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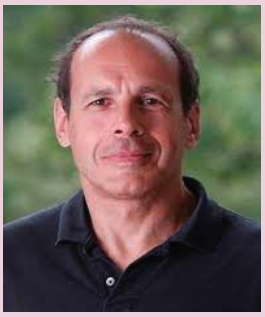

Didier Stainier

Director
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Hosts: Caroline Lei Wee (IMCB)
& Ajay Sriram Mathuru (Yale-NUS College)

Friday, 27 January (Hybrid)
2:00 PM-3:00PM
IMCB Seminar Room 3-46, Level 3, Proteos, Biopolis
Singapore 138673 (or scan QR code for zoom registration)

Transcriptional Adaptation, a Newly Discovered Mode of Genetic Compensation

Each human genome has been reported to contain approximately 100 loss-of-function (LoF) variants, with roughly 20 genes completely inactivated. Some of these completely inactivated genes are essential genes, and yet they are present in a homozygous state in apparently healthy individuals. Various hypotheses have been proposed to explain these findings including Genetic Compensation (GC). GC manifests itself as altered gene/protein expression, or function, which leads to a wild-type-like phenotype in homozygous mutant or heterozygous individuals who would be predicted to exhibit clear defects. We discovered TA while trying to understand the phenotypic differences between knockout (mutant) and knockdown (antisense treated) zebrafish embryos (Rossi et al., Nature, 2015). Further studies identified additional examples of TA in zebrafish as well as examples in mouse and human cell lines. By generating and analyzing several mutant alleles for these genes, including non-transcribing alleles, we found that mutant mRNA degradation is required to trigger TA (El-Brolosy et al., Nature, 2019). Based on these and other data, we hypothesize that all mutations that cause mutant mRNA degradation can trigger TA. We have also observed TA in C. elegans, and through a targeted RNAi screen followed by genetic analysis, found a role for small RNA biogenesis in this process (Serobyan et al., eLife, 2020). This presentation will also go over our unpublished data on TA including the transgenerational inheritance of this process.

Didier Stainier is the director of the Department of Developmental Genetics at the Max Planck Institute for Heart and Lung Research, Bad Nauheim (Frankfurt), Germany. He received his Ph.D. in Biochemistry and Biophysics from Harvard University (1990) where he investigated the cellular basis of axon guidance and target recognition in the developing mouse brain with Wally Gilbert. After a Helen Hay Whitney postdoctoral fellowship with Mark Fishman at the Massachusetts General Hospital (Boston) where he initiated the studies on zebrafish cardiac development, he set up his lab at the University of California San Francisco in 1995, where he expanded his research to investigate questions of cell differentiation, tissue morphogenesis, organ homeostasis and function, as well as organ regeneration, in the zebrafish cardiovascular system and endodermal organs. In 2012, he moved to the Max Planck Institute where he continues to utilize both forward and reverse genetic approaches to investigate cellular and molecular mechanisms of developmental processes during vertebrate organ formation, in both zebrafish and mouse. More recently, he has also started studying mechanisms of genetic compensation in zebrafish, mouse, C. elegans and yeast.