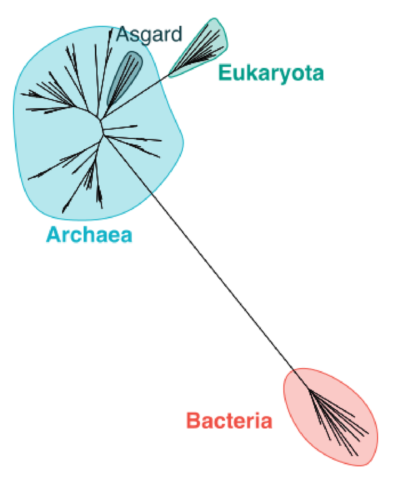
Horizontal Gene Transfer across Asgard archaea

Saioa Manzano-Morales[1 2], Toni Gabaldón[1 2 3]
[1]Barcelona Supercomputing Centre (BSC-CNS), Plaça Eusebi Güell, 1-3, 08034, Barcelona, Spain
[2]Institute for Research in Biomedicine (IRB Barcelona), The Barcelona Institute of Science and Technology, Baldiri Reixac, 10, 08028, Barcelona, Spain
[3]Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain.

INTRODUCTION



Asgard archaea are the **closest prokaryotic relatives of eukaryotes** (Fig. 1), from within which the latter emerged, and therefore key to our understanding of eukaryogenesis.

Figure 1: Tree of Life. Adapted from Williams et al. (2020)

Both successfully cultured Asgards (Fig. 2) are shown to maintain **syntrophic relationships** with other prokaryotes. This prolonged syntrophy is expected to leave **genomic traces** in the form of **Horizontal Gene Transfer (HGT).**

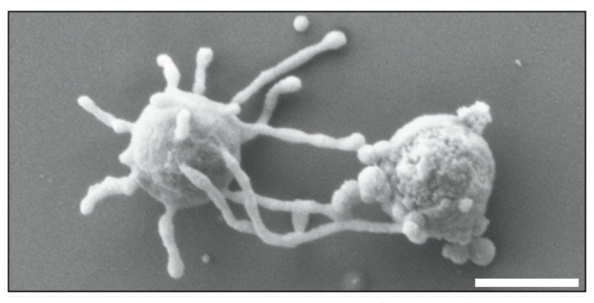


Figure 2: *Ca.* Lokiarchaeum ossiferum. Adapted from Rodrigues-Oliveira et al. (2022)

Therefore, an **analysis of HGT** across the evolution of major Asgard lineages can help shed light on **putative syntrophic interactions** of the archaeal symbiont and the proto-eukaryote during the **first stages of eukaryogenesis**.

METHODS

We selected the most complete representative among the **highest-order Asgard clades**, complementing the sampling with **both cultured Lokiarchaeia** (*Ca.* Prometheoarchaeum syntrophicum and *Ca.* Lokiarchaeum ossiferum) and a representative of the **closest lineage to eukaryotes**, *Hodarchaeales.* We then applied a pipeline that **combines similarity-based screening and phylogenetic analysis** (Fig. 3):

