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Title:	Evolutionary Implications of Telomere and Centromere associated Chromosomal Rearrangements in Mammals
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Abstract:	<p>The hierarchical organisation of the genome allows for it to be regulated at several levels. At the linear level, it involves gene order and neighbourhood, at the chromatin level it involves histone modifications, and at the 3D level it brings in the dynamics of large domains: TADs, cLADs, ciLADs, etc. In this study, we explore the linear ordering of genes and the rearrangements that disrupt them. Chromosomal rearrangements that lead to changes in the linear order of genes are implicated in changes in gene expression. Change in gene expression is, in turn, linked to phenotypic change that is subject to Darwinian selection. Therefore, chromosomal rearrangements play an important role in the course of evolution. Here we explore a subset of chromosomal rearrangements that constrain genes near telomere or centromere in a species specific manner. We hypothesised that genes constrained near or away from heterochromatin (centromere/telomere) via rearrangements experience differential gene expression compared to those genes that maintain their distance from such domains. We studied the rearrangements that shuffle orthologous genes around in human and mouse chromosomes via two methods: using line plots to visualise rearrangements and using distance cut-offs to filter genes constrained within certain distances of the telomere/centromere in a species-specific manner. Through the second approach, we observed that genes constrained near telomeres show high expression divergence as compared to those genes that maintain their distance from heterochromatin in both human and mouse. The genes constrained near telomere in mouse are associated with pathways in immune response and cancer. Since immune responses are just as important as adaptations for the survival of a species, this result warrants further analysis of the hypothesis in other mammalian species. However, a lack of centromere positions for several mammalian chromosomal assemblies is a hindrance. Centromere position prediction was attempted for mammals with complete chromosomal assemblies, with some success for the assemblies of Opossum and Rabbit. We also come to an understanding, through this analysis, that linear rearrangements that disrupt the 3D organisation of the genome (constitutive LAD to constitutive inter-LAD or vice versa) may provide a more comprehensive outlook in elucidating the evolutionary role of rearrangements that displace genes from repressed to expressed compartments or vice versa in a species-specific manner — an outlook that studying linear rearrangements with heterochromatin as a repressed compartment alone may not provide. Keywords: Chromosomal Rearrangements, Heterochromatin, Telomere, Centromere, Expression Divergence, Human, Mouse, Mammals.</p>
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