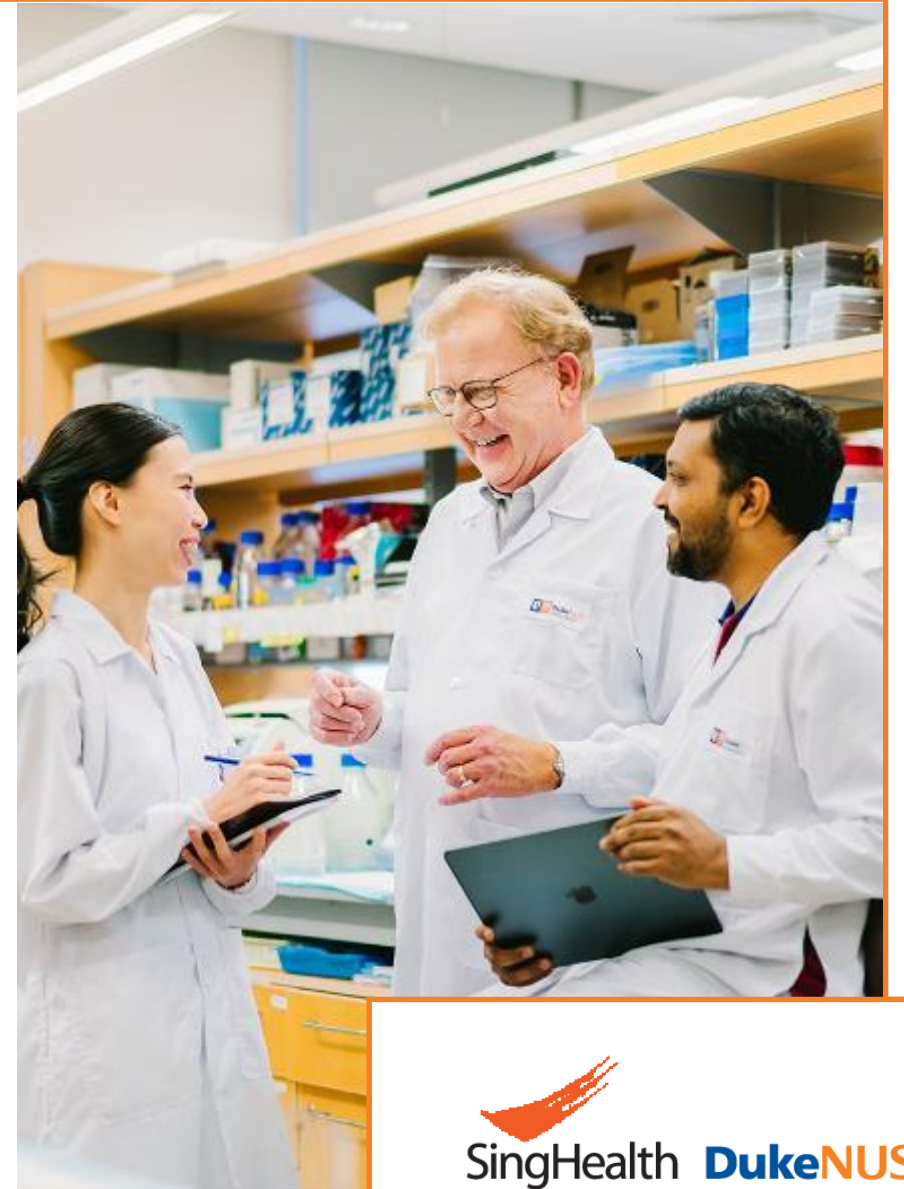


Duke NUS Medical School

Research In Singapore For Asia And The World

Transforming Medicine, Improving Lives



Established in 2005 as a landmark collaboration between Duke University and the National University of Singapore



Duke
UNIVERSITY

Home to USA's **largest and oldest academic clinical research organisation**



DukeNUS
Medical School

Singapore's first and only US-style graduate medical school



NUS
National University
of Singapore

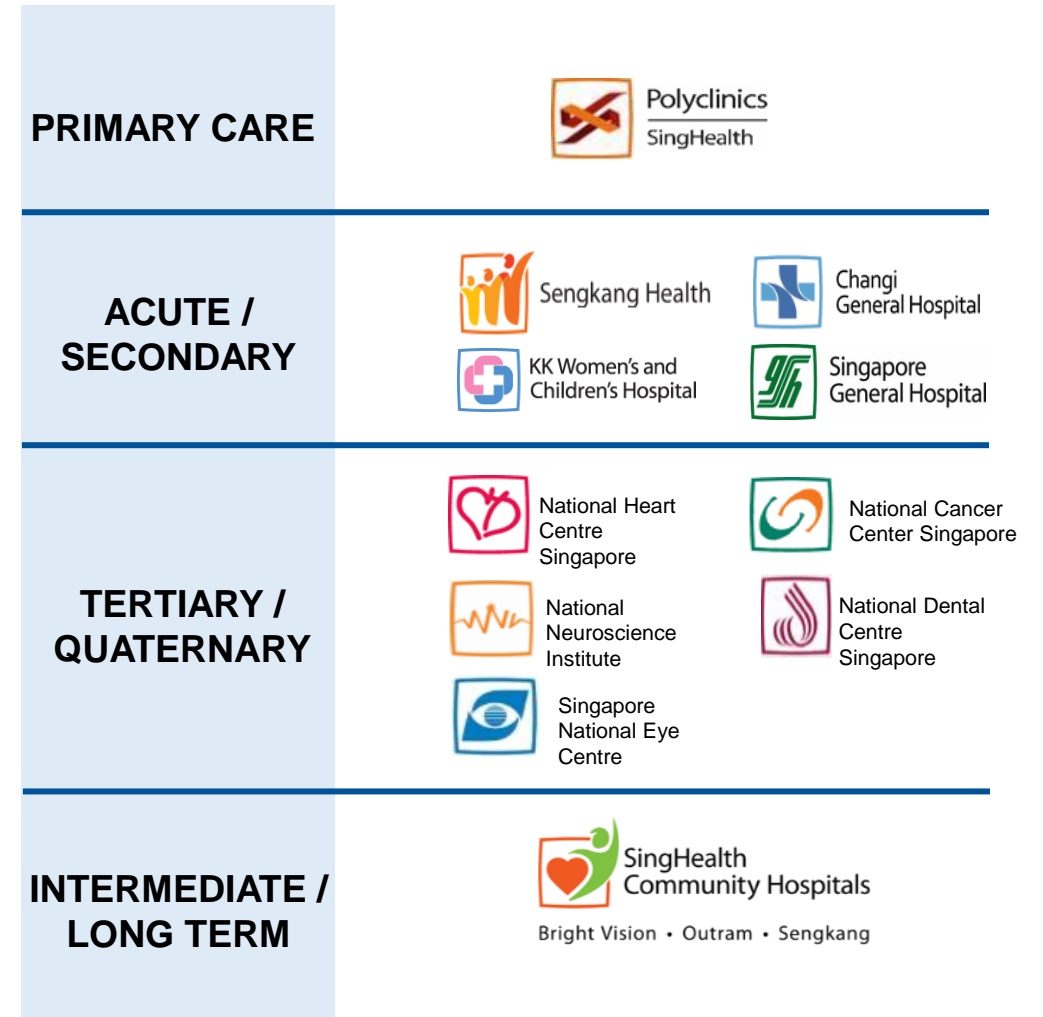
A leading global university and **Singapore's flagship university**

An autonomous school that provides both innovative education & impactful research

Integrated with SingHealth, the largest public healthcare cluster, to form Singapore's premier Academic Medical Centre (AMC)

Singapore Health Services (SingHealth) is Singapore's **largest healthcare cluster** that provides a **real-world setting** for the development of research and education at Duke-NUS

The SingHealth **Duke-NUS Academic Medical Centre (AMC)** operates as a cohesive collaboration, seamlessly blending cutting-edge clinical and translational research with patient care and delivery systems.



