

## Spotlight

## Supergenes promote ecological stasis in a keystone species

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**Structural variation can create supergene architectures through tight genomic linkages that maintain traits in favourable combinations. A new study by Sodeland *et al.* links such supergenes in Atlantic cod with species persistence over millennia, despite the fisheries-induced decline in populations. This links intraspecific supergene diversity to ecological stasis, with significant consequences for ecosystem stability.**

Ecological stasis has long puzzled ecologists and evolutionary biologists alike. Fossil record observations demonstrate that many species evolve in a stepwise manner, despite the broadly acknowledged potential of natural populations to undergo rapid microevolution. A recent study by Sodeland *et al.* [1] on Atlantic cod (*Gadus morhua*) demonstrates that three polymorphic supergene regions facilitate ecological stasis (Figure 1). Supergenes have genetic architectures that can maintain tight associations between genetic elements, jointly controlling complex phenotypes by allowing genetic variants across the linked region to be coinherited. The idea that genomes can harbour such tightly linked supergene regions is not new; however, connecting supergene polymorphism maintenance over long timeframes to species persistence sheds important light on the mechanisms governing biodiversity.

The term ‘supergene’ was first coined during the formulation of the Modern

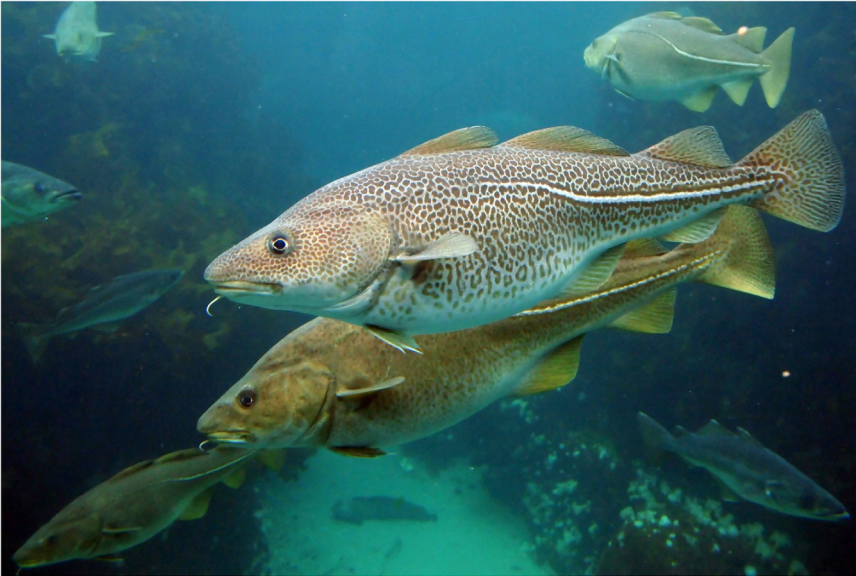
Synthesis by Darlington and Mather [2], who defined it as ‘a group of genes acting as a mechanical unit in particular allelic combinations’. Much of the genetic work then was based on elegant laboratory crossing experiments using *Drosophila*, where large chromosomal changes could be directly observed via light microscopy in giant, puffed-up polytene chromosomes. Applying simple karyotyping techniques, inversion supergenes became visible as distinct chromosome loops in heterokaryotypes (individuals carrying both inversion haplotypes) [3].

Recent work has focused on the processes governing supergene fixation in a population after they arise. A popular idea is that supergene persistence arises from an adaptive benefit, through beneficial linkage between as few as two loci, changes in gene expression, or direct net effects caused by the inversion breakpoints themselves. Supergenes are thought to persist when this advantage remains or becomes even stronger; as such, they facilitate coexistence of multiple, often complex phenotypes. Inversions are also the building blocks of the three supergenes in Atlantic cod [4]. Sodeland *et al.* [1] have combined environmental and genomic data, and knowledge about the fishing intensity since Viking times, to identify the selective forces associated with persistence in this keystone species.

While inversion-induced supergenes have a rich and long history, most of our knowledge comes from laboratory studies or research on model species. Unravelling the eco-evolutionary impacts of supergenes in wild populations has been substantially more difficult. Processes like phenotypic plasticity, gene flow, and spatial population shifts can, for example, lead to substantial phenotypic divergence yet limited genotypic change [5]; deciphering these has been a technical hurdle. Sodeland *et al.* [1] were fortunate because they could leverage recent technical advances

to interrogate whole genomes, and access the recently improved Atlantic cod genome [6]. They could thus deep-dive into the individual genomes of wild Atlantic cod to characterise the demographic history and molecular evolution in the North Sea–Skagerrak–Kattegat system. This area is characterised by pronounced environmental clines, especially salinity, and has thus been nicknamed a ‘natural Darwinian laboratory’. Although visually these Atlantic cod appear phenotypically uniform, genome-wide techniques can reveal hidden structures signifying past survival and mating success. A genome-wide SNP analysis was first applied to detect differentiation in wild populations; this indicated two clearly separate clusters, denoted ‘coastal’ or ‘offshore’ ecotypes. This clustering coincided with the region’s salinity stratification, indicating that coastal ecotypes are probably under environmental selection to cope with reduced habitat salinity [7].

