets were KRAB-ZNF transcriptional repressors; loss of their translation derepresses LINE1 expression, revealing a translation-to-transcription axis that amplifies ribosome-mediated control into broader gene-expression programs. Given the link between LINE1 regulation and pluripotency, we extended RACK1 depletion over longer timescales and found it drove a reversible differentiation trajectory from pluripotent mESCs toward a neural ectodermal fate—revealing an unexpected requirement for a single RP in maintaining stem cell identity. Finally, extending Ribo-Tweezer to the P-stalk proteins RPLP0 and RPLP1, ribosome profiling revealed distinct translational programs for each, including RPLP1's known role in ER-associated translation. Together, these results demonstrate that individual RPs exert non-overlapping regulatory functions, establishing Ribo-Tweezer as a tool for dissecting RP function in gene regulation.

Leaky scanning drives translation of downstream overlapping Open Reading Frames

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Downstream overlapping Open Reading Frames (doORFs) are translated regions that overlap with the main coding sequence and extend into the 3' untranslated region. Their widespread presence across mammalian transcriptomes suggests an important role as regulators of gene expression; however, their annotation remains incomplete and the mechanisms driving their translation are poorly understood. To overcome the challenge of doORFs detection, we merged thousand publicly available ribosome profiling libraries and established a confidence classification system which was compared with Immunopectidome data, confirming that doORFs produce detectable peptides. As they are positioned closer to the 5' cap, suggesting non-random transcript organization, we hypothesized that leaky scanning is the main mechanism driving doORF translation and the translation efficiency depends on the distance from the 5' cap to the doORF start codon, the strength of Kozak sequence recognition, and the availability of initiation factors.

To evaluate leaky scanning, we developed a reporter system to detect the expression of proteins encoded in the main as well as in the doORF. Mutations in the start site of the canonical ORF resulted in increased expression of the doORF consistent with leaky scanning. Moreover, when we evaluated the importance of the Kozak sequence in leaky scanning we found that improving Kozak sequences in the canonical ORF resulted in an increased expression of the main ORF causing a decreased doORF expression compared to wild-type Kozak sequences. Interestingly, worsen Kozak sequences resulted in completely abolish expression of the main ORF with a concomitant increased in doORF expression mimicking the results observed mutating the start codon.

Altogether these preliminary results indicate that we were able to identify doORFs from publicly available data sets which were confirmed by our reporter system, suggesting that leaky scanning is the main driven mechanism of doORF expression although we cannot exclude contribution of other non-canonical mechanisms.

Quantitative proteomics reveals differential translation factor binding between maternal and zygotic ribosomes in zebrafish

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Ribosomes are essential for protein synthesis, translating mRNAs into functional proteins. Although traditionally viewed as uniform machines, recent work has revealed that ribosomes can differ in composition in response to developmental cues, stress, or disease. However, how this heterogeneity affects the ability of the ribosome to interact with translation factors, chaperones, and other regulators remains poorly understood. Zebrafish provides a powerful system to address this question because they exhibit an extreme form of ribosome heterogeneity, where two types of ribosomes, maternal and zygotic, differ in all four ribosomal RNAs. Here, we use quantitative proteomics to investigate how changes in the rRNA sequence and structure affect interactions with protein factors. To determine whether maternal and zygotic ribosomes co-evolved with a unique set of translation factors that differ in availability across development, we performed data-independent acquisition (DIA) proteomics and reanalyzed publicly available zebrafish embryo datasets spanning the 1-cell stage to 5 days post-fertilization. Surprisingly, these data show that most translation factors are present throughout development. To test whether functional differences can arise from differential binding, we used TMT-based quantitative proteomics to compare proteins bound to purified maternal and zygotic ribosomes after puromycin treatment and high-salt washes that disrupt weak protein interactions. These analyses confirmed distinct protein compositions between ribosome types, including enrichment of Rpl5a in zygotic and Rps17 in maternal ribosomes, and further revealed that multiple translation factors are differentially associated with each population. Notably, poly(A)-binding protein (PABP), a key regulator of polyadenylated mRNA translation, is preferentially associated with zygotic ribosomes. Together, these results indicate differential factor binding affinities as a key mechanism by which heterogeneous ribosomes regulate translation, with broad implications for development, disease, and other biological processes.

Ribosome specialization links organelle translation to adipose tissue metabolic flexibility

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Survival in a changing environment requires tissues to rapidly adapt their protein composition to shifts in nutrient availability, energy demand, and cellular stress. Metabolism and translation therefore evolved as deeply interconnected systems, yet how they are coordinated across space within cells remains largely unknown. This question is especially important in adipose tissue, which must continually transition between energy storage and expenditure. White adipocytes store and mobilize lipids, whereas brown adipocytes consume nutrients through mitochondrial oxidative phosphorylation and branched-chain amino acid (BCAA) catabolism. Obesity impairs these transitions, driving metabolic inflexibility, insulin resistance, and cardiometabolic disease. Our findings suggest that ribosomes positioned at lipid droplets (LDs) and mitochondria form a spatially organized translational network that rapidly remodels organelle proteomes in response to metabolic demand. I have built on two technologies in our laboratory: ALIBi, which optogenetically labels organelle-proximal ribosomes, and RiboExM, which visualizes individual ribosomes by expansion microscopy to LDs and mitochondria that provides invaluable resolution on how ribosome composition, localization, and translational output are coordinated within the same cellular system. Our preliminary findings uncover striking evidence for this mechanism. RiboExM reveals a twofold enrichment of polysomes at LD-LD contact sites, identifying unexpected hotspots of localized translation. At mitochondria, ribosomes lacking the sub-stoichiometric protein RPS25 are enriched at the outer membrane and preferentially translate nuclear-encoded mitochondrial and BCAA-catabolic transcripts. BAT-specific RPS25 loss of function increases mitochondrial oxygen consumption, produces smaller, more oxidative LDs, and improves glucose clearance without disrupting adipocyte differentiation. Together, these studies establish how specialized ribosome populations connect nutrient sensing to organelle remodeling and whole-body physiology. This framework explains how cells execute rapid, localized, reversible metabolic responses across physiological and disease states. More broadly, they define spatial ribosome specialization as a fundamental mechanism by which cells adapt their proteomes and how its failure may drive metabolic disease.