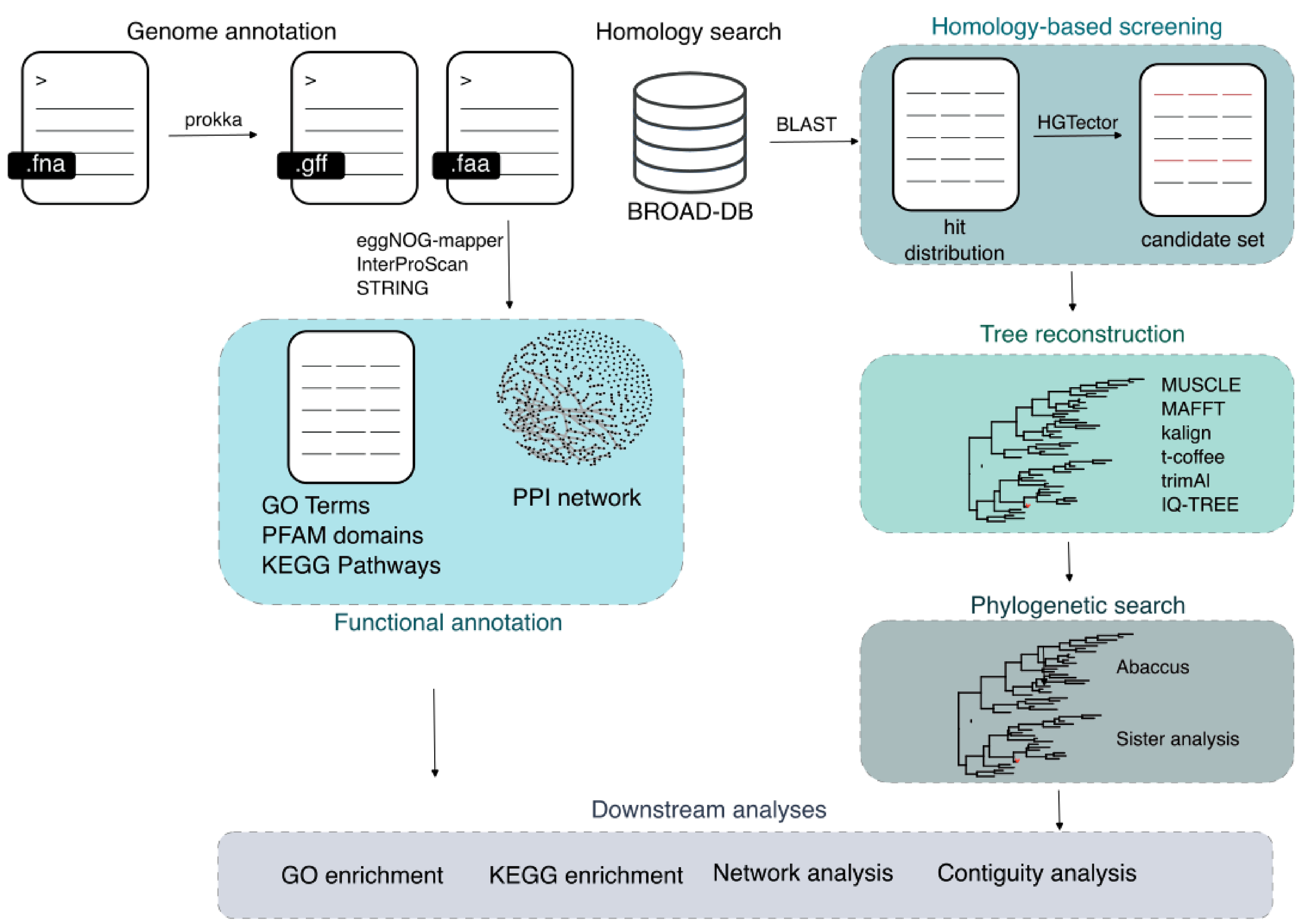
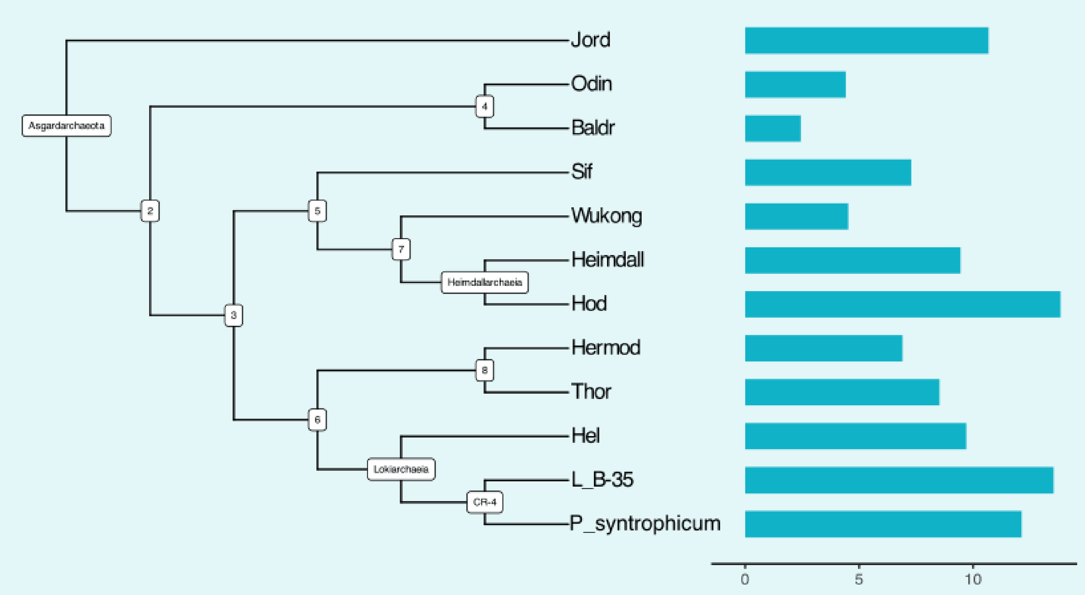


Figure 3: HGT detection pipeline. An initial, similarity-based screening is followed by tree reconstruction and phylogenetic analysis and complemented with functional annotation.

