EuroSciCon

EuroSciCon conference on

Protein, Proteomics and Computational Biology

December 06-07, 2018
Amsterdam, Netherlands

Biochem Mol biol J Volume:4
DOI: 10.21767/2471-8084-C5-021

INTEGRATIVE PROTEOMICS FOR GENE AND PATHWAYS DISCOVERIES IN CELL DEATH AND VIRAL IMMUNITY

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Identifying new genes and members of a protein family and characterizing their structure and function is fundamental in obtaining a complete list of the components that constitute our genomes. One important area of research towards this goal has been to develop more sensitive bioinformatics tools that identify distant relationships between sequence and/or structures. Once the relationship between two sequences or structures is established, one can then infer structural or functional information, develop hypotheses testable in the laboratory, and eventually annotate the function of the newly uncharacterized genes. Existing families can be expanded by adding the newly characterized members. My laboratory has worked extensively at developing new bioinformatics tools and integrative strategies towards this goal. In particular, we focused on a protein superfamily highly represented in the cell death machinery called death domain. In this talk, we will illustrate by a few examples how structural bioinformatics, biochemical and reverse genetics approaches can be integrated to identify and characterize new candidate proteins. The major findings presented will include the discovery of the death domain subfamily PAAD and the functional characterization of some members of the HIN200 family that are novel components of viral innate immunity. Finally, we will present our progress towards the identification of novel OB fold containing genes and their role in viral immunity in *C. elegans* using a promoter: GFP and translational gene fusion screen. To conclude, we will also present a novel method that can deliver any recombinant protein in the gut of the worm and highlight its potential to study host-microbiota interactions in the context of viral immunity.

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