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

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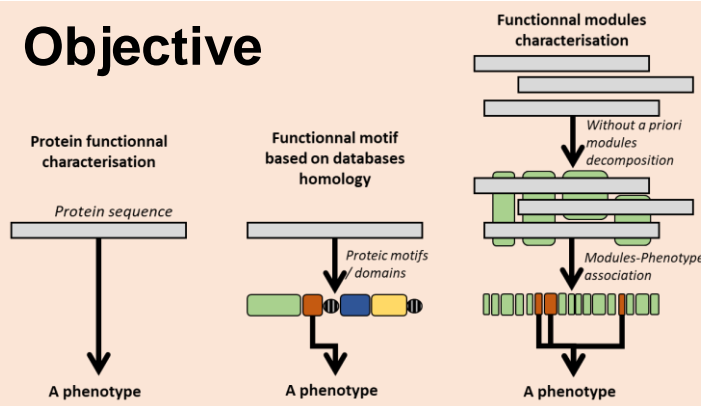
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Introduction

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

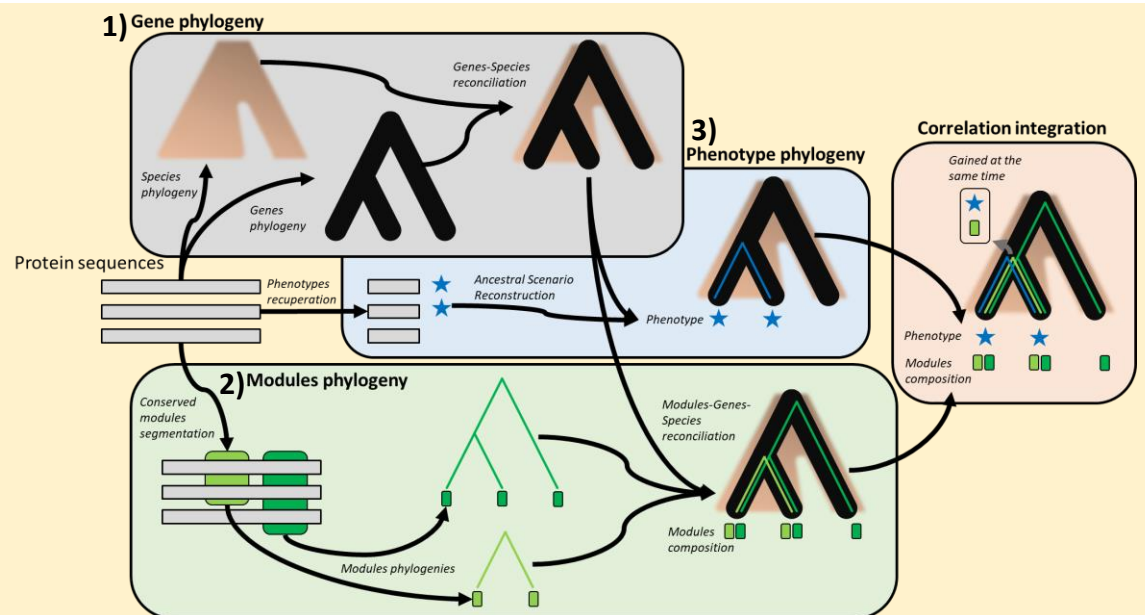
Objective



- ❖ **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

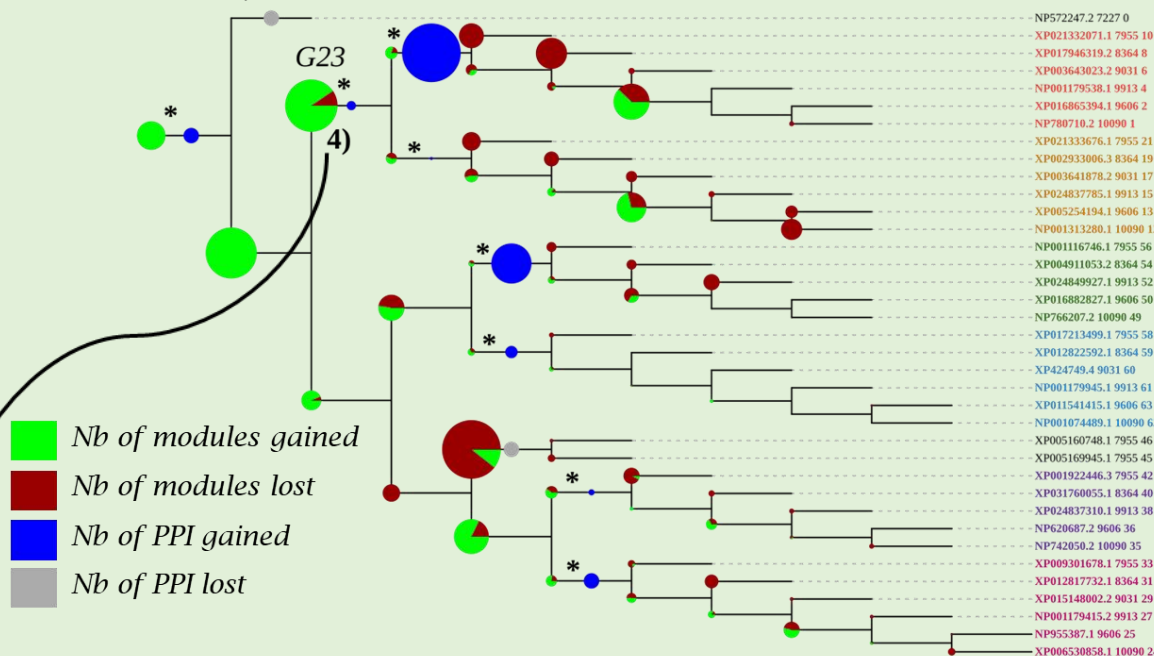


Results

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

2)

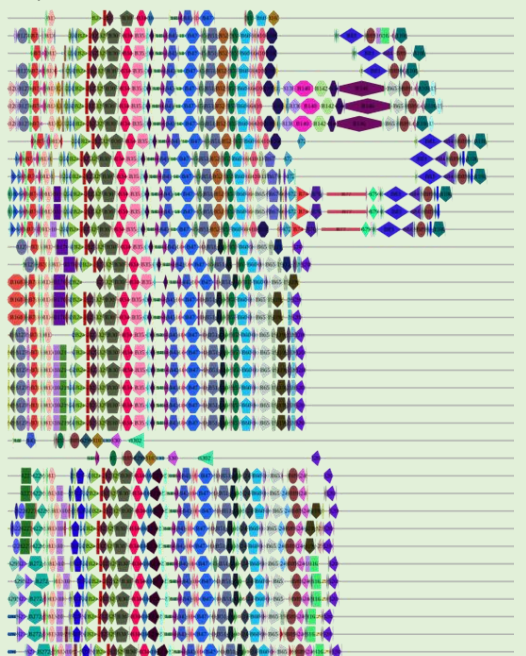
Segmentations *without a priori* in 249 conserved modules (3)



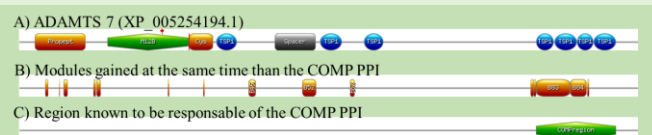
- Nb of modules gained
- Nb of modules lost
- Nb of PPI gained
- Nb of PPI lost

* Ancestral genes, where modules and PPI are gained

ADAMTS 12
ADAMTS 7
ADAMTS 10
ADAMTS 6
ADAMTS 16
ADAMTS 18



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.), 2043:1-12, 2020. [2] Lei Li and Mukul Bansal. Simultaneous Multi-Domain-Multi-Gene Reconciliation Under the Domain-Gene-Species Reconciliation Model. pages 73-86. January 2019. [3] Sohta A Ishikawa, 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.