Abstract Title: Reactivation of human fetal microRNAs in liver cancer
Control Number: 144
Topic: 13. Cancer Genetics
Presentation Preference: Oral Presentation
Applied for Early Career Award and/or Fellowship:

Conference Fellowships of Excellence
Early Career Award

Authors:
Nikita Telkar*[1, 2, 3], Greg Stewart[1], Michelle Pewarchuk[1], Katya Benard[1], David Cohn[1], Wendy Robinson[2, 3], Wan Lam[1]

[1]British Columbia Cancer Research Centre, Vancouver, Canada, [2]British Columbia Children's Hospital Research Institute, Vancouver, Canada, [3]University of British Columbia, Department of Medical Genetics, Vancouver, Canada

Consortium name:

Rapid cell proliferation and differentiation are hallmarks shared by fetal development and cancer. While these highly regulated processes cease functioning after fetal growth, they show aberrant re-activation in cancer (oncofetal). MicroRNAs regulate gene expression and have known clinical roles in normal adult and tumour tissue. However, due to the scarcity of fetal samples, the processes causing this re-activation of fetal microRNAs and the parallels between tumour and fetal development remain to be explored.

We profiled the microRNA transcriptome of 10 fetal liver samples from second trimester elective terminations and compared them with 345 hepatocellular carcinoma and 50 non-malignant (NM) matched samples from The Cancer Genome Atlas (TCGA). MicroRNAs which showed significant differential expression after multiple-testing correction between tumour-NM and fetal-NM but not between tumour-fetal were termed oncofetal microRNAs (n = 113). The Kaplan-Meier survival curve using this 113 miRNA-signature was highly significant (p = 0.0019), and six displayed standalone significant difference (p <= 0.05) in patient survival based on expression. Given the higher incidence of liver cancer in males than females, sex-stratified analysis revealed 121 hepatic oncofetal microRNAs in males and 166 in females – 62 of the 121 and 49 of 166 had significant patient survival curves. Signalling pathways (mTOR, MAPK, HIPPO), immune pathways, and cancer pathways were the top hits output by multiple pathway analysis databases.

To our knowledge, this is the first report of human fetal liver miRnome profiling and comparison with adult liver and tumour tissue. Our results emphasize the clinical importance of oncofetal microRNAs.

CIHR:FRN106430