Cancer Virology Program Winter Newsletter

Published: January 2024

Overview

As we turn the page on the New Year, it is with great enthusiasm and pride that I present the Cancer Virology Program (CVP) Winter Newsletter, highlighting the remarkable accomplishments of the past year and setting the stage for our ambitious goals in the coming months.

Reflecting on the last 8 months, our dedicated CVP members and their labs have achieved significant milestones in their groundbreaking research programs. Notably, on October 10, 2023, CVP collaborated with Community Outreach and Engagement (COE) to organize the inaugural "Viral Cancers and Community Outreach and Engagement Symposium." This event featured distinguished speakers, including the esteemed Nobel Laureate Dr. Charles Rice and The Deputy Director, Dr. Douglas Lowy.

Several of our program members served as keynote speakers or organizers at key national and international conferences, showcasing the global impact of CVP's research endeavors. In an outstanding achievement, CVP Members secured Principal Investigator roles in eight newly awarded NIH grants, amounting to a substantial new $4.4 million funding per year, with over half of them from the National Cancer Institute (NCI). Additionally, our members have collectively contributed to over 90 published articles, shedding light on numerous groundbreaking scientific findings. A selection of these publications is highlighted in this issue, providing readers with a glimpse into the wealth of knowledge generated by our dynamic community.

Throughout the year, CVP continued its tradition of hosting thought-provoking seminars featuring renowned speakers addressing diverse topics such as cancer viruses, innate immunity, and virus-host interactions. These seminars foster an environment of intellectual exchange, fueling the collaborative spirit that defines our program.

In this edition, we showcase the remarkable contributions of CVP Program Member Dr. Yufei Huang, who joined our program in June 2021. As a Professor in the Department of Medicine and the Leader of Artificial Intelligence at the Hillman Cancer Center, Dr. Huang has rapidly forged collaborations with over 10 investigators at the Center. Within the past two years, Dr. Huang has secured a U01 grant and is a Co-Investigator in at least four other new NIH R01 grants. His expertise in computational biology, bioinformatics, and artificial intelligence adds invaluable dimensions to the research programs within CVP and other Hillman Cancer Center initiatives.

As we embark on the journey of the New Year, I extend my heartfelt wishes to everyone and their families for a Happy, Healthy, Successful, and Productive year ahead. May our collective efforts continue to propel us toward new horizons in cancer virology research. With warmest regards! *By Dr. Shou-Jiang Gao*

Inside This Issue:

For more information on the Cancer Virology Program, please contact the CVP Program Leaders:

- Dr. Shou-Jiang (SJ) Gao: gaos8@upmc.edu
- Dr. Haitao Guo: guoh4@upmc.edu

Program Member Highlights

Dr. Yufei Huang

Dr. Huang is a member of the UPMC Cancer Virology Program (CVP) and a Professor in the Department of Medicine. He also holds joint appointments in the Department of Electrical and Computer Engineering (ECE) and the Department of Pharmaceutical Sciences. His previous roles include Professor and Associate Chair of Research of the Department of ECE at the University of Texas at San Antonio, Adjunct Professor at the Department of Population Health Science at the University of Texas Health San Antonio, and Visiting Professor at the Center of Bioinformatics, Harvard Center for Neurodegeneration & Repair.

He holds a Ph.D. in Electrical Engineering from Stony Brook University and has been collaborating with biomedical scientists to utilize his expertise in machine learning to advance genomic data analysis for understanding cancer and cancer viruses. He has been working closely with the CVP PIs to use bioinformatics/machine learning, high throughput profiling, and bench experiments to study the mechanisms of viral-induced cellular transformation and oncogenesis. Together, they have identified the signatures of the oral microbiome in HIV-infected individuals with oral Kaposi sarcoma-associated herpesvirus (KSHV) (PLOS Pathogens, 2019), pre-diagnostic markers for nasopharyngeal carcinoma (Clin Cancer Res, 2022), and potential antiviral target for hepatitis B virus (Antiviral Res, 2023).

Dr. Huang has also been actively studying m6A mRNA methylation and its roles in cancer. He is instrumental in developing exomePeak, the widely used analysis tool for m6A sequencing. Supported by the NCI Informatics Technology for Cancer Research program, his team is developing the informatics pipeline and knowledgebase tailored for m6A and cancer research acceleration. Using informatics tools and through collaboration with Dr. Shou-Jiang Gao and other cancer biologists, they mapped genome-wide viral and cellular m6A profiling in multiple KSHV-infected systems (Nat. Microbiology 2018), uncovered a cross-talk among m6A writers, erasers, and readers that regulates cancer progression (Science Advances, 2018), identified unique m6A regulation of innate immune response during bacterial and viral infection (Cell Death & Disease, 2022).

As Leader in AI for Cancer Research at Hillman Cancer Center, he also works with Hillman PIs to enhance AI in cancer research. He is building AI tools to facilitate research and accelerate discovery. His lab is building AI-powered analysis and visualization pipelines for spatial single-cell data to effectively integrate pathology with genomics to more effectively study tumor and viral infection within their immune microenvironment (JMV, 2023). His team also uses large language models like GPT4 for assembling cancer biology knowledge and designs deep learning models to elucidate the mechanisms behind their predictions (Science Advances, 2021; Cancers, 2023).

Dr. Huang is actively engaged in academic service. He chairs the Biomedical Health Informatics (BHI) Technical Committee of the IEEE Engineering in Medicine and Biology Society (EMBS), a professional organization comprising over > 12K biomedical professionals. He has led a variety of biomedical informatics conferences, including chairing the recent IEEE EMBS International Conference on BHI. He also serves as Associate Editor for Frontiers in Genetics and IEEE Reviews in Biomedical Engineering.

New Lab Members

Our warmest welcome and wishes for success to the following new lab members!

Dr. Shou-Jiang Gao's Lab:

Aru Gupta, PhD: *Postdoctoral Fellow*
Dr. Yupta obtained her PhD from the **University of Arkansas for Medical Sciences, College of Medicine in 2019** with a major in Virology. She then came to Dr. Neal DeLuca's lab in the Department of Microbiology and Molecular Genetics at the University of Pittsburgh School of Medicine until December, 2023 before joining the Gao's lab.

Xiaolu Xie, PhD: *Postdoctoral Fellow*
Dr. Xie obtained her PhD from the Chinese Academy of Medical Sciences & Peking Union Medical College, China in 2019 with a major in Molecular Biology. She then worked for Soochow University as a Medical Laboratory Specialist until January, 2023, then as Postdoctoral Fellow at University of Texas at Tyler until December, 2023 before joining the Gao's lab.

Lianna Huang: *Undergraduate, Carnegie Mellon University*
Vicky Zhao: *Undergraduate, University of Pittsburgh*
Daniel Guo: *Hillman Academy Summer Student and Undergraduate, University of Pittsburgh*
Rami Alhallak: *Hillman Academy Summer Student*

Dr. Haitao Guo's Lab:

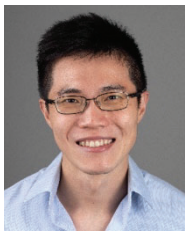
Andrea Jurado: *MD / PhD Student*
Amanda Chan: *Undergraduate Student*
Myles Steed: *PMI Rotation Student*
Anthony Kalvi: *Hillman Academy Summer Student*

Dr. Masa Shuda's lab:

Omkar Betsur is new undergraduate researcher in Shuda lab. He is a senior at University of Pittsburgh and has worked for a former MMG faculty, Dr. Seema Lakdawara and studied a mode of influenza virus transmission using an animal model.

Program Activities

CVP has hosted several visitors and invited speakers this year. Each of them presented a seminar for at UPMC Hillman Cancer Center as well as meeting with faculty members and staffs during their visits. We're thankful for their visits and willingness to share their sciences and experiences with us.



