Bioinformatics Analysis of the Ribosomal Proteins, RPL27, RPL37a and RPL41: 3-D Protein Modeling and Protein-protein Interaction Prediction

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***Abstract*—Ribosomal proteins (RPs) are constituents of ribosome important for protein biosynthesis but likely to have extraribosomal functions. Many RPs are associated with various diseases and cancers. A previous study reported RPL27, RPL37a and RPL41 gene to be downregulated in nasopharyngeal carcinoma (NPC) derived cell lines compared to their normal counterpart. However, their actual physiological roles in organogenesis or tumorigenesis have not been properly defined. In this paper, we report on the findings of structural prediction of these three genes and infer their interactions with other proteins using structural neighbor prediction and molecular docking strategies. Our results revealed that RPL27 interact with SYNJ2 and UBC9. RPL27 is predicted to mediate RNA binding protein and deregulate sumolyation. RPL37a is suggested to interact with CTNNB1, SCMH1 and ATBF1. It is predicted to deregulate Wnt degradation pathway, inhibit β-catenin migration and regulate homeotic transcription. Our studies on RPL41 did not allow logical inference on possible interacting factors. Nevertheless, results on RPL27 and RPL37a provide rational data for the elucidation of their molecular activities.**

***Index Terms*—Protein modeling, extraribosomal functions, protein-protein interaction prediction, ribosomal protein.**

I. Introduction

Ribosomal proteins (RPs) are important ribosomal subunits assembled for protein biosynthesis. Disruption in this process has been associated with deregulated cell growth and altered cell cycle [1], [2]. Ribosomal proteins are structurally distinct and independent polypeptides [3]. Several of them have been found to possess extraribosomal functions that modulate function of important regulatory proteins. Some can even translationally control their targets outside the ribosome [1], [4].

Ribosomal protein genes have been associated with colorectal carcinoma [5]. Recent studies showed that the ribosomal protein large subunit (RPL) genes of *RPL27*, *RPL37a* and *RPL41* are significantly downregulated in cell lines derived from nasopharyngeal carcinoma (NPC) compared to a derivative from normal nasopharyngeal epithelium [6], [7]. However, limited studies on protein-protein interaction activities have made the understanding of their extraribosomal roles difficult. One reason may be the unavailability of experimental structures due to difficulties in obtaining ribosome component structures [8], [9].

To overcome this problem, our study incorporated bioinformatics approach to understand these three proteins. Three-dimensional (3-D) protein models of these proteins was constructed and served as template to search for structural neighbor.

By the assumption that close homologs or analogs almost always interact in the same way [10], interaction models of queried proteins can be extrapolated from known protein behaviors of their structural neighbors with interacting partners. To strengthen our inferences, RPL models were also docked to their candidate partners to further predict RPL functions through their putative interaction sites. Docking is an amenable method to overcome difficulties in crystalizing and modeling transient complexes [11]. The interaction sites evident from other experiments aid to infer RPL functions. As a result of our endeavor, we revealed novel extraribosomal functions for RPL27 and RPL37a.

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II. Methodology

A. Multiple sequence alignment

Protein sequences of human RPL27, RPL37a and RPL41 were retrieved from Ribosomal Protein Gene (RPG) database [12]. The protein identifiers used are: NP_000979 for RPL27, NP_000989 for RPL37a and NP_001030344.1; NP_0667927.1 for RPL41. PSI-BLAST search for each query RPL sequences against Protein Data Bank (PDB) was performed using default parameter to search for templates. For RPL41, the parameter was altered to accommodate short sequence. Template structures with expected value (e-value) above threshold for high sequence identity and structure resolution were selected for multiple sequence alignment. The selected templates were aligned with their respective target sequences using ClustalX program [13]. Protein weight matrix used was from BLOSUM series while clustering algorithm was UPGMA algorithm.

B. Comparative Modeling

SWISS-MODEL workspace [14] was used to build RPL models. RPL27-template alignments were submitted to SWISS-MODEL server pipeline with 3U5E_Z (PDB ID) as structure template. Using the same alignment mode, RPL37a was modeled with 4A17_Y (PDB ID). In contrast, RPL41 was modeled via project mode by structurally aligning 3IZS (PDB ID) to RPL41 raw protein sequence in SPDBV 4.0.1