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



Investigating collective cell behaviors

- Dr. Joseph Campanale
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- School of Life Sciences
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- Website: <u>Campanale Lab</u>



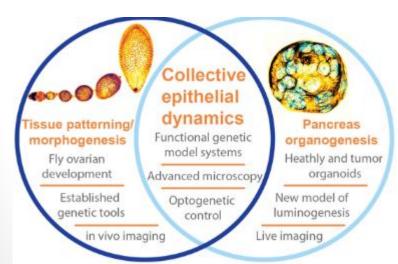


Fig.1: Using flies and mammilian organoids to study collective epithelial dymanics deployed in development.

Expertise

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



How do cells coordinate collective movements to establish barriers?

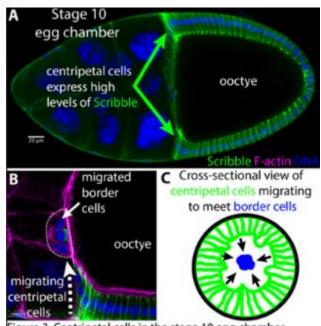


Figure 3. Centripetal cells in the stage 10 egg chamber overexpress scribble (A,B) and migrate toward boder cells (C).

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?

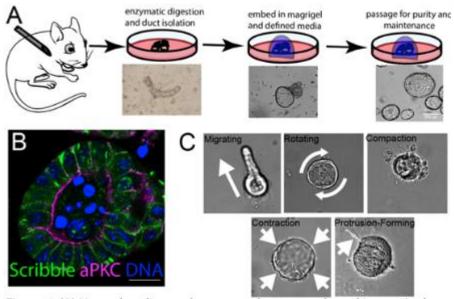


Figure 4. (A) Normal or diseased pancreas ducts are cultured in matrigel before maitenance. (B) Normal organoids are apicobasally polarized and (C) exhibit a range of behaviors during development.

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?



Comparative Biomechanics: Evolutionary, Environmental, & Applied

David V. Lee

Associate Professor

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Web: Laboratory of Comparative Biomechanics

Expertise:

Locomotion and gait

Animal biomechanics

X-ray motion analysis

Joint dysfunction

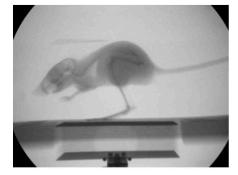


Locomotion

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

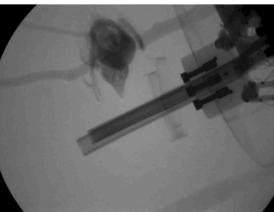






X-ray video of a kangaroo rat on a miniature force platform showing different gaits







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

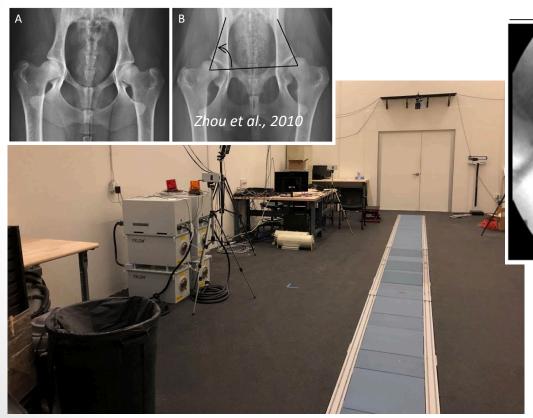


Comparing human, avian, and robotic bipedalism based on whole-body dynamics



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.



