Stem Cells, Tissue Regeneration & Repair, Prosthetics (Biology) Research

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Studies on Degenerative Diseases: Blindness and Alzheimer's Disease

Dr. Nora B. Caberoy
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School of Life Sciences
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Expertise:

- Phagocytosis
- Retinal cell biology
- Retinal degenerative diseases (*Retinitis pigmentosa*, Age-related macular degeneration)
- Functional proteomics by phage display
- Alzheimer's disease therapy

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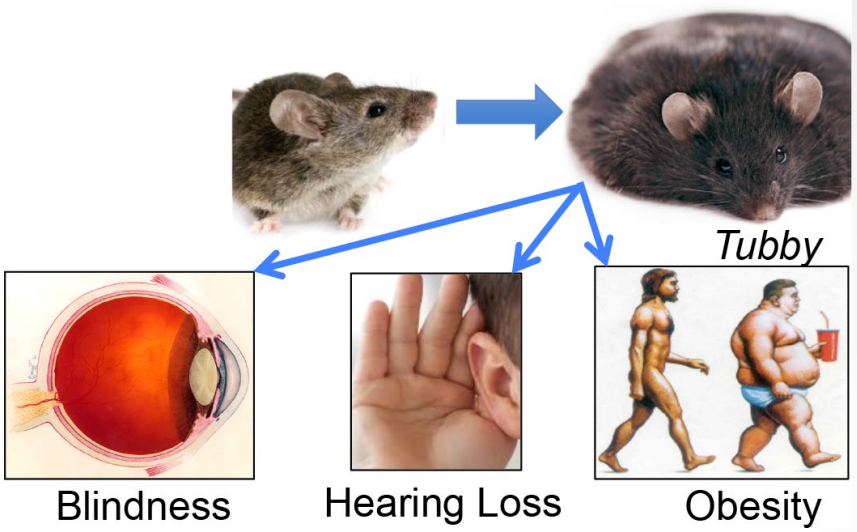
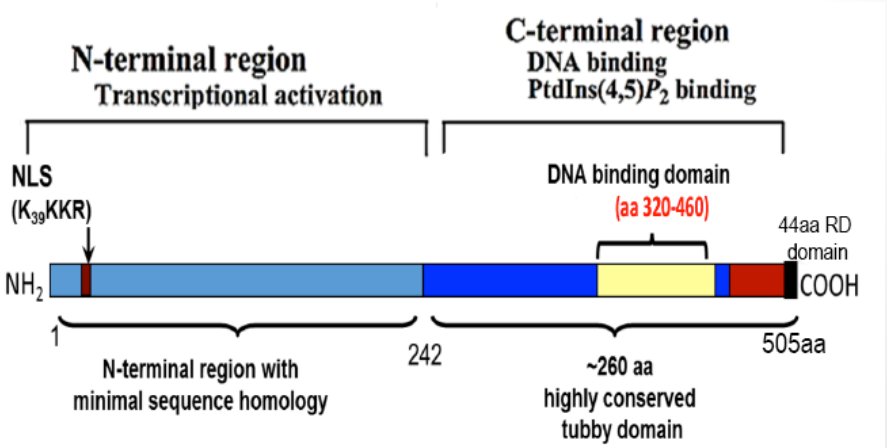
Delineating molecular mechanisms of blindness, hearing loss, and obesity

Mutation in Tubby gene resembles human syndromes:

- Hearing and/or vision - *Usher's, Retinitis pigmentosa*
- Obesity and sensory deficits - *Bardet Beidl, Alstrom's*
- Pathological mechanisms unknown



- Characterizing Tubby as a transcription factor
- Globally identifying genes regulated by Tubby
- Unraveling Tubby protein-protein interaction network



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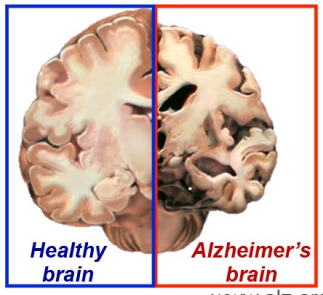
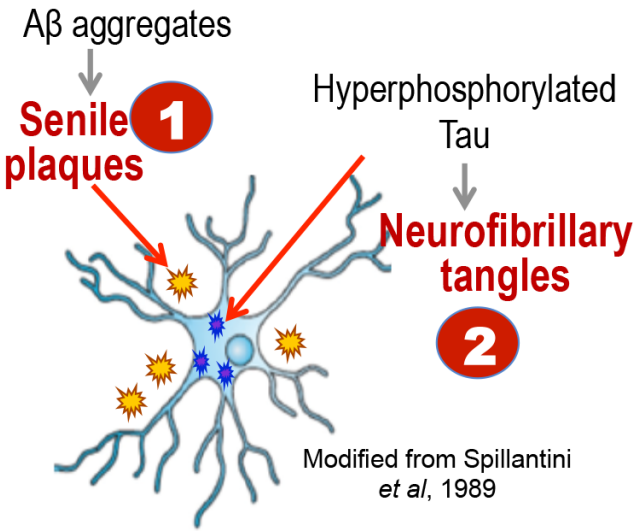
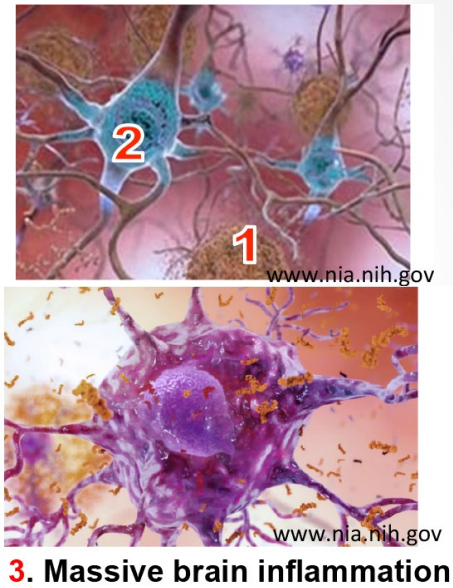
Redirecting phagocytosis of amyloid beta from inflammatory to non-inflammatory pathway