Sizun Jiang, PhD

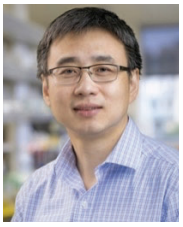
Dr. Sizun Jiang, Assistant Professor, Department of Medicine, Center for Virology and Vaccine Research, Beth Israel Deaconess Medical Center, Harvard Medical School Boston, Massachusetts. He was invited through the CVP and visited us on July 17-18, 2023. He presented a seminar entitled*: "Interrogating Host-Disease Interactions in situ"* at the UPMC Hillman Cancer Center. *Host: Dr. Shou-Jiang Gao.*

Saumendra Sarkar, PhD

Dr. Saumendra Sarkar, Professor, Department of Microbiology and Molecular Genetics, and a CVP Member presented a seminar entitled*: "Mechanistic Specialization of Interferon-stimulated Gene Function"* at the Department of Microbiology and Molecular Genetics on September 6, 2023. *Host: Dr. Tom Smithgall.*

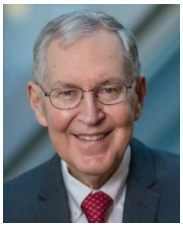
Elizabeth Read-Connole, PhD

Dr. Elizabeth Read-Connole, Program Director, Viral Oncogenesis Cancer Etiology and Section Chief, Cancer Immunology, Hematology and Etiology Branch, Division of Cancer Biology, National Cancer Institute was invited through CVP and visited us on October 9-10, 2023. She attended the Viral Oncology Symposium and presented a seminar entitled*: "National Cancer Institute (NCI) Initiatives for HIV and Cancer"* at the UPMC Hillman Cancer Center. *Host: Dr. Shou-Jiang Gao.*



Yan Xiang, PhD

Dr. Yan Xiang, Professor, Department of Microbiology and Immunology, University of Texas Health Science Center at San Antonio, was invited through the Department of Microbiology and Molecular Genetics. He visited us on November 1, 2023 and presented a seminar entitled*: "SAMD9-Mediated Innate Immunity Against Viruses and Myeloid Tumors"* at the Department of Microbiology and Molecular Genetics. *Host: Dr. Renfeng Li.*



David M. Knipe, PhD

Dr. David Knipe, an Academy Member of the National Academy of Science, and the Higgins Professor of Microbiology and Molecular Genetics, and Head of the Harvard Program in Virology, Department of Microbiology, Blavatnik Institute, Harvard Medical School. He was invited through the CVP and visited us on November 6-7, 2023. He presented a seminar entitled*: "Epigenetics of Herpes Simplex Virus Lytic and Latent Infection and Transduction"* at the UPMC Hillman Cancer Center. *Host: Dr. Shou-Jiang Gao.*

Tongqing Zhou, PhD

Dr. Tongqing Zhou, Investigator, Structural Biology Section, Vaccine Research Center, National Institute of Allergy and Infectious Diseases, NIH. He was invited through the Department of Microbiology and Molecular Genetics and visited us on November 15, 2023. He presented a seminar entitled*: "Structure-based and antibody-guided vaccine design against viral pathogenesis"* at the Department of Microbiology and Molecular Genetics. *Host: Dr. Haitao Guo.*

Michaela Gack, PhD

Dr. Michaela Gack is the Scientific Director and The Arthur and Marylin Levitt Endowed Chair of the Cleveland Clinic Florida Research and Innovation Center. She was invited through the Department of Microbiology and Molecular Genetics and visited us on December 6, 2023. She presented a seminar entitled*: "Regulatory mechanisms of virus infection and immunity"* at the Department of Microbiology and Molecular Genetics*. Hosts: Drs. Kathy Shair and Patrick Moore.*

Xuefeng Liu, PhD

Dr. Xuefeng Liu, Professor, Departments of Pathology, Urology, and Radiation Oncology, James Comprehensive Cancer Center, The Ohio State University. He was invited through the CVP and visited us on December 12, 2023. He presented a seminar entitled*: "Translation of HPV biology and patient-derived cell models"* at the UPMC Hillman Cancer Center. *Host: Dr. Shou-Jiang Gao.*

Recent CVP "Work in Progress" Presentations

Alex Reznik - 9/22/23: "Optimizing CRISPR/Cas9-editing of EBV genomes to address the functional genomics of LMP1".

Benjamin E. Warner - 10/6/23: "Liquid biopsy for cancer prevention: Epstein-Barr virus genetics guides refinement of EBNA1 IgA biomarker for nasopharyngeal carcinoma risk".

Bizunesh Abere - 11/3/23: "Viral encoded circular RNAs"

Suet Kee Loo - 11/17/23: “Arginine Sensor CASTOR1 is a Tumor Suppressor and Biomarker in Viral and Nonviral Cancer: Predicting Patient Survival in Lung Adenocarcinoma”.

Febri Gunawan Sugiokto - 12/1/23: “PIAS1 Regulates Episome Maintenance Proteins to Control the Life Cycles of EBV, KSHV and HPV”.

Luping Chen - 1/5/2024: “Activation of glucocorticoid receptor signaling inhibits KSHV-induced inflammation and tumorigenesis”.

Hongzhao Zhou Thesis Defense

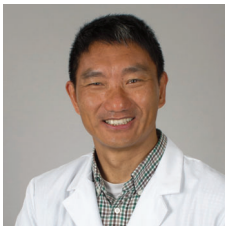
Hongzhao Zhou from Drs. Yuan Chang and Patrick Moore’s Lab successfully defended his thesis on July 31, 2023. He wowed one and all with his data and presentation. Congratulations on this wonderful achievement and best wishes on your continued success!

Awards & Honors

Zandrea Ambrose, PhD

Dr. Ambrose was a keynote speaker at the 27th West Coast Retroviruses meeting in early October and has been asked to be the co-organizer for the 28th West Coast Retroviruses meeting in 2024.

Congratulations on these important recognitions!



Shou-Jiang Gao, PhD

Dr. Gao was invited by the Department of Microbiology, Harvard Medical School on March 15, 2023 to give a seminar entitled: “Arginine sensor CASTOR1 as a tumor suppressor in viral and nonviral cancers and inflammation”.

Dr. Gao was invited by the Society of Chinese Bioscientists in America (SCBA), Virology Division and Association of Chinese Virologists in America (ACVA) on September 21, 2023 to give a virtual seminar entitled: “*N6*-methyladenosine (m^6A) in KSHV infection, cellular transformation and innate immune response”.

Haitao Guo, PhD

Dr. Guo has been awarded the following new editorial appointments:

Deputy Editor: *Journal of Medical Virology*
Editor: *Antiviral Research*
Deputy Section Editor: *Virology Journal*

Congratulations on these impressive appointments!

Sumin Jo

Sumin Jo from Dr. Yufei Huang's lab received the NCI Travel Award for the 2023 NCI Junior Investigator Meeting.

Congrats on winning your award!

Joseph T. Newsome MS, DVM, DACLAM

Dr. Newsome was recently appointed to committee of the NASEM Roundtable that planned and presented on Dec 19-20, 2023.
He's also joined the *"Effective Communication with the General Public about Scientific Research that Requires the Care and Use of Animals Workshop"* committee.

Congratulations on both of these honors!

Sheng Shen, PhD, Professor of Southern Medical University, Guangzhou, China and former member of Dr. Haitao Guo's lab received JGV Best Poster Presentation Prize at the 2023 International HBV Meeting in Kobe, Japan. Their presentation was entitled *"NEDD4 family ubiquitin ligase AIP4 associates with ALIX to enable HBV naked capsid secretion in an ALIX ubiquitination-independent manner."* Congrats on this achievement!

Dr. Benjamin Warner, PhD

Dr. Warner, a Postdoc in Kathy Shair's lab, received the 2nd prize poster award at the HCC Annual Retreat in the Clinical, Translational, Population Research category.

Congratulations to Dr. Warner on this fine achievement!

In the News

Cancer Virology Co-Sponsors the Viral Oncology Symposium

The Cancer Virology Program (CVP), along with Community Outreach and Engagement (COE) organized the first "**Viral Cancers and Community Outreach and Engagement Symposium"**, held on October 10, 2023 at the Assembly Building. The organizers were Drs. Monica Baskin, Robert Ferris, Shou-Jiang Gao, Haitao Guo and Patrick Moore with the support of Greg Benzy (Hillman Administration) and Brittni Prosdocimo (CME Office). Drs. Shou-Jiang Gao, Robert Ferris and Dean Anantha Shekhar commenced the symposium. The symposium showcased how basic research can collaborate, translate into and support translational work including cancer prevention, population study and community outreach. The symposium featured several prestigious guest speakers including Nobel Laureate Dr. Charles Rice, The Deputy Director Dr. Douglas Lowy along with several internal speakers including Drs. Haitao Guo, Masa Shuda, Renfeng Li, Kathy Shair, Robert Ferris, Jose Zevallos, and Monica Baskin who showcased their outstanding works.

All the presentations are available by **clicking here.** Thanks to all those who helped make this excellent day of education and collaboration a huge success!