Research at Duke-NUS is optimised through its wide variety of programmes, institutes and collaborations, which help to translate discoveries and innovations into commercial applications that can enhance healthcare and improve the lives of not only patients, but also the general population

OUR RESEARCH BY NUMBERS



>11000

Papers published in international peer-reviewed journals



>3000

Faculty in research and education



>\$772m

In research funding locally and overseas



11

Current Singapore Translational Research (STaR) Investigators



>300

Synergistic Research Alliances



3

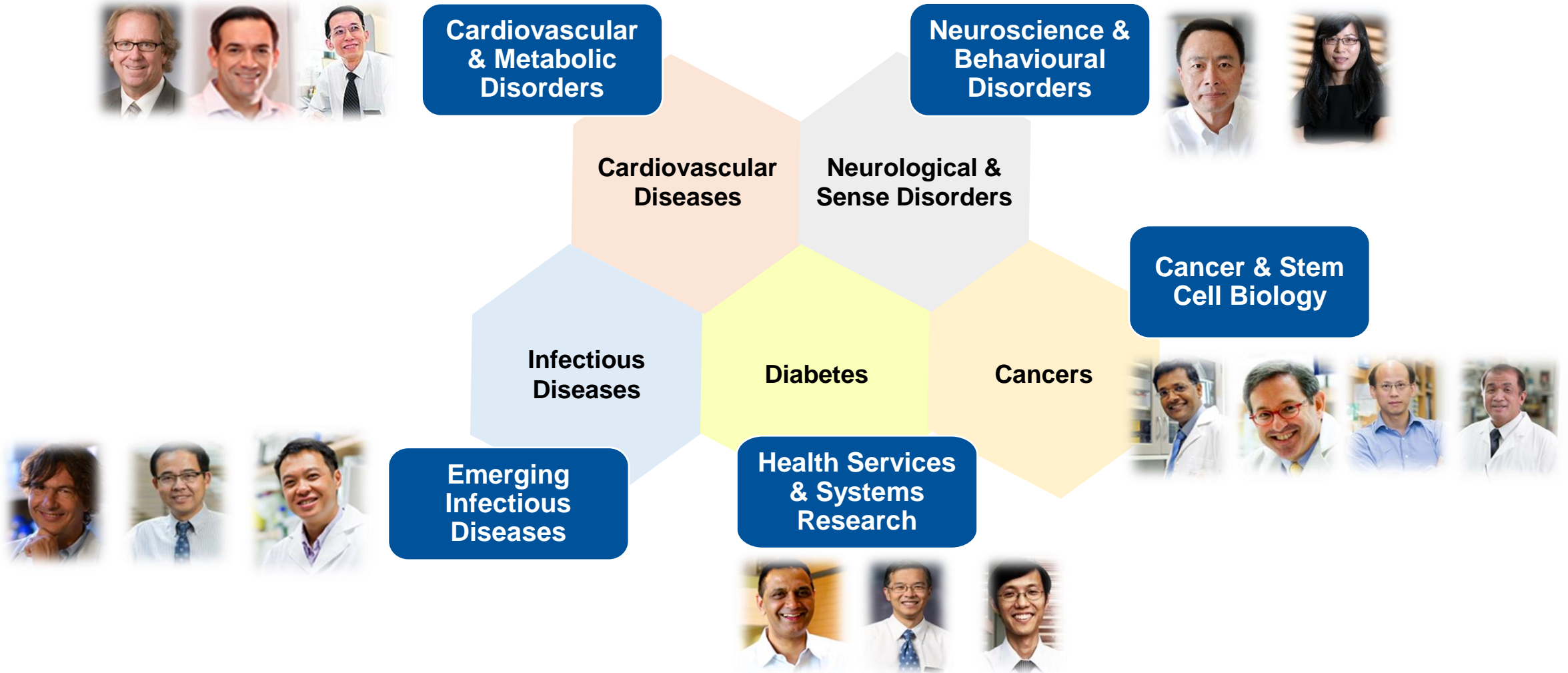
National Research Foundation Investigator ships



8

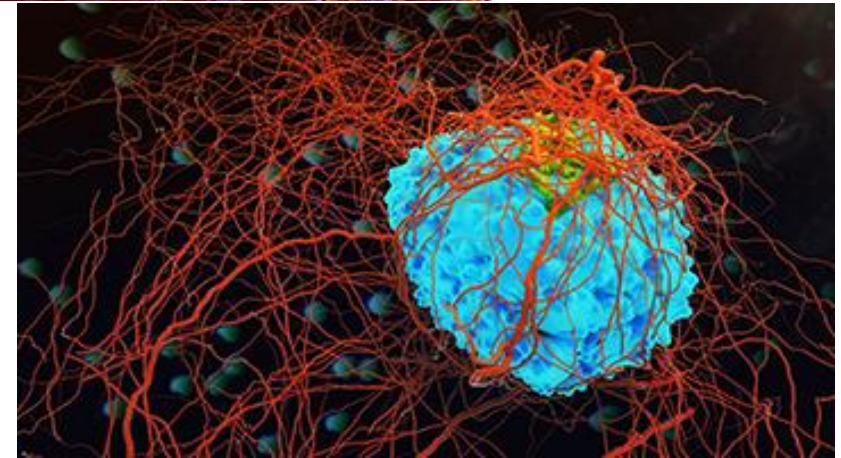
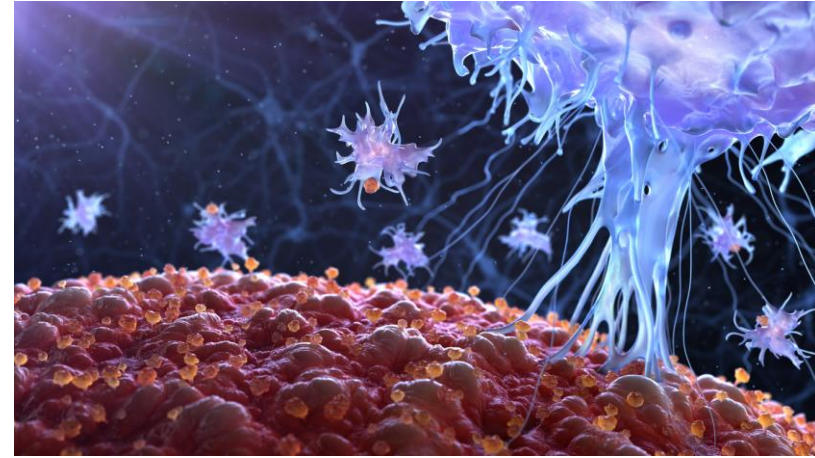
National Research Foundation Fellowships

Duke-NUS Signature Research Programmes



The **Cancer and Stem Cell Biology Program** pioneers diverse research, spanning basic science, disease investigation, drug discovery, and groundbreaking trials.

“Collaborating across Singapore, including National Cancer Centre, Singapore General Hospital, A*STAR, and more, we push boundaries in cancer research and treatment.”



Empowering Breakthroughs: Unleashing Innovation in Cancer and Stem Cell Frontiers.

