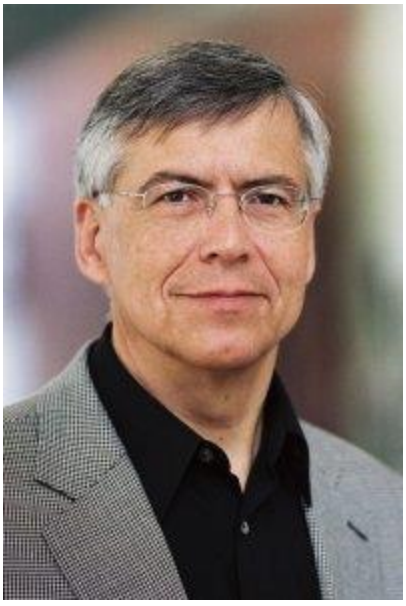
NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

BIOLOGY COLLOQUIUM

Friday, 30 January 2015 | 4pm | DBS Conference Room 1

Hosted by A/P Christoph Winkler

Establishing transcriptional disease signature from fish skin cancer models



By **Manfred Schartl**

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Aberrations in gene expression are a hallmark of cancer cells. Differential tumour-specific transcript levels of single genes or whole sets of genes (transcriptional disease signatures, TDS) may be critical for the neoplastic phenotype and are important for therapeutic considerations or useful as biomarkers. In an approach to filter out the relevant expression differences from the plethora of changes noted in global expression profiling studies, we searched for conserved changes of gene expression. Stable transgenic lines of medaka were produced expressing the *xmrk* melanoma oncogene from Xiphophorus under control of the pigment cell specific *mitf* promoter. Several lines were established that develop pigmentary disorders ranging from benign hyperpigmentation to highly malignant pigment cell tumours. The melanomas perfectly recapitulate the oncogenic molecular changes known from the Xiphophorus system. RNA-seq transcriptomes from Xiphophorus and medaka melanoma were generated and compared to datasets from zebrafish and human melanoma. This revealed molecular conservation at various levels between fish models and human tumours providing a useful strategy for identifying expression signatures strongly associated with disease phenotypes and uncovering new melanoma markers. TDS were established that can be used for high-throughput drug screening. Changes in TDS point to systemic suppression of the innate immune response and break of oncogene-induced senescence as major events for the transition to the malignant state.

Artwork by Ann Nee, DBS, NUS