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Identification of new metabolic enzymes with filament capacity defined by transmission electron microscopy

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Self-assembly of metabolic enzymes into filaments and supramolecular structures coincides with metabolic changes and has been most widely described in bacteria and yeast, with few examples in mammalian cells. Currently, it is believed that the formation of non-membranous compartments may also play a critical role in regulating metabolic networks. (1) A recent study on filament-forming yeast enzymes showed a direct association between metabolic enzymes from connection points of a given main pathway with its metabolic arms to activate or inactivate a given enzyme in times of growth or stress, thus ensuring the metabolic flow to different destinations. Several of the enzymes previously detected in yeast are conserved in humans (2); however, these aggregated states have been functionally and structurally characterized only for a few of these homologs. (3) In this project, 14 human metabolic enzymes, homologous to yeast, will be evaluated for their ability to aggregate in vitro in response to the presence of substrate, product, and co-factors, using biophysical techniques that kinetic assays will complement. Finally, up to three of these enzymes will be selected for electron cryo-microscopy studies, with the objective of high-resolution structural determination.

Palavras-chave: Metabolic enzymes. Cryo-microscopy. Filaments.

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