

**Fairy tale:** Statistical analyses can show that ancient fairy tales have likely evolved from common ancestors of the Indo-European language groups or even from the culture that spoke the Proto-Indo-European language. (Image: From *The Folktales of Bengal* illustrated by Warwick Goble.)

Silva from the New University of Lisbon, Portugal, and Jamshid Tehrani from Durham University, UK, have recently shown that, among dozens of folk tales that share ancient roots in Indo-European cultures, at least one arises from the common ancestor, Proto-Indo-European (R. Soc. Open Sci. (2016) 3, 150645).

Graça da Silva and Tehrani used the Bayesian analysis mentioned above to establish a phylogeny of folk tales involving magic that are found in different Indo-European traditions. To distinguish between vertical transmission through historical time and horizontal spread between neighbours they relied on Atkinson and colleagues' phylogenetic tree of Indo-European languages as a proxy for cultural inheritance.

They discovered strong phylogenetic connections in dozens of common types of folk tales, mostly reaching back to the major branches of Indo-European. For instance, the authors report that the essential content of Beauty and the Beast as well as Rumpelstiltskin harks back to the early days of Western Indo-European languages, so they may have come to Europe with the Yamnaya expansion.

One type of tale, 'the smith and the devil', is found both in European and South Asian branches of Indo-European cultures, and the authors say

they can show with confidence that its root is in the common ancestral culture that spoke Proto-Indo-European. As the smith required in this tale proves the knowledge of metallurgy in the culture of its origin, this finding supports the Bronze-Age localisation of PIE in the steppe rather than the early agriculture link in Anatolia, where metallurgy was as yet unknown at the time when agriculture started to spread.

Intriguingly, premonitions of this wide-ranging connection between Indo-European cultures are as old as the study of their linguistic relationship. Wilhelm Grimm (1786–1859), in the preface of an edition of the traditional German tales he famously collected with his brother Jacob (1785–1863), expressed his conviction that these tales were part of an ancient Indo-European oral tradition.

Now, with the methods of ancient DNA and statistical analyses, scientists can show that Grimm's hunch was true to fact and the genetic, linguistic and cultural connections ranging from the south of Asia to the north of Europe are due to a shared family tree likely rooted in the Pontic Steppe, and not just fairy tales.

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## Book review

# Darwin meets Waddington

Steven Henikoff

*Extended Heredity: A New Understanding of Inheritance and Evolution*

Russell Bonduriansky and Troy Day (Princeton University Press, Princeton, NJ; 2018)

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C.H. Waddington introduced the term 'epigenetic' to describe a conceptual framework for developmental decisions as they were understood by the mid-1900s. Later the term was applied to silencing phenomena that show clonal inheritance, such as the orange and black coat color patches of the calico cat resulting from X-chromosome inactivation. However, in recent years, this term has exploded in popularity, first among researchers interested in mechanisms of development, and then as a fad for describing anything that affects gene expression but is not a mutation. The term has permeated popular culture, often as a marketing gimmick, such as 'epigenetic dentistry'. Excitement about epigenetics has also fueled wishful thinking about controlling one's own genes through epigenetics. Perhaps nurture controlling nature is not such a crazy idea: higher levels of maternal grooming in mice were recently reported to increase mobilization of transposable elements specifically in the hippocampi of offspring [1]. With such surprising findings being reported with increasing frequency, it seems worthwhile to keep an open mind as to what epigenetics is capable of explaining.

Although there is little that is remarkable about levels of gene expression changing in response to environmental perturbations, such as maternal grooming, we are especially intrigued when such effects are transmitted through eggs or sperm. There are many examples of genomic imprinting, in which epigenetic modifications, such as DNA methylation, are passed through the gametes and affect post-zygotic development. However, whether

or not transgenerational effects are sufficiently persistent that they can be subject to natural selection has long been a contentious question. In their new book, *Extended Heredity*, Russell Bonduriansky and Troy Day marshal the arguments in favor of epigenetic and other influences not encoded in DNA sequence as profound contributors to evolution. By bringing together the large body of evidence for non-DNA inheritance in a single narrative, the authors make a persuasive case that genes are not the only determinants of Darwinian evolution.

