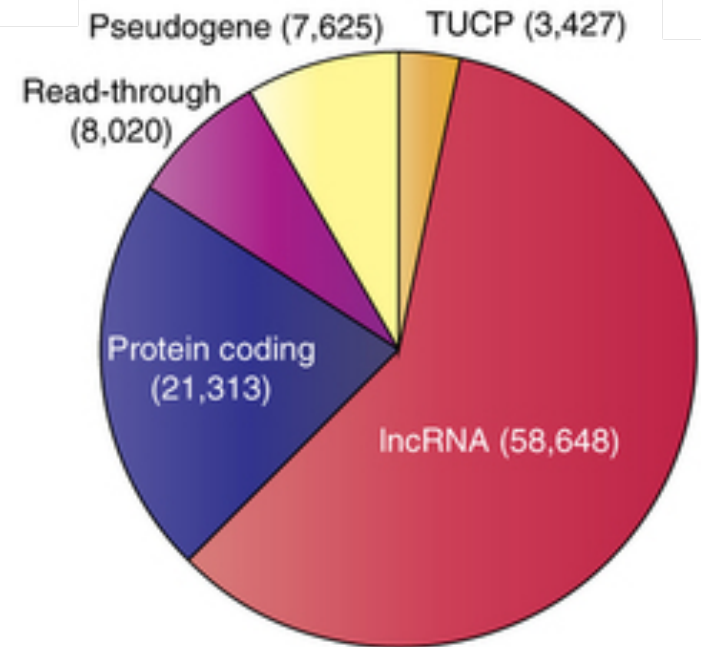
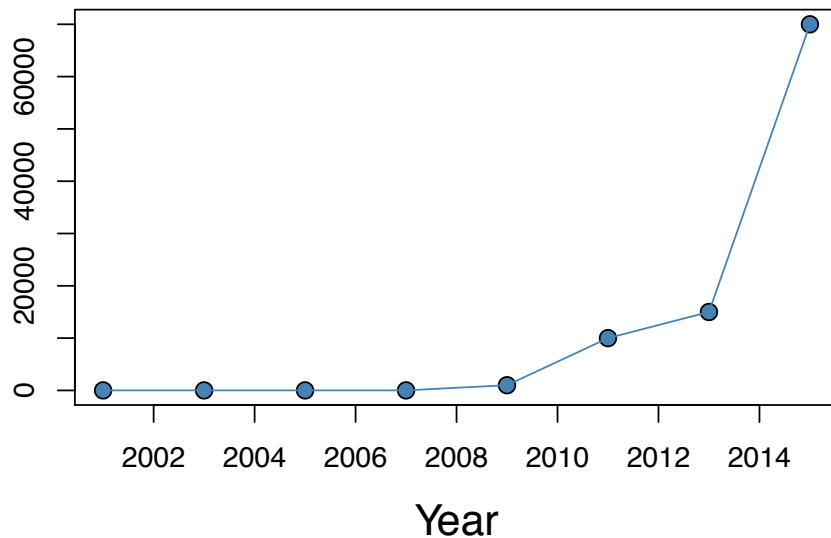


The evolving human transcriptome

Number of non-coding RNAs
in the human genome

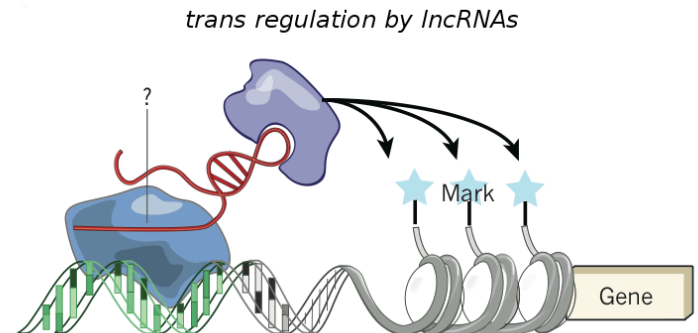


non-coding RNA annotation based on
7,000 RNA-seq samples

Long non-coding RNAs (lncRNAs)

- lncRNAs: long (often poly-adenylated & spliced) transcripts lacking protein-coding potential.
- Reported roles in gene expression regulation:
 - recruitment of chromatin-modifying complexes
 - transcriptional and post-transcriptional regulation
 - regulation in *cis* or in *trans*
 - competition for miRNAs

image from Guttman & Rinn, 2012

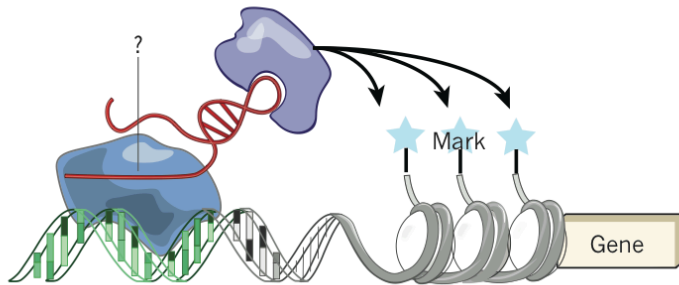


Functional RNAs or transcriptional noise?

- lncRNA functions: experimental evidence for only ~200 lncRNAs at the moment
- What proportion of lncRNAs are simply transcriptional noise?

image source: <http://www.geneticliteracyproject.org>

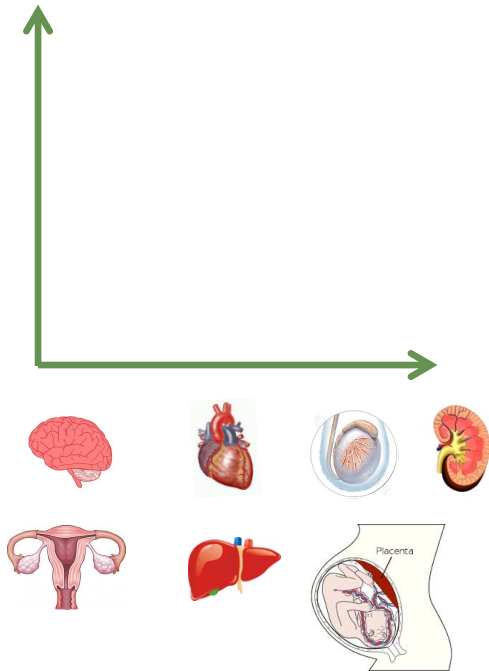
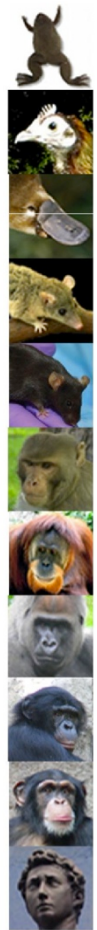




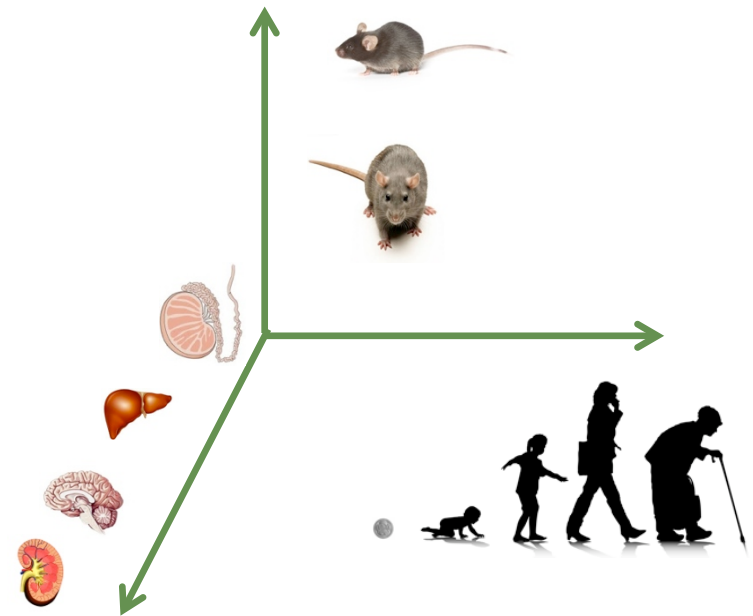
Nothing makes sense in **(lncRNA)** biology except
in the light of evolution.