Widespread Functional Translation of Downstream Open Reading Frames Across the Human Transcriptome

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Beyond canonical ORFs, non-canonical ORFs occur within untranslated regions of eukaryotic mRNAs. Downstream ORFs (dORFs) initiate translation downstream of the canonical start codon and include overlapping dORFs (doORFs), which begin within the coding sequence and extend into the 3' untranslated region (3'UTR), and non-overlapping dORFs located entirely within the 3'UTR. Conservation across eukaryotes suggests evolutionary constraint consistent with functional translation, yet their annotation remains incomplete and the mechanisms driving their translation are poorly understood, partly because overlapping regions dilute CDS-derived ribosome profiling signal.

We aggregated ribosome profiling data from a large collection of publicly available libraries and developed a confidence-based classification system for dORFs (high-confidence, low-confidence, inconclusive) based on transcriptome-wide translation signatures. Validation against HLA immunopeptidomic datasets revealed a dose-response relationship: high-confidence dORFs yielded significantly more peptide identifications than low-confidence or inconclusive candidates, confirming that dORFs produce detectable peptides.

High-confidence dORFs were significantly enriched proximal to the 5' cap, indicating non-random transcript organization consistent with leaky scanning as the primary mechanism of dORF translation, whereby efficiency depends on cap-to-start-codon distance, ATG context strength, and initiation factor availability.

We tested this model using a dual-reporter system in HEK293T cells, in which the canonical ORF is N-terminally FLAG-tagged and a high-confidence doORF is fused to EGFP in an alternative reading frame. Manipulating canonical initiation produced reciprocal effects on doORF expression: disrupting the canonical start codon or weakening its sequence context increased doORF translation, whereas optimizing the context enhanced canonical translation and suppressed doORF expression, confirming leaky scanning as the driving mechanism.

Together, these results establish that dORF translation is functional and widespread across the human transcriptome, driven primarily by leaky scanning, and uncover a regulatory axis in which canonical ORF initiation efficiency, governed by ATG context, directly controls both transcript stability and protein diversity generated from a single transcript.

A new type of ribosome in the zebrafish germline

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Zebrafish (*Danio rerio*) undergo a remarkable shift in the composition of their ribosomes, the machinery responsible for protein synthesis. This heterogeneity has been reported to be driven by two divergent 45S ribosomal RNAs (rRNAs), the maternal and somatic rRNAs, that are transcribed in tissue-specific patterns. The maternal 45S is primarily expressed in oocytes, whereas the somatic 45S is expressed in all adult somatic tissues. However, by performing long-read sequencing of zebrafish DNA, we identified a third type of 45S gene that displays sequence divergence from both the maternal and somatic genes. This new 45S gene was completely uncharacterized, leading us to speculate that deciphering its expression pattern would shed light on its function. We observed that this new 45S gene, termed “germinal 45S”, is expressed in primordial germ cells and incorporated into ribosomes. Hence, we hypothesized that the germinal ribosomes possess specialized functions in the zebrafish germline. To test this, we first determined whether the germinal 45S is expressed in the adult zebrafish germ cells. We utilized publicly available scRNA-seq datasets and found that the germinal 45S is primarily expressed in the germline stem cells (GSCs) of both the ovary and testis. These results were further confirmed by germinal rRNA staining in histological sections of the zebrafish gonads. To address whether the germinal 45S is essential for GSC survival, we used CRISPR-Cas9 to produce a germinal 45S knockout. Our results revealed a strong male bias in the FO₁ phenotype consistent with GSC cell death and sex reversal in zebrafish. Future work will further dissect this knockout to determine its impact on GSC survival. Collectively, these findings illuminate a previously unrecognized layer of ribosome heterogeneity in zebrafish with direct implications for germline biology, reproduction, and sex determination.

Unraveling quality control pathways targeting defective ribosomes in ribosomopathies

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Ribosomopathies are inherited disorders marked by anemia, bone marrow failure, skeletal defects, neurocognitive impairment, and elevated cancer risk, and are caused by mutations in genes required for ribosome biogenesis and maturation. In these diseases, defective ribosomal intermediates are selectively degraded, creating a shortage of functional ribosomes that impairs global translation and cellular homeostasis, yet the surveillance pathways that recognize and eliminate aberrant particles remain poorly defined. Here, we establish a human Diamond-Blackfan anemia (DBA) model driven by RPS19 haploinsufficiency and use it to uncover a previously unrecognized ribosome quality control pathway targeting defective 40S subunits for degradation. Di-glycine remnant proteomics mapped ubiquitination sites on ribosome biogenesis intermediates, providing direct evidence that aberrant pre-40S particles are ubiquitin-marked for clearance. To systematically identify the factors executing this surveillance, we performed a whole-genome CRISPRi screen for defective ribosome clearance and revealed an unexpected quality control role for the cell-cycle regulators CDC20 and PLK1. Depletion of either factor by CRISPRi stabilized defective ribosomal intermediates and restored 40S ribosomal protein levels in RPS19-deficient cells. Consistent with a direct function in this pathway, proximity ligation assays showed selective association of CDC20 and PLK1 with defective ribosomal intermediates in RPS19-deficient but not wild-type cells. Notably, CDC20 or PLK1 depletion similarly stabilized defective ribosome intermediates generated by RPS10 or RPS26 depletion, indicating that these factors act as master regulators operating across multiple DBA-associated perturbations of pre-40S biogenesis. Together, our work identifies a previously unrecognized quality control axis linking core cell-cycle regulators to ribosome homeostasis and establishes CDC20 and PLK1 as key mediators of defective ribosome surveillance, providing new mechanistic insight into ribosomopathy pathogenesis and fundamental principles of ribosome biogenesis fidelity.

