Human embryonic stem cells (hESC) have a unique pluripotency capacity. L1TD1, a novel gene encoding for an uncharacterized protein, was isolated in recent experiments while analyzing the transcriptome data of 21 hESC lines of rapidly regulated genes during the early differentiation. Experimentally it has been shown that L1TD1 is a RNA-binding protein localized in processing bodies (P-bodies), forming a complex with LIN28 and RNA helicase A (RHA), and is essential for the self-renewal of hESCs and expressed in embryonic carcinoma cells. L1TD1 is highly expressed in hESC and rapidly downregulated upon differentiation. It has been thought that L1TD1 could be used as a marker to distinguish undifferentiated hESC as well as for some cancers. There is a huge gap between the numbers of known sequences and known three-dimensional (3D) structures. However, there is only a limited number of different folds making protein modeling possible. Building a model is important in order to understand protein's function and interactions. Aim of this thesis was to model a structural complex including L1TD1 and RHA by using homology modeling and discover their interactions with RNA. Homology modeling is a well-studied analytic tool for constructing the structure of a structurally unknown protein based on knowledge of its primary structure. This method uses sequence similarity of proteins of known structure to build a 3D model for a protein of interest. Structural similarity can usually be assumed, if one can detect sequence level similarity between two proteins as 3D structures of proteins in a family are more conserved than their sequences. Suitable templates were acquired from Protein Data Bank (PDB) and sequence analysis and alignment was obtained from BLAST for L1TD1 and RHA. Computational informatics software for molecular modeling SYBYL was used for the model building process. Automated validation tools were used to validate the model. The findings showed that the interactions between L1TD1 and RHA or RNA are not in fact direct. These discoveries of the L1TD1 structural elements and its place in the functional complex open up possibilities for new direction of experimental research, could lead to new discoveries of pluripotency of stem cells and offer diagnostic tools and better understanding for cell replacement therapies for the treatment of various debilitating diseases.

KEY WORDS: human embryonic stem cells, homology modeling, L1TD1, structural complex, pluripotency factors, interactions, RNA binding