Alzheimer's Disease (AD): Pathological hallmarks

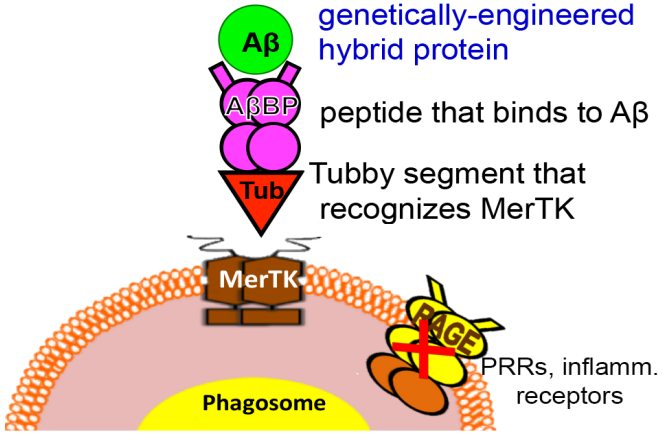






Strategy:

- engineer hybrid proteins
- binds oligomeric and fibrillar amyloid beta
- sequesters and directs phagocytic clearance of amyloid beta through non-inflammatory pathway



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Investigating collective cell behaviors

- **Dr. Joseph Campanale**
- Assistant Professor
- School of Life Sciences
- Email: joseph.campanale@unlv.edu
- Website: Campanale Lab

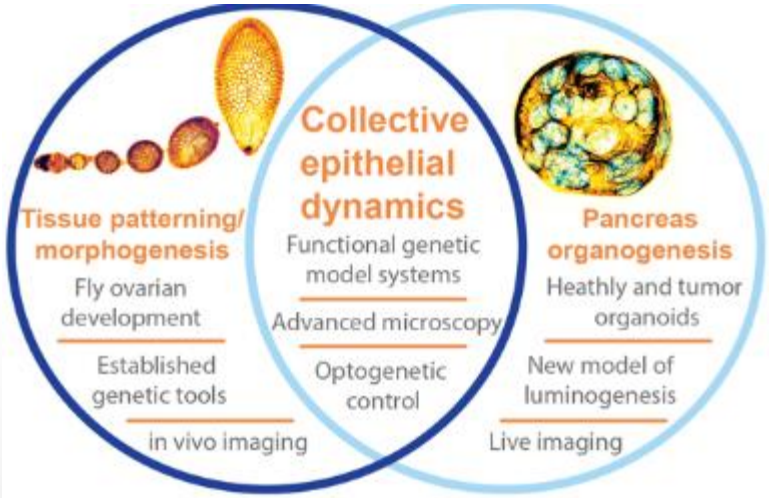

Fig.1: Using flies and mammilian organoids to study collective epithelial dymanics deployed in development.

Expertise

- Collective cell migration
- Cancer cell biology
- Developmental biology
- Fruit fly genetics
- Pancreatic organoid morphogenesis
- 4-Dimensional live cell microscopy

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How do cells coordinate collective movements to establish barriers?

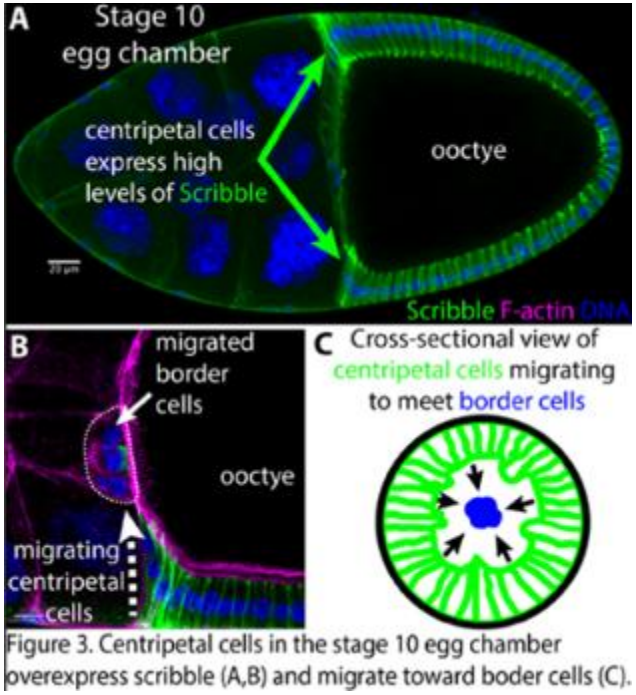

Figure 3. Centripetal cells in the stage 10 egg chamber overexpress scribble (A,B) and migrate toward boder cells (C).

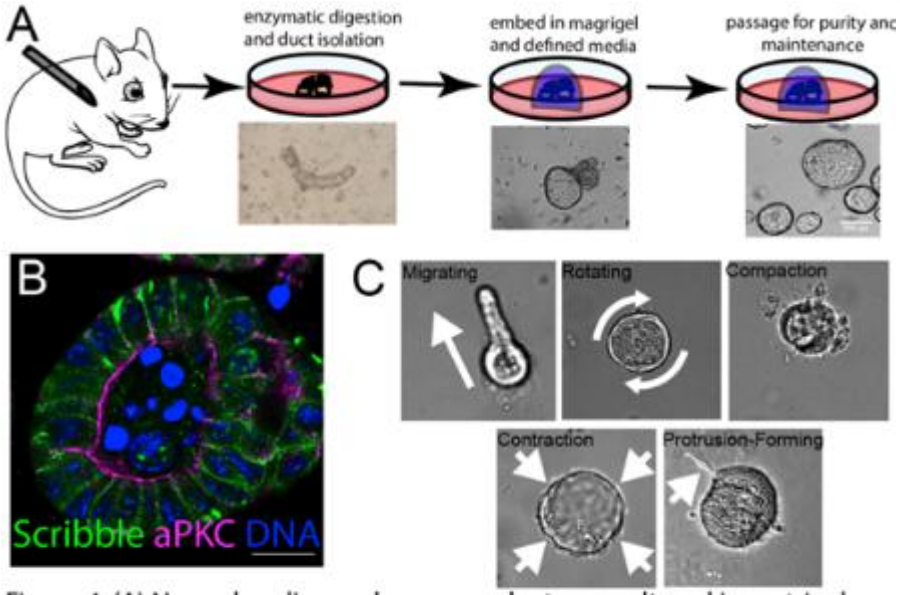

Figure 4. (A) Normal or diseased pancreas ducts are cultured in matrigel before maitenance. (B) Normal organoids are apicobasally polarized and (C) exhibit a range of behaviors during development.

Centripetal cells (CFCs) found in fruit fly eggs offer an unexplored *in vivo* model of epithelial sheet migration. My lab uses these untapped experimental pace to understand the basic principles of how cells migrate as sheets *in vivo* and answer questions such as: 1) What role does epithelial cell polarity signaling play in CFC movement; and 2) Does polarity signaling regulate CFC cell-cell adhesion during migration?