Cancer Virology Program

UPMC HILLMAN CANCER CENTER
VIRAL ONCOLOGY SYMPOSIUM

Tuesday, October 10th, 2023

Organized by the Cancer Virology Program (CVP), Community Outreach and Engagement (COE) and the Head and Neck Program

Douglas R. Lowy, MD
Deputy Director - National Cancer Institute

Charles M. Rice, PhD
2020 Nobel Prize Lauréate

Jeffrey I. Cohen, MD
Chief, Laboratory of Infectious Diseases - NIH

Blossom Damania, PhD
Vice Dean for Research - University of North Carolina at Chapel Hill

Charl Cohen, PhD
President - Hepatitis B Foundation

Shannon Christy, PhD
Department of Health Outcomes and Behavior - Moffitt Cancer Center

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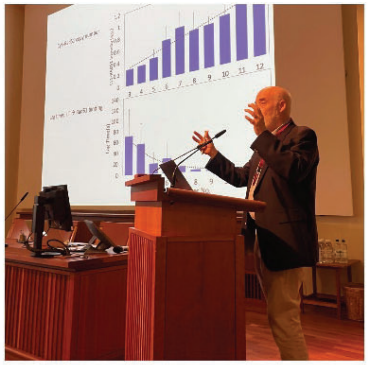
This activity is approved for the following credit: *AMA PRA Category 1 Credit™*

Both Drs. Moore & Dr. Chang were keynote speakers at the 7th Nordic Merkel Cell Carcinoma Meeting:






7th Nordic Merkel Cell Carcinoma Meeting – Stockholm, Sweden – Sept 14 - 15

International Conference on Kaposi's Sarcoma Herpesvirus and Related Agents

Drs. Moore & Dr. Chang, along with Dr. Bizunesh Abere, attended the 25th International Conference on Kaposi's Sarcoma Herpesvirus and Related Agents which was held in Dar es Salaam, Tanzania, Africa this year. Dr. Moore gave a keynote on KSHV Vaccines.

Upcoming Events

Upcoming CVP PhD Thesis Defense

There will be PhD Dissertation Defense and Final Examination by Luping Chen of the Integrative Systems Biology Graduate Program entitled: "Activation of glucocorticoid receptor signaling inhibits KSHV-induced inflammation and tumorigenesis". TIME: 1:00 PM, Friday, January 12, 2024 ; PLACE: Hillman Cooper Conference Center A/B; OR log in through Microsoft Teams.

Click here to join the meeting using passcode: CqUdZt.

CVP / Dr. Gao Lab Special Presentation

There will be a special CVP presentation on **Friday, January 19th - 2:00 p.m.**

Dr. Gao's lab will be hosting Guo Luo, PhD, an instructor at Stanford University.

They will present a seminar entitled *"Antigen-HLA restricted CD4 T cells in narcolepsy, Alzheimer's and Parkinson's diseases."* We hope you can join us.

Guo Luo, PhD

In Person CVP "Work in Progress" Presentations

The CVP-WIP Seminar Series started again this fall in Cooper B/C as in-person only events. It's been nice seeing everyone in person again and a great time of collaboration and learning.

1/19: Wenyu Peng - Chang / Moore Lab

2/2: Cheng-Der Liu - Guo Lab

2/16: Joshua Walston - Shair Lab

3/1: Wen Meng - Gao Lab

MMG Seminar Series Presentation

Dr. Laurie Krug - 1/31/24: Title TBA - *Invited by Kathy Shair*

Newly Funded

Dr. Zandrea Ambrose

1R21AI175795-01, 7/15/23 - 8/31/25, total cost: $195,800/Total annual cost

"Live-cell imaging of SARS-CoV-2 replication organelle formation and RNA synthesis"

SARS-CoV-2 is a novel b-coronavirus identified in 2019 that causes the disease COVID-19, which is responsible for over 6 million deaths since late 2019. While recent virology studies have clarified many aspects of how SARS- CoV-2 infects cells and causes disease, questions remain on the spatio-temporal processes of post-entry replication steps, which may be useful for targeting novel therapies. Using reverse genetics and live cell and super-resolution microscopy of labeled SARS-CoV-2 proteins expressed in cells or during SARS-CoV-2 infection, we propose two aims to gain better understanding of virus-host interactions during infection of human airway cells. We will understand the role of host proteins in the biogenesis of SARS-CoV-2-induced double- membraned vesicles (Aim 1) and visualize the origin and trafficking of SARS-CoV-2 RNA synthesis (Aim 2) for WT virus and variants of concern (e.g., Alpha, Delta, and Omicron). The studies will be performed in real-time in human airway epithelial cell lines and deidentified primary cells. These aims will be performed by fluorescently labeling SARS-CoV-2 proteins and the viral RNA as well as host cell proteins. Small molecules, knock down of host factors, and mutations in the viral genome (including those found in highly circulating variants) will be used to alter these processes and, thus, infectivity to study replication mechanisms. In addition, correlative light- electron microscopy (CLEM) will provide structural information on these replication processes. Improved understanding of SARS-CoV-2 infection may lead to more effective COVID-19 therapies for infected individuals and could prepare us for preventing or treating new coronaviruses that arise in the future.

1R01AI175068-01A1, Multi-PIs: Gjoern Markus Reinhard, Zandrea Ambrose, Suryaram Gummuluru, 3/17/23 - 02/28/27, total cost: $787,467/Total annual cost

"Improved nanoparticle targeting of tissue myeloid cells for HIV-1 long-acting pre-exposure prphylaxis"

Antiretroviral pre-exposure prophylaxis (PrEP) is an important tool for preventing transmission to virus naïve individuals and plays an important role in current efforts to end the HIV epidemic. If taken daily current oral PrEP strategies reliably block HIV transmission. However, the requirement of strict adherence to daily pill uptake, pill fatigue and other institutional barriers to access leave oral PrEP underutilized. Long-acting injectable PrEP strategies have the potential to address many of the problems associated with oral PrEP but the realization of drug formulations and delivery strategies that ensure sustained drug release for at least three months has remained challenging and motivates the development of entirely new long-acting PrEP strategies. This project develops a long-acting injectable PrEP strategy based on membrane-wrapped nanoparticles (NPs) that establish cellular depots for sustained maintenance of inhibitory concentrations of antiretrovirals (ARVs) at primary tissue sites of HIV-1 transmission in the female genital tract (FGT) and rectum. Selective targeting of CD169-expressing macrophages and dendritic cells is accomplished through incorporation of the ganglioside GM3 in the NP membrane. GM3-CD169 binding triggers uptake and sequestration of NPs in non-endolysosomal compartments

that share distinct similarities with virus containing compartments (VCCs) in tissue-associated macrophages and dendritic cells. These compartments represent protected sites from where NPs can release drugs into the surrounding tissue for an extended period of time. Membrane-wrapped inverse micelles of block copolymers will be engineered as a GM3-NP platform for long-acting PrEP. A combination of long-acting tenofovir (TFV) and emtricitabine (FTC) prodrugs will be used as active compounds to validate the approach. The block copolymer NPs will contain TFV covalently linked to a polymer shell that encapsulates an aqueous core holding FTC conjugated to dendrimers. After quantifying drug loading and release in vitro, the GM3-mediated targeting of CD169+ myeloid cells in the FGT and rectum of a humanized mouse model will be tested. In parallel, the GM3-NP platform will be optimized to achieve sustained drug release in the target tissues. The hypothesis that the optimized NPs provide protection from mucosal HIV infection in a humanized mouse model for at least three months will be tested. The specific aims of this application are: Aim 1: To develop membrane-wrapped multicomponent NPs for sustained release of TFV/FTC. Aim 2: To target CD169-expressing myeloid cells in the FGT and SLTs for sustained TFV/FTC release. Aim 3: To demonstrate long-term protection from mucosal HIV-1 transmission in humanized mice by TFV/FTC incorporating GM3-NPs.

