Barrier loci and progress toward evolutionary generalities - Kathryn R. Elmer

This excellent target review by Ravinet and colleagues gives a strong general introduction to the processes involved in speciation-with-gene-flow, issues with identifying barrier loci, and how to study speciation events using genomic methods. The review is divided into three main sections. The first section focuses on "Barriers to gene flow in the genomic landscape". Here the authors clearly outline definitions and concepts that are key to the paper and the research field, such as 'barrier loci' ("loci that contribute to a barrier to gene flow"), the theoretical population genetic conditions under which they arise, and their genome-wide effects. The second section addresses "Other factors modifying the genomic landscape", which considers the role of demographic history, genomic properties such as mutation rates, recombination rates, and gene density, and the influence of background selection. This section is a warning call for the research field, as it highlights processes and properties that may not be given sufficient attention in population genomic studies. Throughout the paper, the authors stress the importance of estimating those modifying factors, in addition to merely estimating differentiation across the genome. These genomic issues can be challenging, especially in non-model systems, and preclude simplistic interpretations.

By the time I had reached the third and final section of the paper, "A road map for the genomic landscape", I must admit I was feeling despair that we could ever disentangle the genomics of speciation in natural systems. The first two sections had emphasised that a formidable range of demographic and structural issues affect genomes and genomic divergence: incomplete lineage sorting, complex population histories of contact and isolation, population size fluctuations, mutation rate variation, genome organisation, and the inconsistent and variable forces of selection and gene flow. These factors vary not only within genomes but also across individuals, across evolutionary time scales, and across space. To add further complexity at all scales, the speciation process itself alters properties of the genome: these are non-linear processes and subject to extensive feedback that amplifies or mutes the effects. This presents great challenges, especially in studying populations in their natural habitats.

But then on this brink, the authors revived and inspired me with their 'road map', which includes concrete suggestions for speciation genomics research. The authors outline six research steps that may facilitate realistic and comprehensive conclusions about barrier loci and genomic divergence. Most or all aspects of the road map cannot be accomplished without an annotated reference genome, genetic maps, and study organisms that can be bred in the lab or subjected to transplant experiments. This remains a challenge for

some research groups and some biological systems. But regardless of resources, the road map can aid researchers in dissecting components of their question, assessing limitations, and reflecting on the most suitable experimental approaches to pursue. Further, throughout the paper the authors make a welcomed effort to clarify terminology, which is important for paving clear comparisons and discussion in the literature.

Understanding evolution in all its complexity will require extensive research on non-model organisms - that is, messy and difficult natural populations adapting and diversifying in their environments. Therefore, I was relieved that the road map has a distinctively non-model air. It includes suggestions for complex systems in nature, where the ability to parameterise all the past and detailed issues is not necessarily available. Yet it is clear from the Target Review and the applied road map that concerted efforts are required to identify true signals of barrier loci and subsequently to validate the functional role of those loci.

In my opinion, this focus on barrier loci - of this review and the research field broadly - begs a question of evolutionary generality. Identifying common processes and patterns of evolution ought to be the long-term goal of the research efforts in evolutionary genomics. But given the great complexity of evolutionary and demographic histories, genomic properties, and environmental selection pressures all fluctuating over time, how often are the lessons learned about barrier loci in a given study species going to be generally applicable? I think this question is far from resolved and only will become clearer with an accumulation of effort across many biological systems.

Therefore, this review led me to reflect on the 'what next' from speciation genomics. In this case, the identification of barrier loci is not the central objective in itself, but rather a key intermediate step in progress towards more generality in understanding the evolution of contemporary biodiversity. To arrive at that goal will require comparisons that go much higher than particular populations of interesting species. For example, what are the properties of genomes in lineages that show particular characteristics? Those that speciate rapidly; that diversify in phenotypic parallels; that colonise new environments readily; that adapt quickly to climate or environmental changes? These questions have direct and immediate utility in biodiversity sciences, medicine, agriculture, aquaculture and conservation. This Target Review focuses on the advances with empirical genomic analyses but has less discussion on how and when barrier loci can, or cannot, aid in discerning common evolutionary patterns.

One example of shared evolutionary patterns touched upon in this review is that of 'parallel evolution'. This is outlined in the road map as part of a step to 'identify selection at barriers, taking modifying factors into account'. Parallel evolution studies are those that assess differentiation at genomic loci or genomic regions across population or species pairs (see review table 2). To that definition, I would add 'while considering the consistency of phenotypes across these replicated environments'. At the fine scale, parallel evolution comparisons across populations within species can explore demographic histories, environmental or ecological contexts of diversification, the formation of barrier loci, and their consistency across stages of speciation and environments. Data from replicated population divergences, including comparing across similar and different environments, have improved power to detect and interpret meaningful signatures of parallelism at the genomic level (Roesti *et al.* 2014). The consistency, or lack of consistency, of barrier loci in contemporary populations can provide key insights to the underlying processes of speciation genomics. This is the case for genomic patterns of evolution from shared ancestral variation, distinguishing *de novo* mutations, and even for the importance of identifying the key phenotypes that are in fact parallel (Elmer & Meyer 2011; Berner & Salzburger 2015).

