

Genome-wide promiscuous transcription in the mammalian testis



High testis transcriptome complexity

Recent human and mouse gene expression analyses revealed an exceptionally large number of transcribed protein-coding genes in the testis. To explore the causes and evolutionary relevance of this observation, we generated extensive transcriptome data for 6 tissues from representatives of all major mammalian lineages using high-throughput RNA sequencing (Figure 1).

Our analyses show that the testis stands out among tissues in all mammals as having the largest number of transcribed protein-coding genes (Figure 1), suggesting that the high testis transcriptome complexity represents an ancestral mammalian feature.

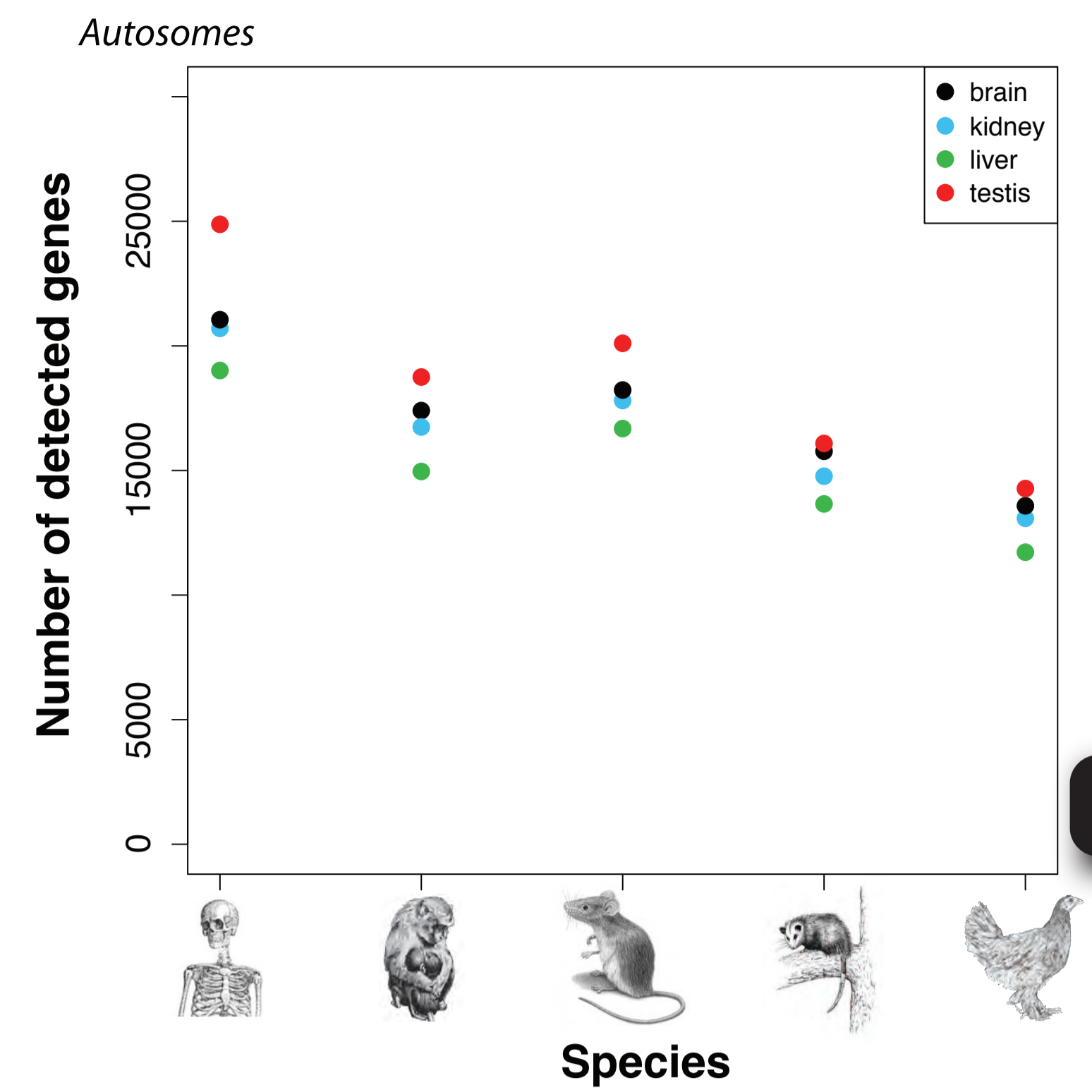


Figure 1

Mouse testis transcriptome and epigenomics project

We further investigated the peculiar testis transcriptome pattern using the mouse as a model organism, producing transcriptome data for meiotic (spermatocytes) and post-meiotic (spermatids) germ cells (Figure 2A).

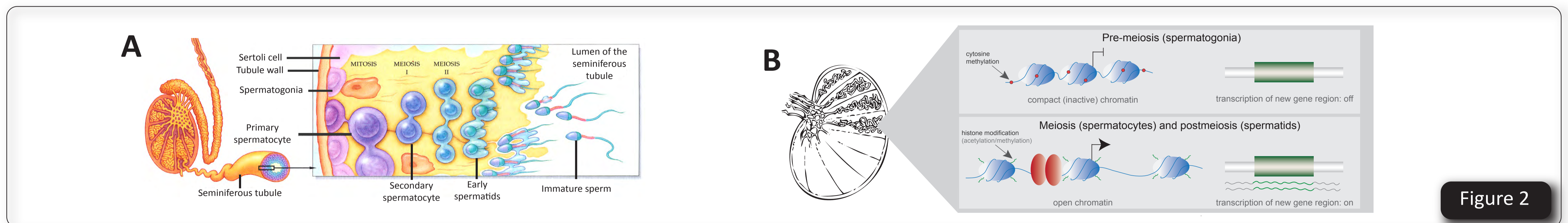


Figure 2

The two types of germ cells transcribe by far the largest numbers of protein-coding genes but also nonfunctional and non conserved genomic elements of various classes (Figure 3A and C). However, while the transcriptome complexity is exceptionally high in these cells, expression levels are generally low for the various transcripts detected in these cells (Figure 3B).