Theodosius Dobzhansky, 1973

An evolutionary approach to understand lncRNA functionality



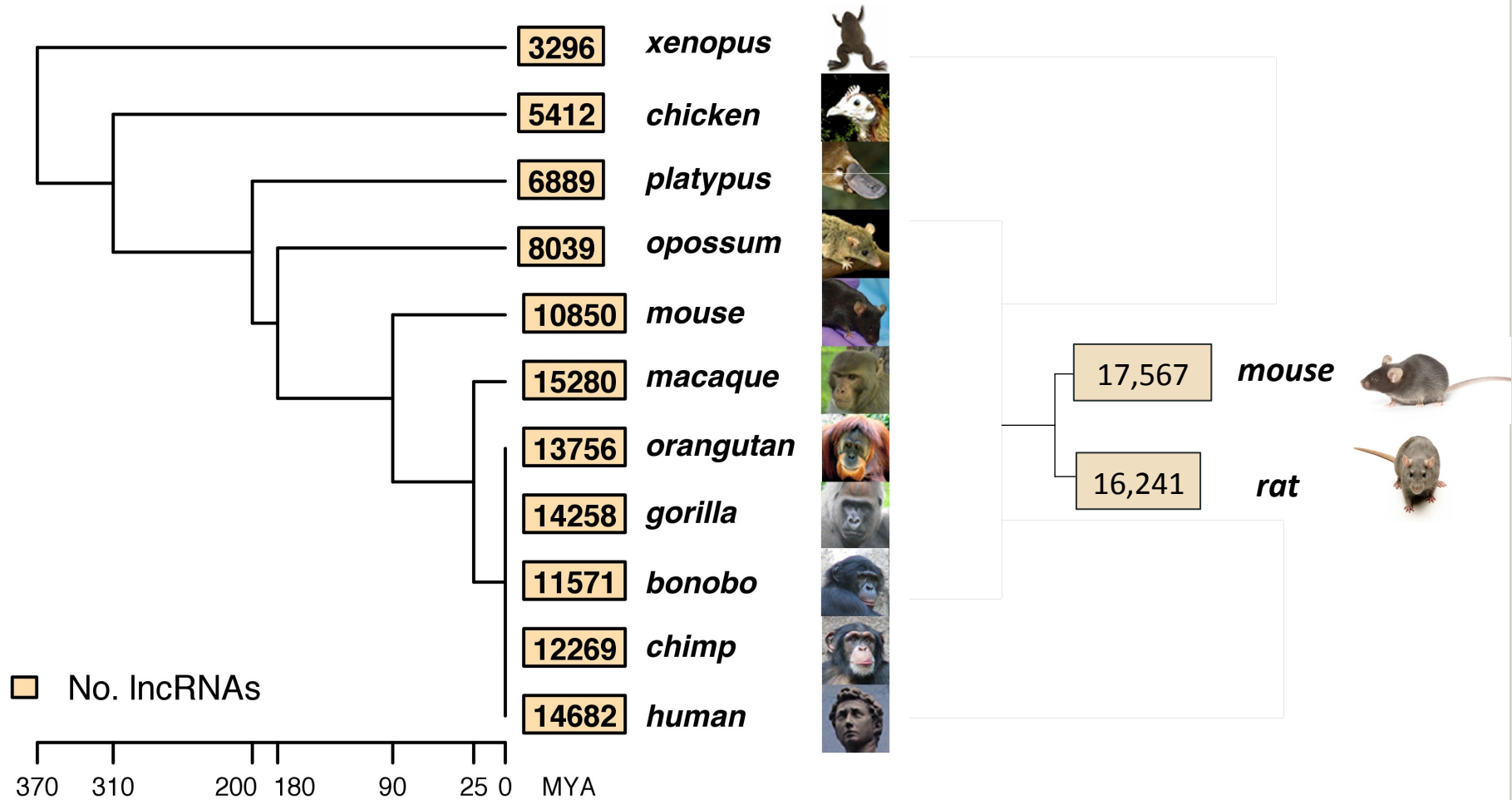
RNA-sequencing for
11 species x 8 organs



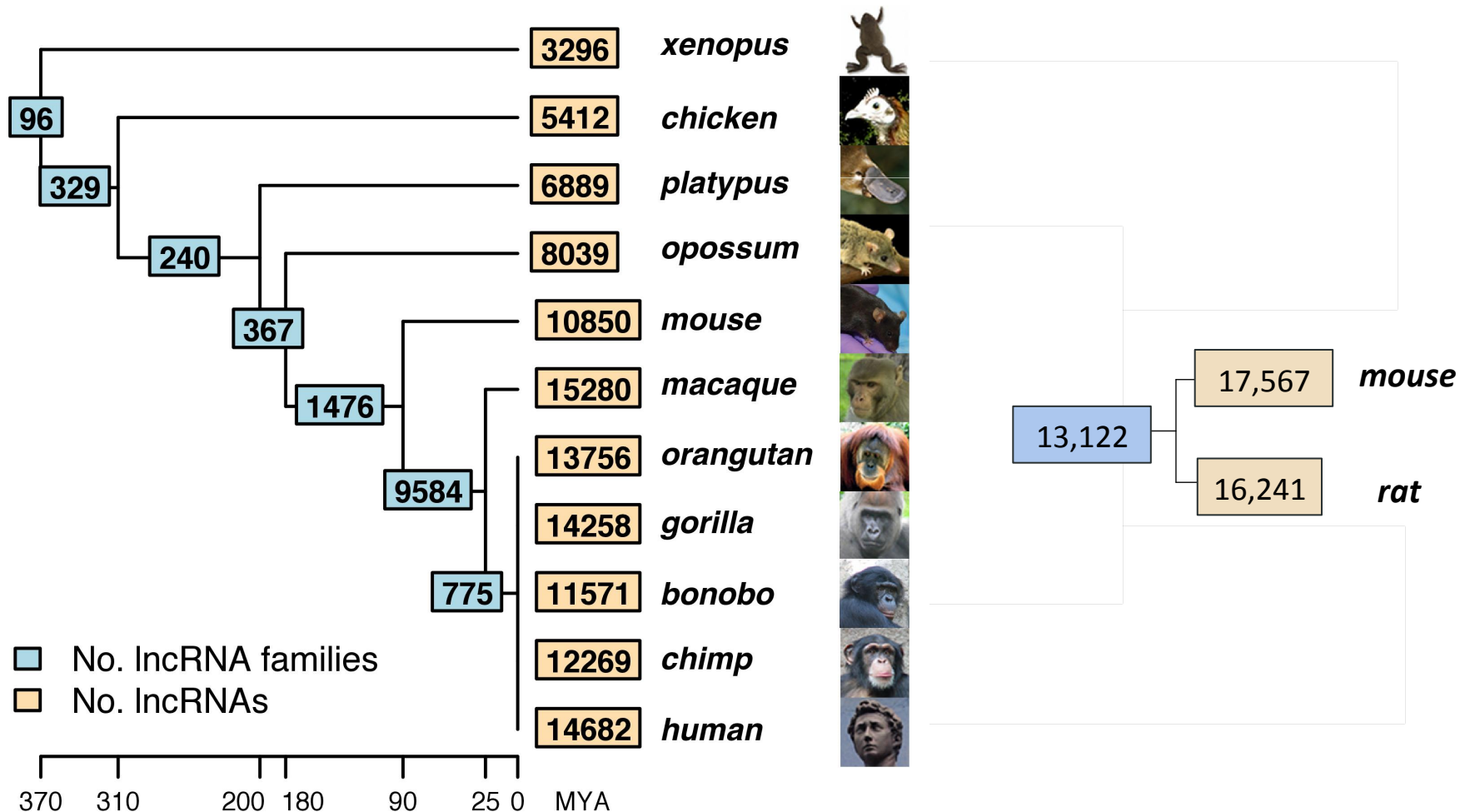
2 species
4 organs
5 developmental stages