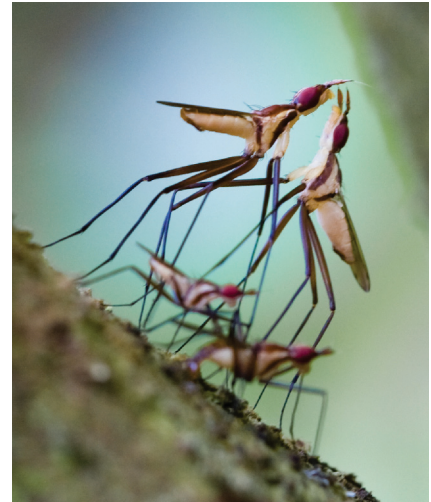
DNA methylation is the clearest example of an epigenetic change that can persist over generations, long enough to be subject to forces of selection. For example, the striking radially symmetric ‘peloric’ floral form of toadflax described by Linnaeus (*Linaria vulgaris*) is caused by a DNA methylation ‘epimutation’, not by mutation of a DNA sequence. The many examples of heritable DNA methylation in flowering plants likely reflect the lack of a global resetting process during gamete and embryo production and the reliance on gene regulation by DNA methylation during the development of endosperm, extraembryonic tissue analogous to the mammalian placenta that provides nutrients to the developing embryo. In contrast, except for imprinted genes, DNA methylation is globally erased in mammalian germ lines, and it remains unclear whether or not mammalian epialleles persist long enough to be subject to Darwinian selection. However, other forms of non-genetic inheritance have been documented, especially small RNAs, which can in principle be transmitted through the germ line and travel through the vasculature to potentially mediate gene regulatory processes.

A striking example that illustrates how non-genetic inheritance of behavior may be subject to natural selection comes from the authors’ own studies of the mating behavior of the neriid fly, *Telostylinus angusticollis*. In nature, males vary remarkably in height, but, when grown in the lab, they are all the same size. By diluting larval food, the size of adult males can be regulated, and the ejaculate of larger males results in the production of larger offspring. A female who first mates with a well-fed male also produces larger offspring

after a second mating with a smaller male fed on diluted food, even when the first male was not their father (a form of extra-parental inheritance classically known as telegony). We might imagine that females who are less choosy about a mate after their first clutch will be more reproductively successful than females who wait for a bigger male to stop by, offsetting likely costs associated with larger size. Note that the evolution of female choice driven in part by non-genetic inheritance in this case can fit comfortably within the standard Darwinian paradigm, and is not a case of Lamarckian inheritance of acquired characteristics.

Unlike mutations, which are very low-frequency events that are strictly heritable, epigenetic changes are frequent, but with low heritability. A change in the local environment is more likely to select for an adaptive epigenotype than an adaptive mutation because there are more of them, but they are short-lived. Extended heredity might work when an adaptive epigenetic change lasts long enough in a population for acquisition of a genetic adaptation in an individual, in which case the epimutation and the mutation can ratchet together along the adaptive landscape. Detecting whether such a process has occurred is challenging because of the transience of epimutations, and one might be skeptical that this is an important evolutionary process. However, the concept becomes compelling by expanding the extended heredity concept to include cultural inheritance. For example, the authors describe the scenario whereby polymorphic alleles causing continued production of the enzyme lactase after weaning in humans are thought to have co-evolved with dairy farming from our lactose-intolerant ancestors. Over the past several thousand years, Darwinian selection has resulted in the near ubiquity of lactose tolerance in parts of the globe where milk is consumed by adults and lactose intolerance where it is not.

By including extrinsic influences, such as parental care and culture, the authors sidestep the nature versus nurture dichotomy. This might seem acceptable from a theoretical perspective, but from a mechanistic perspective extended heredity defined



**Fly tournament.**

*Telostylinus* males size one another up while females observe. (Photo: © M. Janda 2008.)

in this way represents a collection of unrelated phenomena grouped together only because they are not directly encoded in DNA sequence. A key mechanistic distinction is between processes intrinsic to the individual, both genetic and epigenetic, and processes attributable to the individual’s external environment, including nurture and culture. Lumping DNA methylation together with processes that do not directly involve DNA, such as cultural and environmental influences, ignores mechanism, insofar as DNA methylation is a physical feature of DNA. Like DNA sequence, DNA methylation is inherited semi-conservatively and is repaired by some of the same base-excision repair proteins that act on unmodified DNA bases. Likewise, chromatin and DNA-binding proteins that remain associated with DNA during replication and are inherited through the germ line are more sensibly grouped with genetic rather than with behavioral or cultural components of inheritance. Referring to DNA methylation and histone modification as non-genetic processes is a semantic distinction that seems to have no other purpose than to fit biological facts into the authors’ evolutionary scenario.