CONCLUSIONS

HGT has occurred, to a varying extent, **all across the Asgard lineage**, and it appears to be an **on-going process**, via partnership with a **large number of independent donors**. Transferred genes are enriched in the **metabolism of basic building blocks**, despite specific pathways and terms differing across organisms, and they seem to be well-integrated, if **peripheral**, in the organism's interactome, likely reflecting a **stepwise addition** of enzymes into the organism's native pathways.

RESULTS



Asgard lineages **vary in HGT %** (Fig. 4), with the highest corresponding to the isolates and *Hodarchaeales.*

Figure 4: Percentage of transferred genes relative to the whole proteome. Proteins were considered HGTs if the sister group contained less than 10% sequences of archaeal origin, and was assigned the donor taxa as the MRCA of at least 50% leaves.

HGT has been a **continuous (and on-going) process** across Asgard evolution (Fig. 5), involving a **large number of donor clades**, many organism-specific.

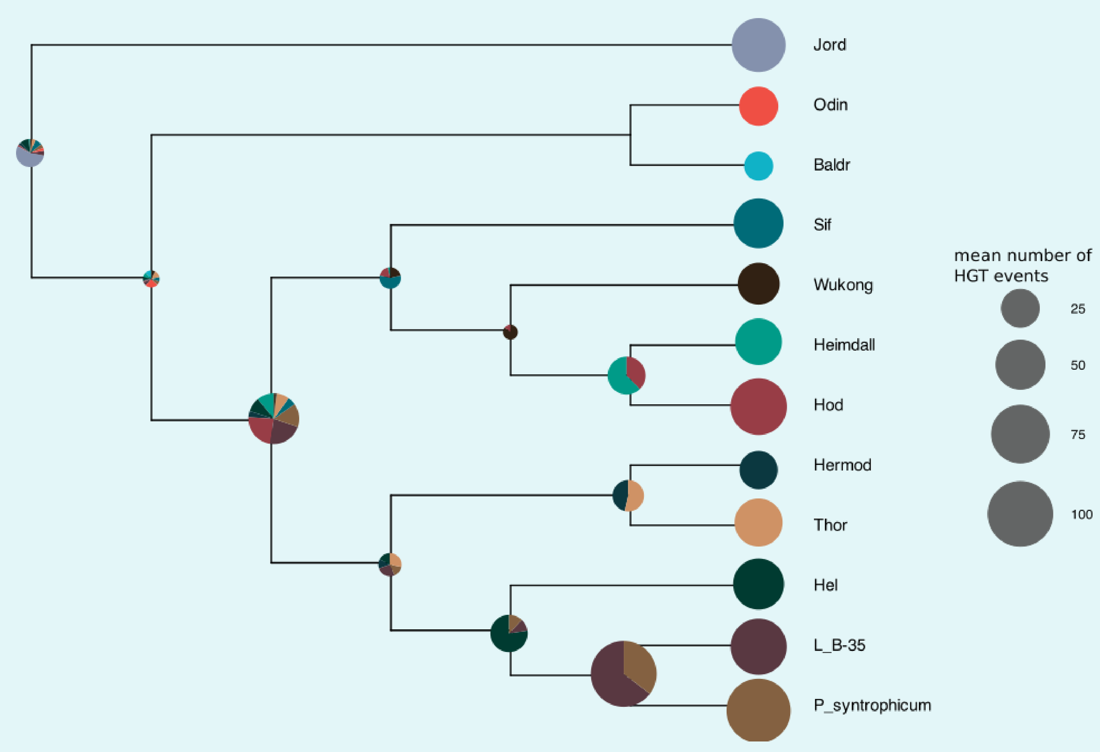


Figure 5: Acceptor analysis. The acceptor was defined as the MRCA of the biggest Asgard monophyletic group stemming from the seed protein. Eukaryotic sequences were considered *de facto* Heimdall. Sub-lineage transfers are collapsed to the tip node.

