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VEGF diversity in the animal kingdom

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https://mjlab.fi — michael@jeltsch.org

Khushbu Rauniyar[2]

Michael Jeltsch[1,2,3]

[1]Drug Research Program, Faculty of Pharmacy, University of Helsinki
[2]Individualized Drug Therapy Research Program, Faculty of Medicine, University of Helsinki
[3]Wihuri Research Institute, Helsinki, Finland

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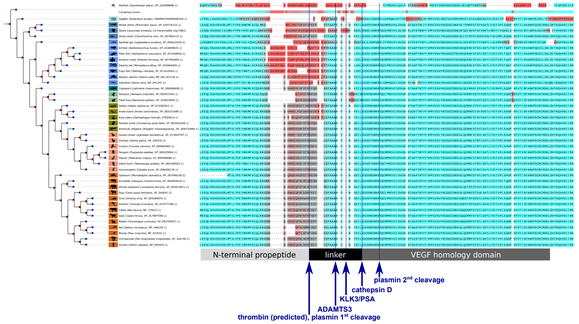

Figure 1. Alignment of VEGF-C orthologs

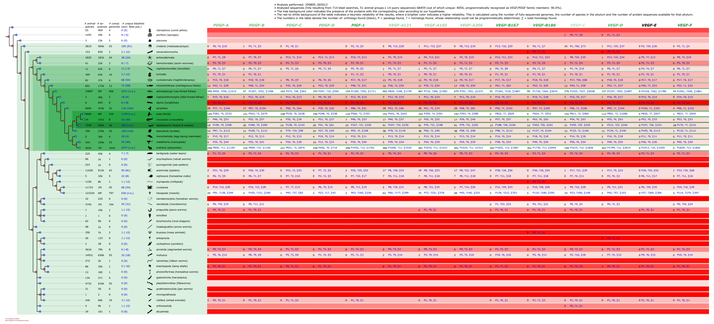

Figure 2. VEGF occurences in the major animal phyla

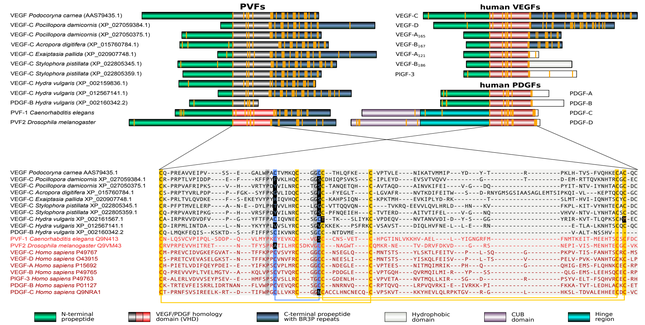

Figure 3. Earliest VEGFs likely resembled VEGF-C

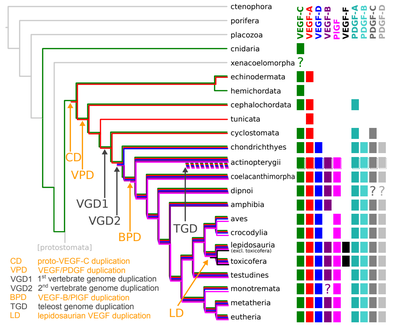

Figure 4. VEGF evolution

Background

The vascular endothelial growth factor (VEGF) family comprises in vertebrates 3 to 6 members, depending on the species: VEGF(-A), PlGF, VEGF-B, VEGF-C, VEGF-D, and VEGF-F. They fulfil mainly functions for the blood and lymphatic vascular systems. Despite the absence of these two vascular systems in most invertebrates, VEGF-like growth factors have also been found in many invertebrate species, e.g. in Drosophila melanogaster and Caenorhabditis elegans. The evolutionary relationships between the VEGFs have never been comprehensively addressed apart from older analyses, which were limited by the low number of sequences and genomes available at the time.

Materials & Methods

We performed a comprehensive bioinformatics analysis of the occurrence of VEGF-like growth factors in all animal phyla, their phylogeny and their conservation.

Results

The vertebrate whole genome duplications play a role in the expansion of the VEGF diversity, but several individual gene duplications account for the temporal pattern of emergence. Some VEGF family members are completely absent in some phyla. E.g. functional genes coding for VEGF-B are absent from the phylum Archosauria, which includes crocodiles and birds, and, by inference, non-avian dinosaurs. The data argue that the phylogenetically oldest VEGFs featured a C-terminus with BR3P-homology repeats, which is a hallmark of the modern-day lymphangiogenic VEGF-C and VEGF-D. Significant differences in the degree of conservation can be found between different parts of the VEGF molecules and between the different VEGF paralogs. The sequence conservation of the VEGF homology domain is remarkable over large evolutionary distances. However, the junctional sequences, which are crucial for proteolytic activation, are highly diverse.

Take-home messages

We conclude e.g. that there is not only a heterogeneity of proteolytic VEGF-C activation within an organism (i.e. several different proteases are able to activate VEGF-C/VEGF-D under different physiological settings), but there is also heterogeneity between animal classes (i.e. deploying different VEGFs and different activating proteases for the same physiological task). Indeed, recent experimental evidence supports this view. Such heterogeneity could have potentially consequences when interpreting or comparing the data generated with disparate animal models.

Bibliography

https://mjlab.fi/IVBM2020biblio

This eposter was created using Open Source Software (Inkscape, Blender, and the Linux Operating System).