

## **The evolution of three-dimensional genome structure following WGDs in the sea lamprey *P. marinus***

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Animal genomes contain regulatory information required for the proper coordination of gene expression in developmental and physiological contexts. This information is carried by non-coding cis-regulatory regions, enhancers, whose action necessitates their physical proximity with their target genes. The organization of vertebrate genomes into self-interacting chromosomal segments called Topologically Associating Domains (TADs) allows both the compartmentalization of long-range promoter-enhancer contacts and their facilitation. Altered three-dimensional genome structure due to chromosomal rearrangements or mutations have been shown to impact gene expression; however, the contribution of this spatial organization to the evolution of gene regulation remains poorly understood. Cyclostome (lampreys and hagfish) genomes constitute an interesting counterpart to gnathostome genomes to explore the potential regulatory constraints and opportunities associated with the evolution of genomes in 3D. Recent studies show that only first of the two rounds of whole-genome duplications (WGD) that have occurred in gnathostomes is shared by cyclostomes. Yet, cyclostome genomes underwent a second independent WGD accompanied by genomic rearrangements. To follow the evolution of 3D genome organization in this lineage, we assessed the genome architecture of the sea lamprey *P. marinus* using Hi-C and examined its relationship to microsynteny by leveraging a high-confidence homology analysis. We also used scRNA-seq to investigate the evolutionarily novel gene expression patterns associated with genomic rearrangements that may have led to the unique morphology and physiology of lampreys. These comparative analyses provide insights into how the evolution of TADs following WGDs may have contributed to shape genomes, gene regulatory architectures, and ultimately morphological diversity.