Salamanders' slow slither into genomic gigantism[*]

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Genome size varies enormously across the eukaryotic tree of life (c. 64,000-fold in animals alone), with the largest reported nuclear genomes found in vertebrates (e.g., salamanders, lungfish) and angiosperms (e.g., mistletoe, fritillaries). Yet despite this huge diversity, most genomes are considerably smaller than the largest reported (c. 150 Gb), with the mean size of both vertebrate and plant genomes being similar, c. 5 Gb.

Although clearly outliers, the existence of giant genomes in this subset of animals and plants provides excellent study systems to unpick those processes likely involved in genomic obesity and that may constrain genome size in most species over evolutionary timescales. Such genome expansion is governed predominantly by amplification of highly repetitive DNA, that is, transposable elements (TEs).

Among tetrapods, salamanders have the largest genomes found, including an average size much larger than related amphibians (Fig. 1). Phylogenetic reconstructions suggest that they have evolved large genome sizes since early in their evolutionary history, over a timescale of approximately 150–200 million years (Organ et al. 2011).

The mutational hazard hypothesis (MHH) states that as genomes increase in size, so does the number of mutations that can directly affect the genome due to the increased target DNA, that is, it poses a "mutational hazard" (Lynch and Conery 2003) and a selective cost. Genomes may have evolved to such gigantic sizes due to an inherently lower mutation rate (thereby negating the increased hazard), or simply by a process of increased genetic drift.

Mohlhenrich and Mueller (2016) test this hypothesis in salamanders using a detailed comparison of protein-coding gene sequences between salamanders and frogs, the latter having much more typical small-sized vertebrate genomes (Fig. 1). By analyzing the number and type of substitutions in the DNA sequences, they are able to estimate the relative effect of different types of selection and genetic drift, and also the relative mutation rate.
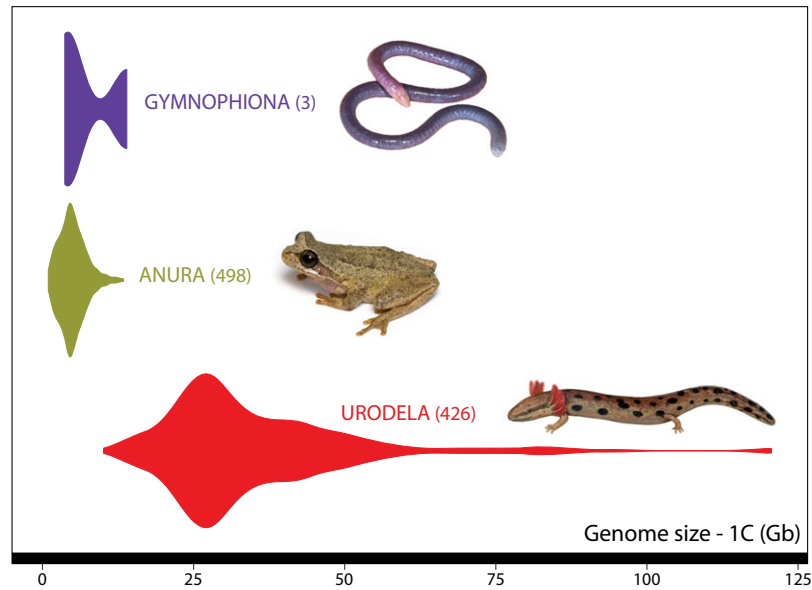
Synonymous substitutions are DNA base changes that do not change the amino acid, whereas nonsynonymous ones do, the latter resulting in functional change. The ratio of nonsynonymous to synonymous substitution rates can therefore reflect selection (directional if >1, purifying if <1, with the strength of genetic drift affecting the efficiency of selection). Compared to frogs, in salamanders, the authors find no clear evidence for increased genetic drift. However, they do find evidence of a lower nucleotide substitution rate in salamanders. This is consistent with the MHH and may explain, in part, why such giant genomes pose less of a "mutational hazard." Nevertheless, the evidence remains equivocal as to whether the reduced "mutational hazard" is the cause or consequence of giant genome evolution.

Giant genomes seem also to be characterized by an inability to remove DNA, when compared to more typically sized genomes (Frahry et al. 2015; Kelly et al. 2015). This in turn is likely influenced by epigenetic processes, such as levels of methylation and how they impact the relative silencing of stretches of DNA.

After genomes reach a certain size threshold, they may be on a "one-way ticket" to becoming obese. In small genomes, however, the disruptive effect of TEs can have a large effect on gene function and are therefore more likely to be silenced and/or efficiently removed (Dodsworth et al. 2015). In brief, as genomes grow, genes become further separated in a sea of repeats, and these elements can then further amplify with minimal effect on gene function (being therefore essentially invisible to selection). Despite the recent insights into the organization of giant genomes, much still remains to be discovered about the mechanistic processes and evolutionary forces that allow genomes to reach such huge sizes.

Figure 1. Violin plots showing the frequency and range of genome sizes in different amphibian groups, together with illustrations on the right for some of the species—from top to bottom *Littoria ewingii*, *Microcarcilia dermatophaga*, and *Necturus lewisi*. Data taken from the Animal Genome Size database (www.genomesize.com). Numbers in brackets following eukaryotic group names refer to the number of genome size estimates incorporated in each plot. Photographs from the top: Wikimedia commons/Wikimedia commons/Joseph E. Trumpey.

LITERATURE CITED

Dodsworth, S., A. R. Leitch, and I. J. Leitch. 2015. Genome size diversity in angiosperms and its influence on gene space. Curr. Opin. Genet. Dev. 35:73–78.

Frahry, M. B., C. Sun, R. A. Chong, and R. L. Mueller. 2015. Low levels of LTR retrotransposon deletion by ectopic recombination in the gigantic genomes of salamanders. J. Mol. Evol. 80:120–129.

Kelly, L. J., S. Renny-Byfield, J. Pellicer, J. Macas, P. Novák, P. Neumann, M. A. Lysak, P. D. Day, M. Berger, M. F. Fay, et al. 2015. Analysis of the giant genomes of Fritillaria (Liliaceae) indicates that a lack of DNA removal characterizes extreme expansions in genome size. New Phytol. 208:596–607.

Lynch, M., and J. S. Conery. 2003. The origins of genome architecture. Science 302:1401–1404.

Mohlhenrich, E., and R. Lockridge Mueller. 2016. Genetic drift and mutational hazard in the evolution of salamander genomic gigantism. Evolution. DOI: 10.1111/evo.13084.

Organ, C. L., A. Canoville, R. R. Reisz, and M. Laurin. 2011. Paleogenomic data suggest mammal-like genome size in the ancestral amniote and derived large genome size in amphibians. J. Evol. Biol. 24:372–380.

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