Fabrice Darbellay

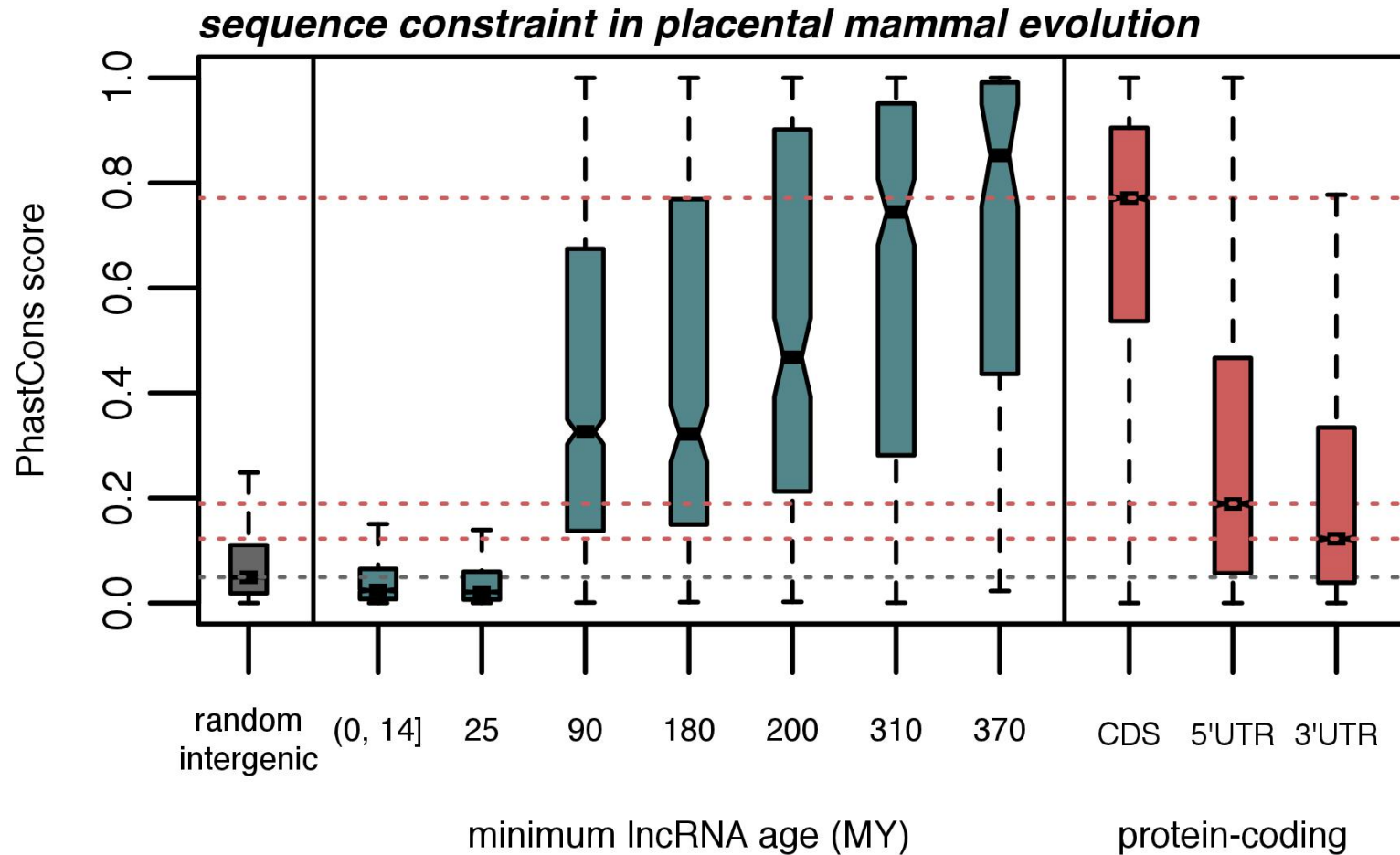
lncRNA repertoires



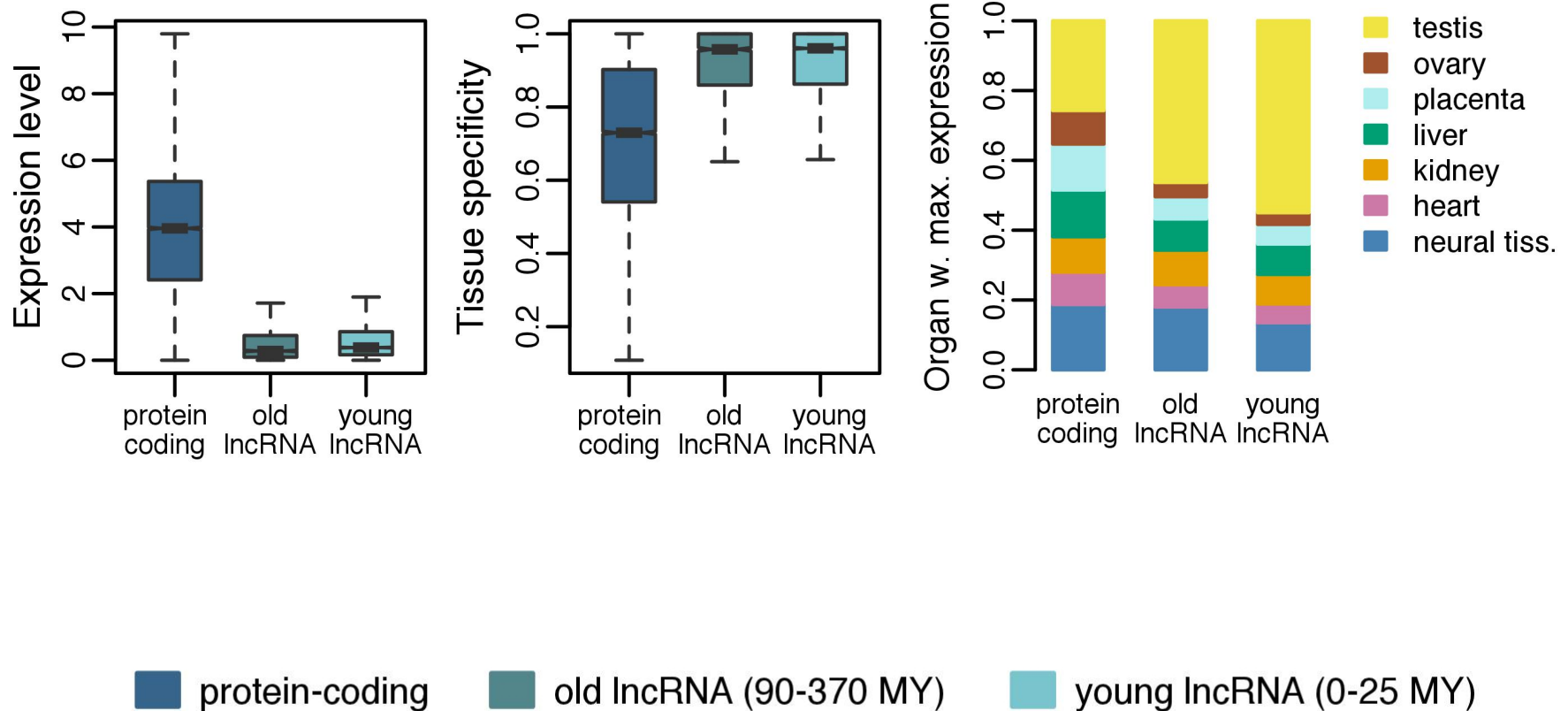
Fast evolution of lncRNA repertoires



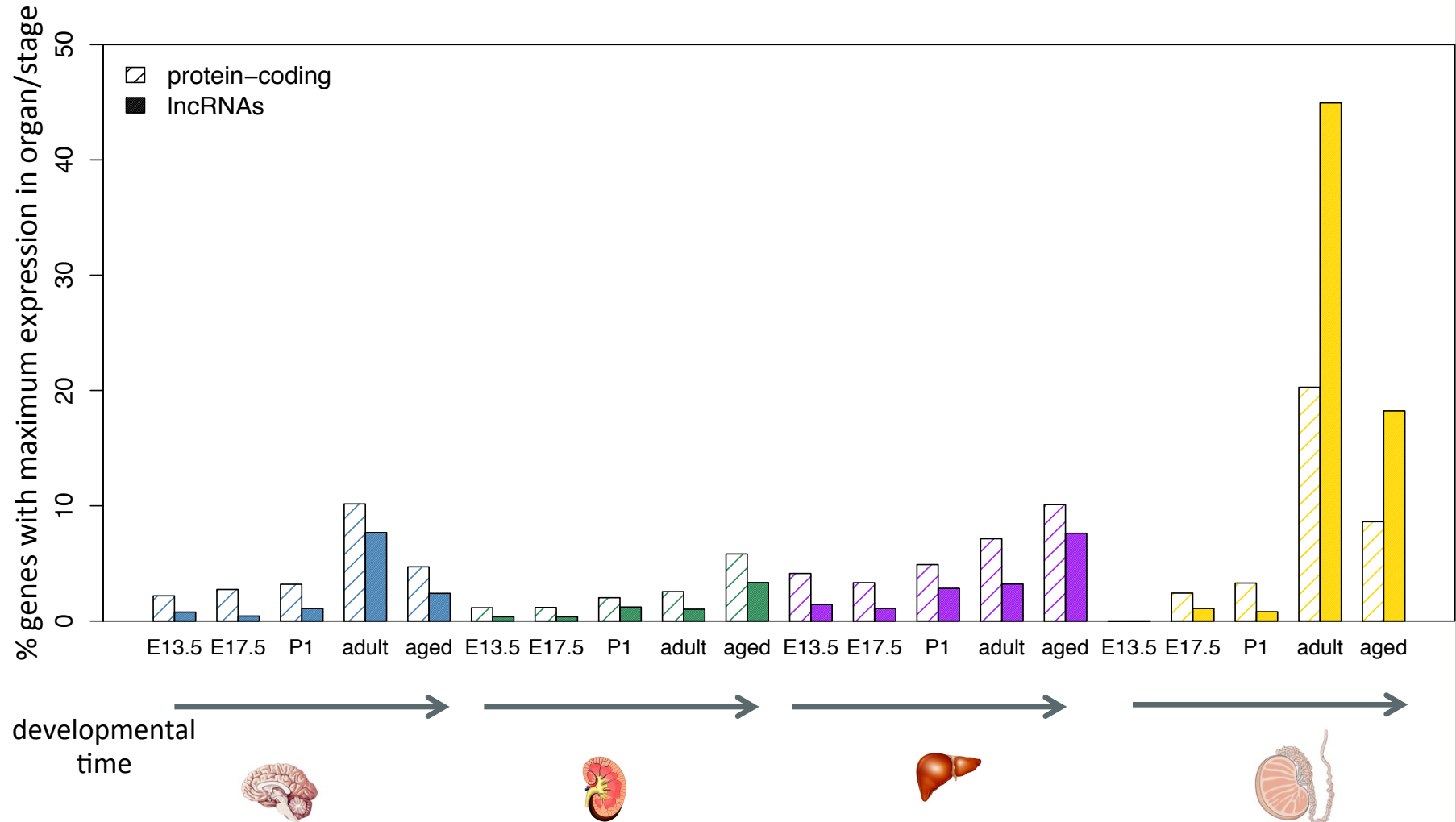
Fast evolution of lncRNA sequences



