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3D heat maps of cancer mutations in the mitochondrial electron transport system to identify driver domain candidates

Estella Chen-Quin and **Trang Dang**
Kennesaw State University, USA

A link between tumorigenesis and mutations in the mitochondrial genes of the electron transport system (ETS) has long been posited, due to the high prevalence of mitochondrial mutations in all tumors. However, whether mitochondrial mutations play a causal role in cancer is unknown. Here, we analyze somatic mutations of ETS complex II (Succinate Dehydrogenase; SDH). People with inherited (germline) mutations in SDH have a known cancer predisposition; however, the path from inherited predisposition to cancer-causing lesions is not understood. Mutational lesions in the ETS disrupt the normal flow of electrons, increasing levels of reactive oxygen species (ROS) and creating a mutagenic source. Increased levels of ROS stabilize the mitogenic factor HIF-1□. To identify and visualize which SDH protein domains are selected for somatic missense mutations during tumorigenesis, we created the 3D protein heatmap to identify potential cancer driver domains. A structural analysis via homology modeling allows us to highlight cancer-associated mutations on the ETS protein structure. This may identify areas of the mitochondrial proteins that promote cancer when altered and inform on the cellular mechanisms involved. Mutations are scored for their predicted protein effect using Polyphen2; and potential driver domains are identified by their mean Polyphen2 score. Cancer data is taken from the Cancer Genome Atlas; control data is from the 1000 Genomes Project. We use Pymol and the porcine crystal protein structure to create the 3D protein heatmaps, providing comparative analysis between the control and cancer set..

Biography

Estella Chen-Quin is an Associate Professor in the Department of Molecular and Cellular Biology at Kennesaw State University. She investigates the cancer genetics of mitochondrial lesions during tumor formation. She has completed her PhD at Yale University and Postdoctoral studies at Emory University

echen1@kennesaw.edu

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