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Development and application of a computational pipeline to analyze genes encoding phospholipase domains in flatworms

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Motivation and Aim: Phospholipases are a group of enzymes (class of hydrolases) that catalyze the process of phospholipid hydrolysis [1]. This work will focus on A2 phospholipases (PLA2), which detach the SN-1 and SN-2 acyl chain. They are known to be venom toxins in snakes [2]. PLA2 are classified into several types, such as secreted, cytosolic, and calcium-independent [2]. Secreted PLA2 (sPLA2) are the best studied and has quite a wide range of functions. In humans sPLA2 are expressed and released by human inflammatory cells including macrophages, monocytes, T cells, mast cells, and neutrophils, and increased concentrations of different isoforms of sPLA2 have been detected in the blood of patients with inflammatory and autoimmune diseases [2]. In contrast to snake or human phospholipases, PLA2 homologs in other taxons are poorly studied. The analysis is complicated by the fact that PLA2 from different groups have a similar structure, despite the variation in domain composition.

In this work, we search for A2 phospholipases in flatworms, a taxon which comprises of an enormous diversity of species occurring in seas, lakes and land masses. As parasites flatworms pose a threat to public health, especially in Siberia and South-East Asia. Diseases caused by parasitic flatworms can cause serious consequences such as cholelithiasis or cancer [3].

The aim of this work is to create a computational pipeline for bioinformatics search and analysis of PLA2 genes in genomes, their functional annotation and study on its basis the features of structure, function and evolution.

Methods and Algorithms: The bioinformatics pipeline inputs annotated phospholipase A2 of vertebrates, and flatworm genomic data. The output of the pipeline is the list of PLA2-domain containing protein sequences, their classification in orthologous groups, phylogeny and domain structure.

Results: PLA2 containing proteins in flatworms were identified and classified according their orthologous groups of 11 families (G1, G2, G3, G4, G5, G6, G7, G10, G12, G15, and G16), which have common ancestors with the molluscan genes, were first identified. We also examined the primary structure and domain composition of the PLA2 proteins. The analysis of gene duplication events showed that the phospholipases of groups G4, G6, G15 are presented in free-living and parasitic flatworms, and the phospholipases of groups G1, G2, G5, G7, G10, G12, G16 are presented mainly in free-living organisms. Group G3 phospholipases among parasitic flatworms are found only in trematodes, include an N-terminal domain with unknown function and are separated into two groups based on the presence of the WxGxG motif in the calcium-binding loop.

Conclusion: From this work follows that flatworms have several groups of PLA2. PLA2 of flatworms and PLA2 of mollusks were diverged from one common ancestor.

Trematodes has an atypical primary structure of PLA2 G3, whether it is associated with carcinogenesis yet to find out.

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