Major Research Themes

Cancer biology & stem cell biology

Computational biology and (epi)genomics

Translational and molecular imaging

Focus / Targets

- **Wnt signalling**, biogenesis, delivery and targets
- **ARF-MDM2-p53** tumor suppressive mechanisms
- Regulation of **telomerase** activity
- **mRNA** modifications and translation
- Targeting the **mTOR kinase**
- **G Protein** signaling (e.g. GNA12 subfamily)
- Inhibition of isoprenylcysteine carboxyl-methyltransferase (**ICMT**)
- Dissecting the role of **Bcl-2 family** molecules
- Stem cell biology in **epithelial tissues**

- **Injury response & oxidative stress**
- Genomic and epigenomic profiling
- Extracellular and post-translational signaling
- **RNA metabolism**, alternative splicing, (epi)transcriptomics
- Long non-coding RNAs

- Imaging cancer immunotherapy
- Image-guided delivery approaches
- Development of imaging biomarkers

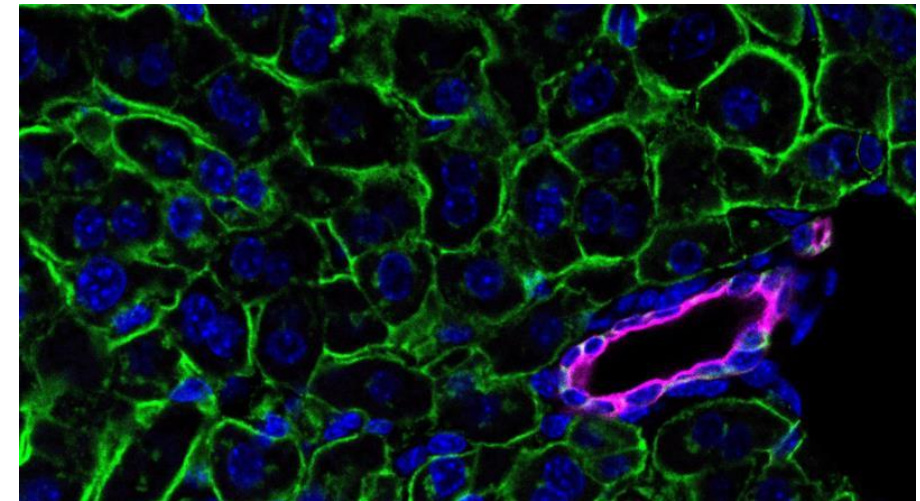
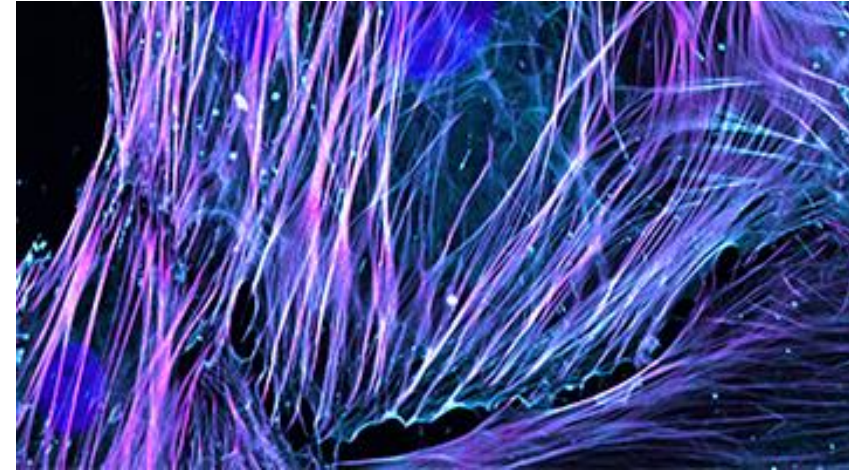
Therapy Areas

- Oncology, including but not limited to:
 - Breast cancer
 - Gastric cancer
 - Biliary tract cancers
 - Liver cancer
 - Head & neck cancer
 - Lung cancer
 - Epithelial cancer
- Haematology, including but not limited to:
 - Chronic myelogenous leukaemia
- Cancer cachexia
- Wound healing
- Ageing
- Infectious Diseases
- Obesity and diabetes

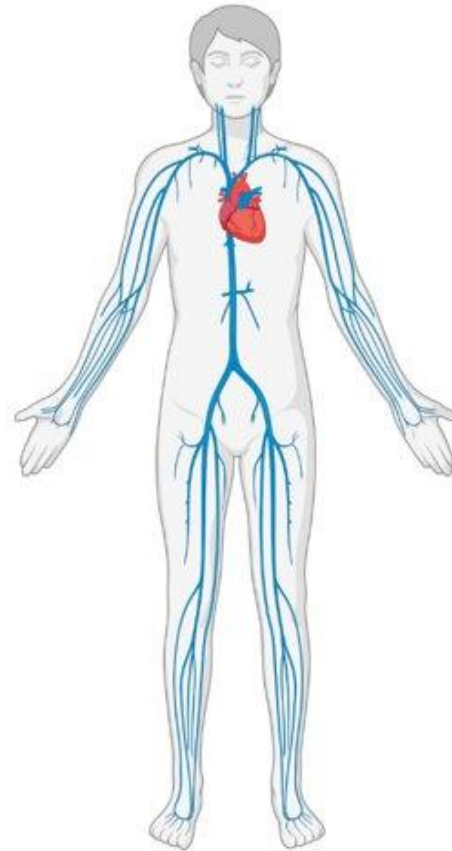
Technologies / Tools

- Radiopharmaceutical chemistry
- In vivo nuclear / fluorescent imaging (rodents, non-human primates)
- Novel mouse models (e.g. for the studies of epithelial stem cells and cancer)
- Budding yeast models
- Drosophila models
- Computational modelling
- Machine learning
- Cancer genomics and epigenomics
- (Epi)transcriptomics

Cardiovascular and Metabolic Disease Program delves into heart and metabolic research, expertise in fat cell biology, blood-brain barrier, mitochondrial health, diabetic kidney intricacies, heart development, genetics, and clinical trials.



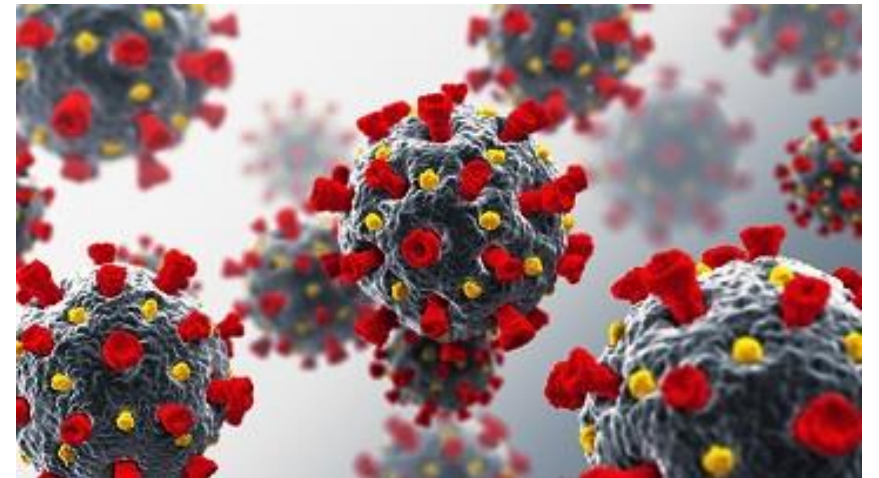
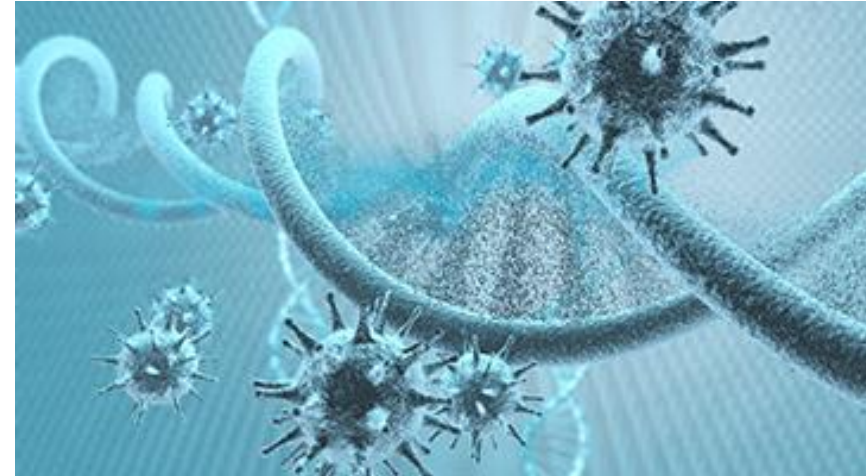
Deciphering Health Intricacies for Innovative Strategies in Preventing, Diagnosing, Treating Cardiometabolic Conditions



Therapy Areas

- Cardiomyopathies
- Myocardial infarction
- Heart failure
- Coronary artery disease
- Diabetic Nephropathy
- Chronic kidney disease
- Ocular angiogenic diseases
- Obesity
- Hypertension
- Diabetes
- Mitochondrial diseases
- Arrhythmogenic Disease
- Fibrotic diseases
- Ageing