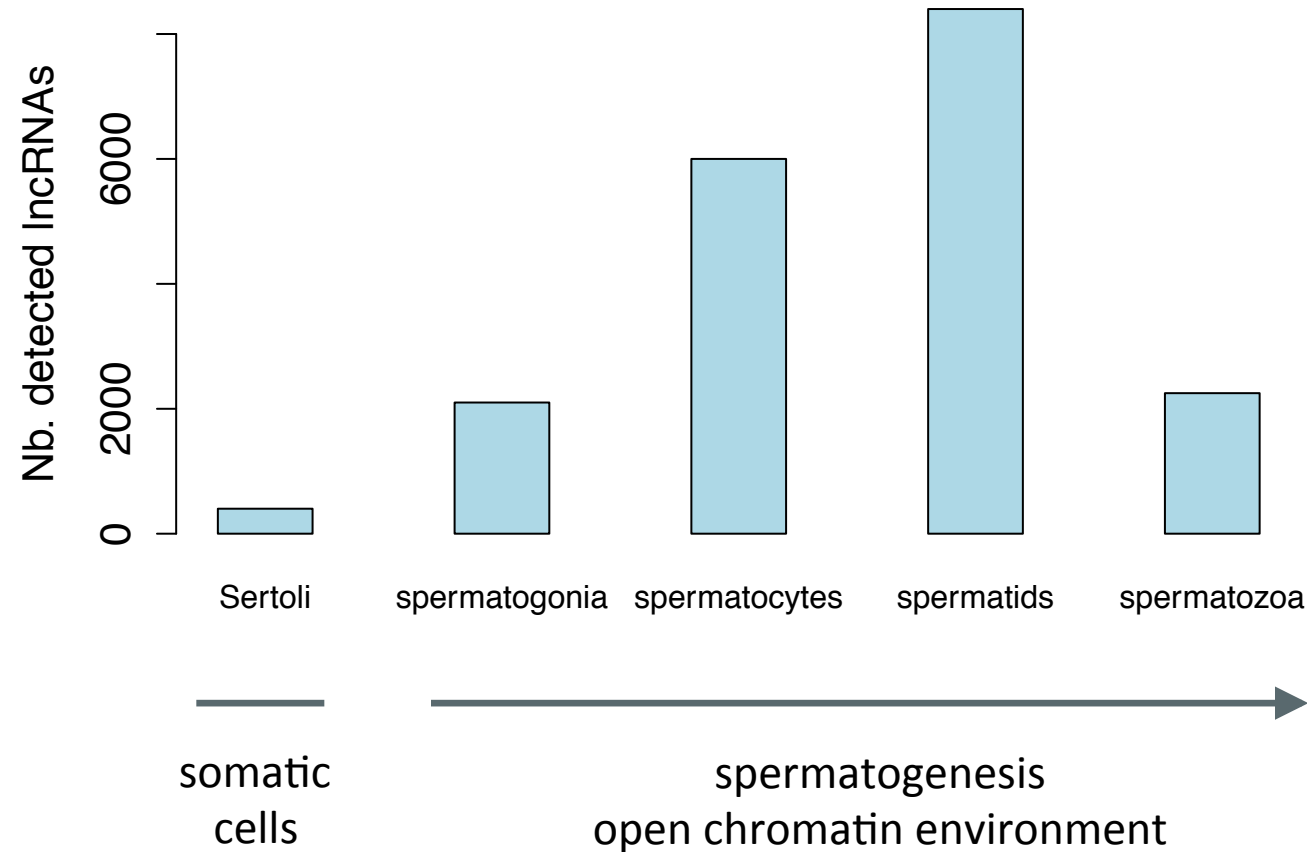
Low expression and high testes-specificity for lncRNAs



lncRNA expressed predominantly in adult testes



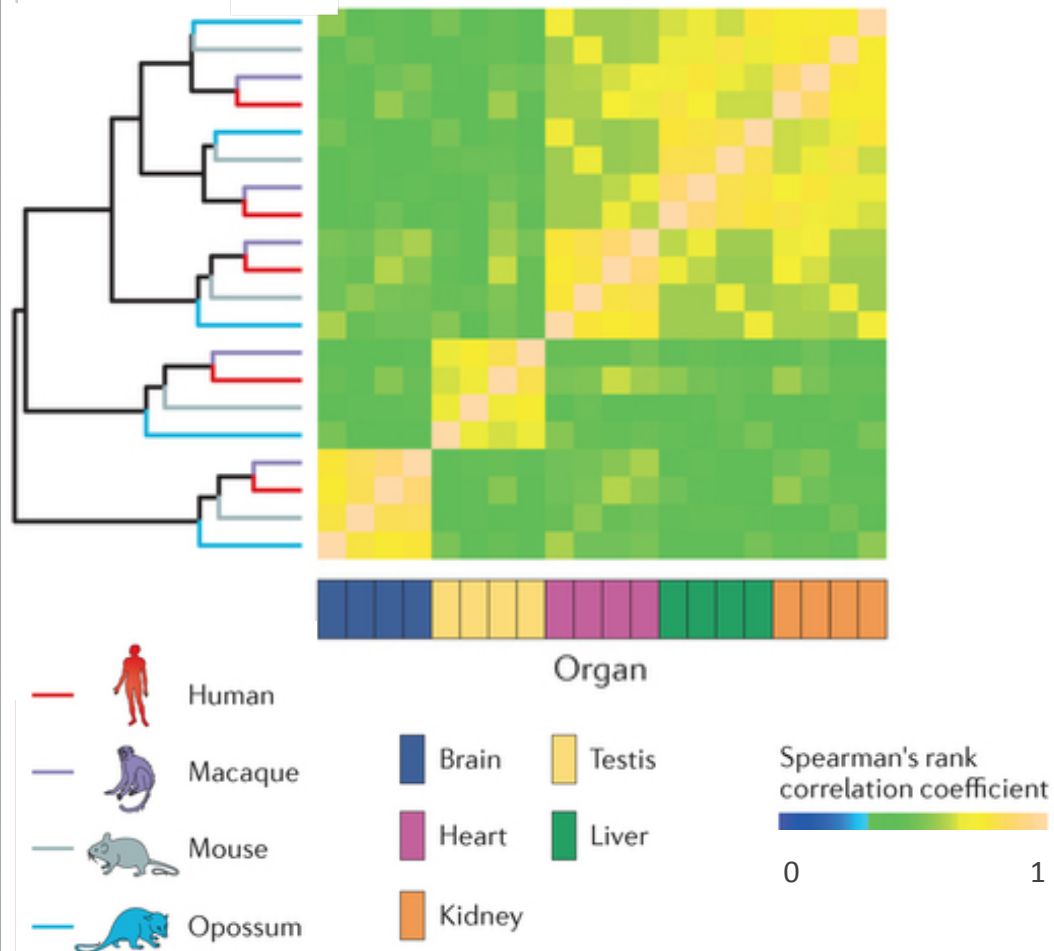
Strong lncRNA expression during spermatogenesis



