REGIONAL CENTRE FOR BIOTECHNOLOGY
Seminar series

Modeling Human Pancreas Adenocarcinoma: Treatment Progression by Real Time Imaging

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Board Room

In cancer biology major challenges we face are several, such as early diagnostics, targeted therapy and preclinical model, which faithfully recapitulates human disease and can be use for all initial platforms for cancer biology. I am focusing on role of oncogenes and the "addiction" of cells on oncogenes. To study this I am using two different cancers, pancreas ductal carcinoma (PDA) and melanoma. My current research is focused primarily on PDA. I created quadruple conditional allele (*Kras*$^{LSL\text{-}G12D/+}$; *Trp53*$^{LSL\text{-}R172H/+}$; *DPC4*$^{flox/+}$; p48$^{cre/+}$) animals. This study revealed that heterozygous loss of tumor suppressor DPC4 shifts the disease phenotype from highly metastatic (*Kras*$^{LS\text{-}LG12D/+}$; *Trp53*$^{LS\text{-}LR172H/+}$; p48$^{cre/+}$) to almost no metastasis. This dramatic switch between highly metastatic to non-metastatic phenotype by heterozygous *DPC4* further suggests an exquisite sensitivity to the level of signaling, rather than its absolute presence or absence. At the same time I am using above model in preclinical drug trials using state of the art small animal imaging techniques such as Ultrasound and Multi Photon Laser Scanning Microscopy. Based on our initial trials, we conclude that mouse model will helpful in predicting efficacy and addition to this the mouse model studies proposed a mechanism that can now be evaluated directly in the earliest clinical trials.