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Phylogenetic Functional Module Characterization of the ADAMTS / ADAMTS-like Protein Family

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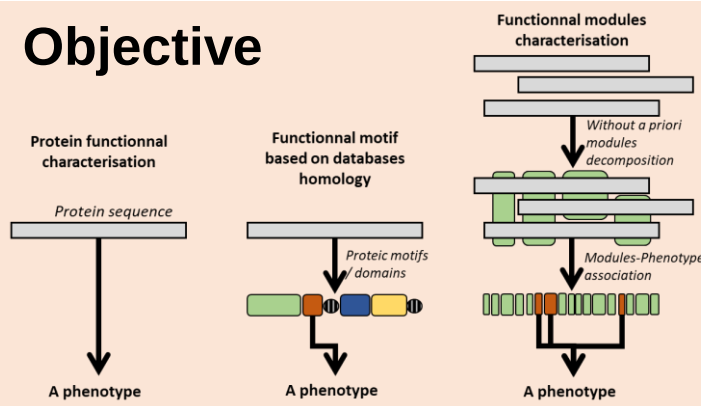
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Introduction

- ❖ Multi-genes (*e.g.*, *paralogs*, *orthologs*)
 - ❖ Multi-domains
 - ❖ Partial knowledge / experimental data [1]
- => A new method to identify functional protein regions

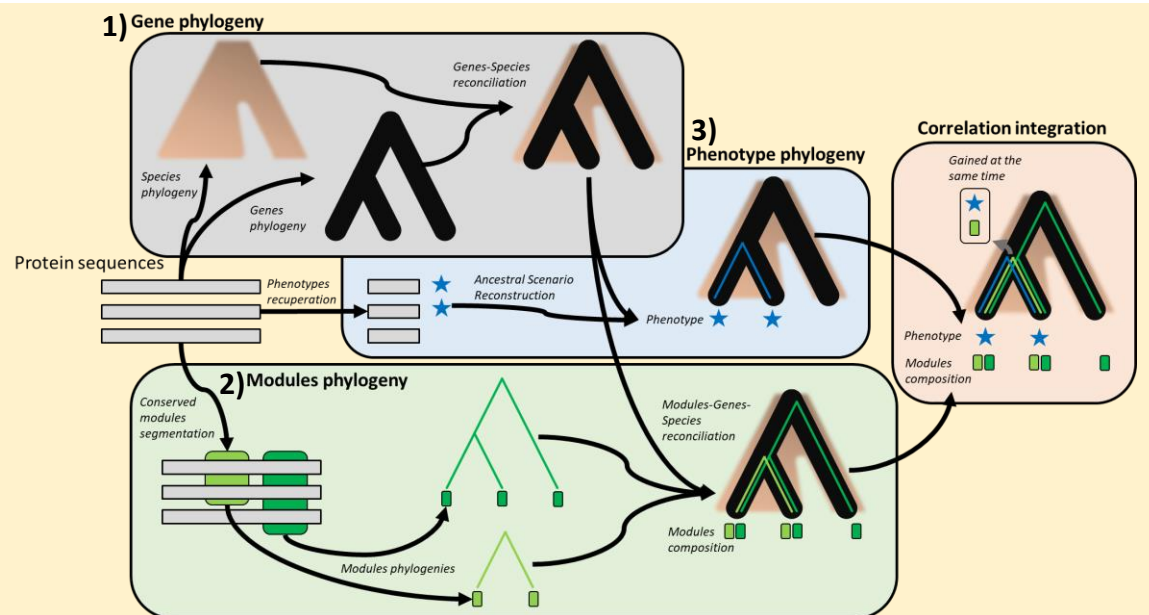
Objective



- ❖ Module: Ungapped conserved sequence regions, shared by at least 2 sequences
- ❖ Hypothesis: During evolution, modules gained at the same time than a phenotype, are involved in this phenotype

Methodology

- ❖ Sequence conservation and phylogenomic inference
- ❖ Segment *without a priori* protein sequences in modules
- ❖ Protein-protein interactions (PPI) [3] and modules evolution [2] on a common gene phylogeny
- ❖ Changes in module composition occurring at the same time than protein-protein interactions

