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

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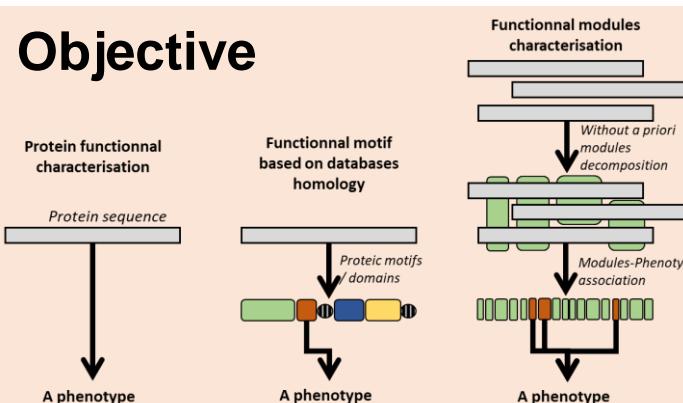
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Introduction

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

Objective

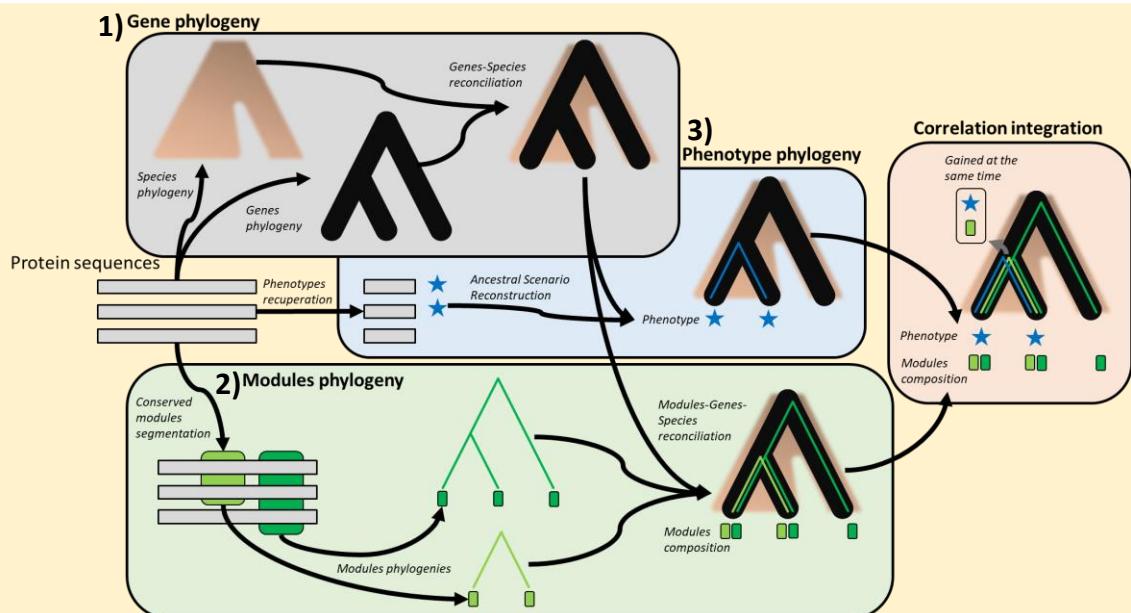


❖ **Module:** Ungapped conserved sequence regions, shared by at least 2 sequences