Polarity complex interactions are well-established in many epithelia; however we lack a detailed understanding of their functions and regulation across organs. We aim to discover the role of polarity in pancreas morphogenesis using live imaging, organoid culture, and developmental biology to ask: 1. What epithelial behaviors drive pancreas development? 2. What mechanistic roles do polarity complex proteins play in controlling these behaviors? 3. What emergent cell properties underlie duct morphology? And 4. Are these properties mechanically controlled?

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Comparative Biomechanics: Evolutionary, Environmental, & Applied

David V. Lee

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Web: Laboratory of Comparative Biomechanics

Expertise:

Locomotion and gait

Animal biomechanics

X-ray motion analysis

Joint dysfunction

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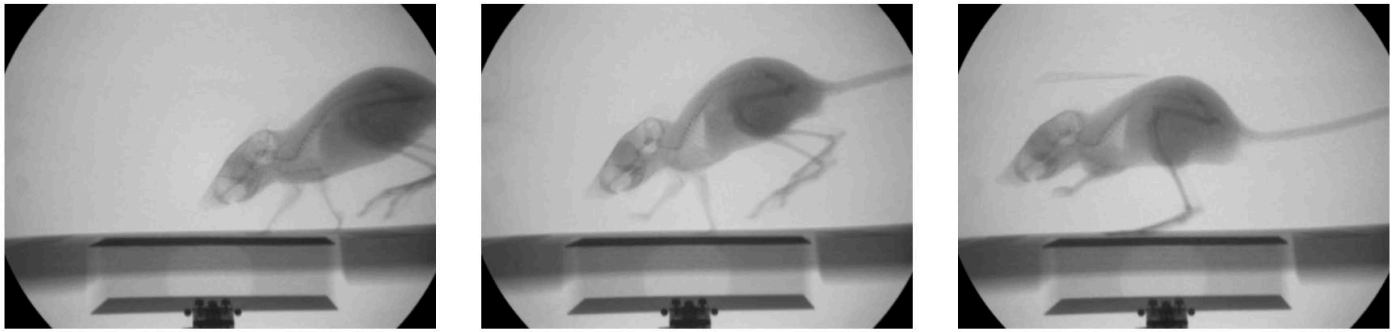
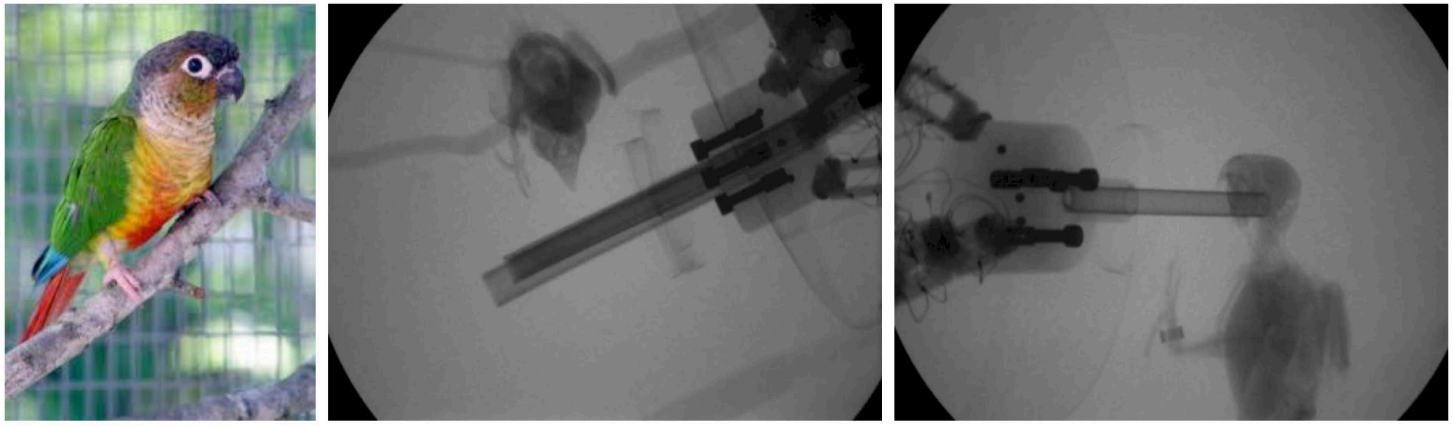
Locomotion

The *Laboratory of Comparative Biomechanics* explores fundamental questions in different modes of animal locomotion, including walking, running, hopping, climbing and digging.



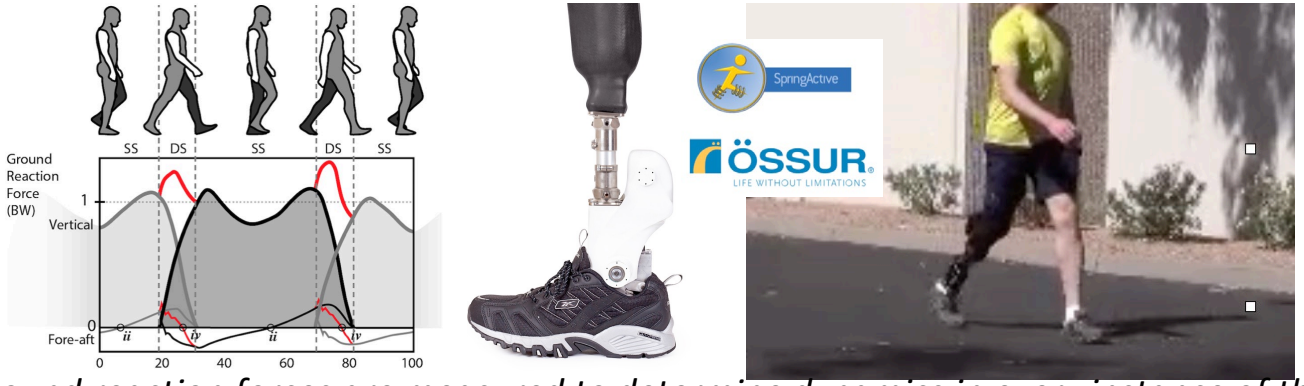
X-ray video of a kangaroo rat on a miniature force platform showing different gaits



X-ray video of a parrot climbing a force-torque ladder in vertical and horizontal views

Human gait and prosthetics

We take a broadly comparative approach to understanding human walking dynamics and the function of both passive and active foot-ankle prostheses in restoring dynamics and speed.



