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Retroviral Links to Cancer

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Introduction.

Cancer at its very base is the out of control growth and replication of cells as a result of intracellular regulatory disruption. Intracellular regulation is controlled through regulatory gene networks that act in much the same manner as any other type of network sending and receiving signals to communicate between nodes. In cellular gene regulatory networks molecular signals are used to send and receive messages to control cellular functions. These molecular signals come in many forms, one of these being micro RNAs (miRNA). These miRNAs are composed of RNA segments of approximately 18-25 nucleotides in lengths. Because of their short lengths it is possible that they can be taken up by retroviruses during the retroviruses self-replication process.

Retroviruses enter and infect cells as RNA the convert themselves into double stranded DNA and insert themselves into the host genome. Once the retrovirus has inserted itself into the host genome, the host will make new copies of the virus that can infect other cells. During this replication process it is possible for the retrovirus to pick small regions of DNA from the host. In the human genome there are many regions of untranslated DNA that could by chance have the same sequence as a miRNA and could be incorporated into a retrovirus during its replication cycle. The incorporation of this miRNA and its subsequent transcription and release into the cell by the retrovirus could cause disruptions in the regulatory network of the cell resulting in cancerous cells.

We propose searching cancer data in the Open Science Data Cloud's (OSDC) Bionimbus database for gene markers that show confidence for incorporation of a retrovirus. Once retroviral gene regions are found we plan to search the regions between genes in the retrovirus for any known miRNAs that have been incorporated into the retroviral genome. Once detected we can determine the regulatory pathways that are being effected and whether they are a contributing factor to the development of cancerous cells.

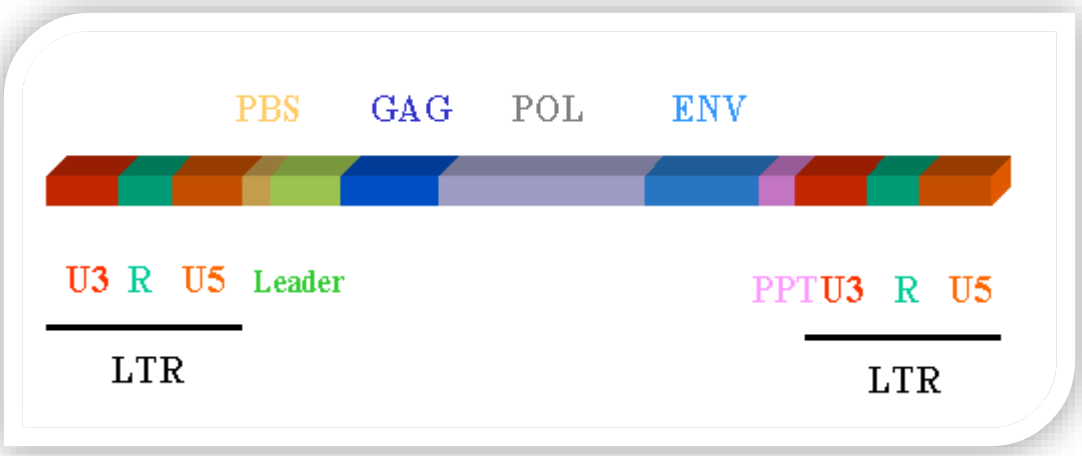

Figure 1 Image of a generic retrovirus with the 4 required genes (GAG, PPT, POL and ENV), repetitive sequence (R), unique sequence (U3 and U5) and primer binding site (PBS)

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Methods.

1) Compile all data required for the experiment.
   The miRNA data necessary can be obtained by the following public repositories and loaded onto the OSDC system.

   miRBase:
   University of Manchester, Faculty of Life Sciences, United Kingdom, funded by BBSRC, and by the Wellcome Trust Sanger Institute
   http://www.mirbase.org/

   miRWalk: microRNA target database
   From Ruprecht-Karls-Universität Heidelberg, Medizinische Fakultät Mannheim, GERMANY.

   The Bionimbus database is available on the OSDC system but access will need to be gained through the proper regulatory bodies.

2) Development of a GPU based search tool.
   The search tool will be written in both CUDA and OpenCL to determine the most efficient GPU method for the search tool. The algorithm will use the 4 genes, gag, ppt, pol and env which are in all retroviruses to find their genome location in the cancer data. Once these regions are found we will search the regions beteween the 4 genes against the miRNA database for matches with high confidence. The tool will search for both the miRNA and its reverse compliment to also find potential interfering RNAs (RNAi). When a match is found the tool will report the match location and miRNA sequence.

Conclusions.

If we can show with confidence that miRNAs are present in human retroviruses we will be able to determine possible regulatory networks being disrupted by the presence of the retrovirus. Once these networks are determined we can find if they are involved in any pathways that are part of cancer formation. If they are involved in cancerous regulatory networks we could develop gene silencing drugs to prevent the formation of cancer.