Abstract
How stable gene expression is maintained by rapidly evolving collections of enhancers and promoters is a fundamental question in evolutionary genetics. To evaluate the consequences of regulatory evolution on mammalian gene expression, we jointly analysed the activity of promoters and enhancers with downstream transcript levels, measured across the same liver samples from over twenty mammalian species. Rapid evolution of enhancers appears a universal feature of mammalian genomes: across all study species half of all liver enhancers are unique to a single species. Most of these arise from exaptation of ancestral DNA, and not from lineage-specific expansions of repeat elements. In contrast, almost all liver promoters are partially or fully conserved across our study species. Recently-evolved enhancers can be significantly associated with genes under positive selection, demonstrating a powerful approach to annotating potential regulatory adaptations in newly sequenced genomes. In contrast, mammalian gene expression levels are largely conserved, with enhanced expression stability for subsets of genes relevant to tissue physiology. Genes associated with complex regulatory landscapes across species generally exhibit high transcriptional levels that remain stable in evolution. Highly-conserved regulatory elements active in most mammals also stabilise gene expression. Conversely, recently-evolved enhancers are typically weak, consistent with a largely neutral role in gene regulation, yet in large numbers can lead to gene expression divergence during evolution. These effects are consistently observed across the entire mammalian clade and robust to potential confounders, such as gene expression level and landscape complexity.

Overall, our results underscore how the evolutionary stability of gene expression is profoundly entwined with both the number and conservation of surrounding promoters and enhancers.

Biosketch
Diego obtained his PhD at the Autonomous University of Madrid in 2010, on the gene expression program controlled by Hypoxia-Inducible Factor, the master transcription factor under oxygen deprivation. After a short post-doctoral stint at the National Biotechnology Center, he joined Duncan Odom’s laboratory in Cambridge in 2012. His research interests focus on the application of functional and comparative genomics to the understanding of mammalian gene expression and tissue function.