Department of Biological Sciences

Graduate Seminar

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Date/Time – **27 Apr. 2017, at 10.00 AM** Venue – **401, AB2**

Nutraceuticals mediated regulation of alternative splicing via epigenetic modifications in oral cancer

Abstract:

Alternative splicing is a highly regulated process which contributes to the transcriptome and proteome diversity in the eukaryotic organisms. It is a complicated process which occurs co-transcriptionally, raising the possibility that alternative splicing may get influenced by the chromatin structure. DNA methylation and histone modifications are determining factors for chromatin structure. Although epigenetics and alternative splicing have been individually very well studied during cancer progression, there is a lack of information regarding role of altered epigenetic marks in generation of cancer-specific alternative spliced isoforms. Epigenetic modifications are involved in cancer progression, and are potentially reversible and could be utilized as therapeutic targets. Here in this study, we explore the use of epigenetic-based therapeutic compounds with minimal toxicity and side-effects on cancer-specific alternative spliced isoform. Nutraceuticals are natural products with food value and have substantial therapeutic effects in cancer.

Curcumin, the principal curcuminoid of turmeric, exert potent effect over a wide range of cancers due to its chemopreventive, antioxidative, anti-inflammatory and proapoptotic activities. Studies also show the role of curcumin as an epigenetic regulator and explain its influence on the level of various epigenetic modifiers like DNA methyltransferase (DNMTs) and ten-eleven translocation (TET), histone acetyl transferase (HATs) and Histone deacetylases (HDAC). In this study, we are investigating the role of curcumin in the regulation of alternative pre-mRNA splicing via modulating epigenetic modifications in oral cancer. In our preliminary experiments, we observed that curcumin could influence the splicing of the oral cancer-specific genes (identified via genome-wide alternative splicing analysis of exon array profile of oral cancer patients). Additionally, we observed changes in the expression of DNMTs and TETs in curcumin treated versus control cells, which led us to investigate the role of DNA methylation in alternative splicing. Interestingly, we observed differential DNA methylation pattern at the cassette exon of model genes in cancer samples. These observations suggest a possible role of curcumin in the regulation of alternative splicing via epigenetics. Based on these observations, the role of curcumin, as well as other nutraceuticals in the regulation of alternative splicing via epigenetic modulation in oral cancer, is in progress.