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Our research concerns the reconstruction, analysis and evolution of biomolecular networks at different scales and their implication on the organisms' susceptibility to genetic diseases such as cancer. We develop quantitative statistical methods and computational tools to infer and analyze causal graphical models from biological data.

Isambertlab website

Evolution of large biomolecular networks

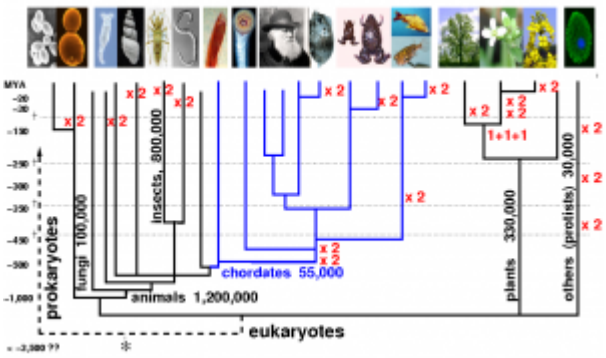

Figure 1: Whole Genome Duplication in eukaryote evolution

We are interested in the analysis of large biomolecular networks and their evolution due to single gene and whole genome duplications, which occurred repeatedly in the course of eukaryote evolution Fig.1, see http://ohnologs.curie.fr

Our early theoretical analyses focussed on duplication-divergence models to account for the generic properties of biomolecular networks. We have shown that duplication-divergence processes bring not only genetic novelty but also evolutionary constraints that restrict by construction the emerging properties of biomolecular networks. In particular, we demonstrated that networks with evolutionary conserved genes display also necessary topological properties by construction (such as hubs and scale-free

degree distribution). We are also interested in the evolution of transcription networks and study the regulatory conflicts that arise through duplication of transcription factors and autoregulators.

More recently, we have analysed the evolutionary constraints on signaling networks implicated in cancer (Fig.2). We investigated the evidence that the emerging properties of these signaling pathways might actually reflect their susceptibility to oncogenic mutations and thus their implication in cancer. We have found, in particular, that “dangerous” gene families implicated in cancer have been greatly expanded through two rounds of whole genome duplication (WGD) (Fig. 2) in early vertebrates. These findings highlight the importance of WGD-induced nonadaptive selection for the emergence of vertebrate complexity, while rationalizing, from an evolutionary perspective, the expansion of gene families frequently implicated in genetic disorders and cancers.

Figure 2: Ras-Ral pathways expansion through Whole genome duplication in vertebrates.

RNA regulatory networks and RNA nanostructures.

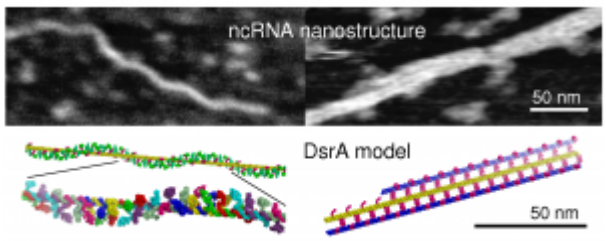

Figure 3 : Novel nanostructures made of DsrA ncRNA from E.coli.

We have developed a server for advanced RNA dynamic simulation (http://kinefold.curie.fr >100,000 online simulations) and studied the properties of small regulatory circuits primary based on RNAs and their interactions. In particular, we have used synthetic biology approaches to design efficient RNA-based repressor and activator modules. These modules control RNA transcription “on the fly” through simple RNA-RNA antisense interactions. We also discovered that DsrA, a small bacterial RNA of *Escherichia coli* could self-assemble, like many proteins do, to form long filaments and larger physical networks (Fig3). This finding further extends the already great versality of natural RNA functions.

Key publications

Year of publication 2019

Beber A, Taveneau C, Nania M, Tsai FC, Di Cicco A, Bassereau P, Lévy D, Cabral JT, Isambert H, Mangenot S*, Bertin A* (2019 Jan 24)
Membrane reshaping by micrometric curvature sensitive septin filaments
Nature communications : DOI : 10.1038/s41467-019-08344-5

Year of publication 2015

Param Priya Singh, Jatin Arora, Hervé Isambert (2015 Jul 17)
Identification of Ohnolog Genes Originating from Whole Genome Duplication in Early Vertebrates, Based on Synteny Comparison across Multiple Genomes.
PLoS computational biology : e1004394 : DOI : 10.1371/journal.pcbi.1004394

Year of publication 2014

Param Priya Singh, Séverine Affeldt, Giulia Malaguti, Hervé Isambert (2014 Jul 31)
Human dominant disease genes are enriched in paralogs originating from whole genome duplication.
PLoS computational biology : e1003754 : DOI : 10.1371/journal.pcbi.1003754

Year of publication 2012

Param Priya Singh, Séverine Affeldt, Ilaria Cascone, Rasim Selimoglu, Jacques Camonis, Hervé Isambert (2012 Apr 12)
On the expansion of “dangerous” gene repertoires by whole-genome duplications in early vertebrates.
Cell reports : 1387-98 : DOI : 10.1016/j.celrep.2012.09.034

Year of publication 2009

Bastien Cayrol, Claude Nogues, Alexandre Dawid, Irit Sagi, Pascal Silberzan, Hervé Isambert (2009 Oct 14)
A nanostructure made of a bacterial noncoding RNA.
Journal of the American Chemical Society : 17270-6 : DOI : 10.1021/ja906076e

Year of publication 2008

Kirill Evlampiev, Hervé Isambert (2008 Jul 16)

Conservation and topology of protein interaction networks under duplication-divergence evolution.
Proceedings of the National Academy of Sciences of the United States of America : 9863-8 : DOI : 10.1073/pnas.0804119105