NUS National University of Singapore

Department of Biological Sciences
Faculty of Science

SEMINAR

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Hosted by Prof Paul Matsudaira

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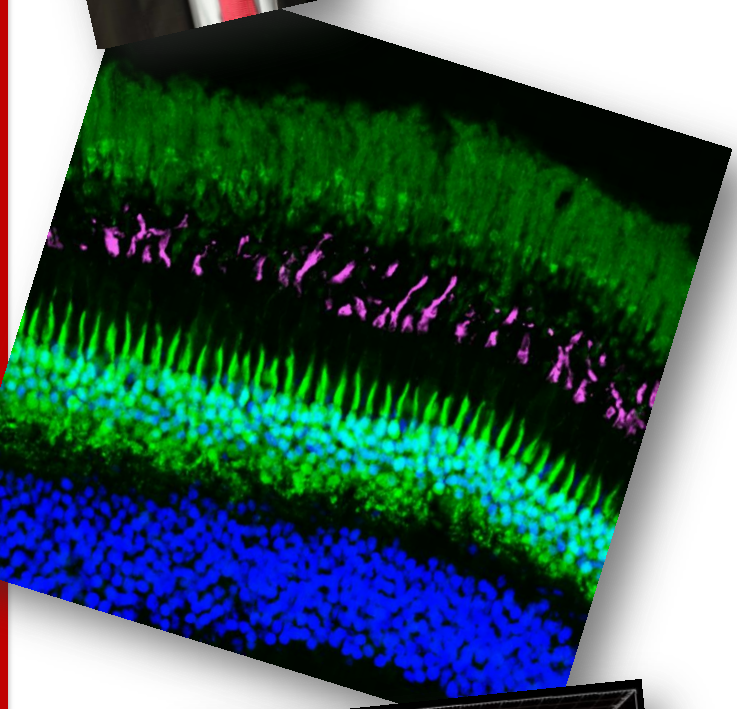
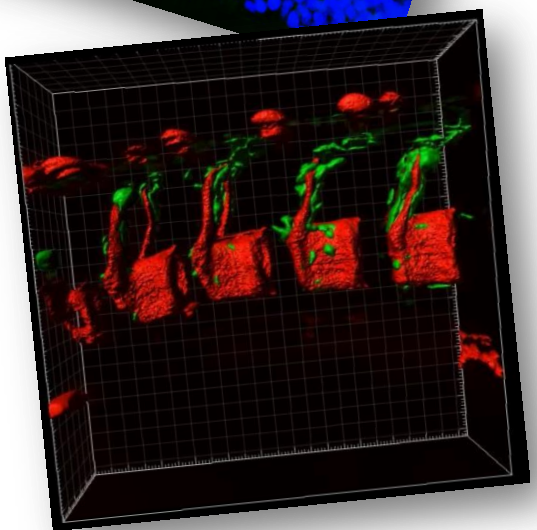
Development, degeneration and repair: New fish models for complex human diseases





Small laboratory fish have become popular model organisms in biomedical research. They allow a combination of live imaging and powerful genetics, which is unique among vertebrate models. Our lab uses zebrafish to understand mechanisms of neural development and degeneration. We generated models for Spinal Muscular Atrophy (SMA) and Retinitis pigmentosa (RP), two common human neurodegenerative diseases with deficiencies in RNA metabolism. SMA, characterized by progressive motor neuron loss, is caused by mutations in the Survival of Motor Neuron (SMN) gene, encoding a chaperone for spliceosomal snRNP assembly. How defects in this ubiquitous protein lead to cell-type specific defects remains unclear. To address this, we used a combination of live imaging and transcriptome analysis in zebrafish and identified neurexin2a (nrxn2a) as a novel SMN target. We show that nrxn2a deficiency phenocopies SMN defects and that nrxn2a splicing is affected in zebrafish and mouse models for SMA.

In a second project, we took advantage of rapid skeleton formation in transparent medaka embryos to study the dynamic behavior of bone forming osteoblasts and bone resorbing osteoclasts in vivo. We show that induced RANKL expression leads to activation of osteoclasts resulting in mineralization defects similar to human osteoporosis. Intriguingly, we find that osteoblast progenitors are recruited to lesion sites suggesting repair processes that involve communication between bone cells and defective bone matrix. We established protocols for isolating individual bone cell populations under osteoporotic and repair conditions and transcriptome profiling. Ultimately, this will help us to better understand the gene regulatory networks underlying bone homeostasis.

Artwork by Ann Nee, DBS, NUS