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Olivier Dennler, Samuel Blanquart, François Coste, Catherine Belleannée, Nathalie Théret. Functional Motif Prediction in ADAMTS-TSL proteins Based on Module(s) and Phenotype(s) Co-appearance. ALPHY/AIEM 2022 - Rencontres Génomique évolutive, Bioinformatique, Alignement et Phylogénie, Mar 2022, Rennes, France. hal-03870590

HAL Id: hal-03870590

<https://hal.science/hal-03870590>

Submitted on 24 Nov 2022

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Functional Motif Prediction in ADAMTS-TSL proteins Based on Module(s) and Phenotype(s) Co-appearance

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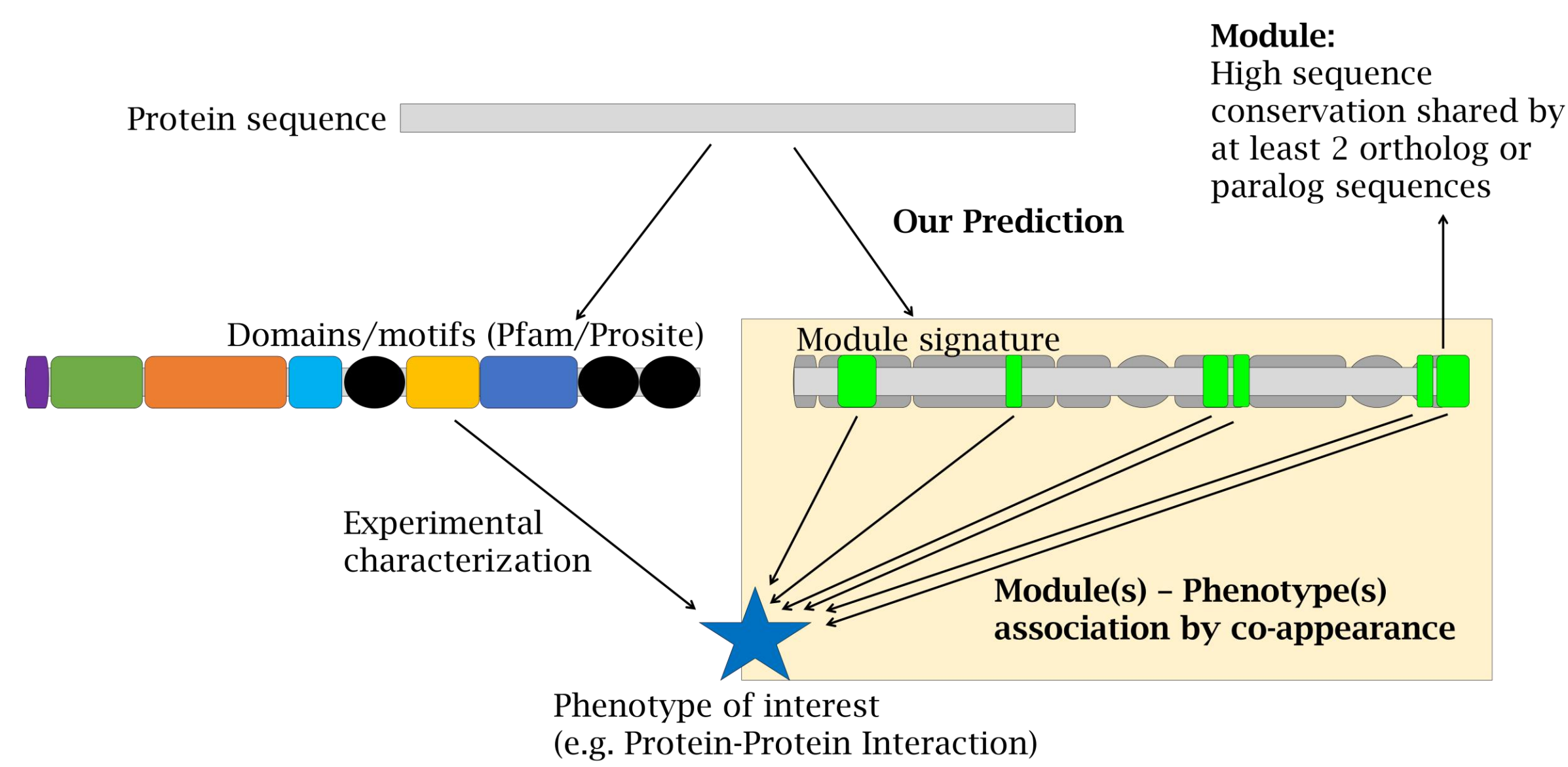
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Introduction and Objective

