

Adaptation despite gene flow? – Low recombination helps.

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15,000 years earlier, the Northern half of Europe and North America was buried under a few kilometers of ice. Since then, many organisms have colonized and rapidly adapted to the new, vacant habitats. Some, like the threespine stickleback fish, have done so more successfully than others: from the sea, stickleback have adapted to a multitude of lake and stream habitats with a vast array of complex phenotypes and life histories. Previous studies showed that most of these ‘ecotypes’ differ in multiple divergently selected genes throughout the genome. But how are well-adapted ecotypes of one habitat protected from maladaptive gene flow from ecotypes of another, adjacent habitat? According to a From the Cover meta-analysis in this issue of *Molecular Ecology* (Samuk *et al.* 2017), low recombination rate regions in the genome offer such protection. While inversions have often been highlighted as an efficient way to maintain linkage disequilibrium among sets of adaptive variants in the face of gene flow, Samuk *et al.* (2017) show that variation in recombination rate across the genome may perform a similar role in threespine stickleback. With this study, theoretical predictions for the importance of low recombination regions in adaptation are for the first time tested with a highly replicated population genomic dataset. The findings from this study have implications for the adaptability of species, speciation and the evolution of genome architecture.

Threespine stickleback inhabit a wide variety of habitats, ranging from their ancestral marine habitat to many newly colonized and diverse freshwater habitats. Among most of these habitats, gene flow occurs to varying extent in thousands of different watersheds across the Northern hemisphere, resulting in many replicate populations that share various gene flow and selection regimes. Samuk *et al.* (2017) assembled a population genomic dataset from populations around the globe by taking advantage of both previously published and newly generated datasets, mostly consisting of DNA sequences obtained by restriction-site associated DNA (RAD) sequencing or genotyping-by-sequencing (GBS) as well as whole genome re-sequencing data. Based on ecological differences, geographical connectivity and distance between 52 stickleback populations, they inferred whether pairs of populations experience divergent selection and gene flow, respectively. The authors used habitat differences as a proxy for divergent selection, for example between marine, lake or stream habitats, between young sympatric limnetic and benthic or marine and white species, or between the 2 million years divergent Sea of Japan stickleback and other stickleback ecotypes. While previous studies have contrasted only few gene flow regimes in a single ecotype pair (e.g. Roesti *et al.* 2012; Marques *et al.* 2016), this global dataset now embraces much of the population-level replication in the stickleback model system.

In order to test whether sets of adaptive variants are maintained in low recombination regions, Samuk *et al.* (2017) first identified potential targets of selection or linked loci from outliers in the genome-wide distribution of relative (F_{ST}) and absolute differentiation (d_{XY}). They found that when two populations experienced both gene flow and divergent selection, then selected loci for both F_{ST} and d_{XY} were strongly enriched in low recombination regions (Fig. 1). In contrast, when two populations of the same ecotype or

without gene flow were compared, associations with low recombination regions were weaker (F_{ST}) or absent (d_{XY}). This is compelling evidence that rarely recombining genomic regions may shield sets of adaptive variants from maladaptive gene flow, at least across many replicated stickleback ecotypes sharing the same recombination landscape and genomic make-up. Thus, the genomic landscape of differentiation in stickleback appears to be shaped by the interaction of gene flow and divergent selection with low recombination in the genome, in line with several theoretical expectations (Butlin 2005; Noor & Bennett 2009; Nachman & Payseur 2012). Stickleback thus contrast with flycatchers and sunflowers, in which linked selection, i.e. background and divergent selection, and low recombination determine genome differentiation in the absence or independent of gene flow (Renaut *et al.* 2013; Burri *et al.* 2015). Although linked selection likely contributed to patterns of divergence in threespine stickleback, Samuk *et al.* (2017) show that gene flow and divergent selection generate an enrichment of adaptive alleles, estimated from both F_{ST} and d_{XY} , in regions of low recombination, above and beyond the effects of linked selection, when gene flow is ongoing.

However, as Samuk *et al.* (2017) point out, further interacting mechanisms remain obscure, in particular what influence did evolutionary history or progress along the ‘speciation continuum’ play in producing these patterns? Some stickleback ecotype pairs which currently experience gene flow have a history of allopatry, i.e. an episode in the past without gene flow, followed by gene flow in secondary contact. Limnetic and benthic stickleback, the nearly completely reproductively isolated Japan Sea stickleback or lake-stream ecotypes from different European watersheds fall into this category, while most marine-freshwater and other lake-stream ecotypes have diverged without such an allopatric episode and represent earlier stages in the speciation continuum. Allopatry may have led to the accumulation of differentiation (in particular for d_{XY}) decaying more slowly in regions of low recombination after populations meet again (Noor & Bennett 2009), or to incompatibilities with a stronger effect on reducing gene flow locally in low recombination regions (Noor *et al.* 2001; Rieseberg 2001). Determining the contribution of different histories to the observed correlations of selected loci and recombination will need further investigation.

Over what time scales may adaptive variants accumulate in low recombination regions? Although nearly all parapatric or sympatric stickleback ecotypes studied have diverged since the last ice age, postglacial ecotype divergence has already occurred in previous interglacial periods. Repeated cyclical adaptation to emerging habitats may thus have favored adaptive variants clustering in low recombination regions, which are in turn ‘easier’ to re-assemble after each glacial retreat. Two observations support such an idea: First, the origin of some adaptive variants frequently involved in divergent adaptation, such as the *Eda* locus controlling the defense trait lateral plates, is much older than the most recent postglacial habitat colonization (Colosimo *et al.* 2005). Second, many variants controlling traits relevant to divergent adaptation co-localize in a few genomic regions and these are mostly characterized by low recombination (Peichel & Marques 2017). It remains to be shown how the age of adaptive variants and recurrent adaptation contributed to their accumulation in regions with low recombination.

The findings of Samuk *et al.* (2017) may have implications for the adaptability of species, speciation and genome evolution. Adaptation to new or changing habitats with ongoing gene flow may be more difficult for species with uniform recombination landscapes. Larger variation in recombination rate might thus be associated with frequent ecotype formation or habitat colonization. Species with regions of reduced recombination in the genome might also be predisposed for ecological speciation: when loci important for reproductive isolation happen to be in low recombination regions, selection for adaptation in these regions will automatically link adaptation with reproductive isolation, which in turn further reduces maladaptive gene flow (Butlin 2005). Also, the recombination landscape may evolve itself or genes may re-arrange in low recombination regions over longer time periods (Butlin 2005; Yeaman 2013). It remains to be shown whether stickleback, with their cyclical adaptation to emergent postglacial habitats, are exceptional in that respect or whether gene flow and divergent selection also frequently interact with recombination rate in organisms with a different genomic make-up. The approach chosen by Samuk *et al.* (2017) with high

replication and genome-wide inquiry will be a guide for future studies comparing recombination rate, gene flow and divergent selection.

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Fig. 1: Loci under divergent selection between different stickleback ecotypes cluster in low recombination regions of the genome when gene flow occurs between them – reduced recombination thus ‘protects’ adaptive variants from maladaptive gene flow. Shown are lake and stream ecotypes from Lake Constance, Switzerland (photo credit: David A. Marques).