Selective translational activation drives *Toxoplasma* latency

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The obligate intracellular parasite *Toxoplasma gondii* cycles between its rapidly growing tachyzoite stage and latent bradyzoite stage in a stress-dependent manner. Parasite latency is coordinated by the selective translational activation of BFD1 mRNA, which encodes a transcription factor that is necessary and sufficient to initiate and maintain parasite latency. Governed by a 2.7kb long 5'UTR, we have shown that stress-dependent translation of BFD1 mRNA occurs independently of eIF4E1 but requires recognition of its 5'UTR by the CCCH zinc finger RNA binding protein, BFD2/ROCY1. Interactome studies of BFD2 have revealed that it binds MKT1 and PBP1, which form a complex that coordinates cell differentiation and mRNA-specific translational control in other eukaryotes. In pursuing this complex, we have determined that MKT1 is required for *Toxoplasma* latency and that it is associated with a pseudouridine synthase, suggesting that stress-induced, BFD2-driven increases in mRNA pseudouridylation may contribute to cellular differentiation and latency.

Ribosomal protein (RP) paralog-specific phenotypes arise from expression divergence and converge on RP dosage-dependent molecular programs

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Ribosomal proteins (RPs) are commonly encoded by paralogous genes in eukaryotes. Despite their conserved role as structural components of the ribosome, disruption of an individual RP paralog often generates a phenotype distinct from that of its sister paralog. However, whether RP paralog-specific phenotypes arise from expression divergence or protein sequence divergence remains controversial. Broad analyses across various RP paralog pairs and direct mechanistic tests, including coding-sequence swaps, are generally lacking. Here, we systematically interrogated 19 RP paralog pairs in *Schizosaccharomyces pombe*, assessing both expression and protein sequence-based mechanisms. Notably, 15 of the 19 pairs exhibited paralog-specific effects on growth rate and heat-shock tolerance across growth phases. Gene-swap assays and multi-omics profiling demonstrated that these prevalent RP paralog-specific phenotypes are driven by expression divergence rather than by protein sequence variation. Furthermore, RP paralog mutants with matched growth rates converge on similar transcriptomic and proteomic states, while *rps* and *rpl* paralog mutants also exhibit 40S- and 60S-specific molecular features. These results support gene dosage balance as a major constraint shaping RP paralog evolution, with expression divergence likely underlying their long-term retention. More broadly, this work provides insights into how tissue-specific RP expression and altered RP dosage may modulate downstream molecular programs in ribosome-related diseases.

Decoding tRNA Gene Redundancy: Sequence Variation Drives Functional Diversification of tRNA-Derived RNAs

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The human genome encodes hundreds of transfer RNA (tRNA) genes despite requiring only 61 codons for protein synthesis. Although this redundancy expands with organismal complexity, the biological significance of individual tRNA isodecoders remains poorly understood. Here, we demonstrate that tRNA isodecoders can be repurposed into functional tRNA-derived RNAs (tDRs) and that subtle sequence differences among isodecoders generate regulatory molecules with distinct mechanisms of translational control.

We identified specific isodecoders of tRNA-His-GTG and tRNA-Gly-GCC that give rise to unique repertoires of 5'-tDRs. A subset of these molecules contains an AUG motif and potentially represses both cap-dependent and cap-independent translation. Mechanistically, these AUG-containing tDRs compete with capped mRNAs for ribosome binding, thereby inhibiting protein synthesis. We next examined 5'-tDRs derived from tRNA-Ala-AGC and tRNA-Cys-GCA, which are unique in their ability to self-assemble into intermolecular guanine quadruplexes (G4s) through 5'-terminal oligoguanine (5'-TOG) motifs. Because many tRNA isodecoders harbor single-nucleotide variants (SNVs) adjacent to these motifs, we investigated how these variations affect tDR function. Remarkably, the nucleotide context surrounding the 5'-TOG motif emerged as a critical determinant of both G4 assembly and translational repression. SNVs flanking the 5'-TOG motif altered the formation and stability of multimolecular G4 structures and dictated the mechanism by which tDRs suppress translation. While some variants function through G4-dependent pathways that target the translation initiation complex, others operate through G4-independent mechanisms that resemble direct competition with mRNA-ribosome interactions.

Together, our findings reveal that tRNA isodecoder diversity extends beyond canonical decoding functions by generating regulatory tDRs with distinct structural and functional properties. These results uncover a mechanistic basis for the biological significance of tRNA gene redundancy and establish tRNA sequence variation as an additional layer of tDR-mediated gene regulation.

How does ribosome heterogeneity impact translation?

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Recent advances in structural biology and biochemistry have revealed the dynamic structure of ribosomes. For example, variance in ribosome composition can range from RNA and protein modifications to differential incorporation of ribosomal protein paralogs. It has been hypothesized that ribosome heterogeneity alters translation kinetics. Directly testing this hypothesis, however, requires isolating highly pure ribosome populations, a task made experimentally inaccessible by the spatial intermixing of these subtle subpopulations within a single cell. These challenges are uniquely circumvented in the dual ribosome system of zebrafish. Zebrafish express two structurally distinct ribosome populations that are temporally segregated. The “maternal” ribosome form is expressed in oocytes and is the sole ribosomal population throughout early embryogenesis until gradual replacement by the “zygotic” form post zygotic genome activation. To understand whether structural differences confer functional specialization, we have developed an in vitro translation system using reconstituted maternal and zygotic ribosomes. In bulk, we measure that maternal ribosomes produce less total protein than zygotic ribosomes. Translation is a highly complex process, however, and to gain mechanistic insight of the underlying kinetic parameters distinguishing maternal and zygotic ribosomes, we expanded the in vitro translation system with nascent-chain labeling and TIRF microscopy. This platform allows us to track individual translation events with high sensitivity to resolve differential initiation efficiency and elongation rates between maternal and zygotic ribosomes. This single-molecule imaging of in vitro translation approach is the first technique to thoroughly investigate how ribosome heterogeneity impacts the kinetics of translation.