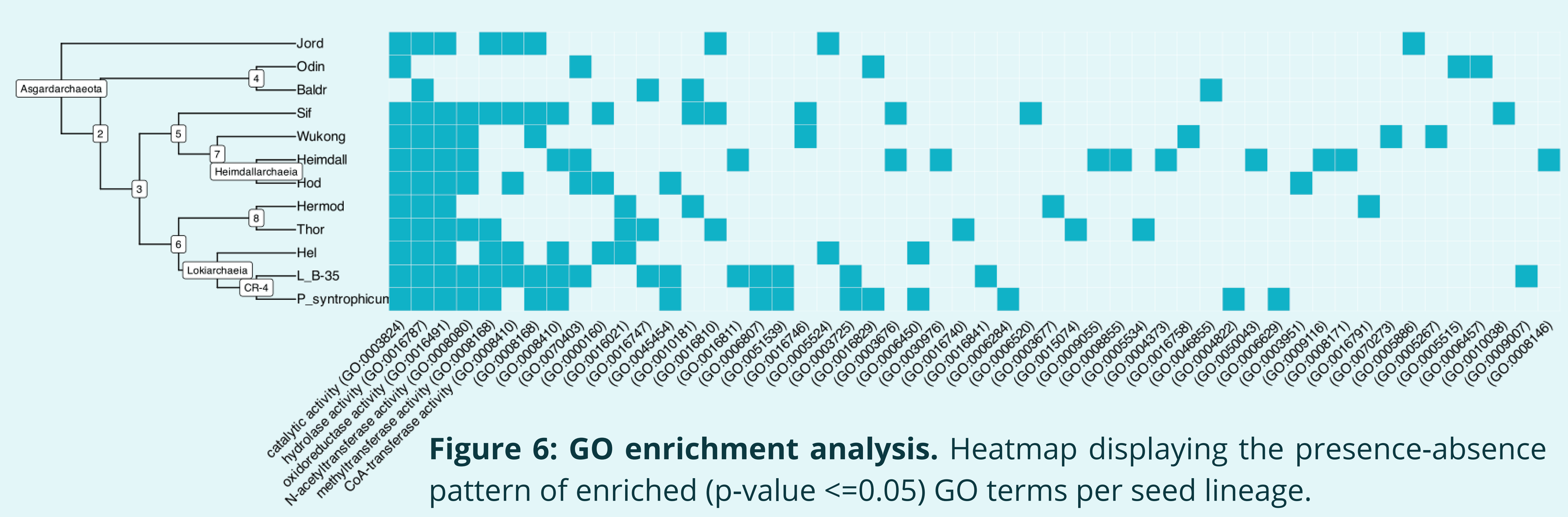


Figure 6: GO enrichment analysis. Heatmap displaying the presence-absence pattern of enriched (p-value <=0.05) GO terms per seed lineage.

Enriched functions (Fig. 6-7) deal with **metabolism of basic building blocks** (amino acids and lipids), but the specific pathways and proteins are organism-dependent.