Emerging Infectious Diseases Program focus spans all facets of emerging infectious diseases - from uncovering pathogens, understanding molecular mechanisms, and exploring immunology, to pioneering therapeutics, vaccine trials, and global health investigations



A premier regional infectious disease hub for reference and research

Major Research Themes

Disease emergence and epidemiology

Immunology

Treatment, detection and control

Molecular biology and computational science

Focus / Targets

- Evolution and emergence of infectious diseases
- Human and animal disease surveillance, virus isolation and characterisation
- Understand viral disease ecosystems
- Roles played by mutation, natural selection, recombination/reassortment and host immune response on virus diversity

- Innate and adaptive immune response
- Mast cell responses to viral pathogens
- Vertical transmission (mother to child)

- Adoptive T-cell Therapy
- HLA-peptide specific antibodies
- Novel vaccination strategies
- Antibody based serological tests
- Animal models for therapeutics studies
- Zoonophylaxis

- Genetic changes and implications for epi/pandemic
- Identify and elucidate the molecular details underlying the interplay between viruses and host cells (e.g. functional genomics)
- Viral morphology, protein structure & function

Therapy Areas

- Infectious diseases due to:
 - Respiratory viruses (influenza, SARS-CoV-2)
 - Enteric viruses
 - Flavivirus (e.g. Dengue, Zika)
 - Zoonotic viruses
- Hepatitis B
- Hepatocellular carcinoma

Platforms

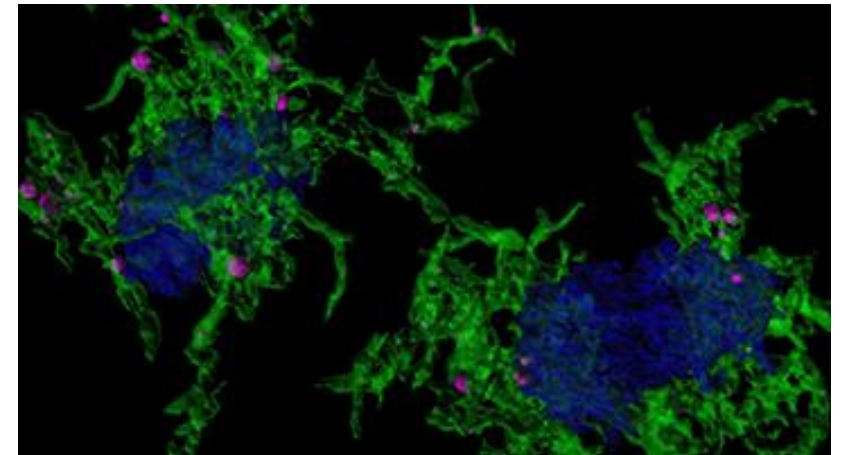
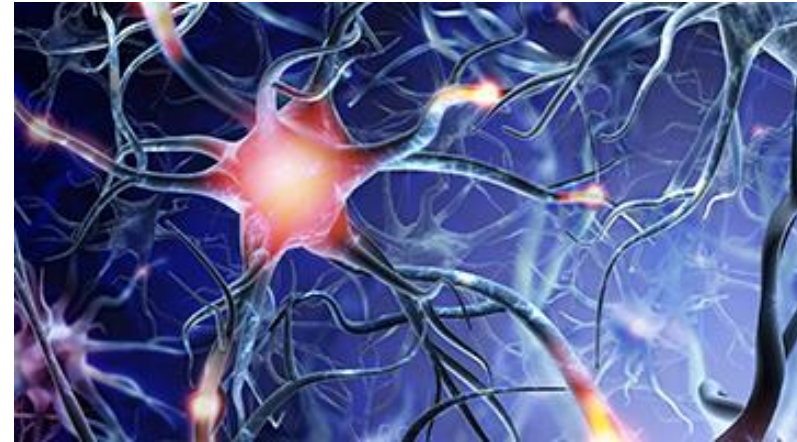
- ViREMiCS

Technologies / Tools

- Genome-scale CRISPR knockout, Haploid Genetic Screen, Genome-wide RNAi
- X-ray crystallography
- Cryo-electron microscope
- 3-D Microfluidics Platform
- 'omics'-technologies
- Imaging
- Novel mouse models (e.g. flaviviral infection) to study new therapeutics

Neuroscience and Behavioural Disorders

focuses on understanding the nervous system's structure, functions, and mechanisms underlying disorders. Collaborating with clinical faculties, we stand strong in neurodegenerative diseases, cognitive disorders, and more.



Deciphering Human Intelligence and Translating Discoveries into Brain Disorder Strategies

Neurodegeneration

Parkinson's Disease

Alzheimer's Disease

Amyotrophic Lateral Sclerosis

Spinal Muscular Atrophy

Huntington's Disease

Neuropsychiatry & Neurodevelopmental Disorders

Autism

Schizophrenia

Attention Deficit Hyperactivity Disorder

Angelman Syndrome

Microcephaly

Depression

Sleep & Circadian Rhythms

Duke-NUS's **Health Sciences and Systems Program** leads in deciphering global health systems.

Unveiling service effectiveness, scalability, and economics, we foster interdisciplinary collaboration. Partnering with government, health systems, and social entities, we employ implementation science, health economics, qualitative research, and more.



Empowering Tomorrow's Health: Unveiling Insights through HSSR Excellence

Major Research Themes

Implementation science

Health economics

Decision science

Survey / qualitative research

Quantitative medicine

Epidemiology

Data science

Research Focus

- Implementation research includes evaluation of existing policies and standard practices, patient needs and the socio-economic factors that impact access to care

- Includes behavioural economic trials, economic modelling, health technology assessments, and preference assessment using state-of-the-art techniques

- Application of modelling methods to promote informed decision-making regarding complex healthcare issues

- Collecting data to understand the demand for healthcare services, medical & social patterns of behaviour, patient & provider perspectives, and to inform modelling efforts

- Developing novel statistical methods and associated clinical trial designs, including artificial intelligence, big data analytics, and longitudinal data analysis

- Population-based epidemiological studies, development of patient-reported outcome measures, new prevention and treatment models, and etiological studies

- Advanced computational and intelligent solutions to improve patient care, including artificial intelligence, machine learning, data science, and leveraging real-world data

Databases

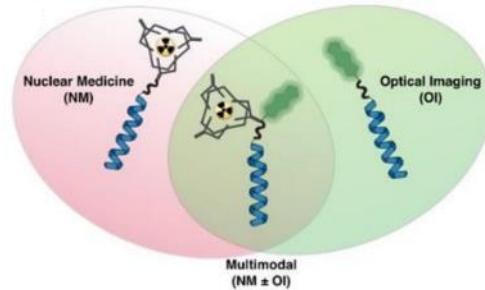
- Diabetes registry
- ED Database
- Cardiovascular Database
- Asthma, COPD
- Colorectal, Breast, Lung, Lymphoma
- Liver Cancer, Distal Pancreatectomy ,Pancreatectomy Databases
- Infection surveillance Registry
- Deidentified Image Database

Platforms

- ODySSEy
- TriNetX
- DEDUCES
- JARVIS

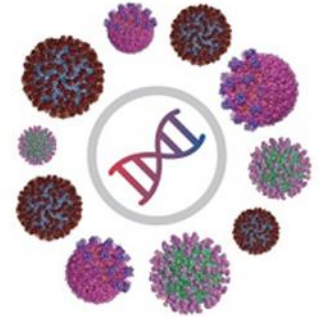
Cancer Immuno-Therapy Imaging “CITI” Programme

An integrated, multidisciplinary platform for translational immunoncology imaging that addresses the urgent call for biomarker-driven approaches to monitor tumour immune response.



Viral Research and Experimental Medicine Centre - ViREMiCS

Aims to accelerate the clinical translation of vaccines and therapeutics by working with academia and industry partners to develop molecular tools that accurately assess the safety and efficacy of vaccines and therapeutics.



