COMPARATIVE GENOMICS TO UNDERSTAND THE ORIGIN OF SCRAMBLED GENES.

X. Chen[1], L. Y. Beh[1], and L. F. Landweber[1], [1]Princeton University, Princeton, NJ USA; lfl@princeton.edu.

The unicellular ciliate *Oxytricha* possesses a dynamic pair of genomes, with massive DNA rearrangements producing a highly fragmented but functional genome from a precursor genome roughly twenty times its sequence complexity. During development, *Oxytricha* eliminates nearly all its noncoding DNA, including all of its transposons, and rearranges over 225,000 remaining short DNA pieces to produce intact genes on tiny gene-sized "nanochromosomes." In the precursor genome, the shattered segments of different genes often interweave with each other, frequently overlap and can even combinatorially assemble to produce multiple distinct loci and gene products [1]. The whole process produces a mature, somatic genome of over 16,000 nanochromosomes that range in size from about 400 to 66,000 base-pairs and typically encode a single protein or RNA, although a small portion contain up to eight genes that may assemble combinatorially by alternative DNA splicing [2].

Remarkably, RNA regulates this entire process. Long noncoding RNAs provide templates for both genome remodeling and RNA-guided DNA repair [3], allowing heritable changes to transfer to the next generation. In addition, millions of tiny 27 nucleotide RNAs provide the critical information to mark and protect the retained DNA pieces of the genome [4]. Together, *Oxytricha's* elaborate epigenome, assembled through complex interacting networks of long and small non-coding RNAs, encapsulates an RNA-driven world packaged in a modern cell. The mechanism for all of these dynamic actions bypasses the traditional modern pathway of inheritance via DNA, hinting at the power of RNA molecules to sculpt genomic information out of smaller pieces.

We are now using comparative genomics of the precursor and rearranged chromosomes from related ciliate species to understand how these broken genomic architectures have arisen over evolutionary time and what they can tell us about the origin of heritable information, as well as the origin of functional, linear genes and chromosomes [5]. Here, I will report our analyses of hundreds of orthologous genes pairs in closely related species whose genetic maps differ radically from each other at these loci. This analysis also allows us to infer many of the steps through which a specific gene or chromosome locus became more complex, relative to its ortholog with a simpler genetic organization.

References:

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