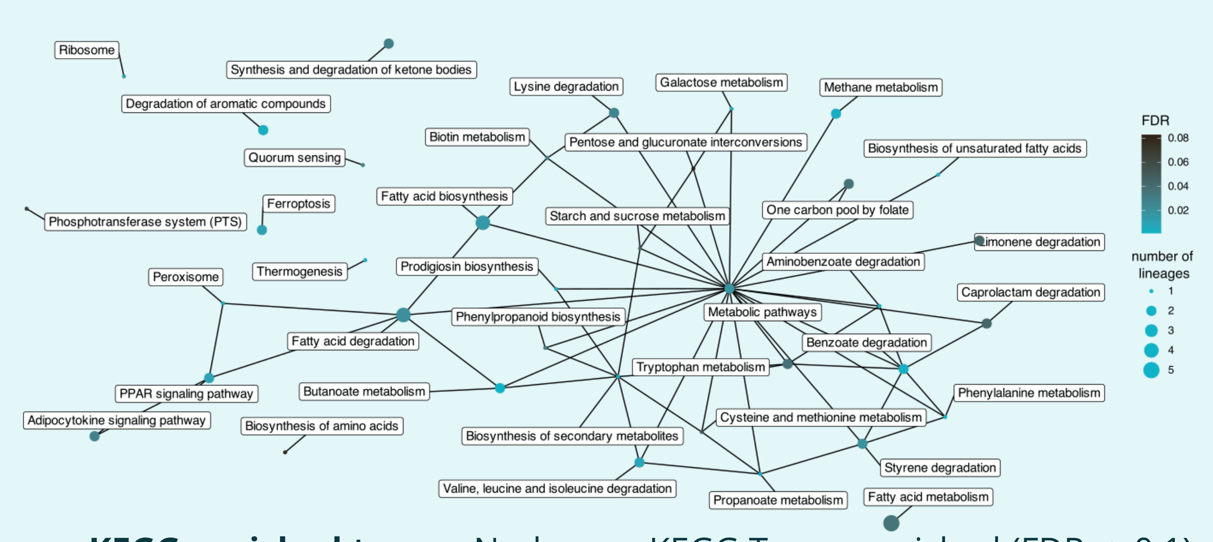
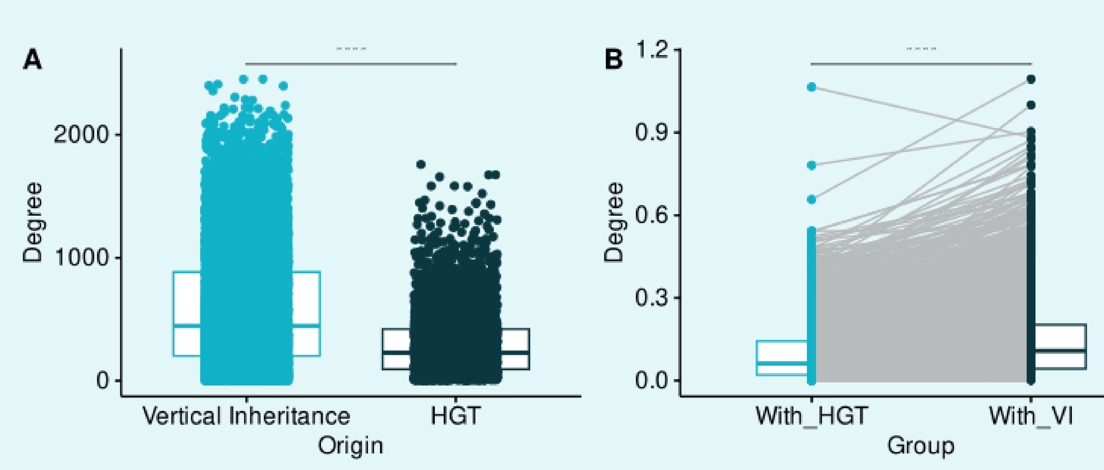


Figure 7: Network of relationships between KEGG enriched terms. Nodes are KEGG Terms enriched (FDR <=0.1) in at least one lineage, edges represent relationships between KEGG terms.



HGT proteins are well-integrated, if **peripheral** (Fig. 8) and seeminlgly **not modular** but stepwise additions to native pathways.

Figure 8: Network properties of HGT proteins within seed organism's interactome. (A) Number of connections (degree) of HGT proteins versus genes of vertical inheritance. (B) Number of connections of HGT proteins with other HGT proteins vs with proteins of vertical inheritance.

BIBLIOGRAPHY

1. Imachi H, Nobu MK, Nakahara N, et al. Isolation of an archaeon at the prokaryote-eukaryote interface. *Nature*. 2020;577(7791):519-525.
2. Zaremba-Niedzwiedzka K, Caceres EF, Saw JH, et al. Asgard archaea illuminate the origin of eukaryotic cellular complexity. *Nature*. 2017;541(7637):353-358.
3. Rodrigues-Oliveira T, Wollweber F, Ponce-Toledo RI, et al. Actin cytoskeleton and complex cell architecture in an Asgard archaeon. *Nature*. 2023;613(7943):332-339.
4. Eme L, Tamarit D, Caceres EF, et al. Inference and reconstruction of the heimdallarchaeial ancestry of eukaryotes. *Nature*. 2023;618(7967):992-999. doi:10.1038/s41586-023-06186-2
5. Zhu Q, Kosoy M, Dittmar K. HGTector: an automated method facilitating genome-wide discovery of putative horizontal gene transfers. *BMC Genomics*. 2014;15(1):717
6. Naranjo-Ortíz MA, Brock M, Brunke S, Hube B, Marcet-Houben M, Gabaldón T. Widespread Inter- and Intra-Domain Horizontal Gene Transfer of d-Amino Acid Metabolism Enzymes in Eukaryotes. *Front Microbiol*. 2016;7:2001

saioa.manzano@bsc.es
github.com/saimanzano

This research was supported by Gordon and Betty Moore Foundation (Grant GBMF9742)