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Bilaterian evolution: Tissue-specificity follows gene duplication

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A comparative transcriptomic analysis of eight tissue types in twenty bilaterian species reveals the long-lasting effects of genome duplication on the evolution of novel tissue-specific gene expression patterns.

The bilaterian clade displays striking morphological and functional diversity, ranging from simpler morphologies in flatworms or nematodes, to more complex body plans in insects or vertebrates. Although the defining feature of this clade is simply the presence of a bilaterally symmetrical body plan during embryonic development, most extant bilaterians also possess elaborate organ systems, including nervous, excretory, and digestive systems¹⁻³. The nature of the last common bilaterian ancestor has been intensely debated⁴. However, it is now accepted that this ancestor – which existed more than 600 million years ago – already possessed primitive forms of the major tissue types and organ systems found in most bilaterians^{5,6}, and that its genome likely encoded the regulatory elements required for cell differentiation from a common genomic blueprint⁷. Writing in *Nature Ecology and Evolution*, Mantica and collaborators⁸ characterize gene expression patterns responsible for tissue-specificity in the bilaterian ancestor and study how these patterns evolved. Through a comprehensive comparative analysis of gene expression patterns in eight tissue types across twenty bilaterian species, the authors show that lineage-specific gains of tissue-specific gene expression were associated with gene duplication events and the emergence of specialized tissue types.

The authors adopted a broad sampling strategy that provided balanced representation of the protostome and deuterostome branches within a mirror-like phylogeny of bilaterians, with insects and vertebrates as focal clades (Figure 1). This species sampling strategy enabled Mantica and collaborators to compare evolutionary events between protostome and deuterostome lineages with the same phylogenetic relatedness and tree topology within each branch. While previous evolutionary analyses of gene expression focused on vertebrates⁹, here the authors sample a much broader phylogenetic range, including insects, vertebrates and other bilaterian species. They compared transcriptomes of the nervous, digestive and excretory tissues; male and female gonads; and the epidermis and adipose tissue. To perform comparative gene expression analyses, the authors identified 7,178 homologous gene families (or orthogroups) that were likely present in the last common ancestor of all studied bilaterian species. These orthogroups included paralogous genes, which enabled authors to study the role of gene duplication in the evolution of tissue-specific gene expression.

Approximately 7% (506) of all orthogroups exhibited conserved tissue-specific expression among bilaterian species and were thus inferred to have been tissue-specific in their last

common ancestor. This will be an underestimation of the complete repertoire of ancestral tissue-specific genes, as descendant clades probably underwent losses of expression specificity. The conserved tissue-specific orthogroups likely reflect the core, ancestral functions of each tissue. For example, the conserved neural-specific module was enriched in genes related to synaptic transmission and neuronal morphology, whereas the conserved testis-specific module was dominated by genes involved in cytoskeleton- and cilium-related biological processes relevant for sperm morphology and motility. Supporting their inferred origin in the bilaterian ancestor, the proximal regulatory regions of conserved tissue-specific genes were also enriched in binding sites for transcription factors considered to be “master regulators” of tissue development.

Mantica and collaborators then investigated the repertoires of tissue-specific genes and the degree of evolutionary conservation of tissue-specificity in each focal species, from which they inferred lineage-specific gains and losses of tissue-specificity (Figure 1). Tissue-specificity showed highly dynamic patterns of gains and losses during bilaterian evolution. Although almost half (47%) of all bilaterian orthogroups were tissue-specific for at least one species and one tissue, tissue-specific expression patterns were largely non-overlapping among species. This illustrates how highly conserved gene families inherited from the bilaterian ancestor were independently co-opted into the tissue-specific gene repertoires of individual descendant species.

