Speaker: Dr. J. Gray Camp, Max-Planck Institute for Evolutionary Anthropology, Leipzig (D)

Title: Multilineage Organoids to Reconstruct Uniquely Human Development

Abstract:

Human pluripotent stem cells (PSCs) can self-organize into complex, three-dimensional (3D) tissues that recapitulate morphological, functional, and genetic aspects of human organ development. I will tell you about two areas where we are using organoids to understand human development, disease, and evolution.

First, we use single-cell transcriptomics to dissect 3D multilineage liver organoids generated by reconstituting hepatic, mesenchymal, and endothelial cell interactions occurring during liver bud (LB) development. We compare hepatocyte-like lineage progression from pluripotency in 2D culture and 3D LB organoids and find that organoid hepatoblasts diverge from the 2D lineage and mature into hepatocytes with a striking correspondence to fetal liver hepatocytes. We use a receptor-ligand pairing analysis and high-throughput chemical perturbation experiment to investigate how inter-lineage communication can impact hepatic maturation in the 3D microenvironment. I will also present preliminary efforts using multilineage organoids to understand dysregulated gene networks in cholesteatosis and pancreatic cancer.

Second, we use great ape organoids to reconstruct uniquely human development. Humans diverged from our closest living relatives, chimpanzees and other great apes, 6-10 million years ago. Since this divergence, our ancestors acquired genetic changes that enhanced cognition, altered metabolism, and endowed our species with an adaptive capacity to colonize the entire planet and reshape the biosphere. We have generated human, chimpanzee, orangutan, and macaque cerebral organoids and have identified cis-regulatory, gene expression, and cell biological features specific to humans. I will tell you about our plans to study the function of these human-specific genetic changes that set modern humans apart from our closest evolutionary relatives as well as all other organisms on the planet.