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What are the mechanisms behind transgenerational epigenetic inheritance?

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Abstract

It has recently become clear that in some circumstances Lamarck may have been right. There are a growing number of examples where a clear case can be made for the inheritance from parent to offspring of environmentally acquired gene expression changes. The more complex and outbred the organism however, the more difficult this inheritance is to study. I am studying this phenomenon using a model organism, the nematode *C. elegans*, and will present data showing a clear case of transgenerational memory as well as some clues to the mechanism by which this may occur.

We show that RNAi-induced silencing of a single-copy GFP transgene can be inherited for multiple generations in the absence of the RNAi trigger, and that this silencing correlates with the presence of small RNAs targeted to the transgene. Through a forward genetic screen and a candidate gene approach we have identified a set of mutants that fail to inherit transgene silencing. These mutants include a core set of nuclear RNAi and chromatin pathway genes, including an RNA-binding argonaute protein, as well as histone methyltransferases, suggesting that both small RNAs and chromatin modifications are necessary for effective transmission of epigenetic silencing between generations. Furthermore our recent data suggest that there are three distinct phases to heritable silencing – Initiation, Establishment and Maintenance. The histone methyltransferase SET-25 and the putative histone methyltransferase SET-32 are required for effective transmission of transgene silencing, but our recent data suggest that they are involved primarily in establishment of a transgenerational mark and not for long-term maintenance of the silencing.

Bio

Alyson completed her undergraduate degree in Molecular Biology and Genetics (Advanced) at the University of Sydney. After completing an Honors project investigating Anarchy in honeybees with Dr Ben Oldroyd, she decided that her real passion lay in the area of epigenetic – the interplay between the environment that an organism encounters during its lifetime and gene expression. Her PhD in genetics and epigenetic (with Dr Emma Whitelaw) was also through the University of Sydney, but she got to spend a couple of happy years at Queensland Institute of Medical Research when the lab relocated.

After a few years in Brisbane she moved over to Cambridge, UK, where she spent four and a half years as a postdoctoral research fellow in the lab of Dr Eric Miska. Here she brought her love of epigenetic to a new model organism – the nematode worm *Caenorhabditis elegans* and established a robust assay for studying transgenerational epigenetic inheritance. She also learnt all about the weird and wonderful world of small RNA molecules, as well as dabbling in the anti-viral innate immune response.

Now back at the University of Sydney Alyson currently holds a DECRA fellowship, and is studying transgenerational epigenetic inheritance, with a particular focus on determining the exact molecular mechanisms by which it occurs.

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