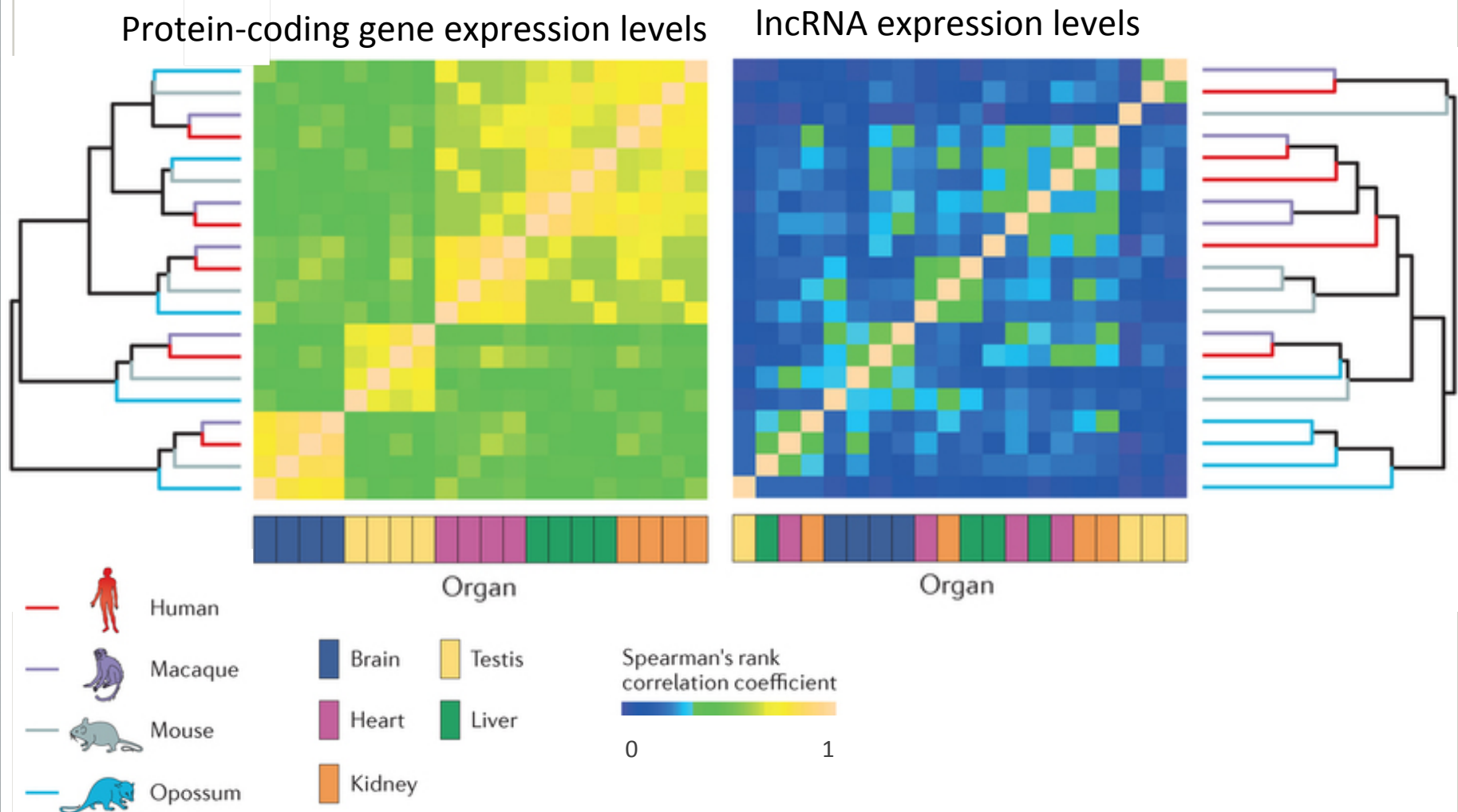
RNA-seq data from Soumillon, Necsulea *et al.*, 2013