Ground reaction forces are measured to determine dynamics in every instance of the stride

Comparing human, avian, and robotic bipedalism based on whole-body dynamics

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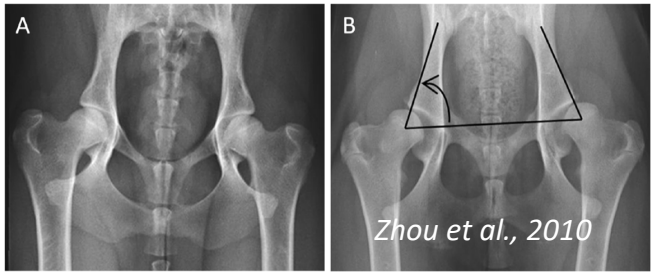
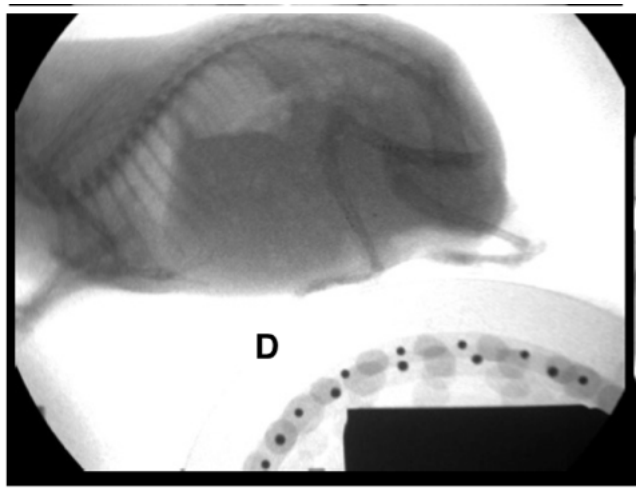
Joint dysfunction and osteoarthritis

Joint dysfunction is a pathway to osteoarthritis and our laboratory investigates mechanical aspects of joint dysfunction preceding spontaneous hip and knee osteoarthritis. We are beginning to use the canine hip dysplasia model to understand biomechanical and genetic determinants of joint health.



Gait laboratory for force and x-ray motion analysis of canine gait



X-ray video of spontaneous osteoarthritis in the guinea pig

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High-dimensional Data Analysis

- **Dr. Farhad Shokoohi**
- Assistant Professor of Statistics
- Department of Mathematical Sciences
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- Website: https://farhad.faculty.unlv.edu

Expertise

- Bayesian and Frequentist Analysis
- Mixture Modelling
- Survival Analysis
- High-Dimensional Genomics and Epigenetic
- Sparse Estimation in Finite Mixture of Regressions
- Machine Learning in Medical and Financial Data
- Differential DNA Methylation Analysis in Cancer Epigenetics
- Hidden Markov Models
- Nonparametric and Semiparametric Regression
- Software Development

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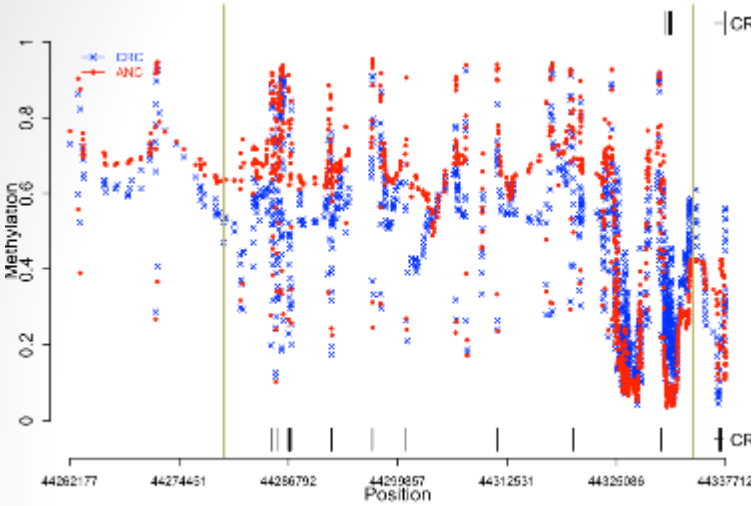
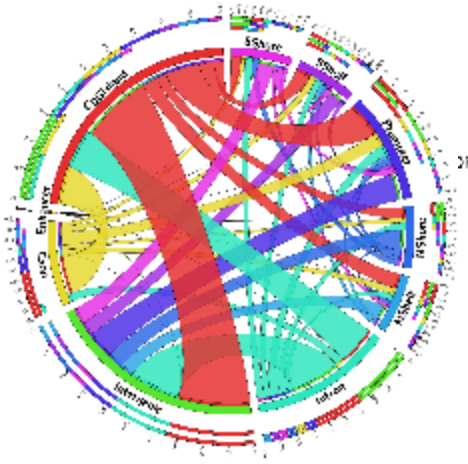
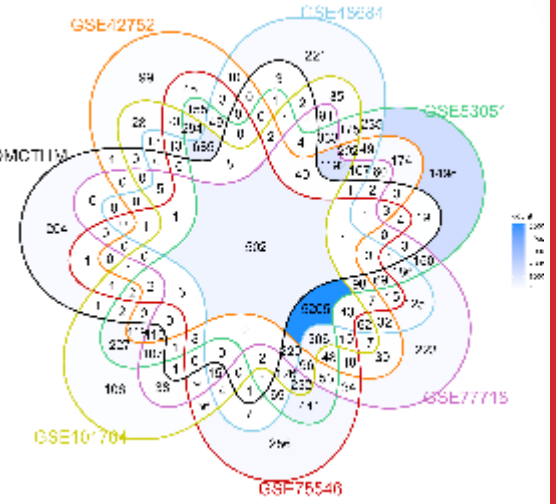
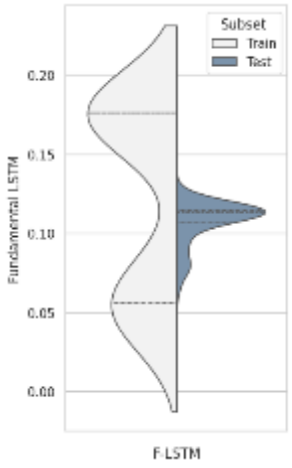
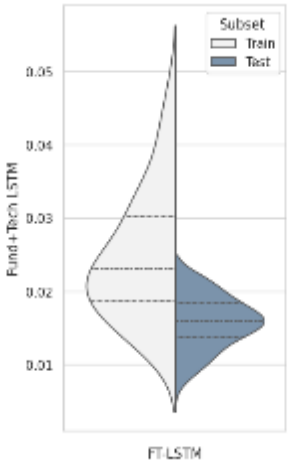
High-dimensional data analysis across a variety of sectors, including finance, healthcare, genomics, market, among others.