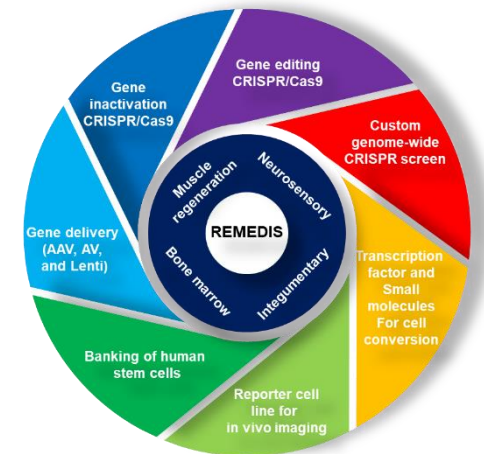
The Diabetes studY in Nephropathy And other Microvascular cOmplications - DYNAMO

A multi-institute research programme developed for research towards reducing diabetic kidney disease (DKD) in Singapore by 30% within the next five years.



Regenerative Medicine Institute of Singapore - REMEDIS

A newly founded institute that is developing cellular-based and regenerative therapeutics and tools as new treatment strategies for key disease areas to improve patient care.



Animal Facilities

Animal BSL 3 [\(video\)](#)

The first facility in Singapore that can house non-human primates in open cage systems in a biosafety level 3 containment.

Behavioral Phenotyping Core [\(webpage\)](#)

Mouse models to study neurological disorder and anxiety behaviors

Mouse Monitoring Core [\(webpage\)](#)

Features the PhenoMaster (Next Generation model) from TSE Systems - a multi-modular platform that allows fully automated and perfectly synchronised metabolic, behavioural and physiological monitoring



Imaging Facilities

Laboratory for Translational and Molecular Imaging [\(webpage\)](#)

- Probe chemistry (conjugation / radiolabeling)
- *In vitro* binding & internalization
- *In vitro/ex vivo* autoradiography
- *In vivo* model development
- *In vivo* pharmacokinetics & pharmacodynamics
- Data analysis & interpretation
- Setup for rodents and non-human primates



Confocal Microscopes

Zeiss LSM 710 Inverted and Upright microscopes

Stem Cell and Gene Editing (SCAGE)

[\(webpage\)](#)

SCAGE provides services involving two Nobel Prize winning technologies – induced pluripotent stem cell (iPSC) reprogramming and CRISPR gene editing.

- Reprogramming of fibroblasts, PBMCs, CD34+ cells, etc
- RNA reprogramming (virus-free method) and Sendai reprogramming methods offered
- iPS characterization assays and karyotyping offered
- Gene knockout
- Targeted mutations at specific sites in gene
- Gene knock-in
- Designing of guide RNAs and donor templates
- Off-target analysis

Insectary Facility [\(webpage\)](#)

BSL2 insectary for infectious oral feeding. Optimized protocols for dengue, Zika and chikungunya viruses. With colonies of *Aedes aegypti*, *Ae. Albopictus* & *Ae. Malayensis*



Metabolomics [\(webpage\)](#)

Providing customized services. Specialized in identifying and quantifying over 1000 biologically relevant metabolites.

- | | |
|---------------------------|---|
| • Amino Acids | • Sphingolipids & Phosphatidylcholines |
| • Acyl Carnitines | • 1- & 3-Methylhistidine |
| • Free / Total Carnitines | • Tryptophan metabolism pathway metabolites |
| • Organic Acids | |

Promising Translational Research



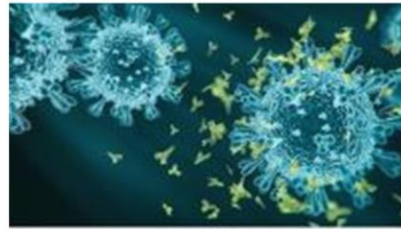
24 Aug 2023

New study classifies SARS viruses and variants into three serotypes,



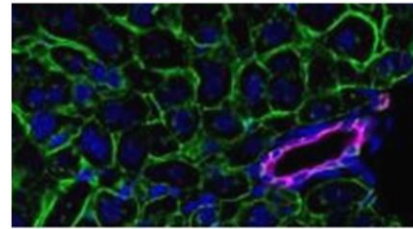
15 Aug 2023

Duke-NUS and Paratus collaborate on a human anti-inflammatory drug



27 Jul 2023

Newly-discovered antibodies can neutralise COVID-19 variants,



19 Jul 2023

Singapore scientists find that a special omega-3 lipid might prevent



08 Jun 2023

Duke-NUS researchers develop promising stem cell-based



01 Feb 2023

Duke-NUS and NHCS scientists first in the world to regenerate diseased



23 Sep 2022

Duke-NUS grants TIIM Healthcare exclusive licence to commercialise technology for intelligently triagl...



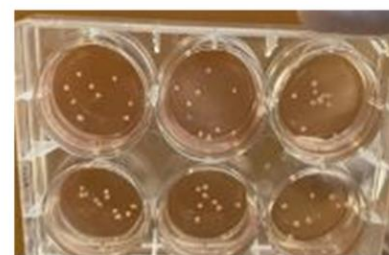
21 Jun 2022

Duke-NUS, Johnson & Johnson join hands to advance dengue innovation through a new discove...



10 Jun 2022

Duke-NUS Centre for Outbreak Preparedness launched in Singapore to enhance regional capacity for...



07 Sep 2021

Scientists grow miniature brains that mimic the major pathological features of Parkinson's disease



-NUS: Cancer mutations caused by bacterial toxin p

24 Jul 2020

Singapore develops first-of-its-kind rapid COVID-19 test to detect neutralising antibodies with high...



14 Nov 2019

Singapore-led global diabetes stud gets special mention at American Society of Nephrology's annual...



14 Apr 2023

Scientists from Singapore and Sweden achieve promising results towards restoring vision in...



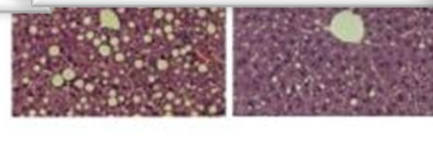
05 Dec 2022

A dengue vaccine? Duke-NUS scientists identify new findings in a key protein that may help



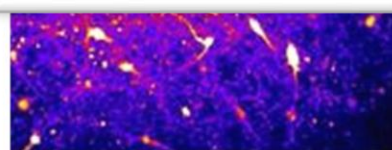
25 Aug 2022

Duke-NUS scientists develop new technique to reveal the hidden genome



21 Sep 2022

Duke-NUS: Preclinical study suggests spermidine can help treat advanced non-alcoholic fatty liver...



15 Jan 2020

Innovative research uncovers mechanism behind epilepsy in Angelman syndrome, may lead to...



09 Jan 2020

Development of first-in-class antibody therapeutics and new partnership bring hope to patient...

Over the last 18 years we have worked with many large companies, biotech's, startups and investors to bring innovative solutions for patients from vaccines to drugs, diagnostics to AI enabled decision making tools, training, education and policies.


