Dr. Shou-Jiang Gao

1R01CA284554-01, 9/8/23 - 8/31/28, total cost: $793,089/Total annual cost

"Impact of microbiota on AIDS-Kaposi's sarcoma development and therapy"

Microbiota imbalance impacts the development and therapeutic outcome of cancer by altering host immune response and inflammation. Kaposi's sarcoma (KS) is the most common cancer in HIV-infected patients caused by infection of Kaposi's sarcoma-associated herpesvirus (KSHV). Despite antiretroviral therapy, KS remains common among HIV-infected patients. It remains unclear what factors might influence the development and therapeutic outcome of AIDS-KS? In response to RFA-CA-22-056 entitled: "Basic/Translational Research on Health Disparities in Underrepresented People Living with HIV (PLWH) and Cancer", this application specifically addresses the underserved African populations that have high numbers of new HIV infections with the long- term goal is to delineate the pathogenesis of AIDS-associated KS (AIDS-KS) and identify effective therapeutic targets and agents as well as prognostic biomarkers. We have recently shown the impoverishment of oral microbial diversity and enrichment of specific microbiota in oral AIDS-KS, and demonstrated that bacteria and their products lipopolysaccharide and flagellin promote KSHV-induced tumorigenesis by enhancing inflammation in a preclinical KSHV-induced KS animal model. Our hypothesis is that specific microbiota regulates inflammation to impact KS development and therapeutic outcome in AIDS-KS patients. We have assembled a strong collaborative team with diverse expertise in HIV infection, KSHV biology, microbiome, clinical sciences, epidemiology, statistics, computational biology and machine learning. We will take advantage of the long-term clinical studies in Africa with well-defined cross-sectional, case-control and longitudinal cohorts of large HIV-infected and AIDS-KS populations directed by investigators of this project. We will determine the impact of specific microbiota on inflammation and AIDS-KS development by performing case-control analyses in naïve AIDS-KS and HIV/KSHV patients without KS (Aim 1); and examine the impact of specific microbiota on the therapeutic outcome of KS by case-control longitudinal analyses of AIDS-KS patients undergoing anti-retroviral therapy followed by validation analyses in an independent cohort (Aim 2). This interdisciplinary project will analyze the molecular, virological, microbial, immunological, single cell spatial omics, and clinical features of AIDS-KS patients using advanced machine learning approaches. We expect to identify factors that influence the development and therapeutic outcome of AIDS-KS patients. The proposed work is highly significant, and will have prognostic, preventive and therapeutic impacts on AIDS-KS patients. This will be the first time that the role of microbiota will be systematically examined in AIDS-KS patients from well-characterized cohorts. The proposed innovative approaches such as spatial single cell sequencing and machine learning will generate unique and unprecedented results, providing novel insights into the pathogenesis and therapeutic outcome of AIDS-KS.

1R01CA278812-01, 7/1/23 - 6/30/28, total cost: $540,484/Total annual cost

"Citrulline-urea cycle in KSHV cellular transformation"

Kaposi's sarcoma-associated herpesvirus (KSHV) is the causal agent of Kaposi's sarcoma (KS) and several other malignancies. We have discovered that, unlike most other types of cancer cells that are addicted to glucose and aerobic glycolysis, KSHV-transformed cells do not depend on glucose and have a reduced level of aerobic

glycolysis. Instead, KSHV-transformed cells are addicted to glutamine. More surprisingly, glutamine is primarily shunted to the syntheses of nucleotides and amino acids. To maintain the metabolic flow and clear the toxic products, KSHV hijacks the citrulline-urea cycle by upregulating the key rate-limiting metabolic enzyme argininosuccinate synthase 1 (ASS1). Significantly, ASS1 is essential for the proliferation and survival of KSHV-transformed cells and upregulation of the citrulline-urea cycle further provides an essential STAT3 oncogenic signal by inducing nitric oxide. Our hypothesis is that KSHV encodes specific gene(s) to hijack the citrulline-urea cycle to support the proliferation and survival of KSHV-transformed cells, and hence targeting this pathway is effective for treating KSHV-induced tumors. We have developed an efficient model of KSHV-induced cellular transformation and tumorigenesis, three-dimensional (3D) culture models KSHV- transformed cells, and advanced metabolic profiling and tracing technologies, all of which are particularly useful for testing this novel hypothesis. We will examine the essential roles of ASS1 and citrulline-urea cycle for maintaining metabolic flow, clearing toxic products and activating STAT3 pathway to support KSHV-induced cellular transformation (Aim 1); determine the mechanism by which ASS1 and active citrulline-urea cycle activate the STAT3 pathway to support KSHV-induced cellular transformation (Aim 2); determine the mechanism by which KSHV upregulates ASS1 and hijacks the citrulline-urea cycle (Aim 3); and determine the therapeutic potential of targeting key enzymes in the citrulline-urea cycle for treating KSHV-induced tumorigenesis (Aim 4). The proposed project is highly significant as it will test a novel hypothesis of KSHV manipulation of a key cellular metabolic pathway using multidisciplinary innovative approaches and model systems. It is our expectations that accomplishment of this project will lead to the identification of novel cancer drivers and vulnerabilities of KSHV-induced cancers, which could provide a scientific basis for developing novel therapies.

1R01CA096512, 1/13/03 - 6/30/28 (renewal: 7/6/23 - 6/30/28), total cost: $584,851/Total annual cost

"Cell model for KSHV infection and genetic manipulation"

Cancer cells depend on reprogrammed metabolic pathways for anabolic proliferation. Discovering these cancer metabolic vulnerabilities can reveal novel targets for therapy. Kaposi's sarcoma-associated herpesvirus (KSHV) is the causal agent of Kaposi's sarcoma (KS) and several other cancers. Despite intensive studies for several decades, there is currently no effective therapy for KS. Our long-term goal is to delineate the pathogenesis of KSHV-induced cancers, providing a scientific basis for developing novel therapies. Toward this goal, we have previously developed an efficient system of KSHV-induced cellular transformation of primary cells and a reverse genetics system for KSHV mutagenesis. Using these powerful systems, in the current funding period, we have delineated viral and cellular genes that are essential for KSHV-induced cellular transformation and identified novel therapeutic targets and agents that have the potentials for translating into clinics. In particular, we have recently discovered that KSHV-transformed cells are addicted to glutamine. Unlike other types of cancer cells that utilize glutamine to replenish the TCA cycle, glutamine is primarily shunted to nucleotides syntheses by providing the critical g-nitrogen in addition to amino acids. KSHV hijacks numerous rate-limiting enzymes in these pathways, including phosphoribosyl pyrophosphate amidotransferase (PPAT) and phosphoribosyl pyrophosphate synthetases 1 (PRPS1), which is upregulated in KS spindle tumor cells. Significantly, knockdown of these enzymes suppresses the proliferation of KSHV-transformed cells but has no effect on the primary/uninfected cells. Our hypothesis is that KSHV encodes specific gene(s) to hijack the nucleotide synthesis pathways to support the proliferation and survival of KSHV-transformed cells, and hence targeting these pathways is effective for therapy of KSHV-induced tumors. We have developed 3D Culture systems that closely representing in vivo metabolic changes, an innovative nanoparticles carbon-dots (Cdots)- mediated delivery approach for locked nucleic acid (LNA)-siRNAs, and cutting-edge technology of metabolomics for tracing the carbon and nitrogen flows. We will determine the essential roles of the dysregulated nucleotide synthesis pathways for KSHV-induced cellular transformation and tumorigenesis (Aim 1); determine the mechanisms by which KSHV hijacks the nucleotide synthesis pathways for supporting the proliferation and survival of KSHV-transformed cells (Aim 2); and target vulnerable genes in the nucleotide pathways using the Cdots-mediated delivery approach for treating KSHV-induced tumorigenesis (Aim 3). The proposed project is highly significant as it will test a novel hypothesis of KSHV manipulation of key cellular metabolic pathways using multidisciplinary innovative approaches and model systems. It is our expectation that the accomplishment of this project will lead to the identification of novel cancer vulnerabilities of KSHV-induced cancers, which could provide a scientific basis for developing novel therapies.

1U01CA279618-01, Role: Co-Investigator, PI: Yufei Huang, 8/3/23 - 7/31/24, total cost: $408,557/Total annual cost
"m6A-suite: an informatics pipeline and resource for elucidating roles of m6A epitranscriptome in cancer"

1R01HG013359-01, Role: Co-Investigator, PI: Kai Wang, 8/3/23 - 7/31/24, total cost: $709,603/Total annual cost
"Novel bioinformatics methods to detect DNA and RNA modifications using Nanopore long-read sequencing"

Dr. Haitao Guo

1R56AI179574-01, Multi-PIs: Daryl T. Lau, Haitao Guo, Ying-Hsiu Su, 8/3/23 - 7/31/24, total cost: $847,428/Total annual cost
"HBV cccDNA and integrated DNA in HIV coinfection and HBV monoinfection"
Chronic hepatitis B (CHB) remains a substantial public health burden despite the availability of effective vaccines and approved therapies. Functional cure with HBsAg clearance is the current HBV treatment endpoint. Although prolonged therapy with nucleos(t)ide analogs can suppress HBV DNA replication, the rate of functional cure remains low. With functional cure, it is expected that the intrahepatic cccDNA would be in a transcriptional inactive state regardless the status of the integrated HBV DNA (iDNA). We and others provided evidence that the iDNA produces a major source of HBsAg especially in HBeAg-negative CHB. The current serum assay cannot distinguish HBsAg generated from intrahepatic cccDNA versus iDNA. In this proposal, we focus to 1) evaluate both the concentrations and the transcriptional activities of cccDNA and iDNA in CHB with and without HIV; 2) assess the roles of epigenetic mechanisms in cccDNA and iDNA transcription in treatment response; 3) compare the intrahepatic and plasma iDNA levels, and to correlate iDNA levels with HBsAg titers and treatment outcomes; 4) evaluate second generation serum HBV pgRNA and novel HBV core Ag (HBcAg) biomarkers as surrogate markers for cccDNA; 5) apply the clinical, serological and virological parameters to generate predictors of treatment-induced transcriptionally inactive cccDNA and HBsAg loss. This is a unique translational research study that utilize well-characterized liver and blood samples as well as advanced molecular technologies and methods to understand the virological mechanisms of HBV persistence, inactivity, and clearance. The success of our study will have significant impacts in the development of novel therapies leading to a complete HBV cure.

