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Oral Defence by PhD Candidate Najmeh Nikpour

Institute of Parasitology

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Abstract

One of the most intriguing features of Trypanosoma brucei, a unicellular protozoan parasite, is its unique way of energy production in different life cycle stages. In the mammalian host, trypanosomes generate energy by glycolysis in glycosomes whereas in the insect vector they generate energy by oxidative phosphorylation in mitochondria. In mitochondria, mRNAs undergo a unique post-transcriptional editing process by guide RNAdependent insertion and deletion of uridine nucleotides that requires a multi-protein complex, the editosome. The edited mRNAs translate into the essential protein subunits of the respiratory chain. Interestingly, RNA editing is differentially regulated between the mammalian and insect life cycle stages of the parasite, resulting in differential mechanisms of ATP generation. However, it is unknown how the developmental regulation of editing occurs. My Ph.D. project tested the hypothesis that differential editing may reflect the differential function and/or composition of the components of the editosome and its associated complexes in the different life cycle stages of the parasite. I tackled this intricate question by studying the composition of the mitochondrial protein complexes from the insect stage of parasites using two orthogonal, complementary biochemical approaches and identification of a few novel proteins Down-regulation of one of the proteins, RBP7910 indicated an essential role for the growth and editing of apocytochrome b mRNA levels in the insect form of *T. brucei*. Structure-based analysis of RBP7910 suggested that it resembles a conserved family of Z-DNA binding proteins (ZBPs), sharing two winged helix-turnhelix (WTHT) structured Z-DNA binding domains. Overall, in the insect form of T. brucei, RBP7910 with two Z-DNA binding domains binds multiple mitochondrial RNA classes and influences the editing and stability of specific transcripts.



About the Candidate

Najmeh did her undergraduate studies in zoology at "Guilan University, Iran" and then joined "Shahid Beheshti University, Iran" for her master's program in biological science. In 2012, she joined Dr. Reza Salavati's lab at the Institute of Parasitology to work on "RNA editing regulation in *Trypanosma brucei*" during her PhD.