Contribution ID: **4** Type: **not specified**

Evolution of transcription factor families along the human lineage.

Wednesday, 28 September 2016 10:40 (20 minutes)

Transcription factors (TFs) exert their regulatory action by binding to DNA with specific sequence preferences.
However, different TFs can partially share their binding sequences. This redundancy" of binding defines a way of organizing TFs inmotif families" that goes beyond the usual classification based on protein structural similarities. Since the TF binding preferences ultimately define the target genes, the motif family organization entails information about the structure of transcriptional regulation as it has been shaped by evolution. Focusing on the human lineage, we show that a one-parameter evolutionary model of the Birth-Death-Innovation type can explain the empirical repartition of TFs in motif families, thus identifying the relevant evolutionary forces at its origin.
More importantly, the model allows to pinpoint few deviations in human from the neutral scenario it assumes: three over-expanded families corresponding to HOX and FOX type genes, a set of ''singleton" TFs for which duplication seems to be selected against, and an higher-than-average rate of diversification of the binding preferences of TFs with a Zinc Finger DNA binding domain.
Finally, a comparison of the TF motif family organization in different eukaryotic species suggests an increase of redundancy of binding with organism complexity.

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Session Classification: Sessione 7