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Inferring protein function in Microsporidia by structural homology

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Pavillon Charles-Eugène Marchand, salle Hydro-Québec (1210)

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Résumé

Microsporidia are spore forming, fungal-related obligate intracellular pathogens exhibiting high levels of genetic divergence postulated to originate from the lack of several DNA repair proteins. In human infecting microsporidian species from the genus *Encephalitozoon*, severe streamlining resulted in sub-3Mbp genomes (the tiniest known in eukaryotes) coding for a mere 2,000 or so proteins. Unfortunately, the divergent sequences found in Microsporidia render functional inferences difficult such that roughly half of these 2,000 proteins have no known function. Most *in silico* inferences are based on sequence homology approaches and thus can fail when in presence of highly divergent sequences. However, because protein structures and their biological roles are intertwined, protein function can also be inferred by searching for structural homology. Recently, we built a structural homology-based pipeline called 3DFI (for tridimensional functional inference) leveraging protein structure prediction, structural homology, and visualisation tools to help assist genome annotation efforts and used it to help infer the functions of unknown Microsporidia proteins. In this talk, I will give an overview of the pipeline, show a few examples of proteins identified with it, and highlight some of the pitfalls and limitations inherent to structural homology-based approaches.

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