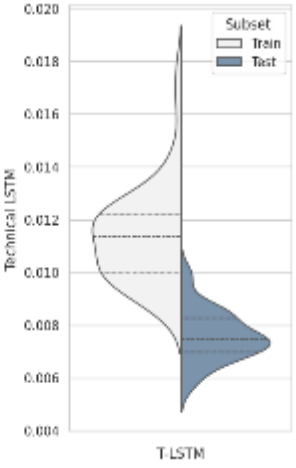


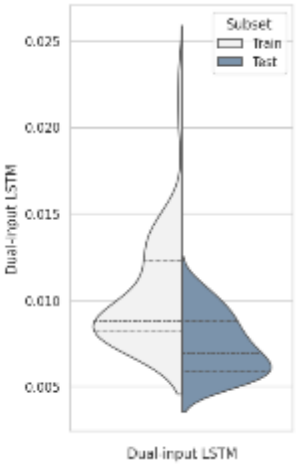


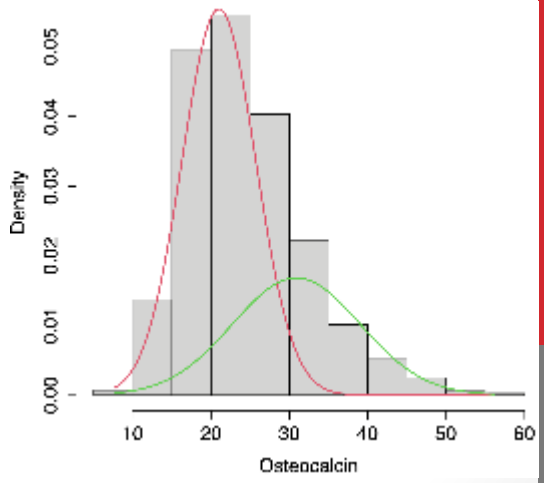












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Biochemistry – Interrogate Cell Signaling Pathways by Molecular, Genetic and Proteomic Approaches

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Expertise

Cell signaling
Cancer cell biology
Stem cell biology
Mouse conditional knockout models

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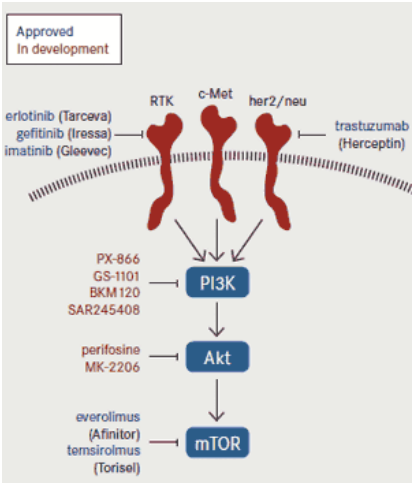
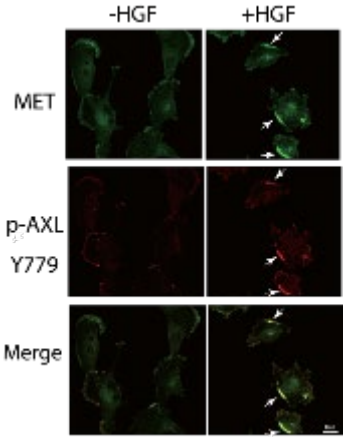
Regulation of cell surface receptor RTKs localization and activation

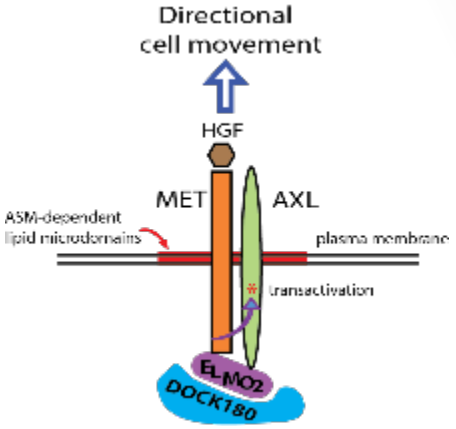
Problem: cancer cells often have multiple receptors (RTKs) activated on cell surface, making targeting inefficient



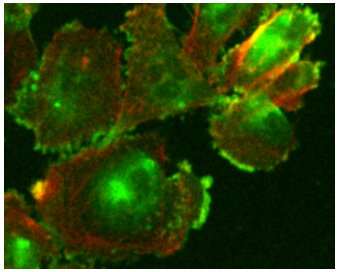
Co-activation of AXL-MET RTKs:
HGF (ligand for MET) also activates AXL, detected by antibodies for p-AXL-Y779



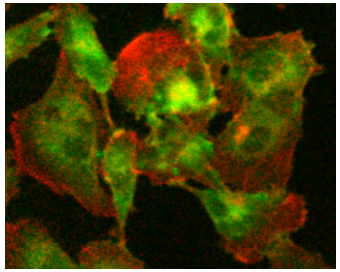
A novel mechanism discovered for RTK-Co-activation and signaling for cancer cell migration and invasion



Li et al., J. Biol. Chem. (2018) 293:15397-15418.

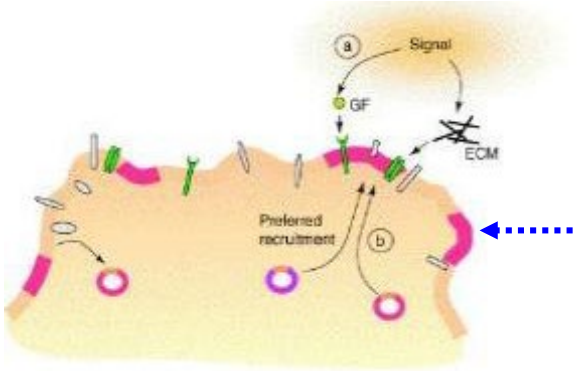


Vehicle



ASM Inhibitor

ASM inhibition prevents the MET RTK to be transported to the cell surface, as revealed by immunostaining (MET, green label; and a control cell surface protein, red label).
Zhu et al, J. Cell Science (2016) 129, 4238-4251.

