

NEWS AND VIEWS

PERSPECTIVE

Linking conceptual mechanisms and transcriptomic evidence of plasticity-driven diversification

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The East African cichlid fishes provide text book examples of adaptive radiation. Diversification and speciation of cichlids associate with variation in diet and trophic morphologies among other ecological, behavioural and morphological phenotypes (Kocher 2004). Numerous case studies in cichlids reveal a role of developmental plasticity in generating jaw ecomorphs in response to variation in feeding ecology that can facilitate niche exploitation and subsequent diversification (e.g. Meyer 1987). Specifically, genetic divergence among such environmentally induced morphs can occur via reproductive isolation due to divergence in habitat and resource use in combination with genetic assimilation of environmentally induced phenotypes (West-Eberhard 2003; Pfennig *et al.* 2010). Expansion of this conceptual model has been hampered in part by the limited knowledge of the molecular mechanisms of plasticity in nonstandard model systems and the associated lack of evidence linking the molecular mechanisms of plasticity to those that generate phenotypic divergence among populations and taxa. In this issue of *Molecular Ecology*, Gunter *et al.* (2013) identify the transcriptional mechanisms of diet-induced lower pharyngeal jaw (LPJ) plasticity in the cichlid fish *Astatoreochromis alluaudi*. Natural populations of *A. alluaudi* exhibit variation in jaw morphology in relation to diet hardness. Among the plastic responses to diet are adjustments to the LPJ ranging from a robust molariform morph in response to a hard diet to a more gracile papiliform morph in response to a soft diet (Fig. 1). Gunter and colleagues induced developmental plasticity of the *A. alluaudi* jaw using diet manipulations and compared LPJ transcriptomic profiles of the resulting morphs. In this foundational work, the authors identify 187 differentially expressed genes that underlie the development and maintenance of diet-induced LPJ morphologies. This list includes a wide range of genes spanning from broad-acting transcription factors to signalling molecules and structural genes. Here, I examine the ontogeny of the

molecular response to mechanical strain imposed by diet hardness and discuss the role of the stages of this response in the evolution of plasticity and plasticity-driven diversification.

Keywords: development and evolution, east African cichlids, phenotypic plasticity, transcriptomics

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Molecular Biology of Mechanotransduction: Transduction of environmentally imposed signals proceeds through a progression of stages that receive and integrate environmental signals ultimately generating a physiological response. The gene expression profiles provided in this study cleverly capture these distinct stages of mechanotransduction. Animals are raised to maturity on diets differing in hardness inducing the development of the two distinct morphs. Once morphs are established, jaws of mature individuals are dissected within 30 min of feeding on their respective hard or soft diets. Thus, the differentially expressed genes identified in their analysis can be putatively assigned to the distinct stages of mechanotransduction based on their predicted function (Fig. 2). This recreates the ontogeny of signal transduction that translates mechanical strain into a LPJ phenotype (for expanded discussions of the molecular biology of mechanotransduction, see Mantila Roosa *et al.* 2011; Nomura & Takano-Yamamoto 2000). Briefly, mechanical strain causes damage and other changes to the physical environment of the cell eliciting a chemical cellular response. At this stage, the intracellular response and intercellular communication are mediated by the action of mechanosensitive ion channels and gap junctions that cause an influx of calcium, activation of calcium-signalling pathways and induction of GTPases (Nomura & Takano-Yamamoto 2000; Mantila Roosa *et al.* 2011). This cellular response leads to a rapid activation of immediate early genes. These broad-acting transcription factors integrate the environmental signal into a molecular level response resulting in the activation (or repression) of signalling molecules and transcription factors that regulate the downstream physiological response that builds the structural change. Specifically, action of growth factors and specific transcription factors results in increases in cell proliferation and differentiation as well as matrix secretion and cytoskeleton organization (*ibid.*). In addition, repression of other signalling molecules such as cytokines and chemokines minimizes bone remodelling and promotes matrix secretion (Mantila Roosa *et al.* 2011).

The Role of Immediate and Downstream Genes in Plasticity-Driven Divergence: Plasticity-driven phenotypic divergence can result from genetic accommodation and/or genetic assimilation of environmentally induced phenotypes among

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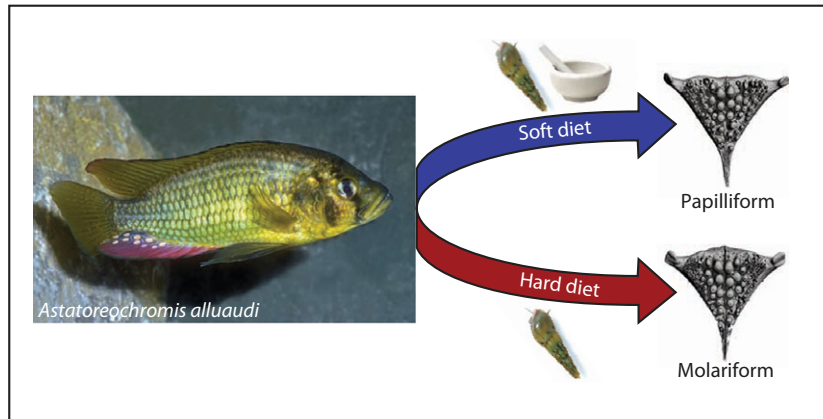


Fig. 1 Phenotypic plasticity in the lower pharyngeal jaws of the cichlid fish *Astatoeochromis alluaudi*. A mechanically stimulating diet such as hard-shelled snails induces a molariform phenotype with larger molar-like teeth set in a larger, denser jaw, in comparison with the papilliform phenotype, which develops in response to a soft, nutritionally equivalent diet of pulverized snails. Photographs were kindly provided by Helen Gunter.