X-ray video of spontaneous osteoarthritis in the quinea pig

COLLEGE OF SCIENCES

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

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

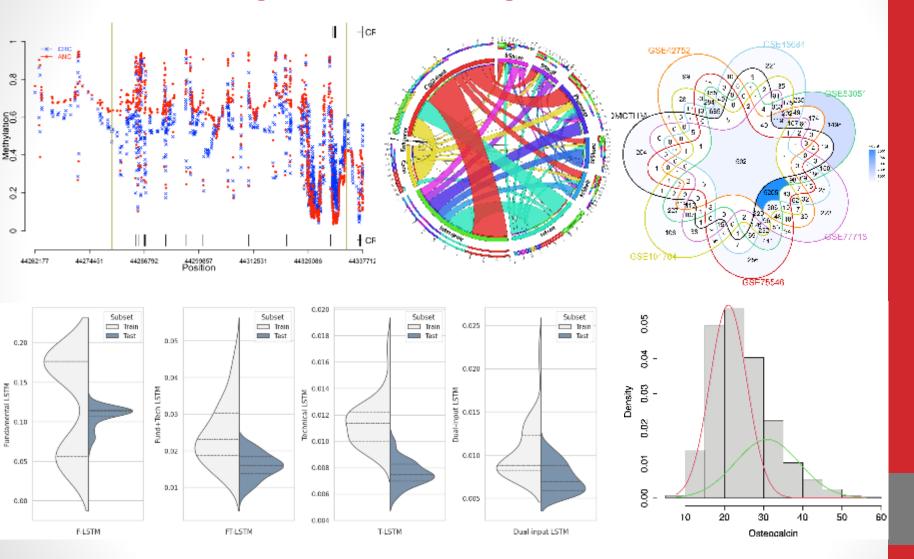


Expertise

- 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



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





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

Dr. Hong Sun

Associate Professor

Department of Chemistry and Biochemistry

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Expertise

Cell signaling

Cancer cell biology

Stem cell biology

Mouse conditional knockout models

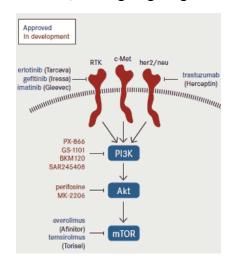


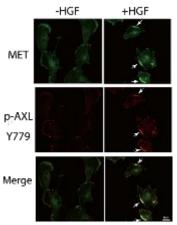
Regulation of cell surface receptor RTKs localization and activation

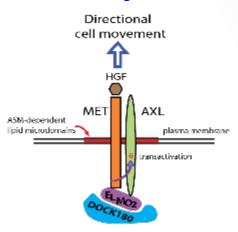
Problem: cancer cells often have multiple receptors (RTKs) activated on cell surface, making targeting inefficient detected by antibodies for p-AXL-Y779

Co-activation of AXL-MET RTKs: HGF (ligand for MET) also activates AXL,

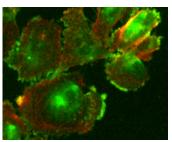
A novel mechanism discovered for RTK-Co-activation and signaling for cancer cell migration and invasion



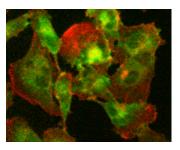




Li et al., J. Biol. Chem. (2018) 293:15397-15418.

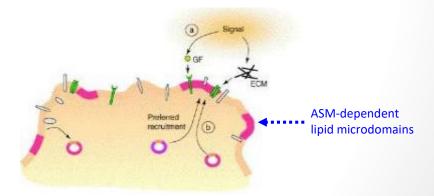






ASM Inhibitor

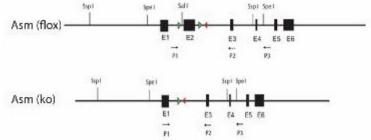
ASM inhibition prevents the MET RTK to be transported to the cell surface, as revealed by immunostaining (MET, green label; and a control cell surface protein, red label). Zhu et al, J. Cell Science (2016) 129, 4238-4251.



Mass-Spectrometry analyses revealed that the ASMregulated 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

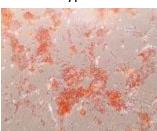


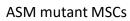


Purkinje neurons immunostained with D28K antibody.