R21/R33AI179929, 1/1/24 - 12/31/28, total cost: $198,750/Total annual cost
"High throughput screening and preclinical development of HBV cccDNA inhibitors"
HBV cccDNA is essential to the virus life cycle, its elimination is considered critical to a cure but has not been achieved by the FDA-approved drugs that exclusively target the viral polymerase. Due to the limitations of current HBV experimental systems, including the impracticality of detecting cccDNA itself, cccDNA has not been rigorously targeted in HTS of small molecule libraries. This is a biphasic project to develop and implement a novel high throughput screening (HTS) system for identification of inhibitors of hepatitis B virus (HBV) covalently closed circular DNA (cccDNA) (R21 phase), followed by preclinical drug development studies (R33 phase). Successful completion of our goals will deliver at least one lead compound to advanced preclinical studies toward development of novel therapy to cure chronic hepatitis B.

Dr. Yufei Huang

1U01CA279618-01, 8/3/23 - 7/31/24, total cost: $408,557/Total annual cost
"m6A-suite: an informatics pipeline and resource for elucidating roles of m6A epitranscriptome in cancer"
Project Summary N6-methyl-adenosine (m6A) is the most abundant mRNA methylation in mammalian cells. Emerging evidence has linked m6A with cancer phenotypes in many cancers, spurring a surge of research in studying m6A and cancer biology. However, dysregulation of m6A effector writers, erasers, and readers and reprogramming of m6A sites are poorly characterized. How different modes of m6A-regulation of gene expression mediate the downstream cancer pathways and phenotypes is mostly missing. We have developed several widely used informatics tools for m6A peak detection, differential m6A analysis, and functional

predictions for m6A targets from MeRIP-seq m6A profiling data. Using these tools, we worked together with cancer biology collaborators to reveal reprogramed viral and host m6A epitranscriptome in cells infected by the oncogenic virus KSHV and discovered a cross-talk between m6A writers, erasers, and readers to regulate cancer growth and progression. However, the fast-moving m6A and cancer research poses many unmet informatics challenges. Among them, the ability to accurately identify single-base m6A sites and predict key m6A regulatory mechanisms from profiling data is seriously lacking. Also, a comprehensive database that catalogs and enables queries of where, what, and how of m6A methylation and function in normal and cancer conditions is highly desirable. To address challenges, we propose to develop m6A-Suite, an informatics toolbox, pipeline, and resources to facilitate the mechanistic study of m6A in cancer. A key obstacle to developing tools in m6A-Suite is a lack of large, high- quality training datasets. Toward this end, we have collected 1,113 human and 680 mouse MeRIP-seq samples from cancer cell lines, tumors, and normal tissues and identified >4M m6A peaks. In parallel, we have also collected 194,060 single-base m6A sites in 9 cell lines and 3 tissues. We propose to leverage this data to construct the highly desirable training datasets. Using these datasets, we will develop efficient and accurate tools for single-base m6A detection and quantification from MeRIP-seq and nanopore data (Aim 1), enable the prediction of m6A-mediated RNA decay and splicing (Aim 2), and establish the comprehensive, queriable m6A- KB knowledgbase to catalog these predictions in an extensive collection of public MeRIP-seq and nanopore data in cancer and normal cells, and tissues in diverse conditions(Aim 3). We will systematically test and evaluate these tools within this project and through many established and emerging collaborations inside and outside the ITCR consortium. We will make the tools and data freely available to the research community and constantly seek feedback from the collaborators and users for improvement. Given the emerging nature of m6A and cancer research, the addition of these tools to the ITCR program will positively impact this important, fast-growing, new area of cancer research.

1R01HG013359-01, Role: Co-Investigator, PI: Kai Wang, 8/3/23 - 7/31/24, total cost: $709,603/Total annual cost

"Novel bioinformatics methods to detect DNA and RNA modifications using Nanopore long-read sequencing"

1R01CA284554-01, Role: Co-Investigator, PI: Shou-Jiang Gao, 9/8/23 - 8/31/28, total cost: $793,089/Total annual cost

"Impact of microbiota on AIDS-Kaposi's sarcoma development and therapy"

Dr. Renfeng Li

1R01CA272710-01A1, Role: Co-Investigator, PI: Anthony Faber, 8/02/2023 - 7/31/2028, $571,084/Total annual cost

"SUMOylation disruption is toxic for SS18-SSX-driven synovial sarcoma"

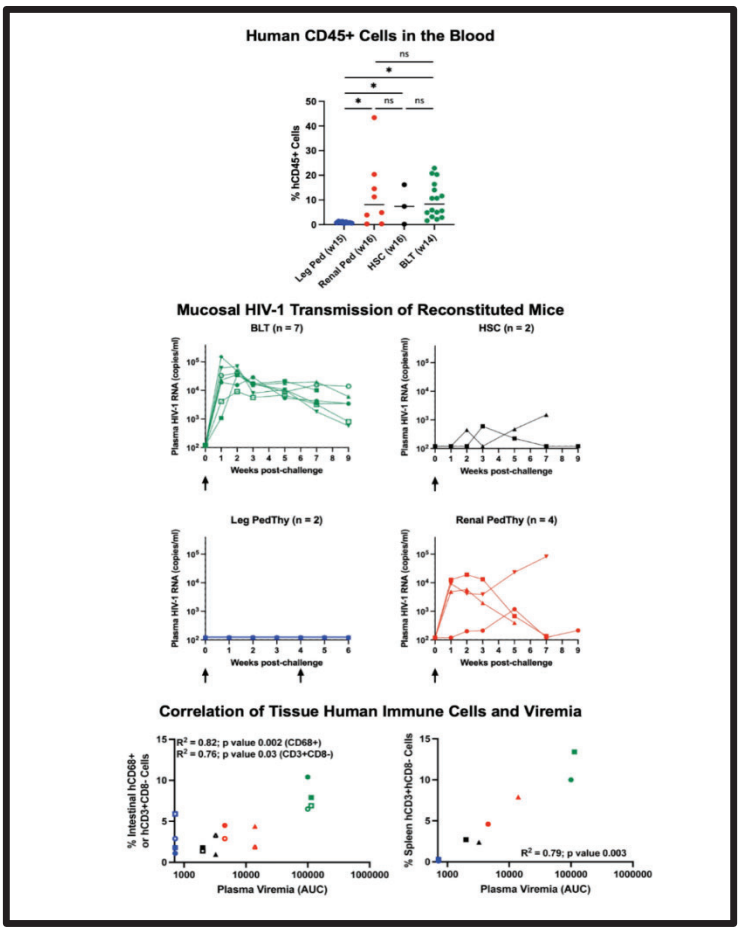
The goal of this project is to test a diverse set of synovial sarcoma (SS) mouse models for efficacy and safety of SUMOylation inhibition and to investigate the relationship between SS18-SSX and the SUMOylated proteome in synovial sarcoma.

DOD-HT9425-23-1-1017, PI: Role: Co-Investigator, PI: Anthony Faber, Renfeng Li, 9/15/2023 - 9/14/2026, $179,922/Total annual cost

"Sabasumstat as a Sensitizer to Radiation Therapy in Synovial Sarcoma"

This project will investigate the SUMO inhibitor sabasumstat as a sensitizer to radiation therapy in mouse models of Synovial Sarcoma (SS).