Supergene variation was then quantified to reveal the next layer of genome complexity in three 4–17 Mb large inversions: SG02, SG07, and SG12. This revealed pronounced abundance and frequency shifts throughout the sampling region, a classic sign that natural selection acts on specific supergene combinations in an environmentally dependent context. Theoretical and empirical research indicates that, after fixation, supergenes can undergo rapid evolution, facilitating the divergence of genomic haploblocks within a species. While the adaptive function of supergenes via their ability to peg genes together is well established, studies are increasingly documenting that these haploblocks also accumulate recessive deleterious mutations owing to their reduced population size, particularly when supergenes persist for long periods [8]. The accumulation of these (often private) recessive variants can cause overdominance, facilitating maintenance and generating strong, nonadaptive haplotype



Trends in Genetics

Figure 1. The Atlantic cod (*Gadus morhua*) is a keystone predator on both sides of the Atlantic Ocean. Photographic credit goes to Joachim S. Müller/FLICKR (CC-BY-NC-SA 2.0).

divergence. Clines in inversion frequencies have been observed in other species, notably *Drosophila*, where parallel frequency clines on different continents have been heralded as some of the strongest canonical examples of local adaptation [3]. Owing to the well annotated Atlantic cod genome assembly, Sodeland *et al.* could pinpoint some tentative candidate genes under selection: for example, ion channel activity genes that regulate salinity tolerance, which were overrepresented on SG07 and SG12 compared with the rest of the genome.

The authors then described selection patterns and the history of population demography to identify the evolutionary landscape that facilitated species persistence over larger temporal scales. Whole-genome analyses of representative coastal and offshore ecotypes measured allele frequency spectra and Tajima's *D* to identify DNA sequences that evolved nonneutrally. These analyses showed that a mix of balancing and directional selection exerts selective pressures on

supergenes, consistent with environmentally dependent haplotype fitness. Balancing selection refers to various selective regimes maintaining advantageous genetic diversity at underlying loci, including overdominance, sexual selection, periodical environmental shifts, pleiotropy, and negative frequency-dependent selection [9]. These differing mechanisms have in common that whether an allele is beneficial or detrimental is at least partially dependent on context. An allele is not advantageous or deleterious *per se*: its contribution to individual fitness depends on the environment. Another common attribute is that selection often favours rare alleles, thus countering genetic drift and any associated stochastic variant losses. Studies of natural populations are revealing that balancing selection can promote maintenance of chromosomal inversion-based supergene systems in insects, birds, and fish [3]; this new study indicates the same for Atlantic cod. More importantly, balancing selection appears to have stabilised the genomic portfolio of variation in this keystone species, despite intense fisheries-induced

population declines. This study thus adds to the accumulating evidence that balancing selection can be a prime selective agent, stabilising a species' genome diversity by slowing allelic turnover [9].

Ecological stasis in keystone species is poorly understood, and this study sheds urgent light on the role of long-lived and balanced polymorphisms in the evolutionary puzzle of life. Disturbances to keystone species like Atlantic cod can cause ecosystem reshuffling, with severe consequences for biodiversity, a scenario that seems more likely than ever. Although Atlantic cod has undergone severe fisheries-associated population declines through the past millennium, there is growing concern that it may not be able to keep pace as multiple stressors accumulate. While the presence of supergenes provides a species with the substrate for potentially rapid evolution, this is not a given. One lesson emerging from comparative studies is that the origins and subsequent evolutionary paths of supergenes are not easily predictable. Future work needs to refine models of supergene evolution to provide mature understanding of their general and system-specific dynamics. These new models should seek to disentangle the genetic contributors inside inversions, to quantify the relative impacts of the accumulation of deleterious recessive mutations [8], while also accounting for rare events such as recombination that can selectively purge variants [10]. Emerging techniques that allow functional genetic manipulation of supergenes – (e.g., CRISPR-Cas9) – hold promise to fine-map different haplotypes and verify causal genes that underlie complex supergene phenotypes. Such work will help disentangle the relative contributions of different selective and stochastic mechanisms that impact supergene evolution and the evolutionary fate of species over long timespans.

#### Declaration of interests

No interests are declared.

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