Within the epigenetics community, there is a lively debate about mechanisms of transgenerational inheritance, with small RNAs, DNA methylation, histone modifications and DNA-binding proteins having their

proponents and critics [2]. The authors provide a comprehensive and up-to-date description of exciting advances in transgenerational epigenetics — a field that continues to be demystified. For example, Waddington's experiments selecting for stress-induced phenotypes that led to his epigenetic framework are now thought to have been caused by insertions and deletions resulting from stress-induced transposon mobilizations [3]. This example emphasizes the importance of first ruling out genetic explanations for transgenerational phenomena before jumping to conclusions about non-genetic inheritance.

Unfortunately, when it comes to observational evidence, the authors are all too ready to propose epigenetic explanations that do not bear scrutiny. For example, there is uncritical acceptance of conclusions from the famous Swedish Överkalix cohort of a century ago based on the supposed effects on health and longevity when previous generations were subjected to different boom-or-bust cycles. Even if the weak associations described for the rather arbitrary subdivisions of data are statistically valid, it is impossible to distinguish true epigenetic effects from confounding environmental variables. The authors recognize the distinction between nature and nurture in familial settings, as they acknowledge that the obesity of offspring of men exposed early in gestation to the Dutch Hunger Winter of 1944–1945 might have been influenced by the habits and resources of their overweight fathers. Such was the conclusion of the authors of the original study based on solid evidence and it was sufficient to fully explain the data [4], but Bonduriansky and Day favor an epigenetic explanation, despite the multiple, unknown steps required for such a mode of inheritance to be at all plausible.

By not delving into the details of molecular processes elucidated in controlled experimental studies, the authors inadvertently overstate the likelihood of epigenetic inheritance being responsible for transgenerational effects. For example, the poster child mechanism for transgenerational inheritance of a starvation response akin to the Swedish and Dutch examples is the transmission of small RNAs in the worm *Caenorhabditis elegans*,

which triggers an evolved starvation response in offspring by targeting nutritional genes [5]. However, a crucial component of this pathway is the enzyme RNA-directed RNA polymerase, which amplifies the transmitted RNAs in the worm, but is missing in vertebrates. This is not to say that abundant small RNAs in sperm cannot provoke an early developmental change in vertebrate embryos — an attractive prospect — but rather that, by not addressing the mechanistic distinctions, the authors overstate the likelihood that epigenetics is responsible. Without a plausible amplification mechanism, the enormous post-zygotic dilution of small RNAs during development makes it an unlikely mediator of behavioral traits. It is unfortunate that the authors use specious examples of supposed transgenerational epigenetic persistence to warn readers of unfounded threats to the welfare of future generations by new technologies, such as gene editing to treat diseases and improve crops.

Despite my reservations about the authors' unlikely mechanistic interpretations and their doomsday speculations that lack a solid foundation, the many fascinating examples of non-genetic adaptations make the book thought-provoking and entertaining. I just hope that the concept of extended heredity will not become the next marketing gimmick.

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## Q & A

### Claus Schwechheimer

*Claus Schwechheimer studied biology at the University of Heidelberg, Germany, and graduated in biotechnology from the École Supérieure de Biotechnologie de Strasbourg (ESBS), France. After a PhD with Mike W. Bevan at the John Innes Centre in Norwich, UK (1994–1998), and a three-year postdoc with Xing Wang Deng at Yale University, USA (1998–2001), he returned to Germany in 2001 to start his own group at the Center for Plant Molecular Biology at Tübingen University. In 2008, he obtained his current position as a Full Professor and Chair for Plant Systems Biology at the Technical University of Munich. Since 2011, he has been the coordinator of a DFG-funded plant research network in the Munich area focusing on molecular mechanisms controlling yield and yield stability in plants (CRC924). In 2015, he was a fellow of the Nirit and Michael Shaoul Fund at Tel Aviv University, Israel. Throughout his career, his research has concentrated on plants, but often addresses questions that are of relevance to other biological systems. Research in his laboratory was originally directed towards understanding the role of the ubiquitin–proteasome system, which brought him to his current research themes on the roles of the hormones auxin and gibberellin in the regulation of plant growth.*

#### What turned you on to biology in the first place?

When I was at high school, I had never considered studying natural sciences. I majored in French, History, Music and, because it was compulsory, Maths and German. In the mid-1980s there were many political and ecological topics that absorbed my attention. I was also active in various music groups and had developed a certain interest in the Middle East. During a consultation at the student counselling office at Heidelberg University, I was told that there weren't any jobs for people graduating in Middle Eastern studies.