- ❖ Multi-genes (26 *H. sapiens* paralogs)
- ❖ Multi-domains
- ❖ Partial knowledge / experimental data [1]

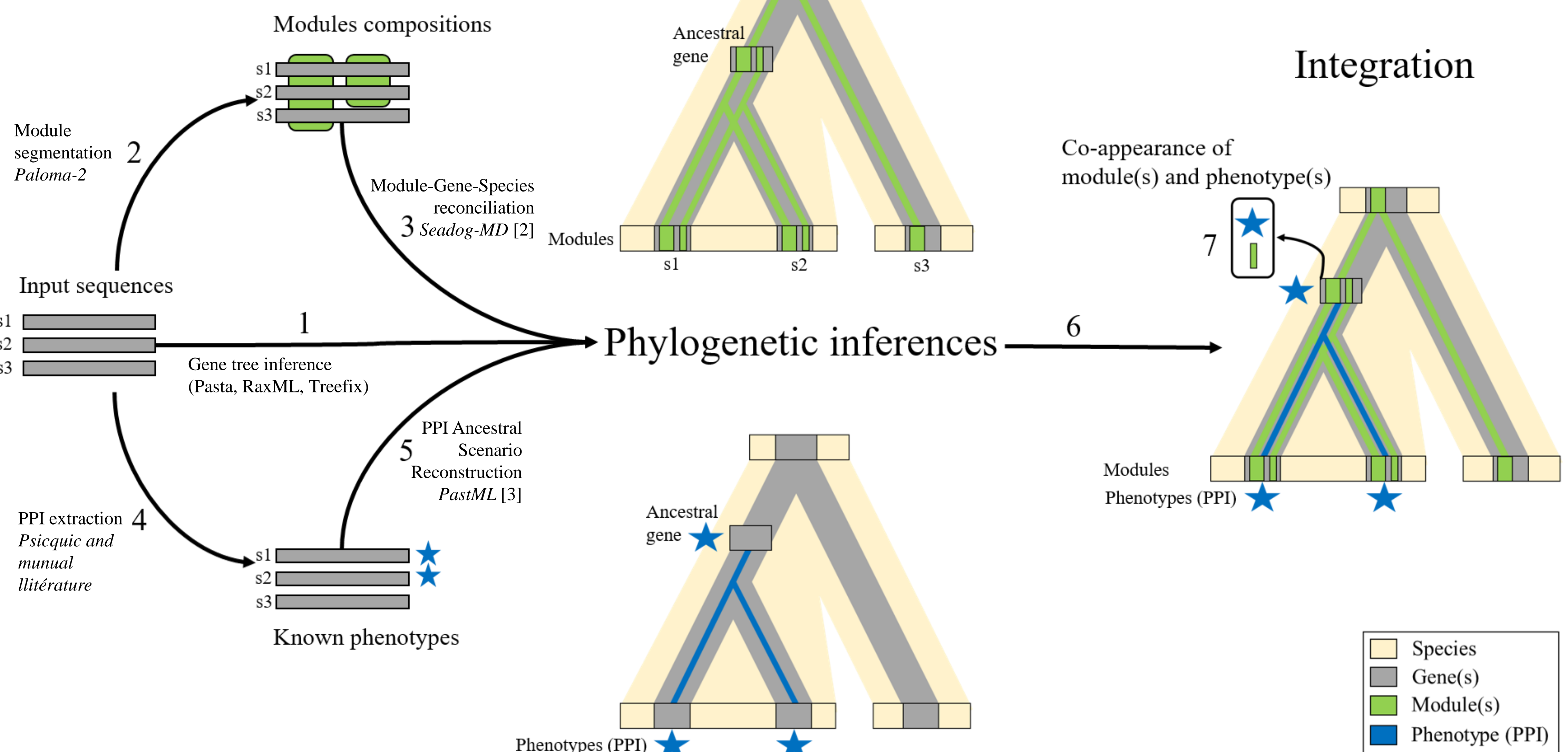
=> A new method to identify functional motif



Hypothesis: During evolution, modules gained at the same time than a phenotype, are involved in this phenotype