Exciting Sciences

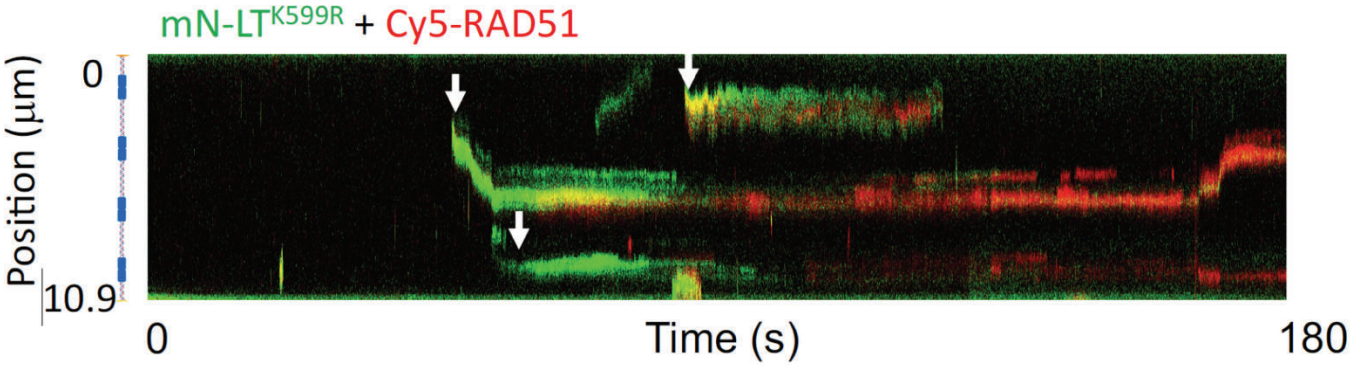


Use of pediatric thymus to humanize mice for HIV-1 mucosal transmission (Drs. Zandrea Ambrose and Tom Smithgall's lab)

The gold standard for HIV studies in humanized mice is the BLT model, which requires fetal thymus prior to injection of hematopoietic stem cells (HSC). Our recent study evaluated pediatric thymus tissue removed during cardiac surgeries and implanted under the renal capsule (Renal PedThy) or in the quadriceps muscle (Leg PedThy) prior to HSC injection. We showed that human immune reconstitution can be achieved in Renal PedThy mice close to that of BLT mice and better than HSC only and Leg PedThy mice. Renal PedThy (but not Leg PedThy) mice could also be infected mucosally with HIV, but not to the level of BLT mice. Virus transmission and replication correlated with human HIV-target cells (CD4+ T cells and macrophages) at the site of transmission or in the spleen. Refinement of the Renal PedThy model with more tissue or different donors is likely still needed.

Roy CN, Shu ST, Kline C, Rigatti L, **Smithgall TE, Ambrose Z**. Use of pediatric thymus to humanize mice for HIV-1 mucosal transmission, Sci Rep 2023, 13:17067. PMCID: PMC10564933.

Unraveling tumor virus DNA (Drs. Yuan Chang and Patrick Moore's lab)



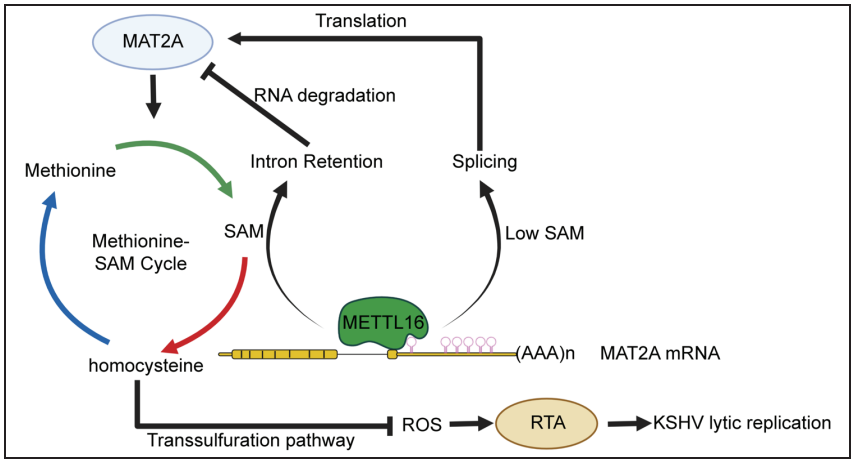
Single DNA molecule binding by Merkel cell polyomavirus large T protein (green) that has a mutation to its ATP hydrolysis site and cannot hydrolyze ATP (Walker A site mutation) still induces DNA melting as measured by Rad51 binding (red).

Unraveling tumor virus DNA: Li "James" Wan and members of the Chang-Moore lab collaborated with Matt Schaich, Sarah Hengel, Nara Lee and Ben Van Houten to look at single DNA molecule replication initiation by Merkel cell polyomavirus and SV40 large T proteins. These oncoproteins bind to their viral origins to unwind

them ("DNA melting"), allowing replication to begin. As they report in PNAS, these proteins begin the unwinding process non-enzymatically by multimerizing and invading the DNA double-strands. This upends a 20-year-old model in which the large T proteins act as helicase enzymes to rachet together an intervening piece of DNA, causing a rupture in the DNA double-strand. Not only do these viral proteins melt DNA without using ATP hydrolysis but for Merkel cell polyomavirus, these CVP investigators show the the entire helicase region can be eliminated from large T and it still begins the initial melting step needed for DNA replication.

Wan L, Toland S, Robinson-McCarthy LR et al. Unlicensed origin DNA melting by MCV and SV40 polyomavirus LT proteins is independent of ATP-dependent helicase activity. Proc Natl Acad Sci U S A. 2023;120(30):e2308010120. PMID: 37459531.

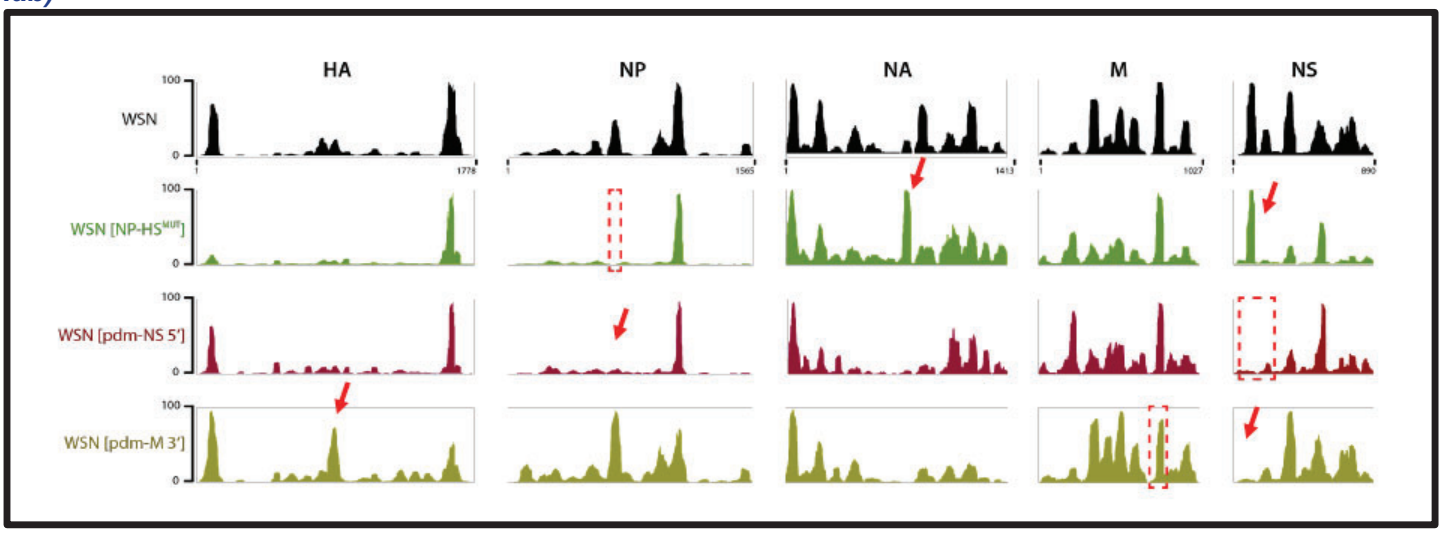
KSHV control life cycle by hijacking an RNA methyltransferse to regulate one carbon metabolism and oxidative stress (Dr. Shou-Jiang Gao's lab)



In this study, the Gao's lab collaborated with Dr. Yufei Huang's lab to identify a suppressive role of METTL16 in KSHV lytic replication. METTL16 binds to and writes m^{6}A on MAT2A transcript to regulate its splicing, maturation and expression in KSHV-infected cells. As a rate-limiting enzyme in the methionine-*S*-adenosylmethionine (SAM) cycle, MAT2A catalyzes the conversion of L-methionine to SAM required for the transmethylation of protein, DNA and RNA, transamination of polyamines, and transsulfuration of cystathionine. The study showed that METTL16 or MAT2A to regulate intracellular SAM metabolism, redox state to control viral latency and replication. This study has illustrated the linkage of KSHV life cycle with specific m^{6}A modifications, and cellular metabolic and oxidative conditions.

