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Title:	Convergent evolution of a genomic rearrangement may explain cancer resistance in hystrico- and sciuromorpha rodents
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Keywords:	Convergent evolution genomic rearrangement cancer resistance in hystrico- and sciuromorpha rodents
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Citation:	Npj Aging and Mechanisms of Disease, 7(1).
Abstract:	The rodents of hystricomorpha and sciuromorpha suborders exhibit remarkably lower incidence of cancer. The underlying genetic basis remains obscure. We report a convergent evolutionary split of human 3p21.31, a locus hosting a large number of tumour-suppressor genes (TSGs) and frequently deleted in several tumour types, in hystrico- and sciuromorpha. Analysis of 34 vertebrate genomes revealed that the synteny of 3p21.31 cluster is functionally and evolutionarily constrained in most placental mammals, but exhibit large genomic interruptions independently in hystricomorpha and sciuromorpha, owing to relaxation of underlying constraints. Hystrico- and sciuromorpha, therefore, escape from pro-tumorigenic co-deletion of several TSGs in cis. The split 3p21.31 sub-clusters gained proximity to proto-oncogene clusters from elsewhere, which might further nullify pro-tumorigenic impact of copy number variations due to co-deletion or co-amplification of genes with opposing effects. The split of 3p21.31 locus coincided with the accelerated rate of its gene expression and the body mass evolution of ancestral hystrico- and sciuromorpha. The genes near breakpoints were associated with the traits specific to hystrico- and sciuromorpha, implying adaptive significance. We conclude that the convergently evolved chromosomal interruptions of evolutionarily constrained 3p21.31 cluster might have impacted evolution of cancer resistance, body mass variation and ecological adaptations in hystrico- and sciuromorpha.
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