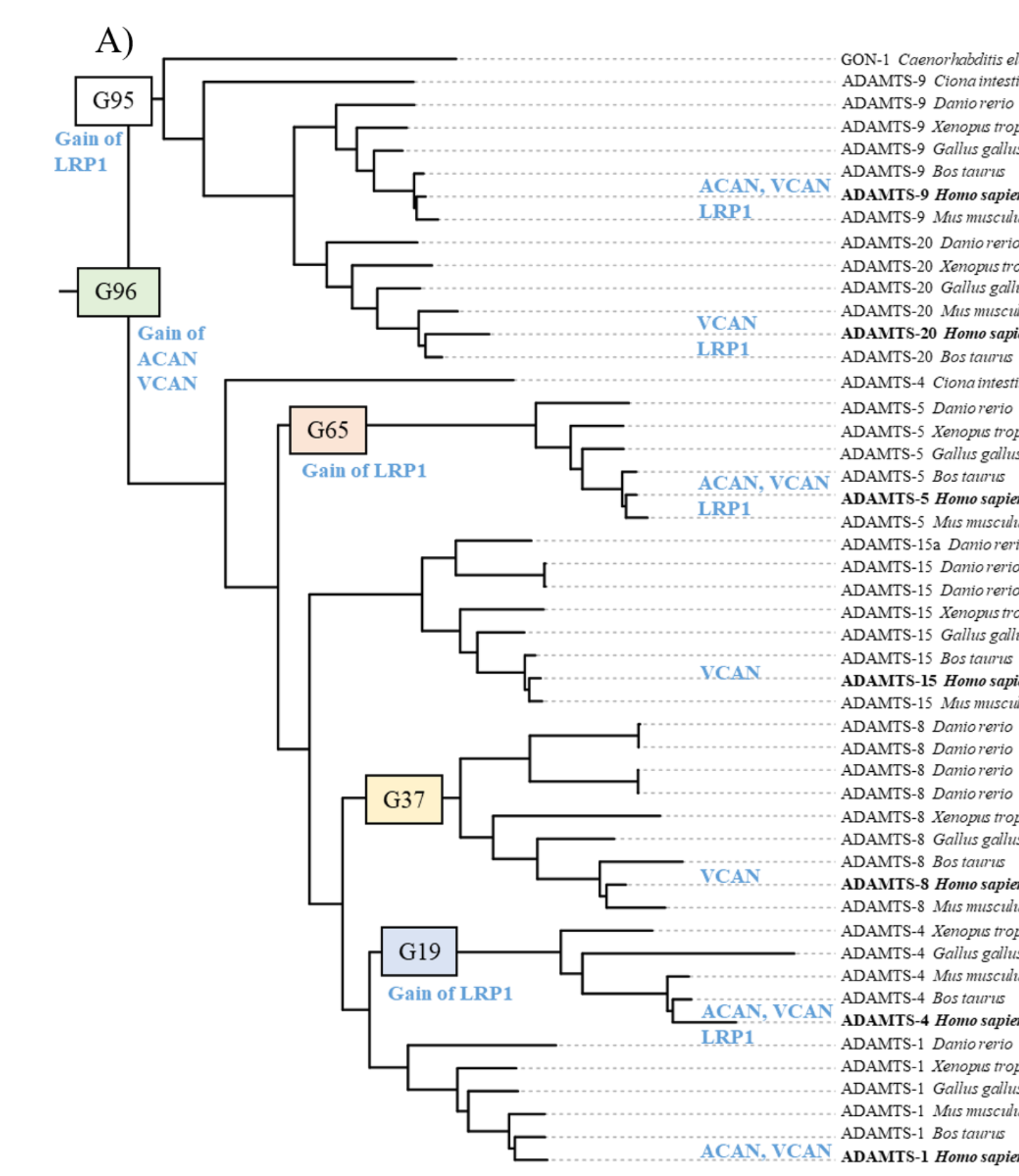
Association of Multiple Evolutionary Histories

- ❖ Ortholog and paralog sequences
- ❖ Protein-Protein Interaction (PPI) and module evolutions on a common gene phylogeny
- ❖ Module(s) and Phenotype(s) Co-appearance(s)

