Using cancer to investigate the interaction between codon usage and tRNA anticodon abundance

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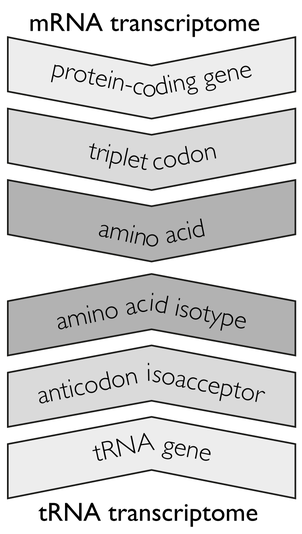
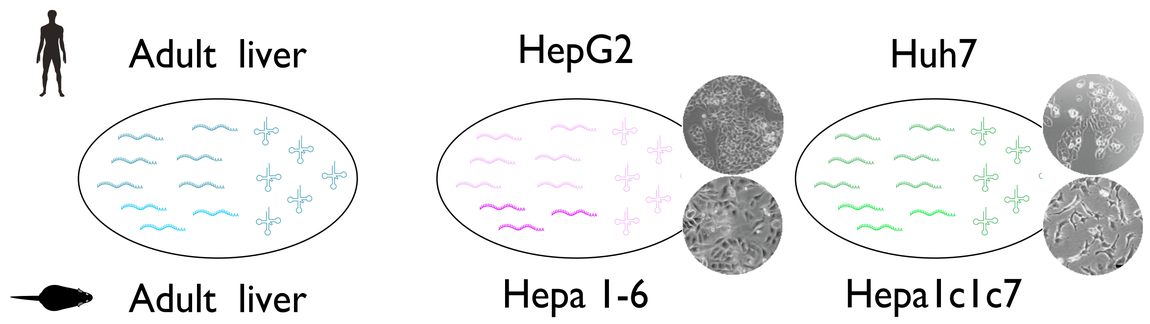
Introduction

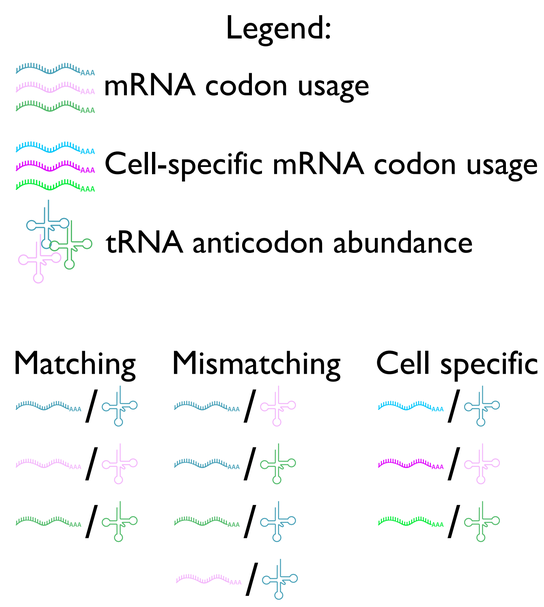
We have previously reported the stability of the codon–anticodon interface during mouse development, where we measured the whole-transcriptome codon usage and the tRNA anticodon abundance of matching stages of development and found remarkable stability, both in codon usage and in tRNA anticodon abundance, despite the drastic phenotypic changes [3]. These findings let us to hypothesise that, unlike in other organisms [1], no widespread translational regulation, mediated by codon bias, is likely to occur in mammals.
In contrast, others have recently reported that codon usage for genes enriched in cell-autonomous function and multicelluarity in humans is adapted to the tRNA abundance of proliferating and differentiating cells, respectively [2].
Here we test this hypothesis using whole-genome expression data from healthy liver tissue and two different tumour cell lines in human and mouse.