In only 18 years, Duke-NUS has achieved an impressive number of invention disclosures, patent applications and licensing, while forming 25 start-up companies, raised \$150M+ in outside capital and 160+ jobs created

CREATING NEW SOLUTIONS



253
Invention
Disclosures



43
Licenses
completed



>130
Patents filed



>27
Patents
granted



25
Active start-up
companies

32 Active “Commercialization Projects”:



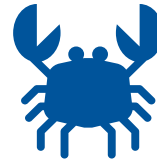
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Neuro



6

Heart + Metabolic



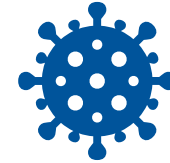
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Oncology



2

Health Sciences



9

**Infectious
disease**



TRAVECTA[®]
THERAPEUTICS

Vanteres 

 **MOGRIFY**
Transforming Cell Therapy

Vitreogel

 **Digital
LifeLine**

 **ENLEOFEN**

PAIRXBIO

STRATIFYCARE
Empowering Personalized Medicine for Tomorrow

 **Neurobit Technologies**

 **evecxia**
therapeutics

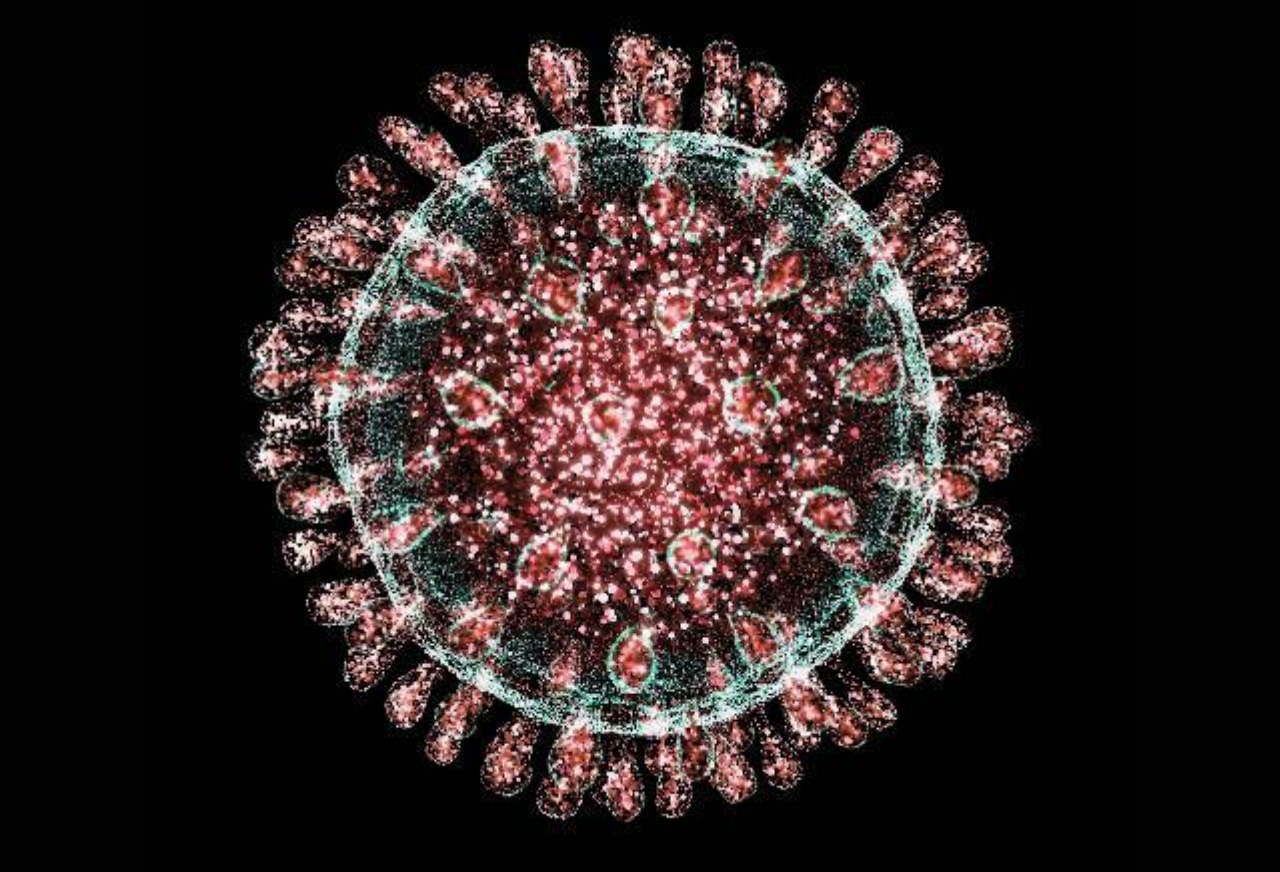

CoVBio

 **CognaLearn**
Exclusive licensee of DukeNUS optimized learning methods & technology

 **LION TCR**
WE HUNT VIRUSES


InFiBiO

 **HEALTHSEQ**



The Problem Statement

Angelman Syndrome is caused by disruptions in UBE3A gene

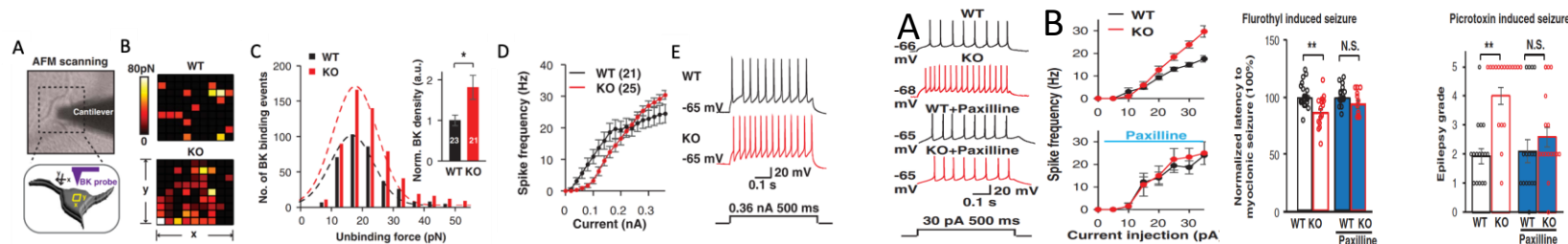
- Serious, incurable, rare (1 in 15,000)
- Epilepsy in 80 to 95% of patients before 3 years of age
- Linked to mutation / loss-of-genes associated with the 15q11-q13 locus mainly, UBE3A
- Disruptions in the expression / function of UBE3A protein can result in AS disease pathogenesis

No targeted approach to treat AS-seizures: a major problem

- Seizures are treated with medications and dietary therapies, while sleep issues are treated with medications and sleep training

BK antagonists provide a promising therapeutic opportunity for the prophylaxis and treatment of seizures in patients with Angelman syndrome

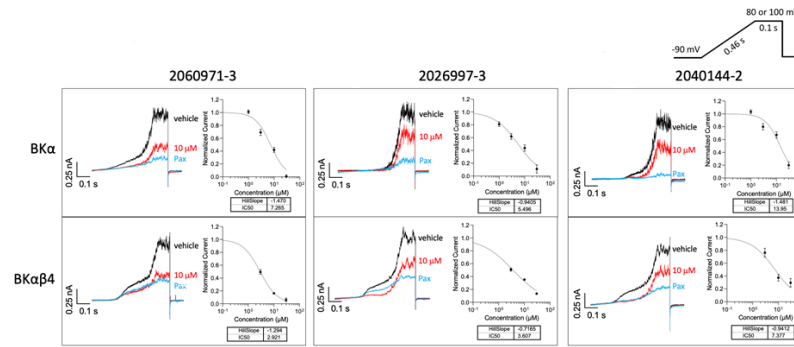
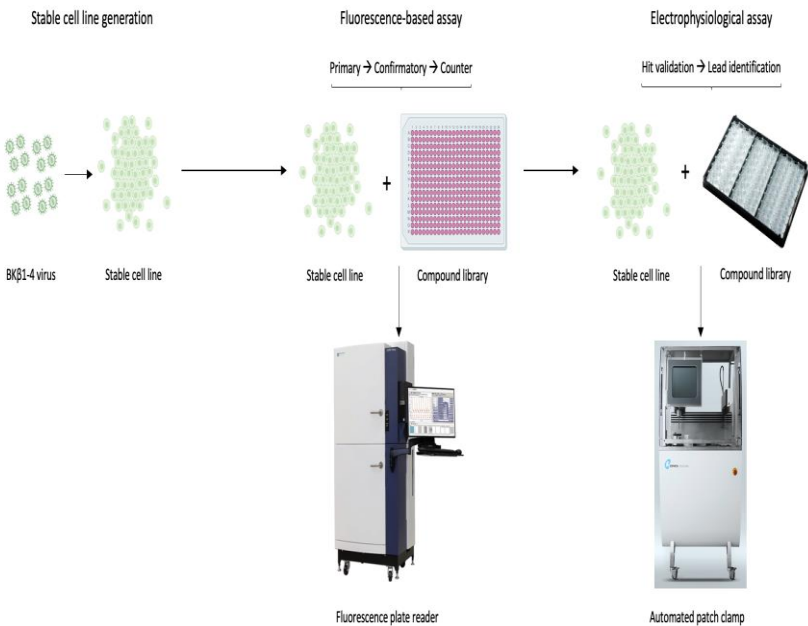
- Our scientists demonstrate that UBE3A suppresses neuronal hyperexcitability via ubiquitin-mediated degradation of calcium and voltage-dependent big potassium (BK) channels
- UBE3A deletions augment BK channel function in human neurons
- Augmented BK channel activity manifests as increased intrinsic excitability in individual neurons and subsequent network synchronization
- The BK antagonist paxilline, normalizes the augmented neuronal excitability changes observed in neurons of UBE3A-deficient organoids
- Other BK antagonists (GAL021, IBTX) also normalized excitability in UBE3A KO human neurons
- BK antagonist reduces seizures/epilepsy in mice caused by Flurothyl or Picrotoxin



