Future Directions

My mentor often says that a doctoral thesis is not the end of a story but an opening to several others since its revelations pave the way and provides background to more comprehensive research. I realize the truth in this statement now when I find that my investigations have revealed only the tip of an ice-berg. Many questions are yet to be answered and many avenues still remain un-traversed. The areas inspiring immediate investigation are as follows:

PMA treatment of U937 cells have revealed increased binding of several proteins to the three (lif-B, lif-C and lif-E) 3′UTR regions of *lif* mRNA. The identities and functions of only 3 of these proteins (Nucleolin, PCBP1 and HuR) have been studied. Other proteins may also have significant roles in *lif* mRNA stability that should be studied.

The nature of interactions between Nucleolin, PCBP1 and *lif* mRNA leading to stabilization have been studied in some details. Further investigations using RNA-footprinting techniques could be utilized to determine the precise binding sites of these proteins on lif-B. Since these proteins have imparitive roles in *lif* mRNA stabilization, identification of non-canonical sequences or mechanisms of their binding to RNA would significantly add to putative RNA recognition motifs of these proteins thereby facilitating the identification of other RNA targets of these proteins.

mRNA stability is a very context dependent phenomenon. It varies with cell type and nature of stimulus as well. Since LIF is also highly pleiotropic, with its expression highly varying in different tissues and also in response to different stimuli, its mRNA stability could be a key determinant of such variation. Therefore post-transcriptional regulation of LIF should be studied in different systems, with respect to different stimuli. For example, as discussed earlier, LIF expression is high in breast cancer cells and directly correlates with their metastatic potential. Increased LIF expression is also implicated in the pathogenesis of osteo and Rheumatoid arthritis. Down regulation of LIF expression by destabilization of its mRNA or by inhibiting its translation in these cells could therefore be a therapeutic strategy.