Séminaire de Biologie

Human endogenous retroviral elements as promoters in normal and cancer cells

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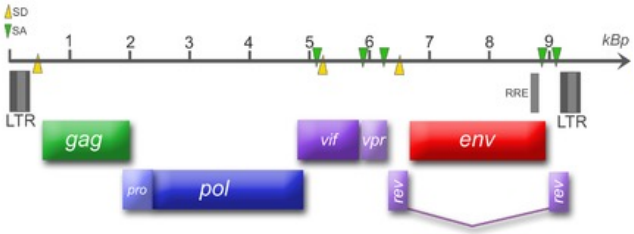
The human genome contains ~500,000 endogenous retroviral sequences, most as solitary long terminal repeats (LTRs) which contain promoters and enhancers. Although most are epigenetically suppressed in normal cells, some LTRs have been co-opted or exapted over evolutionary time to regulate genes or gene networks. Cancer cells represent an abnormal epigenetic environment where LTRs and other transposable elements (TEs) are often hypomethylated or deregulated, leading to transcriptional activation. Such activation could result in abnormal, cancer-specific expression of nearby genes. To study this phenomenon, which we term "onco-exaptation", we developed software to detect and quantify TE-promoted chimeric gene transcripts by mining RNA-Seq data. We analyzed whole transcriptomes from lymphomas and colon cancers specifically to identify gene deregulation due to promoter activity of LTRs or other TEs that are normally transcriptionally dormant. We determined that, in general, cancer transcriptomes have an overall increase in TE-initiated transcripts relative to matched normal tissue or appropriate controls, particularly at LTRs. Specific examples of onco-exaptation will be discussed as well as possible mechanisms underlying recurrent LTR activation in cancers.



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