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Title: PROTEIN COEVOLUTION PREDICTS KNOWN AND NOVEL NUCLEAR-MITOCHONDRIAL INTERACTIONS

Abstract: Correlations in evolutionary rates can be used as a tool to predict protein interactions. We have developed a pipeline that identifies these evolutionary correlations among 12,000 mammalian proteins. The electron transport chain (OXPHOS) combines proteins encoded in the mitochondria and nucleus, which must "work together" for proper function. Here we test the idea that nuclear and mitochondrially encoded proteins with mitochondrial function will show correlated rates of evolution. As predicted, known nuclear partners show high correlations with mitochondrial encoded proteins, such as ERCs among the proteins in Complex I of OXPHOS. In addition, novel protein interactions are found, which are candidates for future research. Examples include connections between Complex V and mitochondrial ribosomal proteins, novel predicted interactions involving autophagy, mRNA and DNA processing. More broadly, this method shows promise for identifying protein-protein interactions in diverse biological processes.