Zhang XQ, Meng W, Feng J, Gao XH, Qin C, Feng PH, Huang YF, Gao S-J. METTL16 controls Kaposi's sarcoma-associated herpesvirus replication by regulating *S*-adenosylmethionine cycle. *Cell Death and Diseases*, 2023, 14(9): 591. doi: 10.1038/s41419-023-06121-3.PMID: 37673880.

Interaction of influenza virus genomic RNA with viral nucleoprotein is regulated in trans (Dr. Nara Lee's lab)

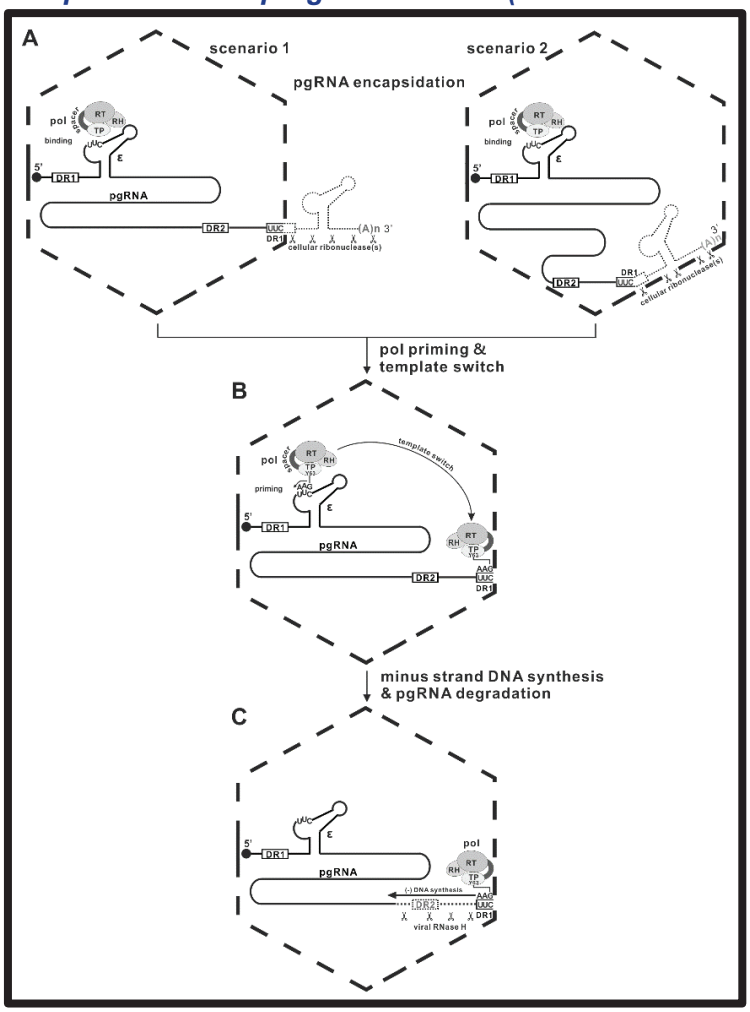


The genome of influenza A viruses (IAV) consists of eight negative-sense RNA segments that are coated by viral nucleoprotein (NP). Until recently, it was assumed that NP binds viral genomic RNA (vRNA) uniformly along the entire segment. However, we have recently proposed a revised model, which posits that NP instead binds preferentially to certain regions of vRNA, while others are depleted for NP binding (PMID: 28911100).

In this study, the Lee lab in collaboration with the Lakdawala lab examined determinants of NP recruitment to the RNA genome. The authors introduced local mutations in IAV strains and mapped NP binding by using a next-generation sequencing-entailing technique. The authors found that NP binding is affected by local nucleotide changes. More surprisingly, these local changes affected NP binding at distant sites on the IAV genome on separate segments. These results suggest that NP binding is not regulated by primary sequence alone, but that a network formed by multiple segments governs the deposition of NP on vRNA.

Le Sage V, Kanarek JP, Lakdawala SS, Lee N. Local changes in viral RNA sequence drive global changes in influenza nucleoprotein binding. J Med Virol. 2023 Jul;95(7):e28896.

Conditional replication and secretion of hepatitis B virus genome uncover the truncated 3' terminus of encapsidated viral pregenomic RNA (Dr. Haitao Guo's lab)

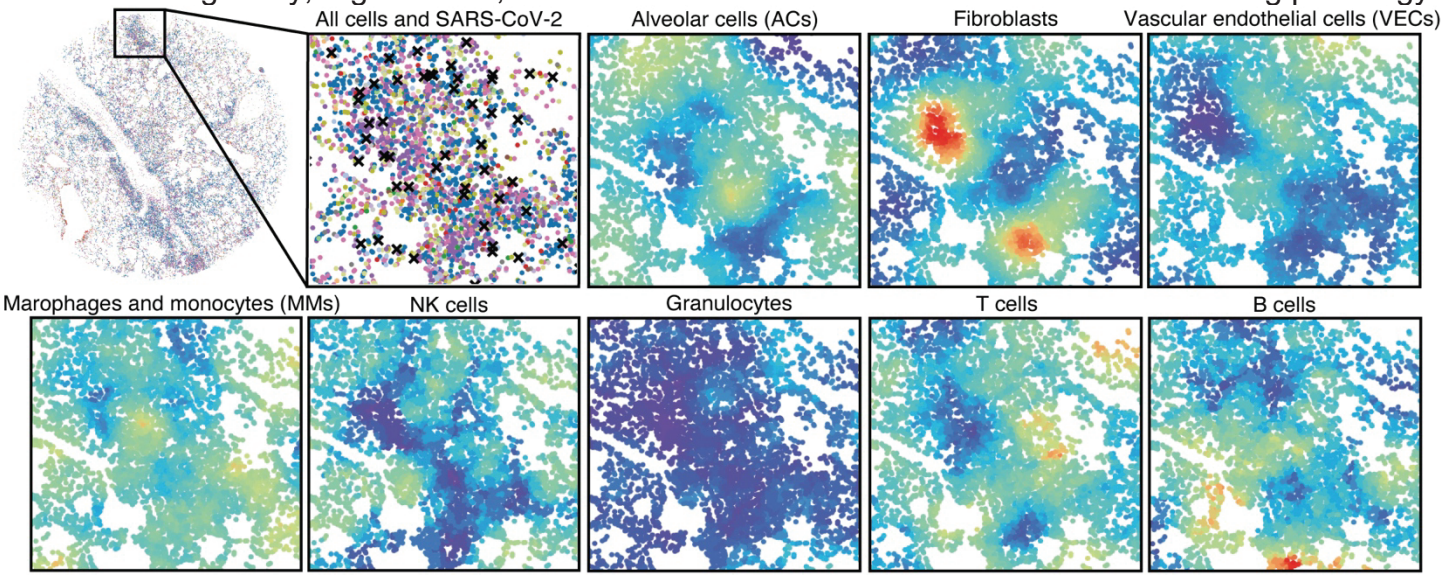


Hepatitis B virus (HBV) pregenomic RNA (pgRNA) is packaged into capsid where reverse transcription takes place to synthesize viral DNA genome, and the encapsidated pgRNA is the predominant species of serum HBV RNA in patients as a serological biomarker. In this study, by utilizing various conditional HBV replication and secretion systems, Shen et al analyzed the intracellular and extracellular capsid pgRNA and revealed that the 3′ terminus of capsid pgRNA is scatteredly distributed between DR2 and poly(A) tail, except that the viral polymerase priming-defective mutant Y63D retained the sequence upstream of 3′ DR1. Mechanistically, the heterogeneity of capsid RNA 3′ terminus is due to the endogenous viral RNaseH activity during reverse transcription and exogenous MNase digestion during capsid RNA isolation; cellular ribonucleases may also participate in this process as the Y63D pgRNA 3′ terminus in the immunoprecipitated capsid without prior MNase treatment remains truncated into 3′ DR1. The major pgRNA splicing variant 1 of 2.1 kb and the artificial 3′ DR1 and ε deletion mutants also possess a truncated 3′ end of capsid RNA, indicating that the underrepresentation of the 3′ end of encapsidated pgRNA is independent of pgRNA length or 3′ terminal sequences. Altogether, this study suggests that the 3′ region of HBV capsid pgRNA downstream of 3′ DR1 is likely positioned outside of the capsid or loosely encapsulated, and thus is ribonuclease accessible. Furthermore, the detailed features of capsid pgRNA 3′ terminus will shed light on HBV pgRNA encapsidation and reverse transcription and aid the development of better diagnostics of serum HBV RNA.