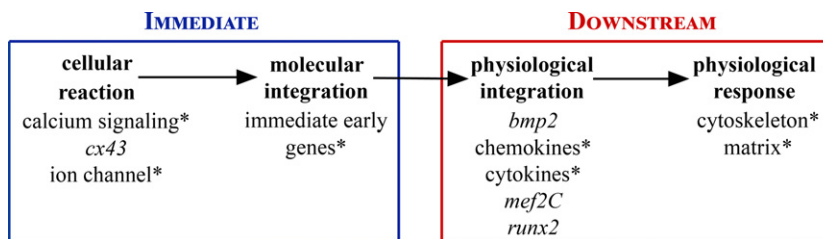


Fig. 2 Genes and gene families differentially expressed in *A. alluaudi* LPJ in response to mechanical strain imposed by a hard diet. Differentially expressed genes are grouped by their predicted role in either the immediate or downstream responses to mechanical strain. While the immediate genes may be the targets of genetic accommodation, only the downstream genes should be the targets of genetic assimilation. See additional discussion in the text. Specific gene names of the listed families (indicated by an asterisks) are provided in Table 2 (Gunter *et al.* 2013).

populations (West-Eberhard 2003; Pfennig *et al.* 2010). Genetic accommodation is a mechanism by which an induced phenotype becomes evolutionarily adaptive through quantitative genetic changes (Suzuki & Nijhout 2006). This can result in either increases or decreases in environmental responsiveness of phenotype development. Genetic assimilation is the specific case in which the development of an induced phenotype loses environmental responsiveness and is constitutively expressed even in the absence of the original trigger (Waddington 1953). Whereas loss of responsiveness to environmental signals results in the consistent development of the ground state phenotype, genetic assimilation results in the consistent development of the induced phenotype. Thus, when variation among environments favours the evolution of distinct developmental strategies, phenotypic divergence among populations can become fixed. For example, populations of *A. alluaudi* may differ in their developmental responsiveness to diet with some populations exhibiting fixed development of the papilliform morph and others the molariform morph regardless of diet hardness (see discussion in Gunter *et al.* 2013).

The genes and developmental pathways that make up the immediate and downstream components of the response to

mechanical strain (Fig. 2) should play different roles in genetic assimilation versus genetic accommodation. The immediate-level genes trigger the plastic response by modulating existing pathways—the downstream genes—that regulate skeletal development, growth and metabolism both in the presence and in the absence of mechanical strain. Loss of environment dependence associated with genetic assimilation requires decoupling of the external signal from phenotype development. Thus, at the transcriptional level, genetic assimilation should reflect fixation of expression patterns in the downstream genes rather than the immediate genes. On the other hand, adjustments to the level of environmental responsiveness associated with genetic accommodation can result from changes in reactivity of immediate-level genes to environmental signals, from interpretation of this response by downstream genes or a combination. The relative importance of these mechanisms for plasticity evolution is an empirical question open for investigation.

Hypothesis Testing Using Comparative Transcriptomics: Next-generation sequencing techniques are increasingly applied in a diversity of taxa including ecological and evolutionary model systems like cichlids. These methods generate an unprecedented wealth of data that can inform longstanding

debates on the mechanisms and evolutionary significance of developmental plasticity (Aubin-Horth & Renn 2009; Beldade *et al.* 2011). Evidence will come in part by showing that the mechanisms that underlie the response to environmental signals also result in phenotypic divergence among taxa (Pfennig *et al.* 2010). However, what this means at the transcriptional level is unclear. In fact, the sheer number of genes differentially expressed, even between intraspecific morphs, can be overwhelming (Aubin-Horth & Renn 2009). How can we sift through similarities and differences in gene expression profiles to find evidence of a role for plasticity in evolutionary diversification? It will certainly require hypotheses of what broad gene expression patterns look like under different mechanisms of plasticity-driven diversification (e.g. see Renn & Schumer 2013). For plastic phenotypes like the *A. alluaudi* LPJ, the environmental trigger is clear, and the ontogeny of the molecular response can be tracked. In this case, assigning differentially expressed genes to their specific roles in generating the phenotypic response to the environment highlights gene expression patterns expected to associate with distinct models of plasticity-driven diversification. This type of approach enables the use of comparative transcriptomic data—for example comparisons of LPJ transcriptomes of fixed molariform and plastic populations of *A. alluaudi*—as evidence of genetic assimilation.

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