Spatio-temporally regulated maternal RNA decay factor essential for zebrafish development

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The maternal-to-zygotic transition (MZT) requires extensive remodeling of the embryonic transcriptome, including the timely clearance of maternally deposited mRNAs. Although the temporal regulation of maternal mRNA decay has been studied extensively, how transcript degradation is controlled across space during early vertebrate development remains poorly understood. Here, we identify *cth1* as the first known maternally encoded spatiotemporally regulated RNA-decay factor in vertebrates outside the germline. By integrating SLAM-seq with single-cell RNA-seq, we found that *cth1* is highly abundant maternally and undergoes rapid, spatially restricted decay during early zebrafish development. CRISPR-Cas9 mutants revealed an essential role for Cth1 in gametogenesis and fertility, preventing analysis of maternal-zygotic mutants. We therefore used RfxCas13d-mediated depletion of *cth1* transcripts, which caused delayed development and severe anterior-posterior patterning defects. Mechanistically, Cth1 acts independently of zygotic genome activation and promotes the decay of maternal transcripts enriched for AU-rich sequences in their 3'UTRs. We further identified conserved cis-elements within the *cth1* 3'UTR that control its spatio-temporal localization and stability. Together, our findings reveal Cth1 as a key component of the maternal regulatory program and provide direct evidence that maternal mRNA decay is controlled not only temporally but also spatially during vertebrate embryogenesis outside the context of germ cells. These results establish spatiotemporally regulated RNA stability as an important layer of post-transcriptional control during early development.

From Screens to Mechanism: Discovering Translational Activators for Human Disease

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Medicine has learned how to inhibit nearly every major step of protein synthesis, yet it has almost no means of increasing protein production when insufficient translation drives disease, as in Diamond-Blackfan anemia (DBA), amyotrophic lateral sclerosis (ALS), and the thousands of haploinsufficiency disorders defined by inadequate protein output. Here we ask whether deficient translation can instead be pharmacologically corrected. We developed a translation activator discovery toolbox

that couples O-propargyl-puromycin (OPP) labeling of nascent peptides with high-throughput microscopy, allowing global protein synthesis to be measured directly at single-cell resolution across chemical libraries, and pairs it with a novel inducible genome-wide, CRISPRi modifier screen using the same OPP readout. To sensitize the platform, we lowered global translation by approximately 60% through knockdown of Ribosomal Protein RPL11, modeling the deficit observed in DBA. In a pilot screen we unexpectedly identified macrolide antibiotics, best known for inhibiting bacterial ribosomes, as mammalian translation activators; the clinically favorable analog azithromycin (AZI) nearly restored protein synthesis in RPL11-deficient cells. Remarkably, AZI increased hemoglobin and extended survival in a lethal DBA mouse model of bone marrow failure in vivo. Photoaffinity chemical proteomics and CRISPRi converged on RUVBL1, the catalytic core of the cotranslational PAQosome chaperone complex, and on its client EFTUD2, which moonlights as a ribosome-associated protein, revealing a previously unrecognized ribosome-associated chaperone axis that mediates AZI-induced protein synthesis. Expanding the screen to more than 10,000 bioactive and clinically tested compounds, we identified an additional 91 activators spanning diverse chemical classes and mechanisms. One compound, indomethacin, restored erythroid differentiation in an ex vivo DBA model and protected primary neurons from TDP-43-induced degeneration and death in an ALS/FTD model. Together, these findings establish a discovery-to-mechanism pipeline for translation activators and position pharmacological enhancement of protein synthesis as a therapeutic strategy across mechanistically distinct diseases.

Ribosome biogenesis

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Ribosome biogenesis is a highly regulated process essential for protein synthesis that occurs within the nucleolus, a membraneless, liquid-like organelle. Although nucleolar architecture is known to change in response to stress and disease, how it is dynamically remodeled to accommodate changing translational demands during cellular development remains poorly understood. Here, we use zebrafish oogenesis as a developmental model involving rapid growth and protein synthesis demands to study the dynamics of nucleolar architecture, throughout oocyte development. Here, we discovered changes in nucleolar number, volume, sub-nuclear distribution and layering throughout oogenesis. We further show that these nucleoli assemble around extrachromosomal maternal rDNA circles. Interestingly, we also found that mouse oocytes undergo similar changes in nucleolar layering, suggesting that nucleolar remodeling is broadly conserved across vertebrate oogenesis. These findings suggest that the nucleolus is a dynamically regulated structure that undergoes developmentally programmed remodeling to meet the biosynthetic needs of the developing oocyte.

HSP-1/HSPA8 directs selective translation towards longevity or immunity

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As organisms age there is a progressive decline in protein homeostasis, yet how mRNAs are selectively translated during aging remains poorly understood. Since cells do not have limitless energy, choices must be made as to which set of proteins are translated at the expense of other proteins which might be less essential. Here, we identify that the Hsp70 chaperone protein HSP-1/HSPA8 binds to the ribosome and helps to direct selective translation in *Caenorhabditis elegans*. We find that depletion of HSP-1, specifically in the intestine, accelerates aging and abolishes the longevity conferred by reduced translation. Intestinal transcriptome profiling revealed that HSP-1 depletion decreases ribosome occupancy on lysosomal transcripts while increasing occupancy on immune- and stress-response mRNAs, including MAPK pathway components. This translational shift activates the p38 TIR-1-MAPK innate immune pathway and impairs autophagy through impaired lysosomal acidification. Similarly, depletion of the human ortholog HSPA8 increases p38 phosphorylation and decreases lysosomal acidification suggesting that this could be a conserved regulator of selective translation. Although this response enhances resistance to bacterial infection in *C. elegans*, it comes at the cost of shortened lifespan, revealing a trade-off between host defense and longevity. While decreased lifespan is dependent on the autophagy pathways, increased resistance to infection depends on the p38-MAPK pathway. Together, these findings identify HSP-1 as a ribosome-associated chaperone that couples selective translation to autophagy, innate immunity, and aging.

m6A alters ribosome dynamics to initiate mRNA degradation

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Degradation of mRNA containing N6-methyladenosine (m6A) is essential for cell growth, differentiation, and stress responses. Here, we show that m6A markedly alters ribosome dynamics and that these alterations mediate the degradation effect of m6A on mRNA. We find that m6A is a potent inducer of ribosome stalling, and these stalls lead to ribosome collisions that form a unique conformation unlike those seen in other contexts. We find that the degree of ribosome stalling correlates with m6A-mediated mRNA degradation, and increasing the persistence of collided ribosomes correlates with enhanced m6A-mediated mRNA degradation. Ribosome stalling and collision at m6A is followed by recruitment of YTHDF m6A reader proteins to promote mRNA degradation. We show that mechanisms that reduce ribosome stalling and collisions, such as translation suppression during stress, stabilize m6A-mRNAs and increase their abundance, enabling stress responses. Overall, our study reveals the ribosome as the initial m6A sensor for beginning m6A-mRNA degradation.

