MOSIMANN LAB

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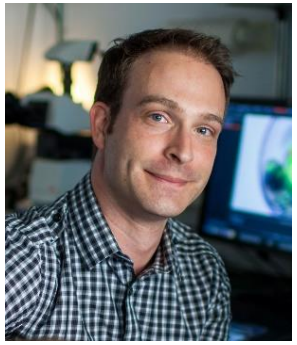


KEYWORDS – Cell Fate, Signaling, Genetics, Cancer Models, Zebrafish

SUMMARY & MISSION STATEMENT

Our lab aims to reveal the molecular mechanisms of cell fate determination and how they become malignant in disease. We use the zebrafish (*Danio rerio*) to understand how embryonic cell programs are harnessed by cancer and to model tumor formation *in vivo*.

OVERVIEW

The goal of my lab is to elucidate the gene-regulatory mechanisms of cell fate determination. As main paradigm, we study the developmental emergence of mesodermal lineages with focus on axial and lateral plate mesoderm (LPM). In addition to cardiovascular diseases, several devastating cancer types arise from these lineages, including leukemia, kidney tumors, mesothelioma, and the rare chordoma. In addition, the LPM forms the endothelial lineages that are crucial for tumor survival. We hypothesize that different mesodermal tumors re-initiate early developmental programs that provide unique cellular properties, including migratory behaviour and tissue invasiveness.

We study mesodermal lineage determination using advanced transgenic approaches, enhancer discovery, genome editing, and live imaging in the zebrafish (*Danio rerio*). The zebrafish provides a unique model to study development and cancer with its rapid development, optical translucency, and potent genetics. We have previously harnessed our transgenics expertise to study leukemia oncogenes, endothelial cell emergence, and to model early melanoma and chordoma formation. In ongoing our work, we combine transgenesis, live imaging including lightsheet/SPIM, genetic lineage tracing, CRISPR-Cas9-based genome editing. Uncovering the molecular programs that govern mesodermal cell fates has the potential to provide genetic sensors for compound screening, and to reveal developmental pathways amenable for therapeutic intervention.

SELECTED CANCER RELATED PUBLICATIONS

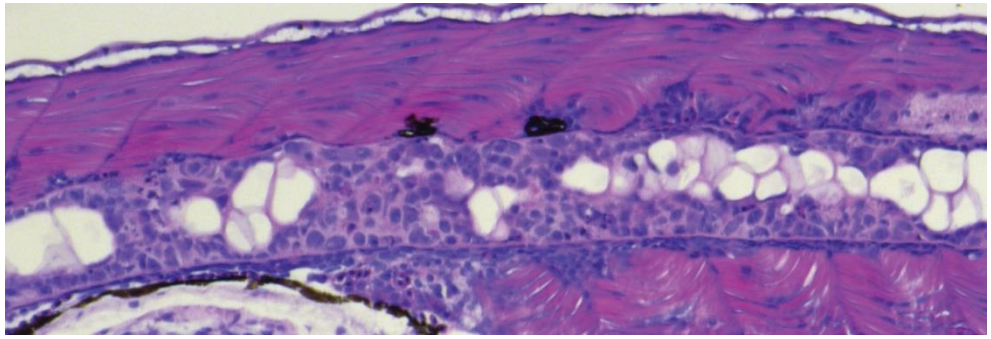
Cancer modeling by Transgene Electroporation in Adult Zebrafish (TEAZ). Callahan SJ, Tepan S, Zhang YM, Lindsay H, Burger A, Campbell NR, Kim IS, Hollmann TJ, Studer L, Mosimann C, White RM. **bioRxiv**, doi:10.1101/297234

CrispRVariants charts the mutation spectrum of genome engineering experiments. Lindsay H, Burger A, Biyong B, Felker A, Hess C, Zaugg J, Chiavacci E, Anders C, Jinek M, Mosimann C*, Robinson MD*. **Nat Biotechnol.** 2016 Jul 12;34(7):701-2.

Maximizing mutagenesis with solubilized CRISPR-Cas9 ribonucleoprotein complexes. Burger A, Lindsay H, Felker A, Hess C, Anders C, Chiavacci E, Zaugg J, Weber LM, Catena R, Jinek M, Robinson MD, Mosimann C. **Development.** 2016 Jun 1;143(11):2025-37.

A zebrafish melanoma model reveals emergence of neural crest identity during melanoma initiation. Kaufman CK, Mosimann C, Fan ZP, Yang S, Thomas A, Ablain J, Tan JL, Fogley RD, van Rooijen E, Hagedorn E, Ciarlo C, White RM, Matos D, Puller AC, Santoriello C, Liao E, Young RA, Zon LI. **Science.** 2016 Jan 29;351(6272):aad2197.

Parafibromin/Hyrax activates Wnt/Wg target gene transcription by direct association with beta-catenin/Armadillo. Mosimann C, Hausmann G, Basler K. **Cell.** 2006 Apr 21;125(2):327-41.



Sagittal section through a transgenic zebrafish embryo that expressed oncogenic Ras in the developing notochord. This genetic manipulation results in hyperproliferative notochord cells that recapitulate human chordoma as the first animal model for this rare tumor.