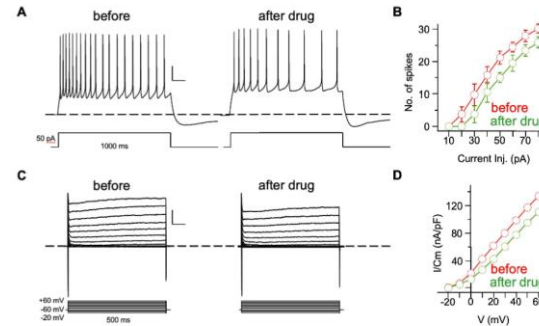
Our Solution

Targeting the BK $\alpha\beta_4$, a CNS-specific BK complex in the brain, by identifying specific antagonist(s) reduced neuronal hyperexcitability and ameliorate seizures in AS patients.

Identified CNS-specific BK channel modulators using high throughput screening of compound libraries



Three compounds could reduce BK currents in Qpatch-HTX automated patch recording.
Lowest IC₅₀ in BK alpha-beta – 3.236 μM



The BK $\alpha\beta_4$ specific antagonist treatment reduces neuronal excitability in human-induced neurons derived from UBE3A KO hESCs.

The Problem Statement

Tissue fibrosis causes harmful scarring due to disrupted healing.

Lack of safe, targeted cures for fibrosis-related disorders leads to global burdens.

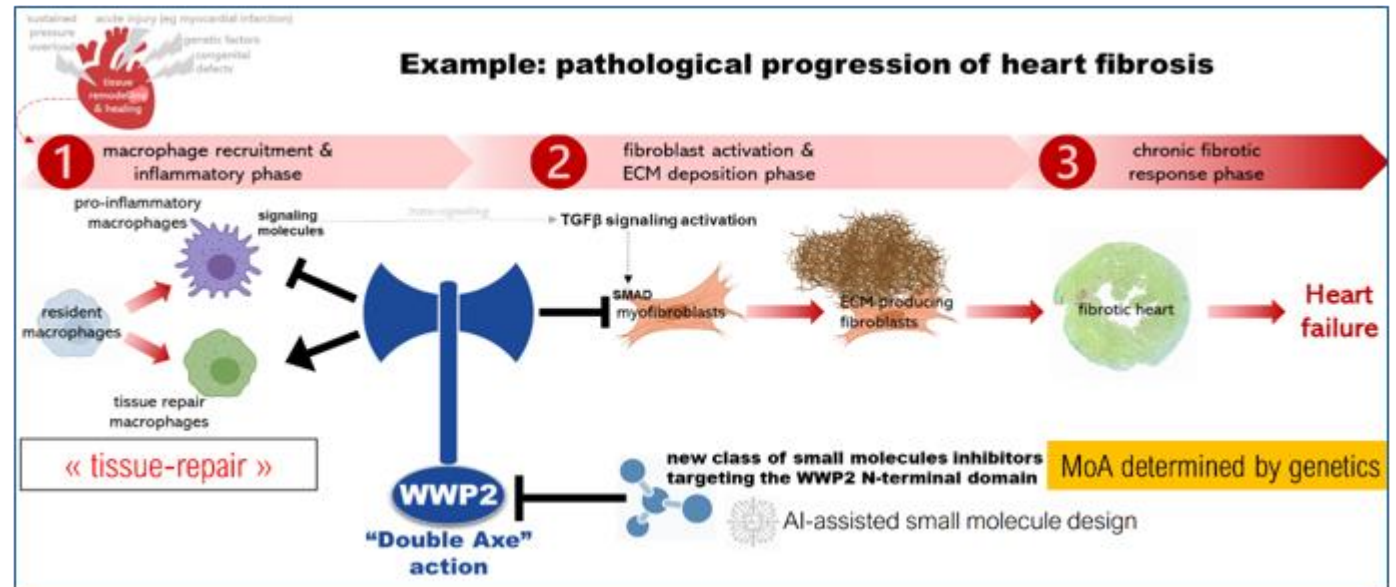
Common diseases lack preventive treatments; current therapies lack specificity and may cause toxicity. **Unmet needs persist for safe and effective fibrosis treatments.**

WWP2 is a new anti-fibrotic target which directly regulates the development of pathological fibrosis in different tissues

WWP2 is a new anti-fibrotic target which directly regulates the development of pathological fibrosis in different tissues -experimentally validated (*in vivo*) using disease models of:

- **dilated cardiomyopathy (DCM), myocardial infarction (MI) & heart failure (HF)**
- **chronic kidney disease (CKD) & acute kidney injury (AKI)**
- **idiopathic pulmonary fibrosis (IPF)**

Different from traditional upstream inhibition of TGF β (e.g., by drugs Losartan, Tranilast) WWP2 inhibition exerts a compelling “Double Axe” regulatory action on different phases of fibrogenesis, working both upstream(1 in macrophages) and downstream(2 in fibroblasts) of TGF β signaling activation

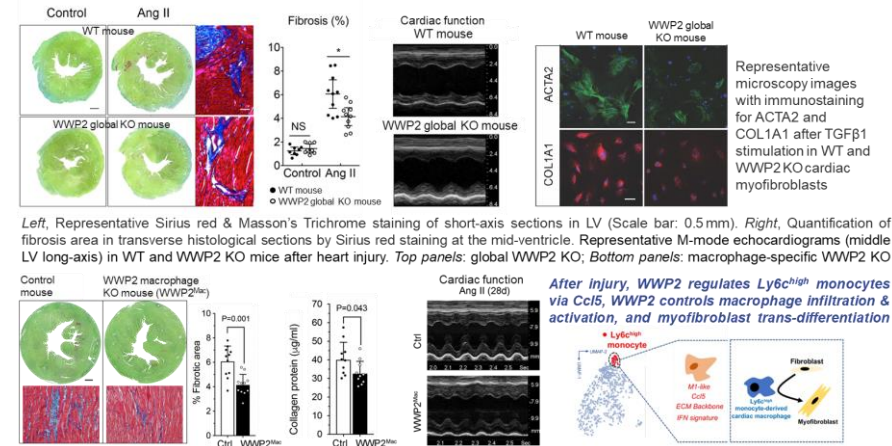


WWP2: Orchestrating TGF β Signaling for Cardiac Fibrosis Control

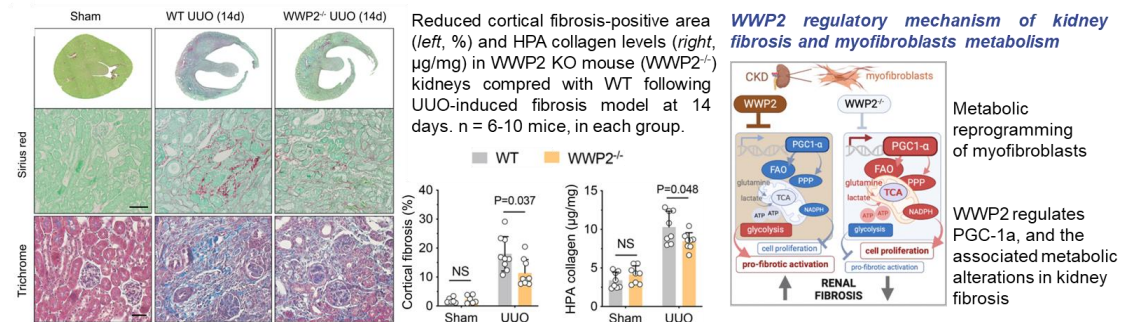
- **Operating both upstream and downstream** of TGF β signaling, WWP2 holds sway over cardiac fibrosis regulation.
- **In the early-inflammatory phase** of fibrosis, WWP2's pivotal role involves a "Double Axe" action, influencing macrophages.
- **Revolutionizing WWP2 Inhibition:** Unveiling a Novel Mechanism through AI-Guided Drug Prediction and Screening.
- **Emergence of a New Class:** N-terminal-targeting WWP2 Inhibitors as Innovative Antifibrotic Therapy