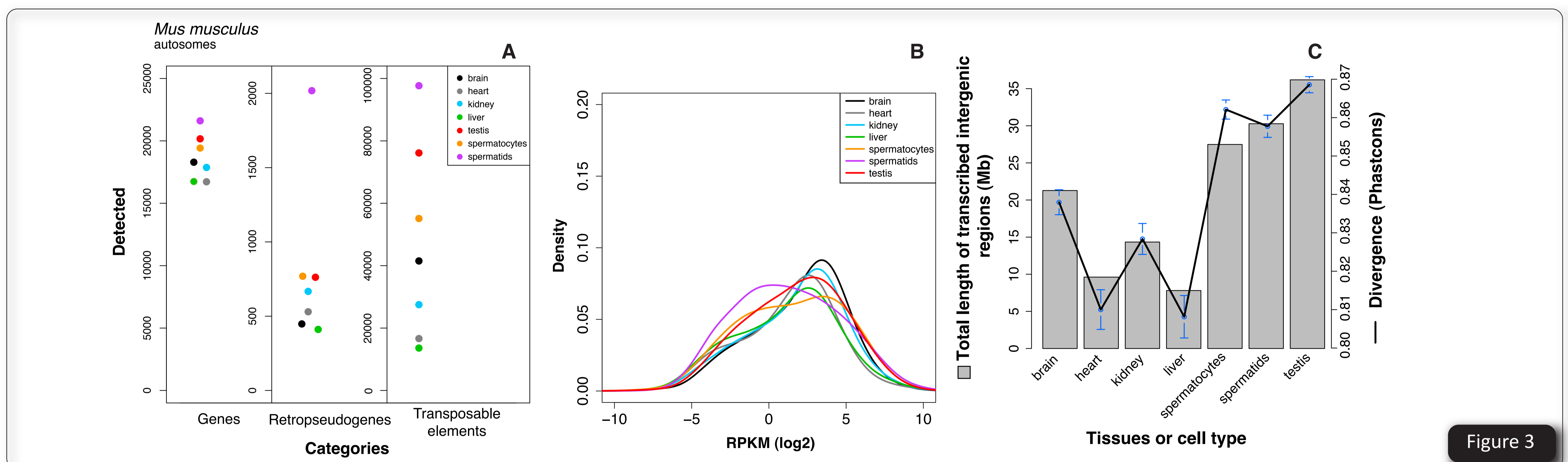


Figure 3

To explore whether the active transcription state of the genome is caused by chromatin remodeling during spermatogenesis (Figure 2B), we generated large-scale epigenome data. To assess the chromatin state, we produced genome-wide histone (ChIP-seq for H3K4me2, an open chromatin marker) and DNA (cytosine) methylation data (low methylation levels are indicative of an open chromatin state).

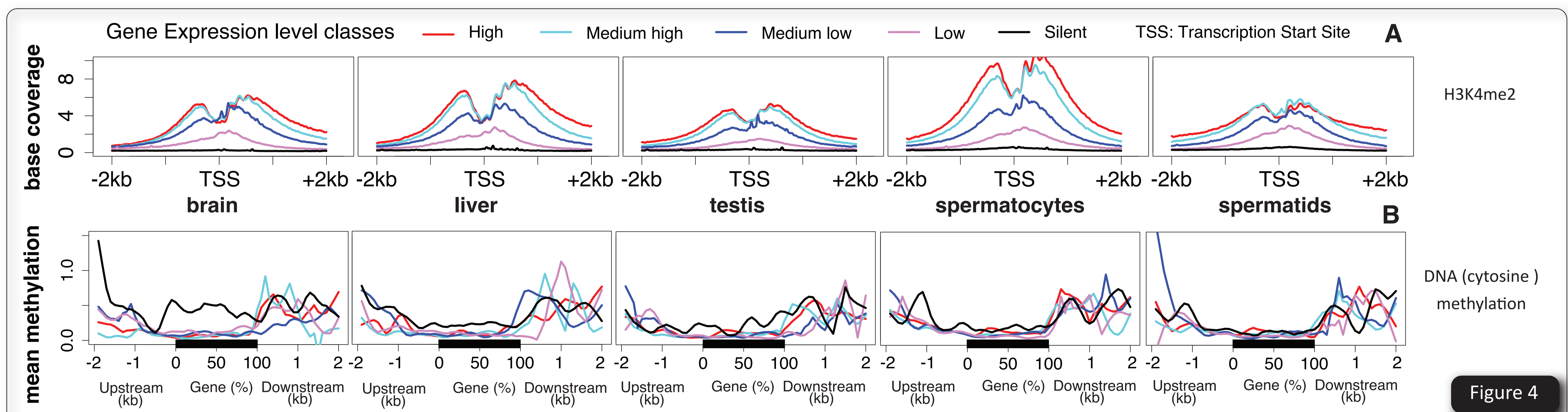


Figure 4

The histone methylation data confirms the enrichment of H3K4me2 near the TSS and its overall high level in spermatocytes is suggestive of a particularly open chromatin state in these cells, which may facilitate transcription (Figure 4A). DNA methylation levels seem to be generally high in brain and liver and overall lower in spermatocytes and in particular spermatids (Figure 4B). The open chromatin state in these cells may be due to the massive chromatin remodeling in late spermatogenesis.

Our findings suggest that many transcripts in the testis may not be functional and transcription levels may be selectively less constrained. This might have contributed to the rapid divergence of expression levels in testis between species (see presentation by Brawand et al.). The active chromatin conformation in male germ cells may also have catalyzed the birth of new genes by facilitating their initial expression.