Interestingly, the authors found that evolution of tissue-specific expression patterns was tightly linked to gene duplication events throughout the bilaterian phylogeny. The number of gains in tissue-specificity was highest in the ancestor of Vertebrata, which is known to have undergone two rounds of whole genome duplication¹⁰. This is consistent with Ohno’s proposal from more than fifty years ago, which suggested that gene duplications are a major source of evolutionary novelty¹¹. Functional divergence between duplicated gene copies is often thought to occur through subfunctionalization (where each gene copy retains a distinct subset of its ancestral roles) or neofunctionalization (where one of the gene copies acquires a novel function). In this case, Mantica and collaborators show that gene duplication can lead to the emergence of tissue-specific expression through specialization – a process in which one of the two gene copies becomes tissue-specific while the other one retains the broad expression pattern of the ancestral gene. Intriguingly, the association between gene duplication and tissue-specificity was not restricted to the evolutionary period immediately following the duplication event, but appeared to linger throughout evolutionary time. This suggests that the impact of whole genome duplications on the functional diversification of the ancestral gene repertoire may be even stronger than previously suspected.

The study by Mantica and collaborators brings unprecedented insights into the origin and evolution of tissue-specific expression patterns in bilaterian organisms. Understandably, some bilaterian lineages were under-represented or not included in this analysis, mainly due to the difficulty of collecting comparable biological samples. As such, numerous intriguing questions remain to be addressed, including the fate of ancestral tissue-specific genes in bilaterian lineages with secondary body plan simplifications¹². Additional studies are also required to determine whether the association between gene duplication and emergence of tissue-specific gene expression is persistent across other eukaryotic clades. Fortunately, the present study not only represents an important resource for researchers, but also provides a

strong conceptual foundation for future studies attempting to elucidate the early evolution of tissue-specific gene expression.

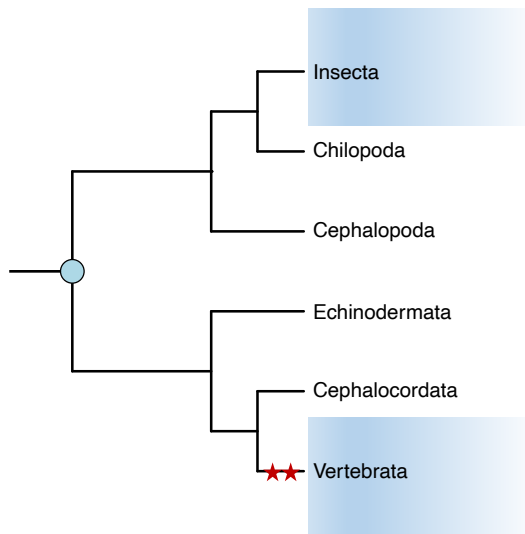
Competing interests policy: The author declares no competing interests.

Figure 1. Evolution of tissue-specific gene expression patterns. a) A simplified phylogenetic tree of the Bilaterian lineages studied by Mantica and collaborators⁸. Stars indicate the two rounds of whole-genome duplication that occurred in the Vertebrata ancestor. b) An example of an ancestral tissue-specific expression pattern that is conserved in Insecta and Vertebrata. c) An example of a gain of tissue-specificity in Vertebrata, with the expression level of a gene being distinctly higher in the testis tissue (T). By contrast, the same gene retains relatively similar expression levels across all tissues in Insecta.

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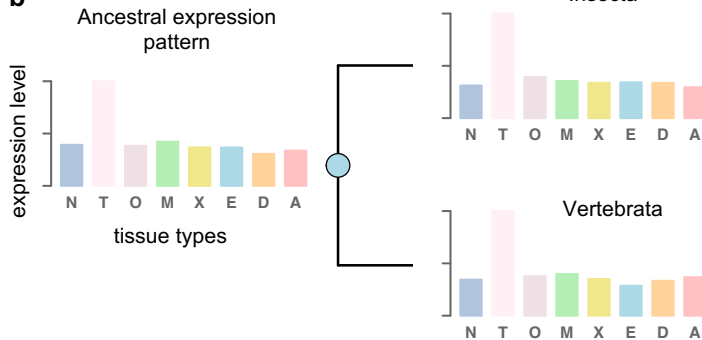
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a

- ★ Whole-genome duplication
- Last common bilaterian ancestor

Tissue types

N Neural	X Excretory
T Testis	E Epidermis
O Ovary	D Digestive
M Muscle	A Adipose

b**c**