Shen S, Liu W, Zeng G, Liang H, Yu X, Zhang H, Sun J, **Guo H**. Conditional replication and secretion of hepatitis B virus genome uncover the truncated 3' terminus of encapsidated viral pregenomic RNA. J Virol. 2023; 97:e0076023. PubMed PMID: 37754759.

***Spatial single cell transcriptome analysis of COVID-19 lung tissues revealed** complex spatial cellular **heterogeneity, organization, and interactions** (Dr. Yufei Huang and Shou-Jiang Gao's lab)*

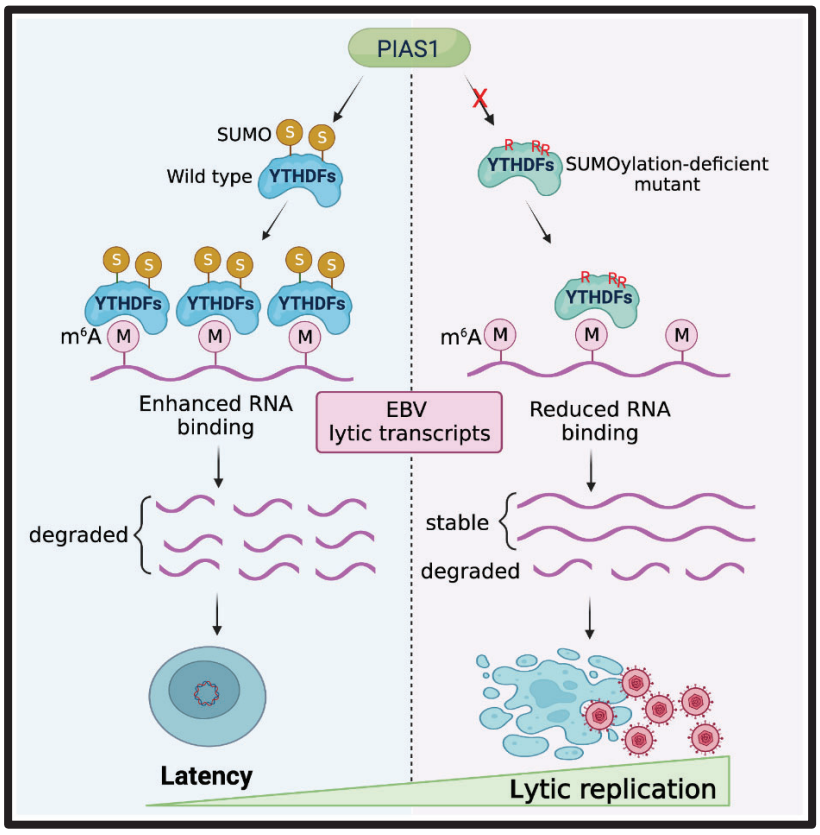
In collaboration with Dr. Shou-Jiang Gao's lab, Dr. Huang's lab used advanced spatial single transcriptome analysis to investigate the spatial single-cell molecular and cellular features of postmortem COVID-19 lung tissues. A total of 10,414,863 transcripts of 221 genes in whole-slide tissues were detected and segmented into 1,719,459 cells, and further mapped to 18 major parenchymal and immune cell types, all of which were infected by SARS-CoV-2. Compared to the non-COVID-19 control, COVID-19 lungs exhibited reduced alveolar cells (ACs) and increased innate and adaptive immune cells. Spatial analysis of local infection rates revealed regions with high infection rates that were correlated with high cell densities (HIHD). The HIHD regions expressed high levels of SARS-CoV-2 entry-related factors including ACE2, FURIN, TMPRSS2, and NRP1, and co-localized with organizing pneumonia (OP) and lymphocytic and immune infiltration, which exhibited increased ACs and fibroblasts but decreased vascular endothelial cells and epithelial cells, mirroring the tissue damage and wound healing processes. Sparse **n**on-negative matrix factorization (SNMF) analysis of niche features identified 7 signatures that captured structure and immune niches in COVID-19 tissues. Trajectory inference based on immune niche signatures defined two pathological routes. Trajectory A primarily progressed with increased NK cells and granulocytes, likely reflecting the complication of microbial infections. Trajectory B was marked by increased HIHD and OP, possibly accounting for the increased immune infiltration. The OP regions were marked by high numbers of fibroblasts expressing extremely high levels of COL1A1 and COL1A2. Examination of single-cell RNA-seq data (scRNA-seq) from COVID-19 lung tissues and idiopathic pulmonary fibrosis (IPF) identified similar cell populations consisting mainly of myofibroblasts. Immunofluorescence staining revealed the activation of IL6-STAT3 and TGF-b-SMAD2/3 pathways in these cells, likely mediating the upregulation of COL1A1 and COL1A2 and excessive fibrosis in the lung tissues**.** Together, this study provides a spatial single-cell atlas of cellular and molecular signatures of fatal COVID-19 lungs, which reveals the complex spatial cellular heterogeneity, organization, and interactions that characterized the COVID-19 lung pathology.



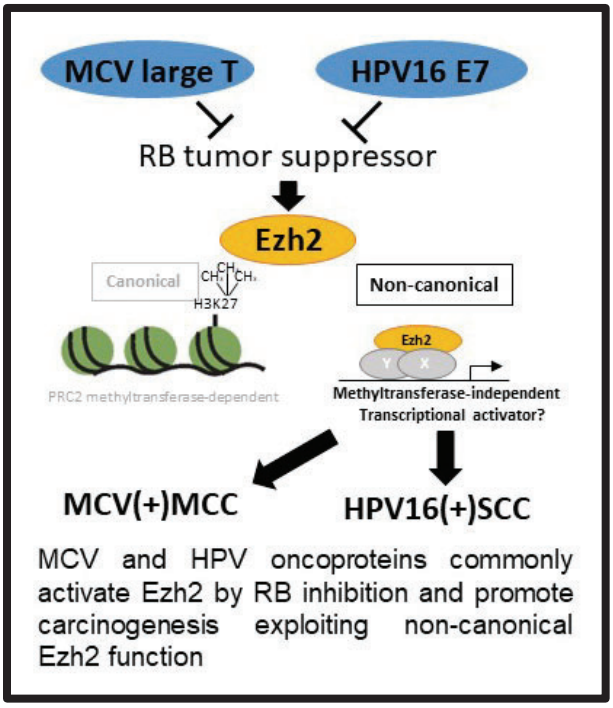
Das A[#], Meng W[#], Li ZT, Hasib MM, Hugh G, da Silva SR, Chen LP, Sica GL, Paniz Mondolfi AE, Bryce C, Grimes Z, Sordillo EM, Cordon-Cardo C, Rivera, KP, Flores F, Chiu YC, Huang YF, Gao S-J. Cellular and immune signatures, and pathological trajectories of fatal COVID-19 lungs defined by in situ spatial single-cell transcriptome analysis. J Med Virol, 2023, 95: e29009. doi: 10.1002/jmv.29009. PMID: 37563850. (#Equal contribution)

SUMOylation of the m6A reader YTHDF2 by PIAS1 promotes viral RNA decay to restrict EBV replication (Dr. Renfeng Li's lab)

A model outlining how PIAS1 facilitates SUMOylation of m6A RNA readers (YTHDFs) to regulate EBV latency and lytic replication. When YTHDFs are SUMOylated, they show increased binding affinity to EBV lytic transcripts, facilitating their decay to maintain viral latency. Conversely, SUMOylation-deficient YTHDFs display reduced viral RNA binding capabilities, leading to increased RNA stability that fosters EBV lytic replication.



Sugiokto FG, Saiada F, Zhang K, **Li R**. SUMOylation of the m6A reader YTHDF2 by PIAS1 promotes viral RNA decay to restrict EBV replication. bioRxiv [Preprint]. 2023 Aug 9:2023.08.08.552509.



Methyltransferase-independent function of enhancer of zeste homologue 2 maintains tumorigenicity induced by human oncogenic papillomavirus and polyomavirus (Dr. Masa Shuda's lab)

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Recently Published

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Dr. James Conway's Lab:

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Drs. SJ Gao & Yufei Huang Labs Summer Picnic

Halloween 2023 in the Chang - Moore Lab
"Where The Wild Things Are"

About the Cancer Virology Program (CVP):

Viruses are the cause of approximately 15% of human cancers. CVP is dedicated to research on the viruses causing human cancer as well as using viruses as tools to fight cancer. The study of tumor viruses has led to important discoveries in cancer research, including the identification of numerous oncoproteins and tumor suppressor proteins critical for the development of all cancers.

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Cancer Virology Program

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