Ribosomal protein paralog switching modulates translation elongation rates and protects against pathological cardiac aging

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Heart and skeletal muscle cells generate heterogeneous ribosomes by replacing the essential ribosomal protein RPL3 with its paralog RPL3L in a process called paralog switching. Paralog switching occurs when RPL3L is induced in muscle cells during development, which downregulates RPL3 by activating a poison exon within RPL3 mRNA. During adult hypertrophy, this pattern is reversed as RPL3L is transiently downregulated, concomitant with RPL3 upregulation. The physiological purpose of both the initial induction of heterogeneous RPL3L ribosomes and the subsequent reversion to canonical RPL3 ribosomes remains unclear.

The significance of paralog switching is evident in patients with severe neonatal heart failure caused by RPL3L missense mutations, which are non-functional for translation while simultaneously inhibiting RPL3 upregulation. In contrast, Rpl3l knockout mice survive to adulthood, while Rpl3 remains uninhibited and thus maintains expression in adult muscle. As RPL3 induction in patients represents a clear therapeutic avenue, a greater understanding of the functional differences between RPL3 and RPL3L ribosomes is required.

To identify these differences, we investigated paralog ribosome function using human cell culture models. Through multiple orthogonal assays to measure nascent translation, we discovered that RPL3L ribosomes have reduced protein synthesis independently of ribosome abundance. Synthesis is reduced at the level of elongation, which coincides with higher fidelity and altered codon occupancies for RPL3L ribosomes. By generating paralog chimeras in an RPL3 knockout background, higher fidelity of RPL3L ribosomes was traced to the N-terminal extension embedded within the ribosome.

To investigate the long-term impact of RPL3-induced higher protein synthesis in the heart, we generated cardiomyocyte-specific Rpl3l knockout mice. In 12-month-old mice, chronic Rpl3 expression reduces cardiac function and produces an epigenetic signature associated with pathological aging. Together, our findings demonstrate that muscle-specific paralog switching is essential for long-term cardiac homeostasis through translation elongation modulation.

Restoring CELF2 Disrupts SREBF1/2-Dependent Lipid Metabolic Reprogramming to Suppress Colorectal Cancer

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Background: Metabolic reprogramming is a hallmark of colorectal cancer (CRC), with dysregulated cholesterol and fatty acid metabolism driving tumor growth and metastasis. Key lipogenic enzymes have emerged as promising therapeutic targets for restraining tumor progression, and while the genetic basis of these metabolic alterations has been extensively characterized, the post-transcriptional mechanisms governing lipogenic metabolism remain poorly understood. This study investigates the role of the RNA-binding protein CELF2 in regulating genes involved in lipid metabolism and CRC progression.

Results: Stable CRC cell lines (DLD1 and HCT116) expressing CELF2, alongside vector controls, were generated via lentiviral transduction. CELF2 restoration inhibited proliferation and migration in-vitro and suppressed tumor growth in xenograft models. Integrated transcriptomic and proteomic analyses revealed that CELF2 broadly represses lipid metabolic pathways by targeting the master lipogenic regulators SREBF1 and SREBF2, leading to reduced expression of key enzymes in cholesterol biosynthesis (HMGCS1, HMGCR, FDFT1, LDLR) and fatty acid synthesis (ACACA, FASN, SCD1). Mechanistically, crosslinking immunoprecipitation (CLIP)-coupled RT-PCR confirmed direct binding of CELF2 to SREBF1/2 mRNAs at the 3'UTR, which was further confirmed using dual-luciferase reporter assays. Additionally, polysome profiling showed that CELF2 suppresses SREBF1/2 translation by redistributing SREBF1/2 transcripts from actively translating to translationally inactive ribosomal fractions. Functionally, CELF2 reduced mitochondrial respiration and glycolytic activity, driving CRC cells toward a hypometabolic state.

Conclusion: CELF2 acts as a critical post-transcriptional brake on lipid metabolic reprogramming in CRC, directly binding SREBF1/2 transcripts to repress their translation and thereby restrain de novo lipogenesis. This CELF2–SREBF axis defines a previously unrecognized layer of metabolic control in CRC, linking RNA-binding protein activity to the lipogenic phenotype that fuels tumor growth. By identifying CELF2 loss as a driver of metabolic rewiring, these findings nominate CELF2 both as a mechanistic tumor suppressor node and as a therapeutic entry point for targeting metabolic vulnerabilities in CRC.

Licensing 60S for translational debut by SBDS and eIF6

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Surveillance of the mature conformation of the 60S catalytic center by SBDS and eviction of eIF6 is essential to license 60S for translation. eIF6 is released from the 60S by the coordinated action of SBDS and the EFL1-GTPase. In Shwachman-Diamond syndrome, mutations in SBDS impair the eviction of eIF6 from 60S. However, the mechanism of how disease-associated missense variants of SBDS that retain 60S binding disrupt 60S licensing and eIF6 eviction remains poorly understood. To address this question, we determined high-resolution Cryo-EM structures of wild type and disease-associated missense variants of SBDS bound to the human 60S. These structures reveal that pathogenic SBDS variants perturb the mature conformation of the peptidyl transferase center and remodel the GTPase-activating center. In addition to the proof-reading activity of SBDS, we find that 60S licensing is also regulated by phosphorylation of eIF6 at the S239 site that we had previously uncovered. Our studies showcase an important role for S239 phosphorylation in maintaining the stability of free pools of eIF6. Depleting the free cytoplasmic pool of eIF6 alters ribosomal subunit balance and attenuates translation throughout the cell cycle with marked effects on mitotic exit. The intersection of cell cycle and phosphoregulation of eIF6 correlates with its high levels in rapidly dividing aggressive cancers. Together, these findings establish a structural basis for defective 60S maturation in Shwachman-Diamond syndrome and underscore the importance of regulatory mechanisms governing late cytoplasmic maturation of the 60S subunit.

Ribosome heterogeneity arising from common and rare rRNA sequence variants affects diverse human phenotypes

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The ribosome, the molecular machine that translates messenger RNA into protein, is increasingly recognized as heterogeneous. Ribosomal RNA (rRNA) genes are encoded by hundreds of copies across five acrocentric chromosomes, making them the most repetitive genes in the human genome. Our prior work showed that rDNA copies carry sequence variations that could generate ribosome heterogeneity associated with development and cancer. Yet population genetics has largely overlooked rDNA: it's absent from SNP arrays due to its repetitive nature, and rRNA is routinely depleted from transcriptome sequencing. Whether rRNA sequence variation affects human phenotypes remains largely unknown.