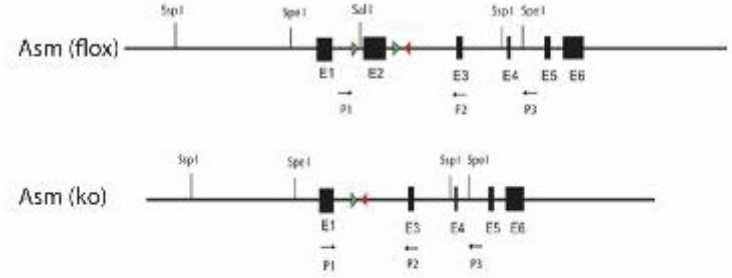


ASM-dependent
lipid microdomains

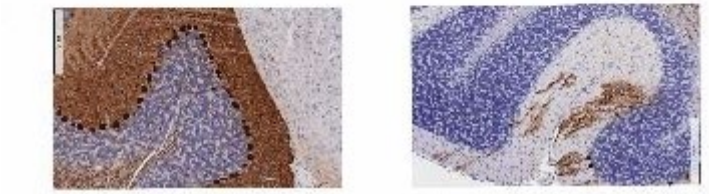
Mass-Spectrometry analyses revealed that the ASM-regulated local lipid microdomains were enriched with many signaling molecules.
Xiong et al. Biol. Open (2019) 8, bio040311.

Regulation of stem cell maintenance: insights from the genetic studies in novel mouse knockout models

A. Gene locus

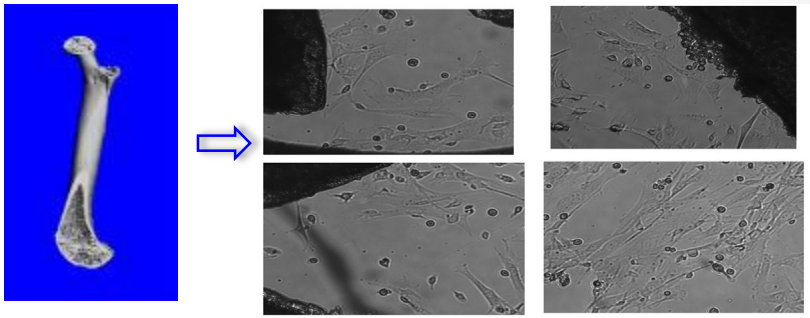


B. Loss of Purkinje neurons in cerebellum



Purkinje neurons immunostained with D28K antibody.

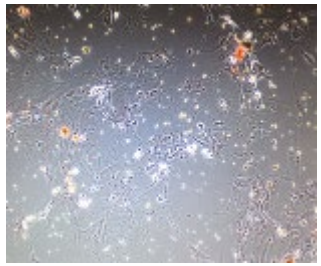
C. Mesenchymal stem cells (MSCs) cultured from bones



D. ASM mutant MSCs failed to become bone-forming cells

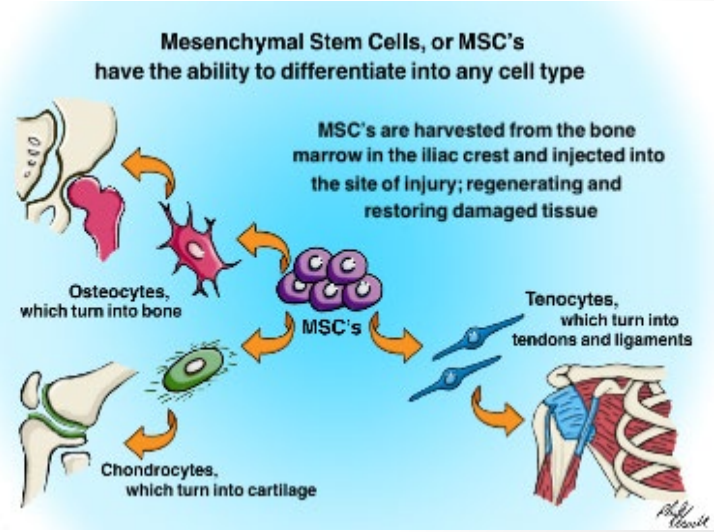
Wild-type MSCs

ASM mutant MSCs



(*in vitro* differentiation assay, then stained with alizarin red)

E. Potentials of MSCs for tissue repair



Regeneration and Stem Cell Biology

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Adjunct Associate Professor, School of Medicine

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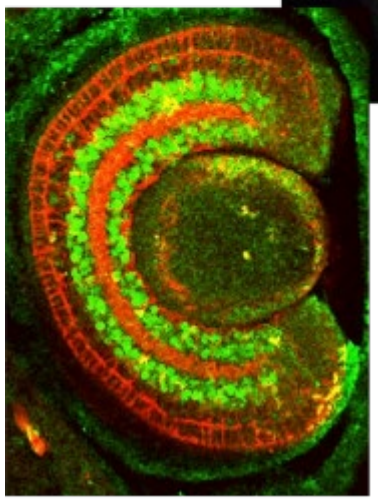

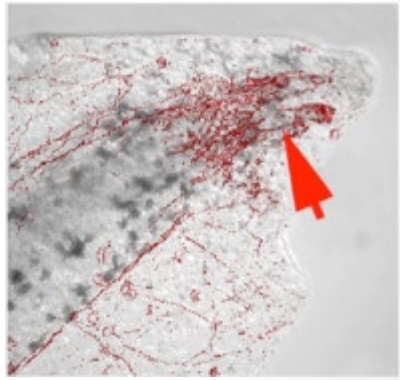

Expertise

- Eye regeneration
- Limb regeneration
- Stem cell biology
- Bioelectrical signaling
- Cell proliferation and growth