Rates of lncRNA expression evolution

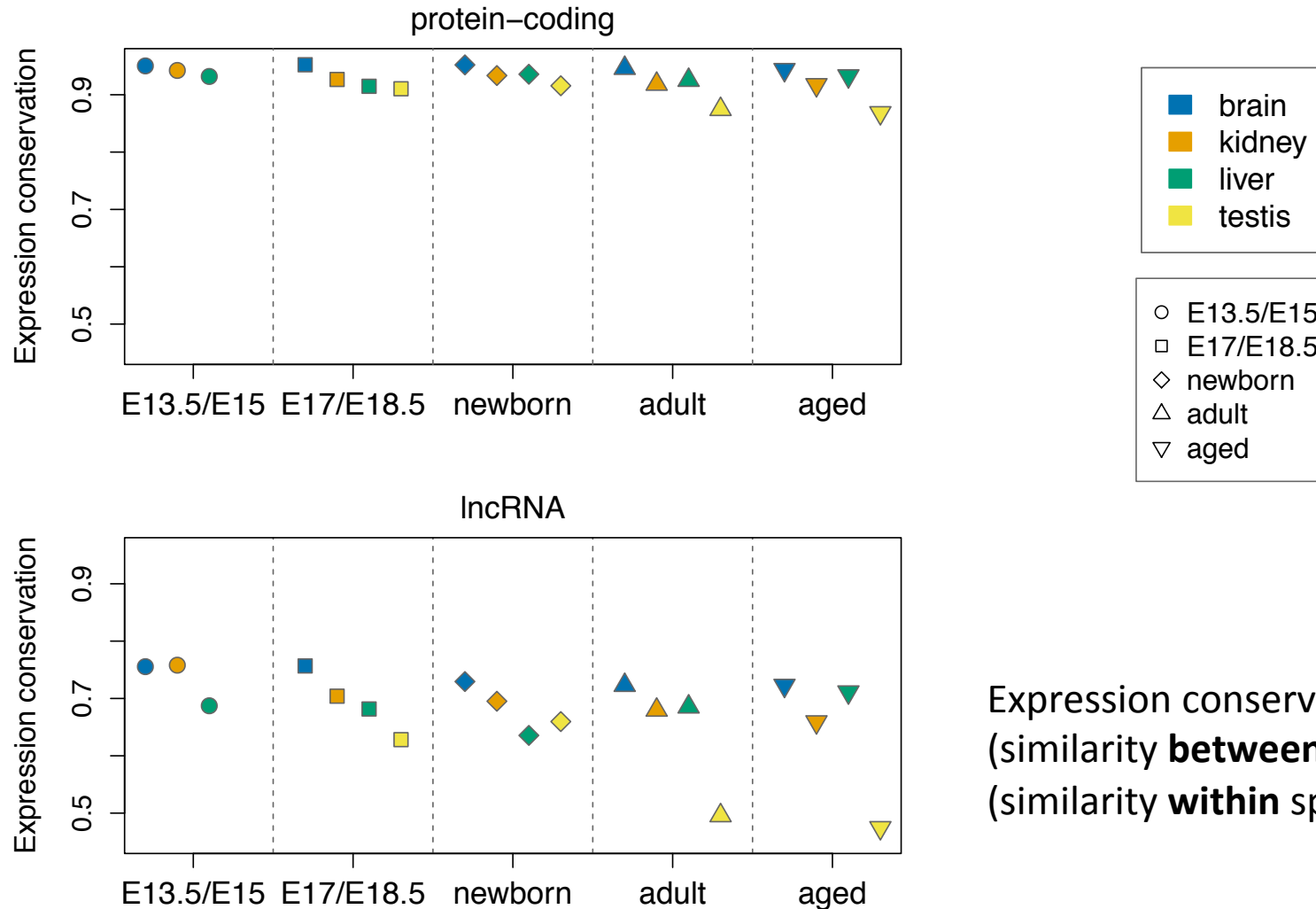
Protein-coding gene expression levels



Rates of lncRNA expression evolution

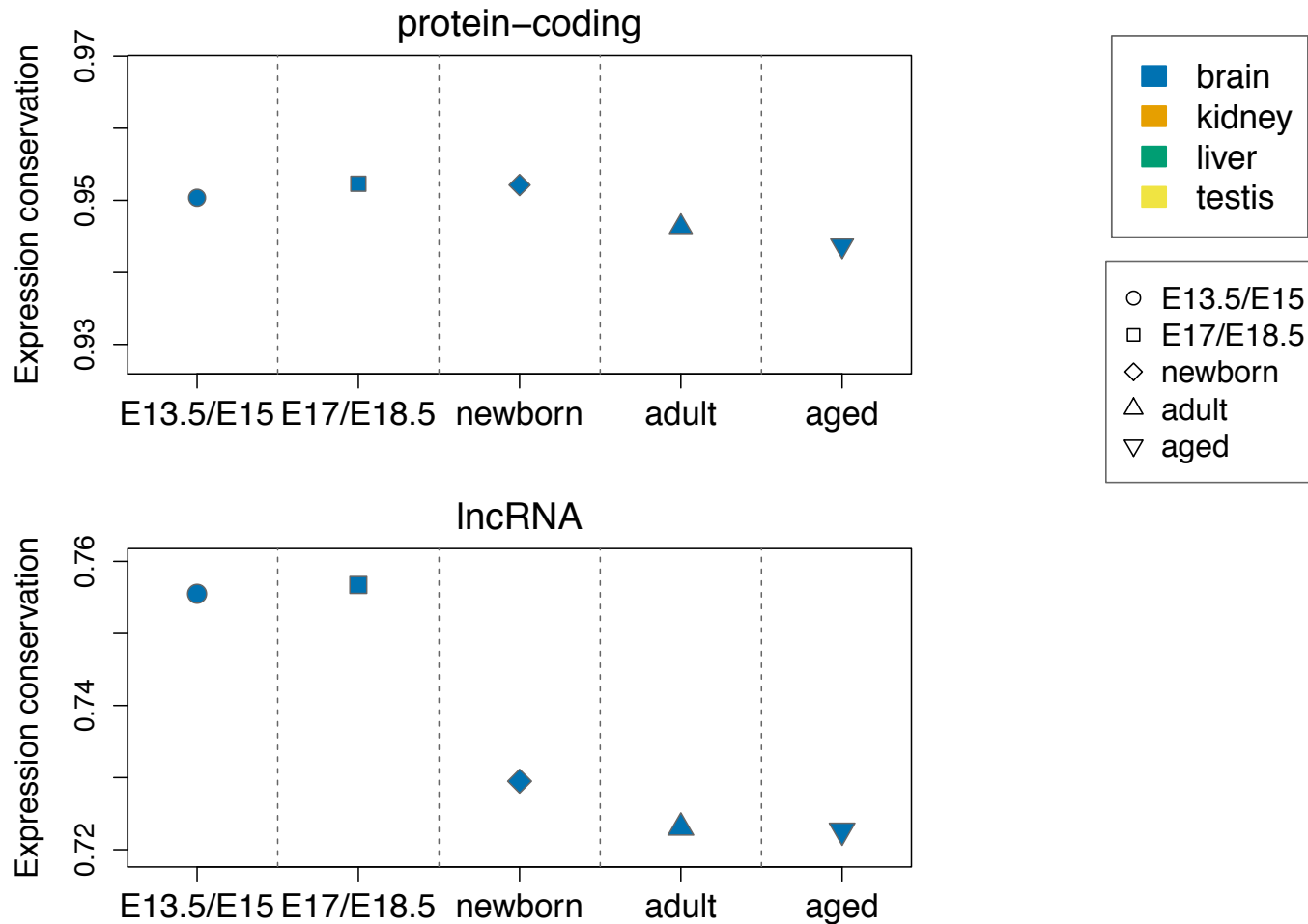


Is there selective constraint on lncRNA expression?

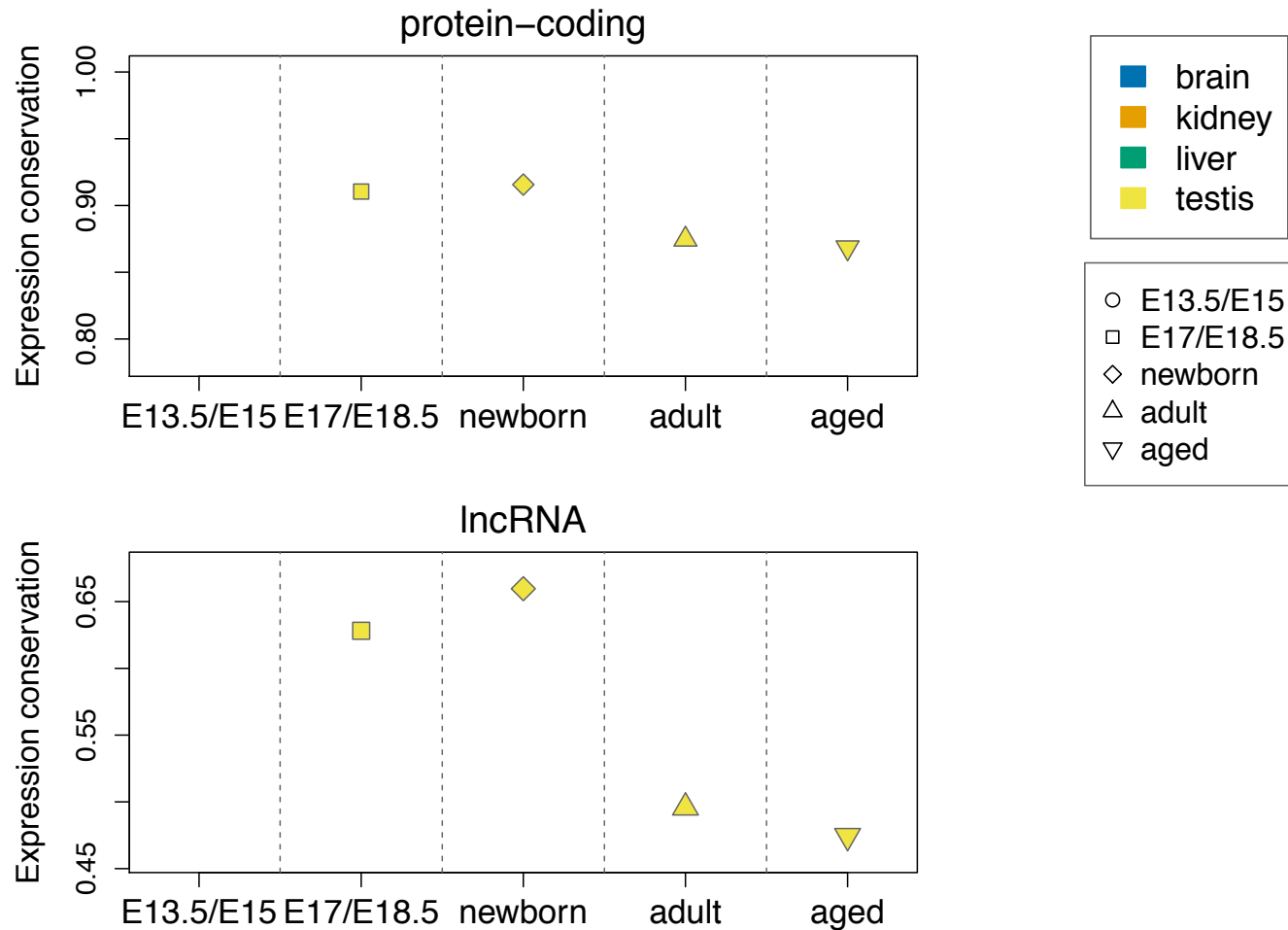


Expression conservation:
(similarity **between** species) /
(similarity **within** species)

Slower lncRNA expression evolution during embryonic development



Slower lncRNA expression evolution during embryonic development



Long non-coding RNA evolutionary patterns

- Fast evolution of lncRNA repertoires and primary sequences
- Low expression levels
- Predominantly expressed during spermatogenesis
- Little evolutionary constraint on lncRNA expression levels
- Most (but not all) lncRNAs may be transcriptional noise