Here we analyze whole-genome sequencing from 487,822 UK-Biobank individuals using our curated atlas of rRNA variants confirmed in translating ribosomes, including tens of common and about a thousand rare variants. We developed RiboVAn, a pipeline for calculating rRNA variant frequencies from short-read data, enabling population-level analysis of ribosome heterogeneity. Using monozygotic twins, we found rRNA variants include both highly heritable germline variants and somatic mutations, with heritable variants concentrated in four expansion segments (ESs) of 28S rRNA: es7I, es15I, es27I, and es39I. These heritable ES variants associate with distinct traits, independent of rDNA copy numbers: es15I with adiposity, es39I with body dimensions, and es27I with blood-related traits and diseases. Rare variant burden analysis further showed that mutations in constrained rRNA regions raise risk for diverse diseases, including type 2 diabetes, myocardial infarction, congenital disorders, and cancers.

Since 95% of cell-free circulating RNA is rRNA, we asked whether rRNA variants could serve as disease fingerprints. In lung adenocarcinoma and hepatocellular carcinoma, rRNA variants predicted both cancer incidence and progression. Together, this study shows that ribosome heterogeneity from rRNA sequence variation meaningfully shapes human physiology and disease, revealing functional specialization of ES regions and proposing rRNA variants as a new blood-detectable biomarker class.

Programmed Ribosomal Frameshifting Regulates Pioneer-Factor Activity Through Differential DNA-Binding-Domain Usage

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Stem cells must balance self-renewal with differentiation to prevent excess proliferation and tumorigenesis. These fate transitions require rapid remodeling of the proteome in response to developmental and environmental cues. Although transcriptional regulation of stem-cell fate has been extensively studied, transcript and protein abundance are poorly correlated in stem cells, revealing an important layer of regulation at the level of translation. Notably, stem cells maintain low rates of global protein synthesis despite high levels of ribosome biogenesis, suggesting that their proteomes are shaped by tightly regulated translational programs. Yet, how these programs contribute to stem-cell identity remains poorly understood. We study the *Drosophila* pioneer transcription factor Zelda (Zld), which promotes the undifferentiated state in both the early embryo and neural stem cells (neuroblasts). We showed that Zld activity is mediated by the usage of distinct DNA-binding domains in each developmental context: a C-terminal zinc-finger cluster mediates Zld binding in the embryo, whereas an N-terminal zinc finger is required for binding and function in neuroblasts. The context-specific use of the Zld DNA-binding domains is partially explained by the existence of two different protein isoforms. The canonical 1596-amino-acid Zld protein is enriched in embryos. By contrast, an alternative Zld proteoform that lacks the C-terminal DNA-binding domain is the predominant form of Zld in neuroblasts. Unexpectedly, we discovered that this truncated, neuroblast-enriched proteoform results from ribosomal frameshifting. Ribosomal frameshifting is well established as a mechanism used by viruses to diversify their proteomes but is highly unusual on cellular mRNAs. Because frameshift-derived proteoforms are encoded by the same transcript and evade standard proteomic identification, this form of protein diversity is largely invisible to conventional approaches. Our discovery

therefore raises the possibility that programmed ribosomal frameshifting represents an underappreciated mechanism used to diversify the proteome in *Drosophila* stem cells, with implications for development and disease

Streamlined mRNA targeting in zebrafish embryos supports non-essential roles for maternally encoded microproteins

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A crucial early step in animal development is the switch in control from maternally provided to zygotically produced factors, known as the maternal-to-zygotic transition (MZT). During this window, loss-of-function approaches face the unique challenge that maternally provided mRNAs and proteins can mask the effects of mutations in the zygote alone (like in FO CRISPRants). Zebrafish is an excellent vertebrate model of this transition, but generating maternal-zygotic mutants remains tedious and risky and established, morpholino-based mRNA targeting can elicit toxicity and off-target effects. Towards overcoming these barriers, our lab previously established the RNA targeting CRISPR-RfxCas13d system. Here we bolster RfxCas13d in zebrafish with 1) automated staging of 2–6 hours post-fertilization (hpf) embryos, 2) removal of problematic RfxCas13d guide RNAs, and 3) cost-minimized bulk RNA-seq. With this approach, we successfully target 29 maternally provided mRNAs that encode short proteins (< 100 amino acids) called microproteins. RfxCas13d reduces mRNA levels by >50% for over half of selected microproteins, with negligible transcriptomic perturbations at 4 hpf or organismal effects through 24 hpf. Finally, we find an extremely low frequency of off-target and non-target knockdown across all 52 unique knockdown paradigms. Overall, our work defines an improved RfxCas13d workflow and increases throughput for organismal and molecular analysis in early zebrafish development.

Developmentally controlled co-translational assembly of the synaptonemal complex

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Co-translational assembly ensures that subunits of multiprotein complexes reach correct stoichiometry and avoid the premature aggregation of orphaned subunits. Yet how RNA regulation, translation, and assembly are coordinated in space and time, especially during developmental transitions, remains poorly understood. Here, we use the *C. elegans* synaptonemal complex (SC), a zipper-like scaffold comprising SYP-1 through SYP-5 and SKR-1 that assembles at meiotic entry, as a tractable system to dissect this coordination.

Biochemical reconstitution identifies two stable SC subcomplexes, SYP-1/SYP-2/SYP-5 and SYP-3/SYP-4/SKR-1, that fail to associate when produced separately and then mixed, suggesting that productive assembly requires co-translational engagement. Single-molecule imaging in intact gonads reveals that *syp-3* and *syp-4* mRNAs specifically colocalize in the cytoplasm, with their colocalization rate peaking immediately before meiotic entry. This colocalization diminishes upon translation inhibition, and nascent SYP-4 protein is detected at *syp-3* and *syp-4* mRNA foci, directly linking mRNA organization to ongoing translation. Systematic RNA immunoprecipitation defines an ordered co-translational pathway: SYP-3 and SYP-4 form an early core that recruits additional subunits before engaging nascent SYP-5 as the final step, a directionality matching known structural interfaces. Notably, most mRNAs of SC subunits are bound by PUF RNA-binding proteins that are downregulated at meiotic entry, relieving translational repression and enabling synchronous SC translation, thereby coupling developmental timing with co-translational assembly.

