Title: Post-transcriptional regulation of mitochondrial gene expression

Human mitochondria contain a small and compact genome that is transcribed as long polycistronic transcripts that encompass each strand of the genome, which are processed into mature mRNAs, tRNAs and rRNAs within the mitochondrial matrix. Despite their common polycistronic origin, we observe wide variation between individual tRNAs, mRNAs, and rRNA amounts, indicating the importance of RNA-binding proteins in the regulation of mitochondrial gene expression. We have investigated the roles of the mammalian pentatricopeptide repeat (PPR) proteins and found that these RNA-binding proteins are all localized to mitochondria where they regulate mitochondrial gene expression. Mammalian PPR proteins have diverse roles in RNA metabolism and translation that are important for mitochondrial function and cell health. To investigate the importance of RNA-binding proteins in mitochondria globally we have established new methods for massively parallel sequencing and analyses of RNase-accessible regions of human mitochondrial RNA. We have identified specific regions within mitochondrial transcripts that are bound by RNA-binding proteins. These mitochondrial protein footprints indicate that RNA-binding proteins as well as small RNAs play a significant role in the regulation of mitochondrial gene expression.