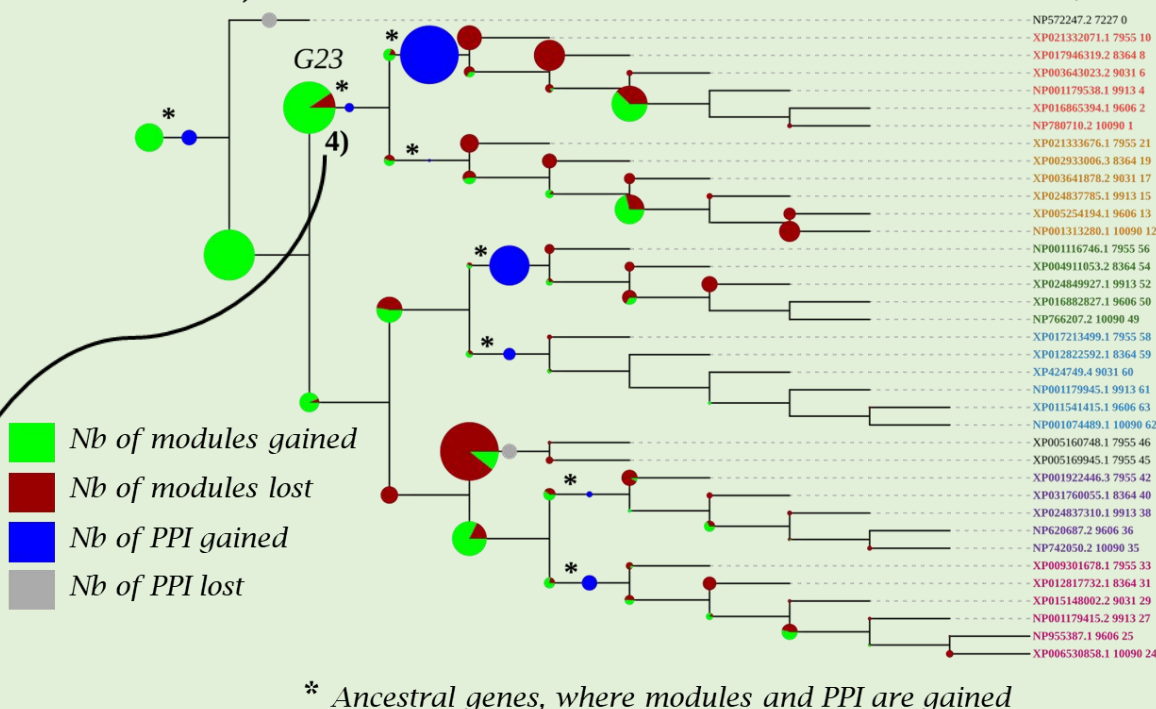


Results

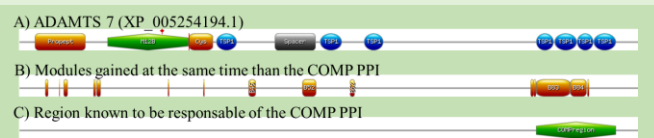
ADAMTS-12, -7, -16, -18, -6, -10 and their associated orthologs, distributed in 7 species (1, 2)

2)

Segmentations *without a priori* in 249 conserved modules (3)



G23 : Apparition of COMP-ADAMTS PPI and 32 Modules gained (4)



Conclusion

- ❖ Pipeline
- ❖ Correlate conserved sequence modules and phenotypes evolution
- ❖ Identify the co-appearance of conserved modules and phenotypes.

References

[1] Suneel S. Apte. ADAMTS Proteins: Concepts, Challenges, and Prospects. Methods in Molecular Biology (Clifton, N.J.), 2043:1412, 2020. [2] Lei Li and Mukul Bansal. Simultaneous Multi-Domain-Multi-Gene Reconciliation Under the Domain-Gene- Species Reconciliation Model. pages 7386. 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] Chuan-Ju Liu, Wei Kong, Kiril Ilalov, Shuang Yu, Ke Xu, Lisa Prazak, Marc Fajardo, Bantoo Sehgal and Paul E. Di Cesare. ADAMTS-7: a metalloproteinase 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.