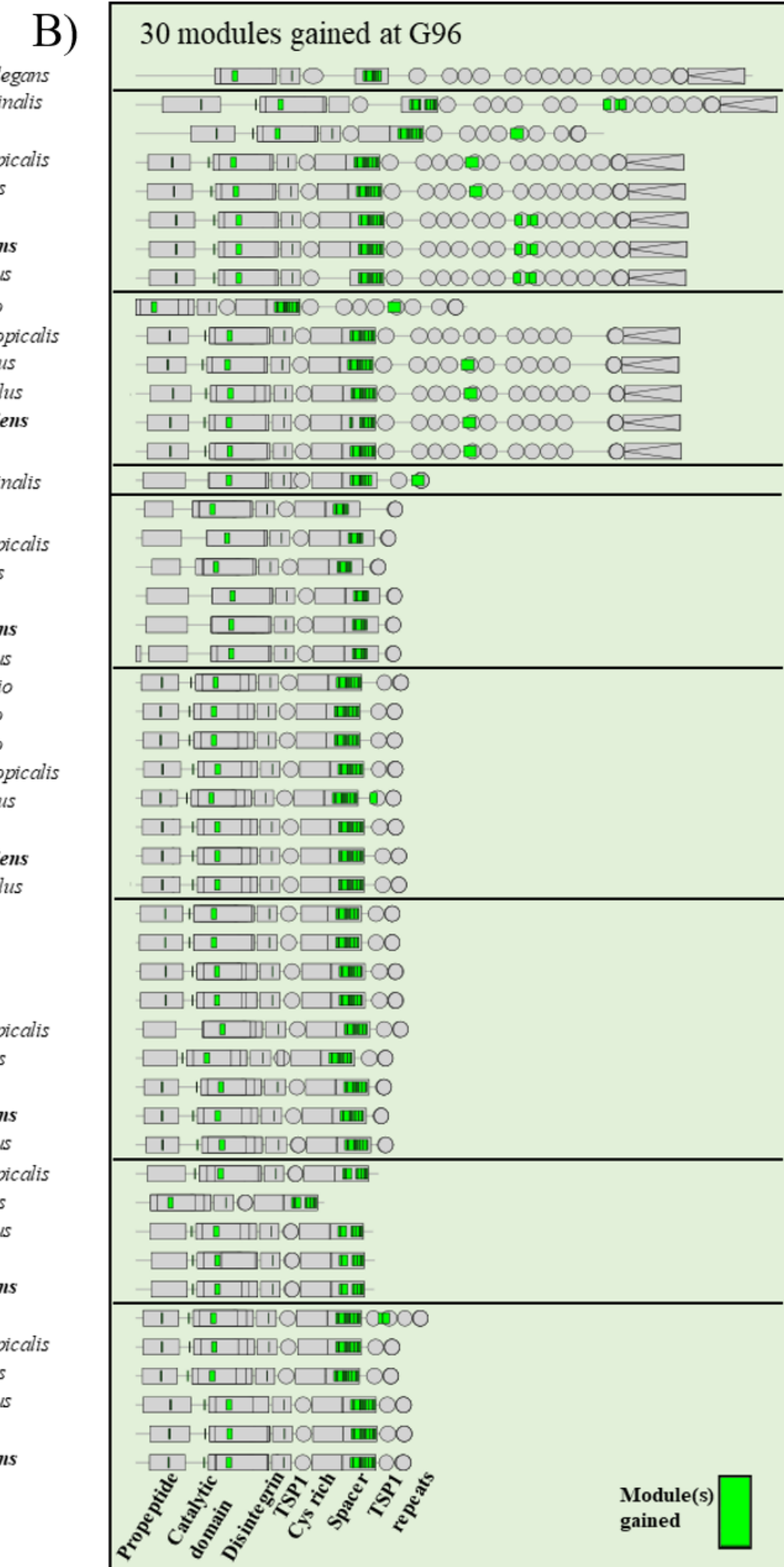


The Hyalactanase Spacer: Validation, Prediction and Diversity

Hyalactanases gene tree



Module signature

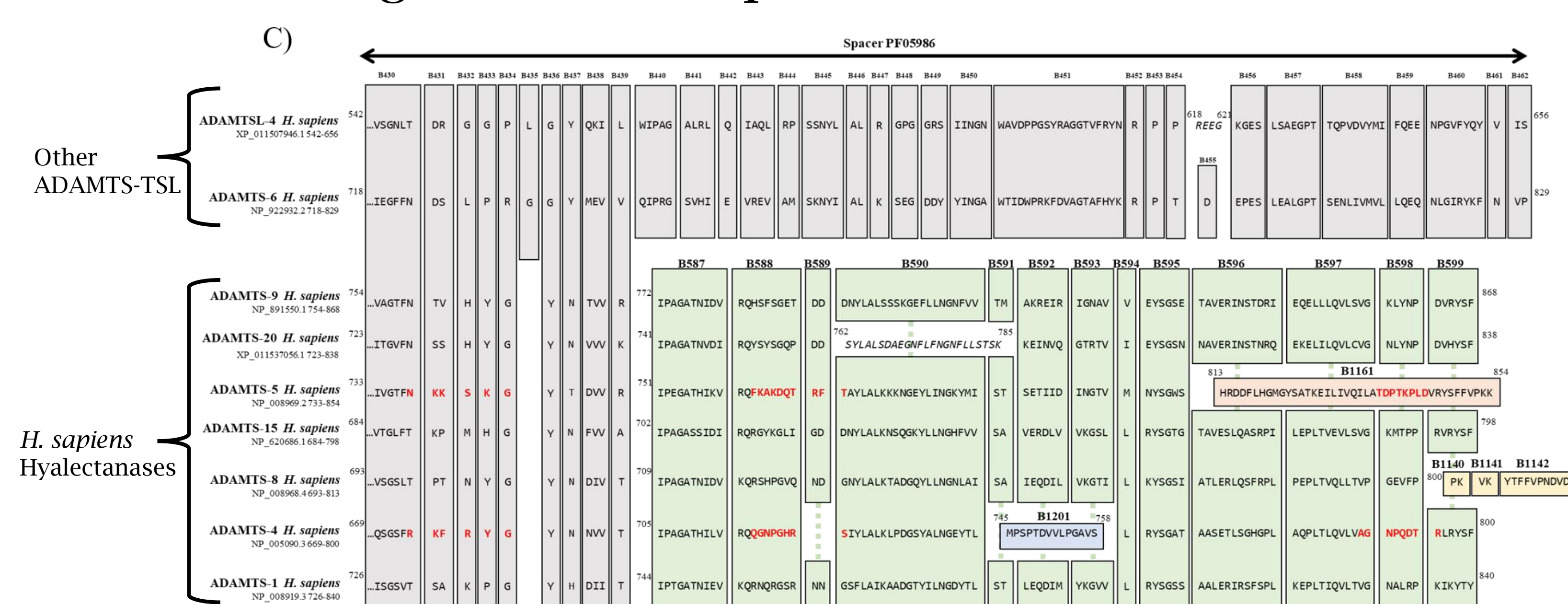


Hyalactanases domains composition



Co-appeared Modules

Module gained in the spacer



- ❖ 173 ADAMTS-TSL in 9 species
- ❖ 1700 modules, 119 PPIs
- ❖ 36 Co-appearances

[1] Suneel S. Apte. ADAMTS Proteins: Concepts, Challenges, and Prospects. *Methods in Molecular Biology* (Clifton, N.J.), 2043:111-2, 2020. [2] Lei Li and Mukul Bansal. Simultaneous Multi-Domain-Multi-Gene Reconciliation Under the Domain-Gene-Species Reconciliation Model. *pages 73186*, January 2019. [3] Sohta A. Ishikawa, Anna Zhukova, Wataru Iwasaki, and Olivier Gascuel. A Fast Likelihood Method to Reconstruct and Visualize Ancestral Scenarios. *Molecular Biology and Evolution*, 36(9):2069/2085, September 2019. [4] Chun-Ju Liu, Wei Kong, Kiril Iakov, Shang Yu, Ke Xu, Lisa Frazak, Marc Fajardo, Santoo Sehgal and Paul E. Di Cesare. ADAMTS-7: a metalloprotease that directly binds to and degrades cartilage oligomeric matrix protein. *FASEB journal: official publication of the Federation of American Societies for Experimental Biology*, 20(7):988/990, May 2006.

Legend:
 [] Module(s) gained early in ADAMTS-TSL evolution
 [] Module(s) gained at the Hyalactanases ancestor (G96)
 [] Module(s) gained at ADAMTS-5 orthologs ancestor (G65)
 [] Module(s) gained at ADAMTS-8 orthologs ancestor (G37)
 [] Module(s) gained at ADAMTS-1 orthologs ancestor (G19)
 [] Hypervariable loops in ADAMTS-4, -5 (from left to right: [β1-β2, β3-β4, β9-β10] as described in Santamaria et al. 2019)
 [] Sequences without any detected conservation