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

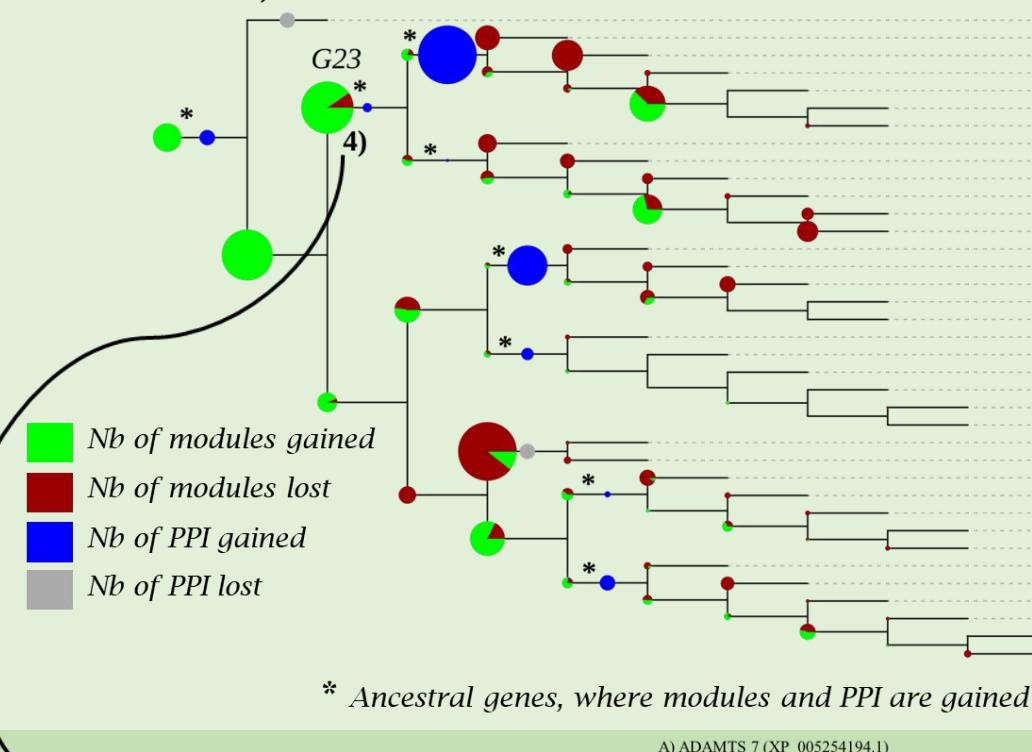
Methodology

- ❖ 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

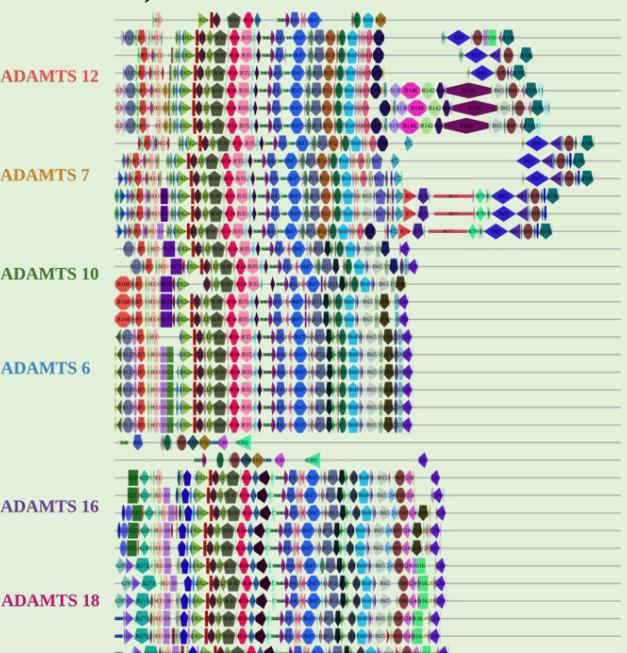
1) ADAMTS-12, -7, -16, -18, -6, -10 and their associated orthologs, distributed in 7 species (1, 2)



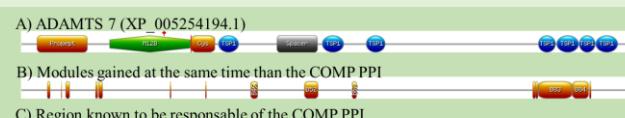
2)

NP572247.2 7227 0
NP021332071.1 7955 10
XP017946319.2 8364 8
XP03643023.2 9831 6
NP001179538.1 9913 4
XP016865394.1 9606 2
NP780710.2 10090 1
XP021333467.1 7955 21
XP02933006.3 8364 19
XP03641878.2 9031 17
XP024837785.1 9913 15
XP005254194.1 9606 13
NP001163280.1 10090 12
NP00116746.1 7955 56
XP04911053.2 8364 54
NP001074492.1 9913 52
XP016882827.1 9606 50
NP766207.2 10090 49
XP017213499.1 7955 58
XP012822592.1 8364 59
XP242749.4 9031 60
NP001179945.1 9913 61
XP011541415.1 9606 63
NP001074489.1 10090 62
XP005160748.1 7955 46
XP005169945.1 7955 45
XP001922446.3 7955 42
XP031760055.1 8364 40
XP024837310.1 9913 38
NP620687.2 9606 36
NP742056.2 10090 35
XP009301678.1 7955 33
XP009301678.1 7955 33
NP001179415.2 9913 27
NP955387.1 9606 25
XP006530858.1 10090 24

3) Segments without a priori in 249 conserved modules (3)



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



References

- [1] Sunee 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, 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 Ilarov, 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.

Conclusion

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