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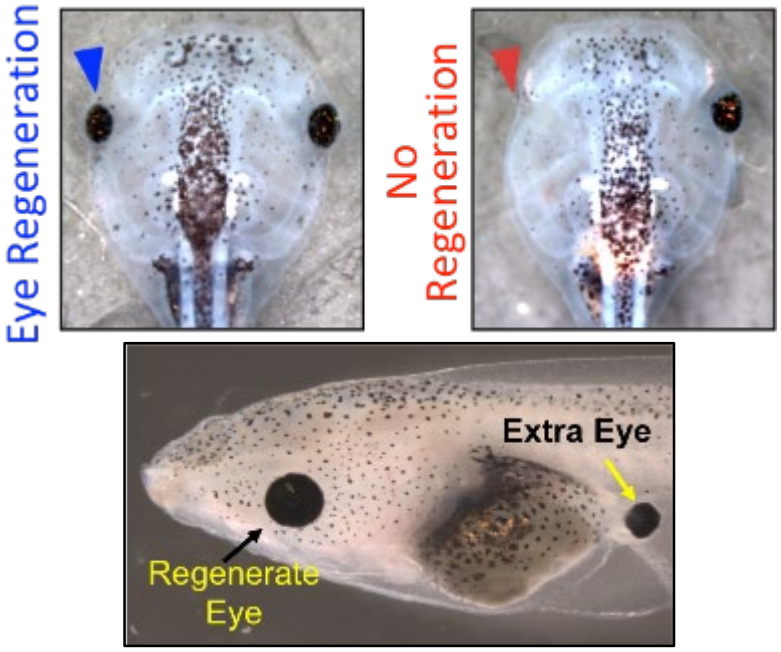
Understanding Vertebrate Organ Regeneration

Kelly Tseng

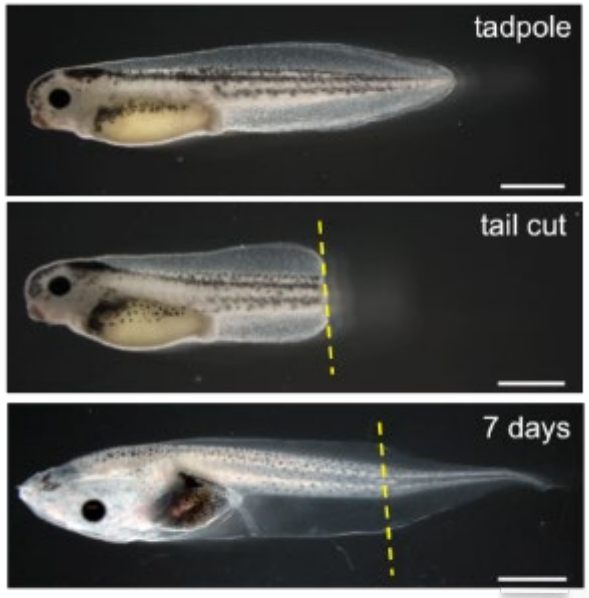
Why Can Some Animals Regenerate Body Parts but Others Cannot?

Goal: understand natural regeneration using a model system with high regenerative ability (clawed frog)

Eye Regeneration



Spinal Cord Regeneration



Projects:

1) Identify and define mechanisms that drive tissue regeneration
2) Develop successful strategies to regenerate lost tissues and organs

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Understanding Vertebrate Organ Regeneration

Kelly Tseng

Recent Publications:

- Kha, C. X., Guerin, D.J., and Tseng, K. A.-S. (2020) Studying *in vivo* Retinal Progenitor Cell Proliferation in *Xenopus laevis*. In: Mao CA. (ed) *Retinal Development. Methods in Molecular Biology*, *2092:19-33*. Humana, New York, NY.
- Kha, C. X, Guerin, D.J., and Tseng, K. A.-S. (2019) Using the *Xenopus* Developmental Eye Regrowth System to Distinguish the Role of Developmental Versus Regenerative Mechanisms. *Frontiers in Physiology*, May 8;10:502. doi: 10.3389/fphys.2019.00502.
- Kha, C. X., and Tseng, K. A.-S. (2018) Developmental Dependence for Functional Eye Regrowth in *Xenopus laevis. Neural Regeneration Research, 13*:1735-38.
- Kha, C. X., Son, P. H. , Lauper, J., and Tseng, K. A.-S. (2018) A Model to Investigate Developmental Eye Repair in *Xenopus laevis. Experimental Eye Research, 169*:38-47.
- Tseng, A.-S. (2017). Seeing the future: using *Xenopus* to understand eye regeneration. *genesis: The Journal of Genetics and Development, 55*(1-2), e23003. http://dx.doi.org/10.1002/dvg.23003

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Stem Cells, Genetic and Epigenetic Inheritance, Cancer

Dr. Hui Zhang
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Department of Chemistry and Biochemistry
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Email: hui.zhang@unlv.edu

Expertise:

- Biochemistry and developmental regulation of pluripotent embryonic stem cells, adult stem cells, and related diseases

- Regulation of chromatin structure, epigenetics, and transcription by protein methylation and ubiquitin enzymes

- DNA replication, DNA repair, cell cycle, genome instability, and cancer

- Targeting the vulnerability of human cancers

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Current research areas in Zhang Laboratory:

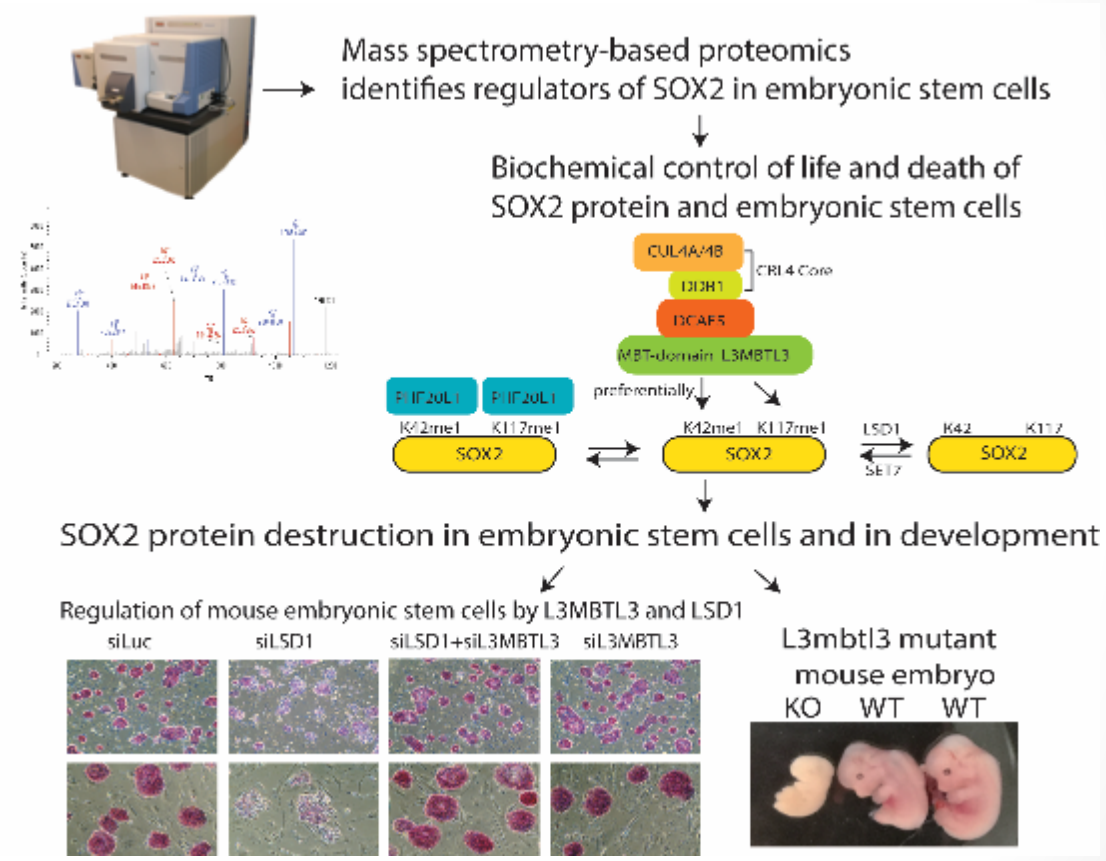
• Discover novel proteins essential for stem cell regulation, examples:

How SOX2 is regulated in embryonic stem cells and many other stem cells in development?

- Sox2 is a master stem cell protein that controls the self-renewal and pluripotency of embryonic stem cells that can develop into any tissue types of cells in development.

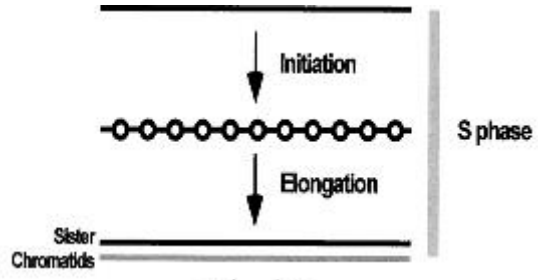
- SOX2 is also a master regulator of many adult stem cells including the stem/progenitor cells for brain, lung, colon, breast, liver, cochlea/ear, skin, retina, ovary, bladder, esophagus, and testes for tissue repair/regeneration.

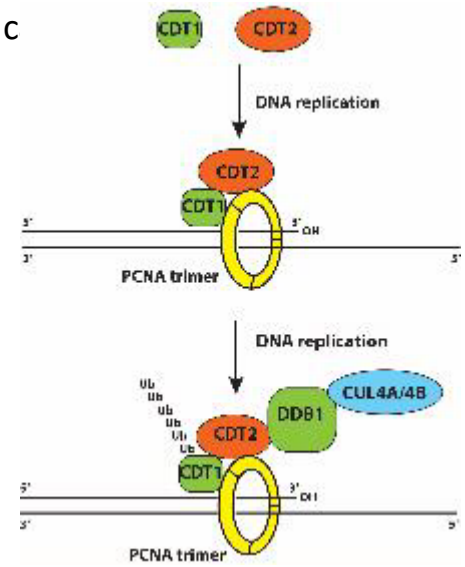
- Artificial Sox2 expression (together with Oct4 and accessary Klf4, and Myc) can virtually convert any differentiated cells, such as skin or blood cells, into induced pluripotent stem cells (iPSCs), the embryonic stem cell-like cells.

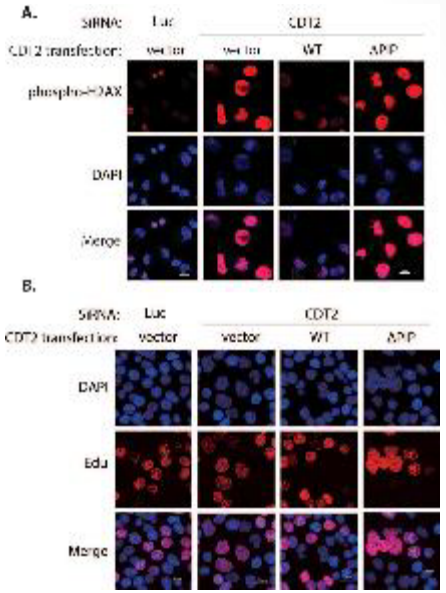


- Discover novel proteins important for epigenetic and cell cycle regulation, examples:
- **Regulation of DNA replication and DNA methylation in normal and cancer cells**

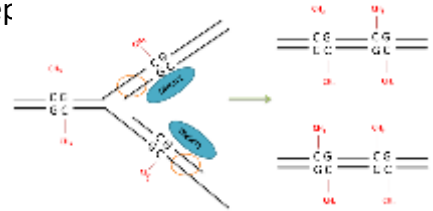
  - How DNA replicates only once in one cell cycle in animal cells? How re-replication is prevented that causes genome instability and c





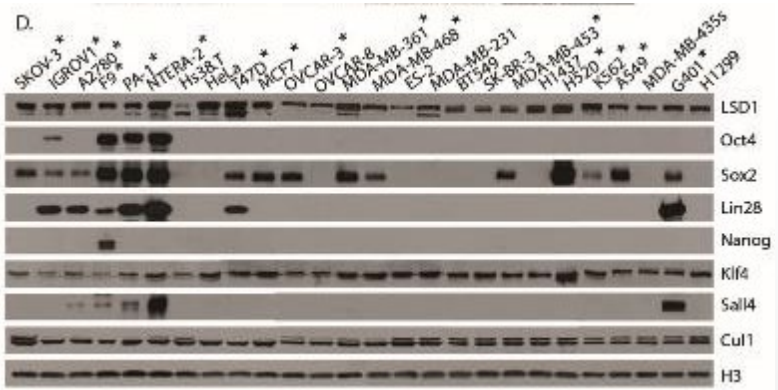


  - How the fidelity of epigenetic DNA methylation is maintained during DNA rep



- **Cancer Biology and therapy development**

Elevated SOX2 levels cause many cancers including cancers of lung, brain, breast, and ovary. These cancers are hard to treat because they behave like stem cells due to SOX2 expression. We are developing novel LSD1 chemical inhibitors that target the epigenetic vulnerability of these cancer cells.



The presence of SOX2 in different types of cancer cells is responsible for sensitivity towards our LSD1 inhibitors. *: Sensitive to LSD1 Inhibitors

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