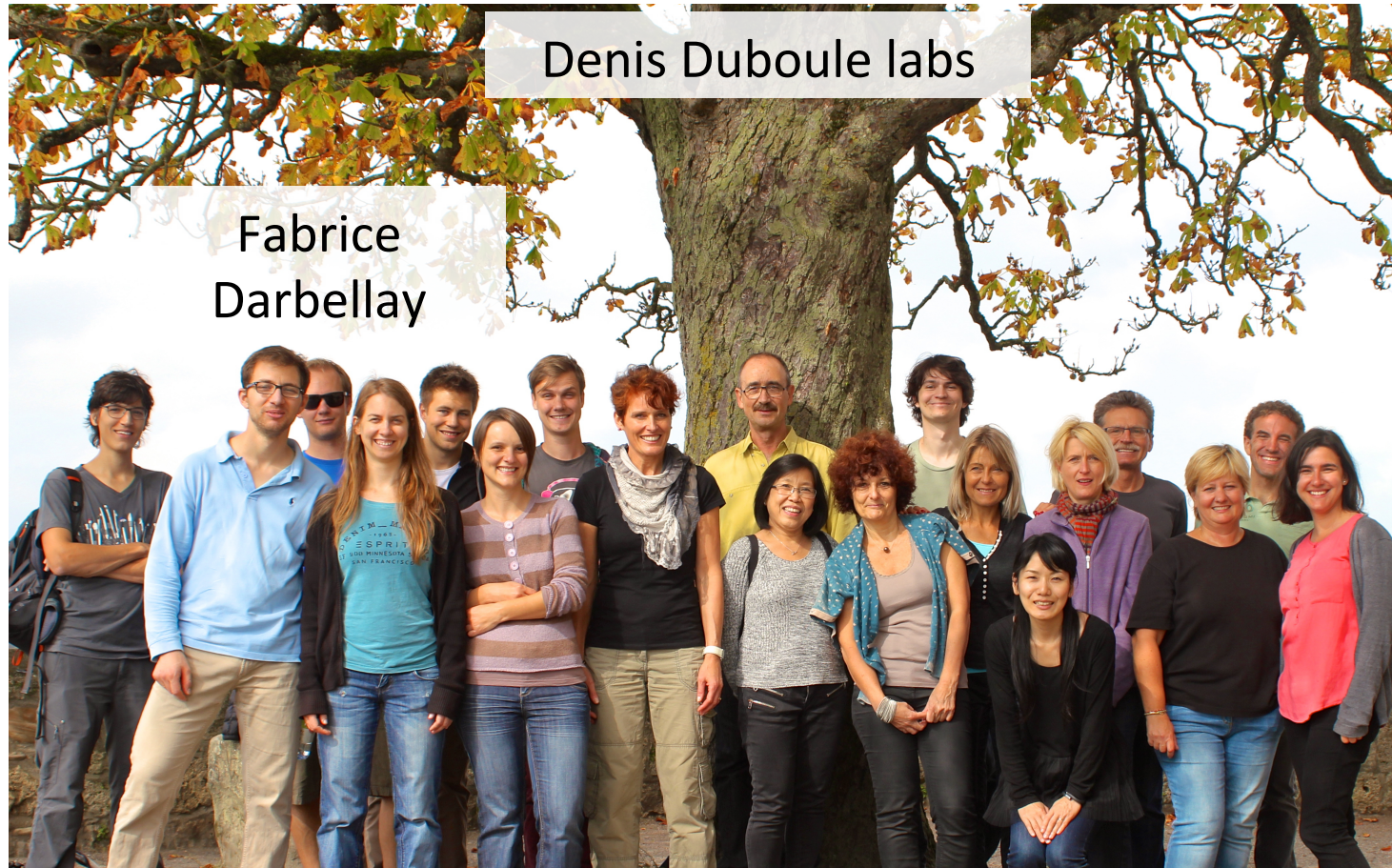


Acknowledgements

Henrik Kaessmann lab

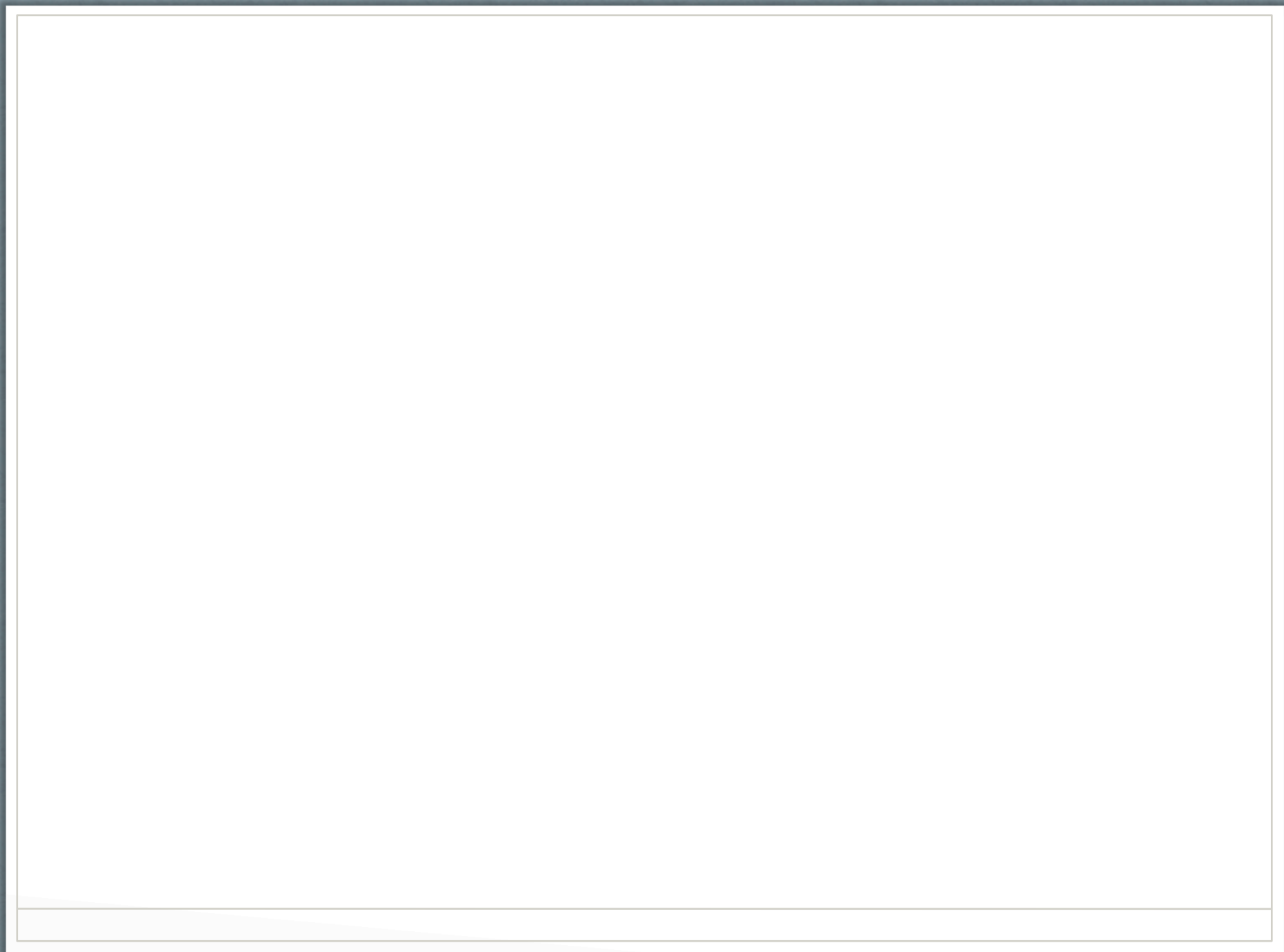


Acknowledgements

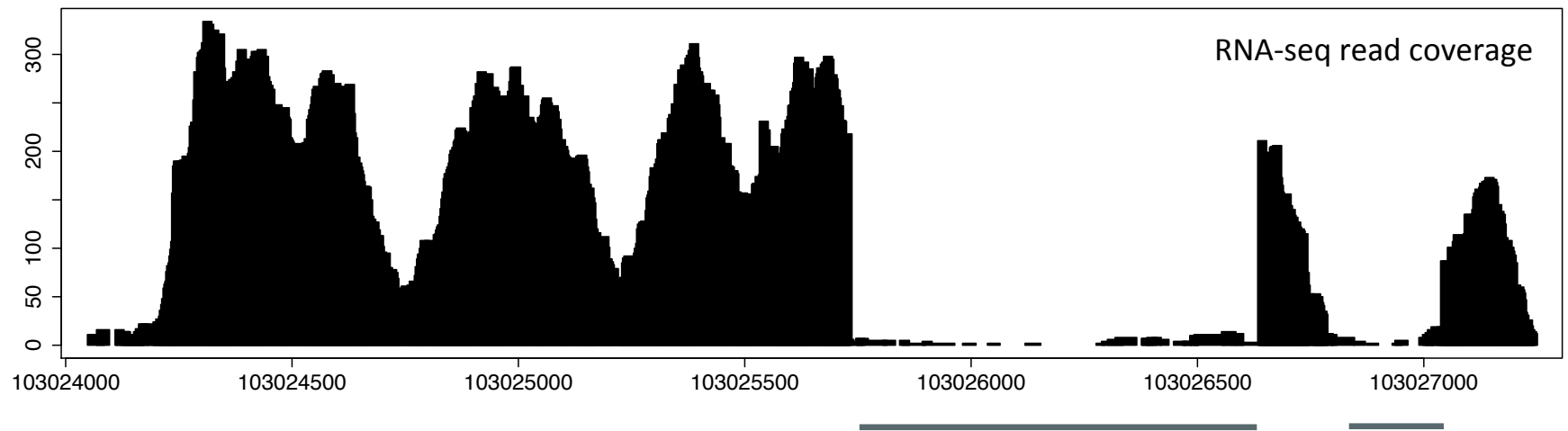


Denis Duboule labs

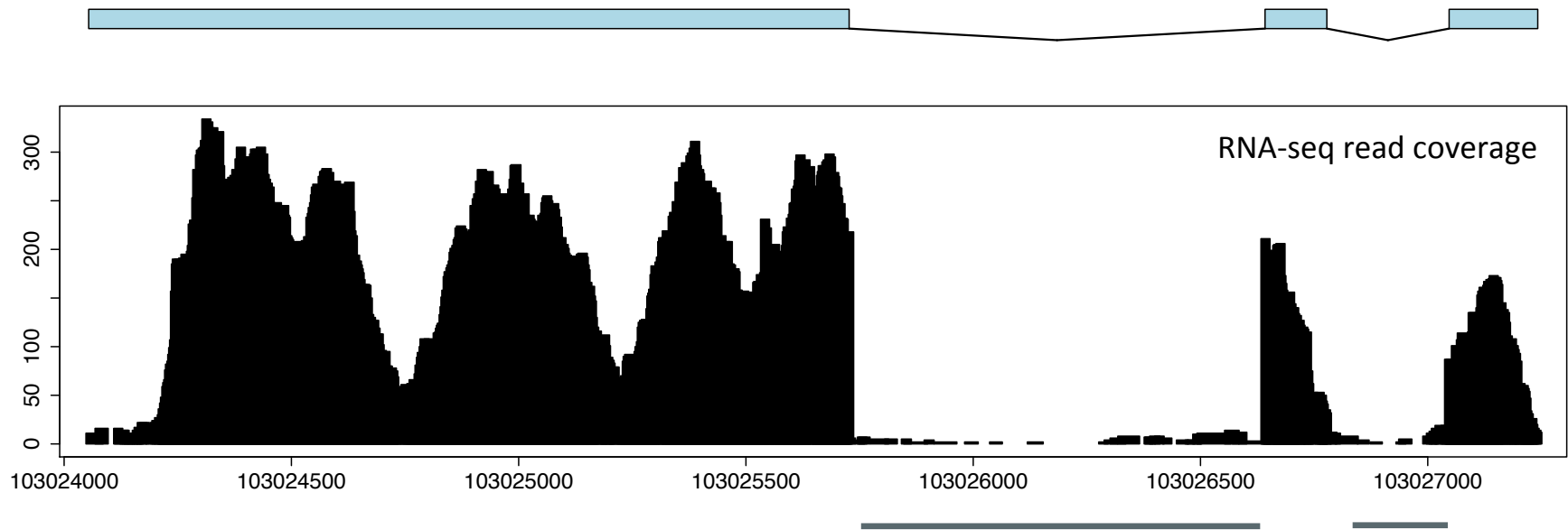
Fabrice
Darbellay



lncRNA detection: *de novo* prediction with RNA-seq



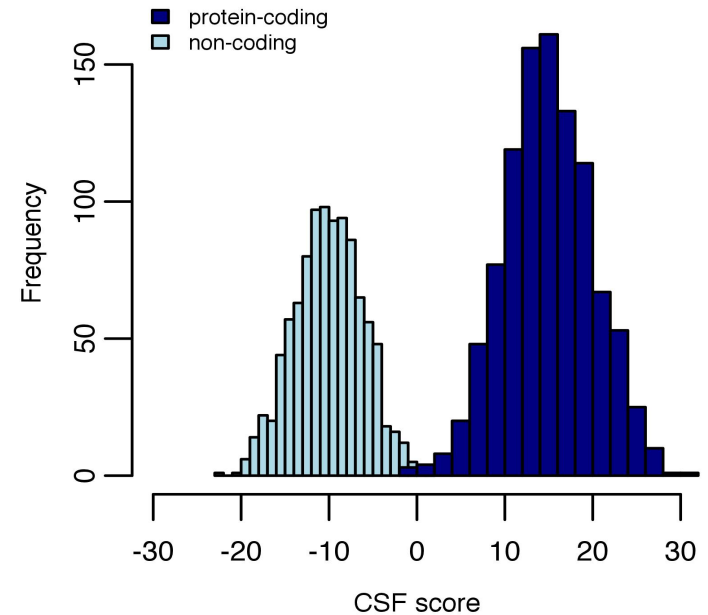
lncRNA detection: *de novo* prediction with RNA-seq



- challenges: gene fragmentation (10% of annotated lncRNAs may be alternative UTRs)