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

Wild-type MSCs

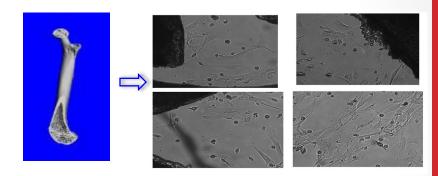






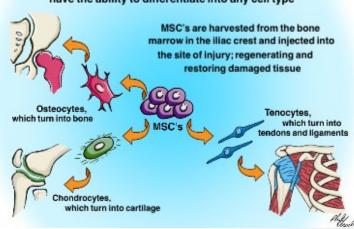
(in vitro differentiation assay, then stained with alizarin red)

C. Mesenchymal stem cells (MSCs) cultured from bones



E. Potentials of MSCs for tissue repair

Mesenchymal Stem Cells, or MSC's have the ability to differentiate into any cell type



Regeneration and Stem Cell Biology

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Expertise

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





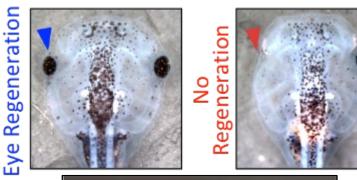
Understanding Vertebrate Organ Regeneration Kelly Tseng

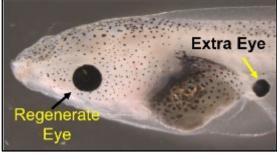
Why Can Some Animals Regenerate Body Parts but Others Cannot?

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

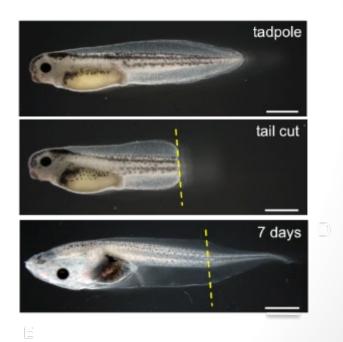


Eye Regeneration





Spinal Cord Regeneration



Projects:

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



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

Associate Professor

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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

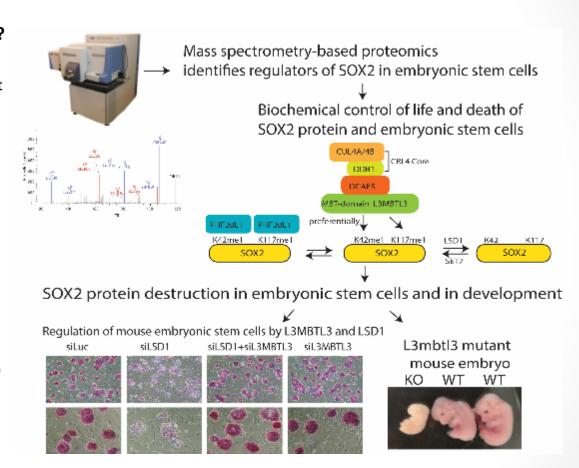


Current research areas in Zhang Laboratory:

• 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.

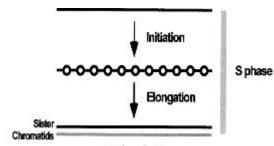




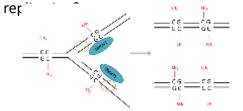
• Discover novel proteins important for epigenetic and cell cycle regulation, examples:

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

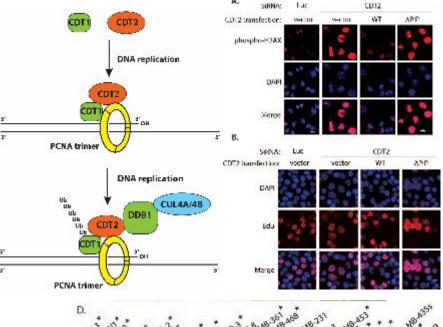


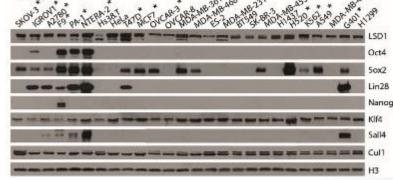
 How the fidelity of epigenetic DNA methylation is maintained during DNA



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