Together, our findings support a model in which SC biogenesis is coordinated by developmentally timed mRNA organization and ordered co-translational assembly. More broadly, we propose that developmental RNA regulons can coordinate the timing and spatial organization of functionally related transcripts to enable rapid, accurate complex formation during developmental transitions.

Global Regulatory Functions of the Human CCR4–NOT Complex in mRNA Deadenylation and Decay

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6 Biofrontiers Institute, University of Colorado, Boulder, CO 80303, USA (* Equal contributions)

Shortening of the poly(A) tail initiates mRNA decay, and the human CCR4–NOT is the principal cytoplasmic deadenylase. Although its subunits have been defined, their functions have not been comprehensively evaluated in cells. We depleted each CCR4–NOT subunit and measured transcriptome-wide effects. CCR4–NOT regulated transcripts from thousands of genes. Distinct groups of transcripts responded according to the modular organization of the complex, while subsets exhibited unique responses to specific subunits. Transcriptomic and poly(A) tail analysis revealed that the CNOT7 and CNOT8 deadenylases are the predominant regulators of poly(A) tail length in these cells. Additional bioinformatic analysis identified sequence determinants associated with CCR4–NOT regulation. The results define the breadth and specificity of CCR4–NOT-mediated mRNA decay and provide a resource for dissecting regulatory mechanisms and biological roles.

Attendee Resources

Location: Stowers Institute for Medical Research – 1000 E. 50th Street, Kansas City, MO 64110

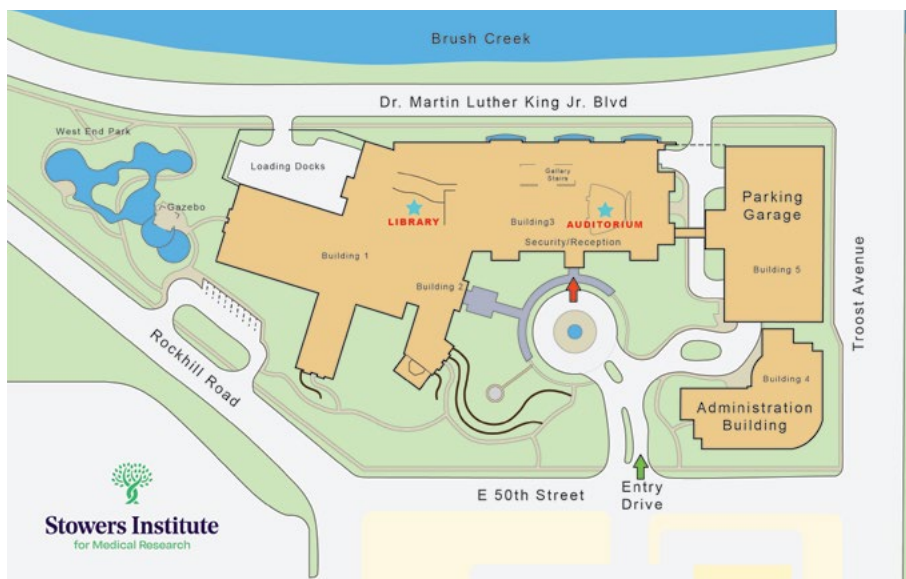
General Phone Number: 816-926-4000

Driving directions from Kansas City International Airport:

(approximately 30 minutes under normal driving conditions)

1. Follow the signs on International Circle to the airport exit.
2. Take Cookingham Drive to I-29 South (right ramp), heading toward Kansas City.
3. Continue to follow I-29 South as it merges into I-29 South 71 (merge in left lane), then I-35 South (merge in left lane again).
4. Cross the Paseo Bridge and get in the lane for I-70 South 71 (Exit 3)
5. Merge right and follow sign to South 71 Highway (Exit 2M).
6. Take the Emmanuel Cleaver II Boulevard exit and turn right onto Emmanuel Cleaver II Boulevard.
7. Follow Cleaver II to Troost Avenue and turn left on Troost.
8. Turn right on 50th Street and take another immediate right at the Stowers Institute's entrance (1000 E. 50th Street, Kansas City, MO 64110).

Campus Map



Parking: Visitor parking is available in the parking structure located between the Administration Building (to your right as you enter the campus) and the Research Building (to your left). Please park on the 5th floor of the parking garage and take the elevator down to the 1st floor to enter the Research Building.

Restrooms: Located by the two large planters on the 1st floor of the Research Building. All-gender restrooms are available at the base of the stairs on the B1 level.

Mother's Room: At the base of the stairs on the B1 level, located next to the all-gender restrooms. An entry key will be provided by security to guests that request to use it.

Tobacco Free Campus: Tobacco of any kind is prohibited in all the Institute facilities and on the Institute grounds. The Institute does not offer any designated smoking areas.



Wireless Access: Stowers Guests may connect to the **stowers_guest SSID**. When connected, you will see a captive portal. Click on the link at the top of the page to register for guest access.

A screenshot of the Stowers Institute Guest Portal. The header shows the Stowers Institute logo and the text "Guest Portal". Below the header, there is a "Welcome" message. A link "Register for guest access" is highlighted in blue. Below the link, there is a message: "Guests: Please register before login. Stowers Members: Please use your Stowers credentials for BYOD access." There are two input fields: "Username:" with the text "xxx" and "Password:" with a masked password "xxxxxxxxxx". To the right of the password field is a "Reset Password" link. Below the input fields are two buttons: "Change Password" and "Sign On".

- You will be prompted to enter their information. Name and email are the only required fields.
- After entering the required information click Register.



Guest Portal

Registration
Please complete this registration form:

First name*

Last name*

Email address*

Company

Reason for visit

Register Cancel

- You will see a page like this with sign on information. You can use the userid and password to connect other devices without going through the registration, by entering the userid and password in the first page of the captive portal.
- Click the "Sign On" button.