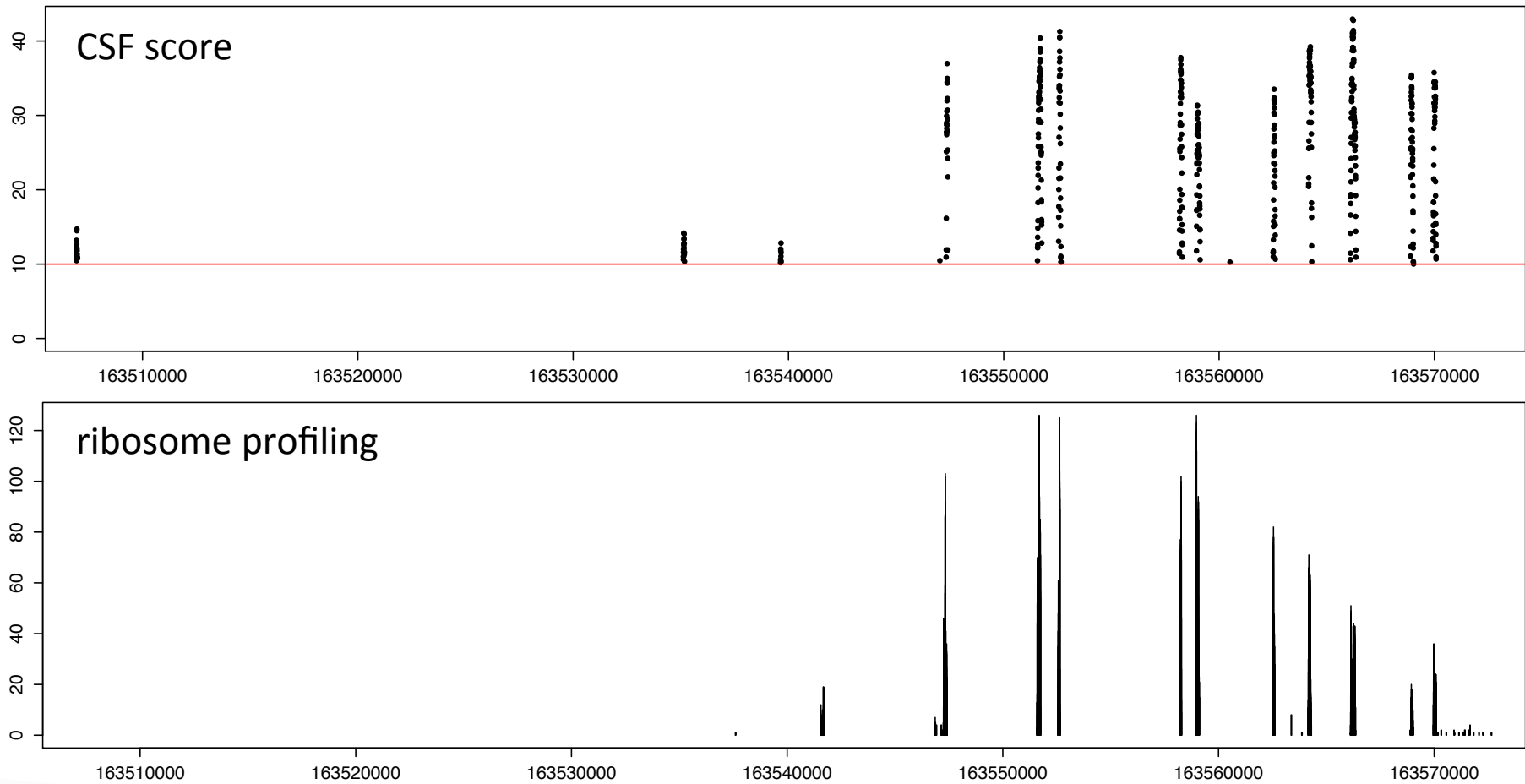
lncRNA detection: protein-coding potential

- ***In silico***: codon substitution frequency (CSF) score
 - Avoidance of mis-sense and non-sense changes in coding regions
- ***In vivo***: ribosome profiling
 - Isolation and high-throughput sequencing of ribosome-bound mRNA fragments (Ingolia, Weissmann, Bartel groups)



lncRNA detection: protein-coding potential

HNF4a



Fast evolution of lncRNA sequences