Experimental setup

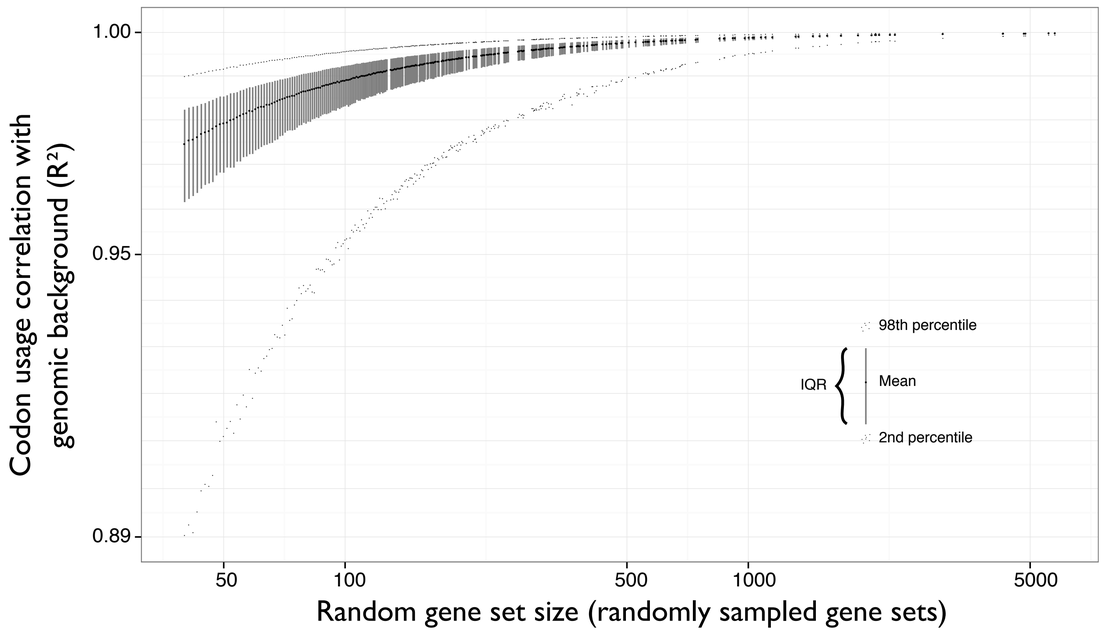




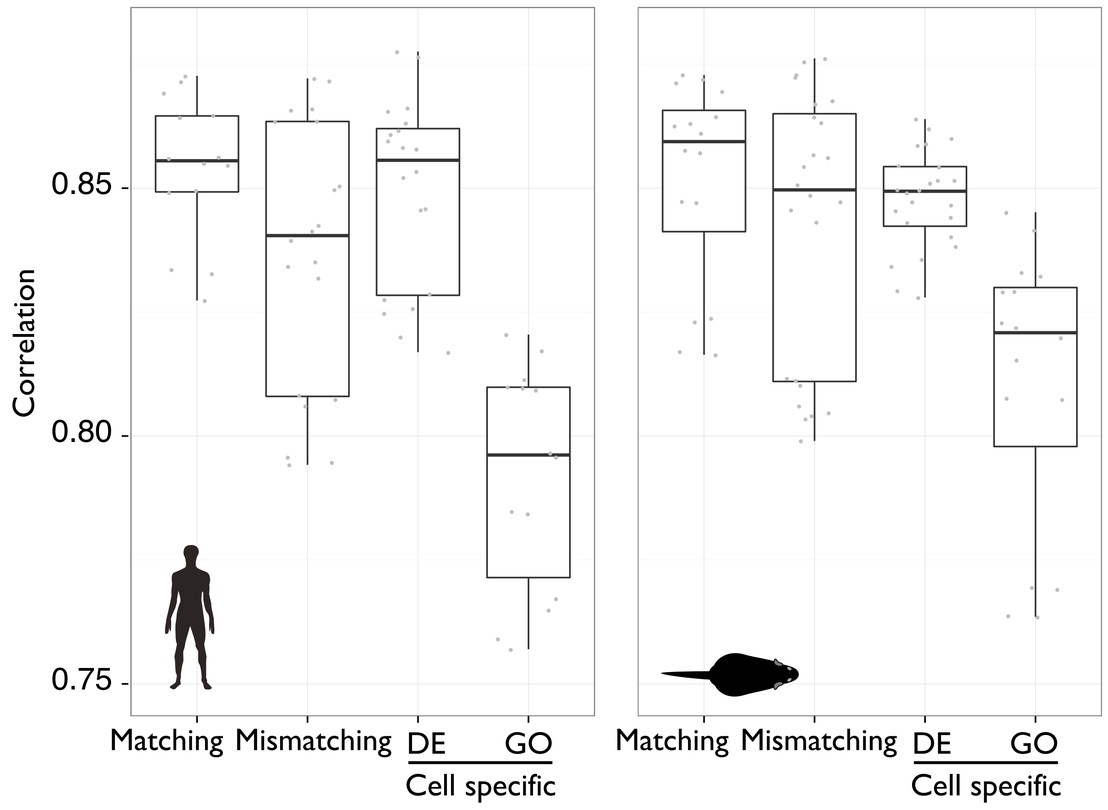
Codon usage and anticodon abundance of healthy adult liver and two cancer cell lines were correlated to estimate their adaptation in each cellular condition. Higher correlation implies better adaptation of the codon usage to the anticodon abundance. The GO terms used for cell-specific functions are "pattern specification process" and "M phase of mitotic cell cycle" for healthy and tumour cells, respectively [2].



Codon usage bias correlates with gene set size



No evidence of codon–anticodon adaptation



Conclusion

Codon–anticodon correlation is not significantly higher in matching than in mismatching cellular condition. The same is true in genes in condition-specific gene sets (determined either via **D**ifferential **E**xpression or **G**ene **O**ntology). Gene sets determined from Gene Ontology, on the contrary, show significantly less codon–anticodon correlation, consistent with the stochastic effect of small gene set sample sizes ($N < 100$ in all cases) on codon bias.

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References

[1] Carlini D.B. et al. (2003) *Genetics*, 163:239–243. ISSN 0016-6731.

[2] Gingold H., et al. (2014) *Cell*, 158:1281–1292. ISSN 0092-8674. doi: 10.1016/j.cell.2014.08.011.

[3] Schmitt B.M., et al. (2014) *Genome Res*, 24:1797–807. ISSN 1088-9051, 1549-5469. doi:10.1101/gr.176784.114.

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