I do not propose that parallel evolution is a panacea to solving all the challenges of speciation genomics, but I think there are some strengths that can be drawn from research on barrier loci, which are very relevant for seeking evolutionary generality. Thus my reasoning for further exploring the strengths of the parallel evolution framework in the context of speciation genomics are twofold here. First, it is an approach that compares replicate phenotypes, and these replicate phenotypes are a proxy for similar adaptations to environmental challenges. In a manner of speaking, this is a way of seeing evolutionary problems being solved in equivalent ways. However, these can be by similar or dissimilar evolutionary routes (Elmer et al 2014). Second, parallel evolution research intrinsically involves a structured analysis of populations or lineages in replicate. These comparisons can provide insight for testing barrier loci, assessing properties of the surrounding genome, and the continuity of barrier loci across evolutionary scales. Such a context is important for delimiting the genetic variation that is shared ancestrally vs. derived, or pervasive vs. unique, and thereby may facilitate disentangling factors such as selection, shared genomic elements, or recombination patterns that result in contemporary patterns of similarity across genomes (Brawand et al. 2014; Burri et al. 2015; Berner & Salzburger 2015). This will be most powerful when it involves explicitly controlled phylogenetic comparisons. I realise a detailed exploration of the utility of parallelism and evolutionary replicates was beyond the scope of this Target Review. My aim here is simply to offer an extension of the road map and explore the potential at some of its intersections.

In short, such replicated comparisons, at shallow and deeper evolutionary scales, may have the power to inform about genomic characteristics within lineages that are associated with diversification and then the consistency of those characteristics across higher taxonomic levels. Importantly, such an understanding might then facilitate predictions about which loci act as barriers and the generality of those barriers across lineages and across a breadth of taxa. This in turn may feed back into our advancing knowledge of fundamental evolutionary processes, and subsequently new research directions. Accurate inference of barrier loci is a key first step.

The progress of speciation genomics from barrier loci to evolutionary generalities is well underway, as evidenced by the range of empirical examples and mechanisms explicated in this Target Review. It has an excellent spirit of blue skies thinking, of pushing the envelope of where speciation genomics research can go, and of inspiring ideas of 'if you could do anything, what would you do with your study system'. This is mixed with some practical suggestions and cautions with an emphasis on rigour at each research step. This review and my notes scrawled across in pencil will sit on my desk as a resource for my own work as it is a useful and timely addition to the literature.

Acknowledgements

I thank Mike Ritchie for the invitation to contribute and Kevin Schneider, Arne Jacobs, Barbara Helm, and Konrad Lohse for valuable comments on an earlier draft.

References

Berner, D. & Salzburger, W., 2015. The genomics of organismal diversification illuminated by adaptive radiations. *Trends Genet* **31**: 491-499.

Brawand, D., Wagner, C.E., Li, Y.I., Malinsky, M., Keller, I., Fan, S., Simakov, O., Ng, A.Y., Lim, Z.W., Bezault, E., Turner-Maier, J., *et al.* 2014. The genomic substrate for adaptive radiation in African cichlid fish. *Nature* **513**: 375-381.

Burri, R., Nater, A., Kawakami, T., Mugal, C.F., Olason, P.I., Smeds, L., Suh, A., Dutoit, L., Bureš, S., Garamszegi, L.Z., Hogner, S. *et al.* 2015. Linked selection and recombination rate variation drive the evolution of the genomic landscape of differentiation across the speciation continuum of *Ficedula* flycatchers. *Genome Research* **25**: 1656-1665.

Elmer, K.R. & Meyer, A., 2011. Adaptation in the age of ecological genomics: insights from parallelism and convergence. *Trends Ecol Evol* **26:** 298-306.

Elmer, K.R., Fan, S., Kusche, H., Spreitzer, M.L., Kautt, A.F., Franchini, P. & Meyer, A., 2014. Parallel evolution of Nicaraguan crater lake cichlid fishes via non-parallel routes. *Nature Communications*, *5*, p.5168.

Huang, W., Massouras, A., Inoue, Y., Peiffer, J., Ràmia, M., Tarone, A.M., Turlapati, L., Zichner, T., Zhu, D., Lyman, R.F. & Magwire, M.M., 2014. Natural variation in genome architecture among 205 *Drosophila melanogaster* Genetic Reference Panel lines. *Genome Research* **24**: 1193-1208.

Nosil, P. 2012. *Ecological Speciation*. Oxford University Press, Oxford, UK

Roesti, M., Gavrilets, S., Hendry, A.P., Salzburger, W. & Berner, D. 2014. The genomic signature of parallel adaptation from shared genetic variation. *Mol. Ecol*. **23**: 3944–3956.

Seehausen, O., Butlin, R.K., Keller, I., Wagner, C.E., Boughman, J.W., Hohenlohe, P.A., Peichel, C.L., Saetre, G.P., Bank, C., Brännström, Å. *et al*. 2014. Genomics and the origin of species. *Nature Rev Genet* **15**: 176-192.