Key Data

WWP2 regulates pathological cardiac fibrosis via its action in fibroblasts and macrophages



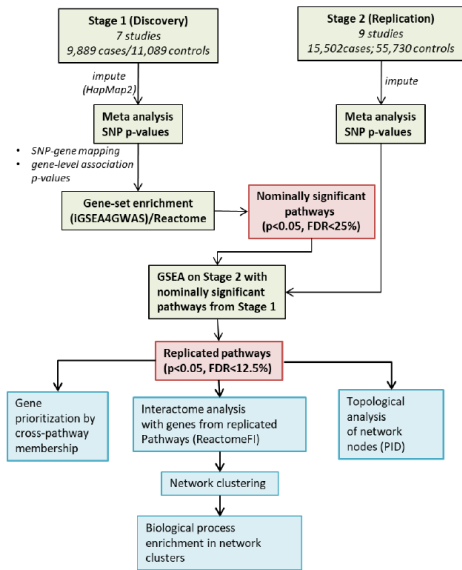
WWP2 regulates the metabolic reprogramming of renal myofibroblasts to promote kidney fibrosis in chronic kidney disease (CKD)



Representative images of WT and WWP2^{-/-} (WWP2 global KO) mouse kidneys following UUO model for 14 days. (n=8 for each condition). Top and middle panels, Sirius Red staining for whole section and representative fibrotic area. Scale bars, 50 μ m. Bottom panels, representative images of Masson's trichrome staining for representative fibrotic area. Scale bars, 20 μ m.

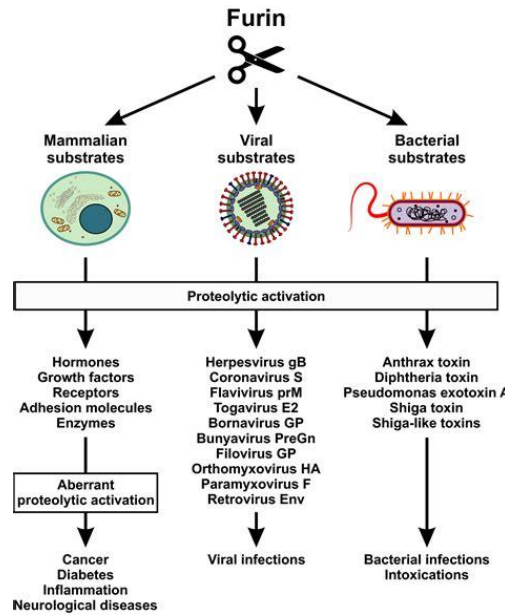
Furin: Why are we interested?

We discovered **FURIN** to be a common component of six biological pathways significantly associated with atherosclerosis



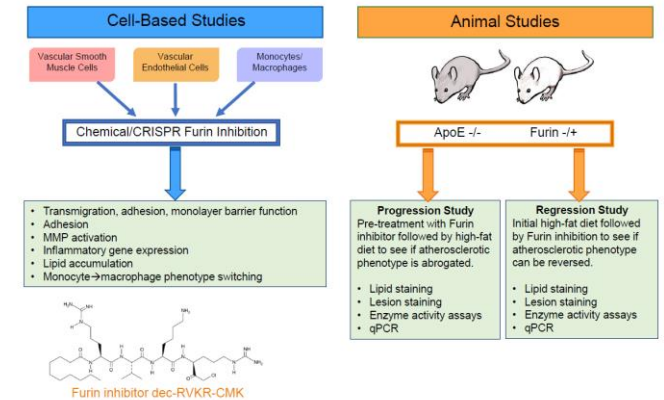
(Ghosh et al., 2015)

Pathway analysis of a large genotyped CAD case: control cohort (Cardiogram consortium)



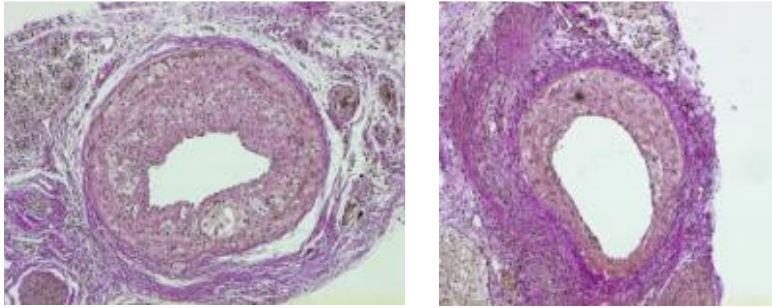
FURIN is a protease that cleaves a wide variety of proteins and thereby regulates a large number of biological processes including embryogenesis, homeostasis and disease

Furin: Target Validation in Cell Culture and Animal Models



Furin inhibition showed positive effects, including reduced atherosclerosis in *Ldlr*^{-/-} mice, decreased plaque formation in *ApoE*^{-/-} mice, lower monocyte migration and inflammation in cell-culture, and decreased systemic inflammation. Additionally, it lowered matrix metalloprotease activation and increased HDL-cholesterol levels in *Ldlr*^{-/-} mice, while furin overexpression increased plaque area in *ApoE*^{-/-} mice.

Atherosclerotic plaque thickness upon inhibition or overexpression of FURIN



We studied FURIN inhibition's impact on monocytes/macrophages in atherosclerotic plaques via cell-culture experiments. Utilizing CRISPR, we knocked down FURIN in monocytes and compared knockout cells to wild-type. FURIN inhibition led to reduced cell growth, lipid uptake, and monocyte migration. Inflammatory gene expression varied, and genes related to "complement/coagulation cascade" were significantly downregulated in FURIN deficient cells. Phagocytic activity remained unchanged.

Next Steps

- Explore targeted cell-specific FURIN inhibition for improved efficacy and fewer side effects compared to systemic inhibition.
- Investigate whether FURIN deletion in monocytes/macrophages, endothelial cells, and vascular smooth muscle cells can yield anti-atherosclerotic effects in animal models.
- Additionally, broaden the spectrum of disorders benefiting from FURIN inhibition and evaluate small molecule FURIN inhibitors as potential anti-infective agents.

Publication

[Meta-Analysis](#) > *Arterioscler Thromb Vasc Biol.* 2015 Jul;35(7):1712-22.

doi: 10.1161/ATVBAHA.115.305513. Epub 2015 May 14.

Systems Genetics Analysis of Genome-Wide Association Study Reveals Novel Associations Between Key Biological Processes and Coronary Artery Disease

Sujoy Ghosh, Juan Vivar, Christopher P Nelson, Christina Willenborg, Ayellet V Segrè, Ville-Petteri Mäkinen, Majid Nikpay, Jeannette Erdmann, Stefan Blankenberg, Christopher O'Donnell, Winfried März, Reijo Laaksonen, Alexandre F R Stewart, Stephen E Epstein, Svati H Shah, Christopher B Granger, Stanley L Hazen, Sekar Kathiresan, Muredach P Reilly, Xia Yang, Thomas Quertermous, Nilesh J Samani, Heribert Schunkert, Themistocles L Assimes, Ruth McPherson

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FURIN Inhibition Reduces Vascular Remodeling and Atherosclerotic Lesion Progression in Mice

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