Guest Portal

no@email.com

Account Created
Use the following information to sign on to the network.
You can only click the button 5 times.

Email Me attempts left:5

Username:
Password:
First name:
Last name:
Email:

Email Me

Sign On

After clicking sign on, you will be prompted to accept the "Acceptable use Policy". After clicking accept you should now have internet access.

If you have any questions, please contact the Stowers Help Desk at 816-926-4150.



Kansas City Fun: The Kansas City area offers a wealth of cultural, educational, and entertaining opportunities to explore, many of which are inexpensive or free of charge. The following is a brief listing of local attractions, event calendars, and resources.

Useful Resources

Information about Kansas City and the surrounding area can be found at kcmo.gov or at visitkc.com. Two publications to help you discover things to do in the area are: "Insider's Guide to Kansas City" by Katie van Luchene and "Day Trips from Kansas City" by Shifra Stein. Both can be found in local bookstores.

Linda Hall Library

5109 Cherry Street, 816.363.4600

The Linda Hall Library in Kansas City is one of the world's foremost independent science research libraries. Founded in 1946 through a philanthropic bequest, it houses vast collections spanning science, engineering, and technology, serving researchers, students, and the public. Known for its international research programs and collaborations, the Library promotes lifelong learning with innovative programming, digital access, and educational resources. The Library also maintains its grounds as a public urban arboretum, offering both scholarly and community engagement opportunities.

www.lindahall.org

Nelson-Atkins Museum of Art

4525 Oak Street, 816-751-1278

Opened in 1933, the Nelson-Atkins Museum has more than 50 galleries and several period rooms. The museum's outstanding feature is its collection of Asian art. The collection of Chinese landscape paintings is one of the finest in the West, and the museum's holdings of Chinese ceramics and decorative arts are also noteworthy. Besides European paintings from the Renaissance on, the museum also has notable collections of ancient Egyptian sculpture, Japanese porcelains and lacquer, and English pottery. The E.F. Pierson Sculpture Garden was dedicated

in 1972, and the Henry Moore Sculpture Garden opened in 1989. Admission is free.
nelson-atkins.org

Kemper Museum of Contemporary Art

4420 Warwick, 816-753-5784

Founded in 1994, the Kemper Museum of Contemporary Art presents modern and contemporary art of the highest quality and significance. It collects, preserves, documents, interprets, and exhibits a growing permanent collection; develops and presents special exhibitions; and offers a variety of educational programs. Admission is always free, and the Museum serves a diverse and inclusive public population.

kemperart.org

Union Station

30 West Pershing Road, 816-460-2020

This fully restored 1914 landmark is Kansas City's most prominent destination for entertainment and cultural activities. The Station is home to a permanent rail exhibit with vintage rail cars, an interactive science center, a vibrant Theater District featuring giant screen movies and live theater, fine restaurants, unique shops, spaces for meetings and events and much more. Of course, you can still catch the train at Union Station, once again among Amtrak's busiest stops.

unionstation.org

Loose Park

Intersection: Wornall Road and 51st Street, 816-784-5300

Loose Park is one of Kansas City's most beautiful parks. The park is home to a lake, a walking path, a shelter house, Civil War markers, tennis courts, a wading pool, picnic areas and the famous Rose Garden. The Rose Garden is popular for all types of outdoor special events including theatrical performances and wedding ceremonies.

Westport

Westport is one of Kansas City's premier destinations for dining, shopping, site seeing and is the heart of the city's nightlife. Located in the midtown, Westport is just north of the Country Club Plaza and a few miles south of downtown Kansas City. Historically, Westport was built along the Santa Fe Trail as an outfitting center for wagon trains heading west. Today the area is filled with renovated and new buildings housing trendy shops, restaurants, and nightspots.

SRC Meeting Policies

The Stowers Research Conference (SRC) series supports an environment for the exchange of scientific ideas that is grounded in dignity and respect for all program participants. SRC believes that a diverse, inclusive and collegial community culture promotes scientific creativity and progress. The conference code of conduct outlined here has been adapted from the policies outlined by the Society for Developmental Biology, sponsor of the first SRC meeting.

No Harassment Policy

Program participants are expected to conduct themselves in a professional manner and to treat each other with dignity and respect. This expectation applies to the organizers, event attendees, volunteers, employees, consultants, vendors, and others while on Stowers premises, while representing SRC elsewhere, and while attending events organized by SRC.

SRC will not tolerate any discrimination in the form of sexual harassment and other forms of harassment. Program participants shall not engage in any conduct that could reasonably be construed as unlawful harassment against an individual. Program participants shall not make unwelcome sexual advances, make requests for sexual favors, or engage in other verbal or physical conduct of a sexual or offensive nature.

No Violence Policy

SRC does not tolerate any type of violence or threats of such violence while on Stowers premises, while representing SRC elsewhere, and while attending events organized by SRC. SRC prohibits acts or threats of violence by or against any program participants. In addition, SRC does not permit the possession or the concealed or open carrying of weapons anywhere on the Stowers premises.

Reporting

If a program participant discovers any conduct which they believe violates this policy or is otherwise detrimental to the organization, they are asked to promptly report it to the organizers.

Recording, Photography, and Session Etiquette

While in sessions, please mute all cell phones and other electronic devices. Photography or the electronic capture of scientific sessions and posters is not permitted without the expressed consent of the presenting author(s). Respect other individuals' and organizations' intellectual property and confidential information.

Photo Release

SRC has an official photographer for the meeting. Photos taken at the meeting may be used in future SRC publications, on the SRC website, or in other materials.

By registering for the meeting, you agree to allow SRC to use your photo in and SRC related publication or website.

Smoking Policy

The use of tobacco, in any form, or the use of any smoking device is prohibited in all Stowers facilities and on the Stowers campus. Stowers facilities are defined as common work areas, auditoriums, classrooms, conference and meeting rooms, private offices, elevators, hallways, food service facilities, employee lounges, stairs, restrooms, vehicles, the parking garage, and all facilities owned by the Stowers Group of Companies.

Creative, innovative, fearless science

At the Stowers Institute, we aim to attract scientists who are visionary risk-takers, who seek to solve the most challenging and intractable problems in biology.

Meet the Scientists at the Stowers Institute for Medical Research
stowers.org/scientists

