Medical Xpress

Insight into DNA reprogramming during egg and sperm cell development

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Scientists at the Babraham Institute have gained a new understanding of when and how the DNA in developing egg and sperm cells is 'reset', in preparation for making a new embryo. It is well known that small chemical groups can be added to DNA to alter gene activity, these modifications to the DNA are acquired during development in the womb and throughout adult life and can arise from changes in environment. Most of these modifications are removed in immature egg and sperm cells to 'reset' the DNA and to erase any 'environmental memory', but some remain. Decoding this reprogramming has major implications for our understanding of development and how these modifications can be inherited from one generation to another.

All the cells in the body of one individual have the same DNA sequence (genome) and it is how the DNA sequence is interpreted that results in the formation of different cell types, for example different genes can be switched on and off. Inactive genes often have a small chemical modification, called a methyl group, added to them outside the coding sequence which promotes this regulation. This study, published today (6 December) in the journal *Molecular Cell*, is the first genome-wide study to look at what happens to the methyl groups during early stages of egg and sperm cell (primordial germ cell) development. This type of research, investigating modifications to the DNA which do not alter the underlying DNA sequence, is called epigenetics.

Dr Stefanie Seisenberger, lead author from the Babraham Institute, which receives strategic funding from the Biotechnology and Biological

Sciences Research Council (BBSRC), explained, "We produced a high resolution map showing the location and timing of methyl group removal from primordial germ cell DNA. We discovered that the majority of demethylation occurred much earlier than people previously thought and this has allowed us to shed light on the process of methyl group removal in mammals, a mechanism which has remained elusive for many years. An even more exciting finding is that we have identified regions of DNA that avoid demethylation and are therefore candidates for how environmental information can be transferred from parent to offspring. Interestingly, one of these areas has a link with type 2 diabetes."

Professor Wolf Reik, senior author of the paper, a Group Leader at the Babraham Institute and an associate faculty member at the Wellcome Trust Sanger Institute, added, "Several recent studies in other laboratories have confirmed that environmental information can be transferred from parent to offspring in mammals, for example mice fed a high-fat diet produce offspring with altered metabolic regulation, but it is not known how this occurs. One interesting observation from our study, which backs up work performed elsewhere, is that incomplete removal of methyl groups from DNA occurs more frequently in sperm than egg forming cells, suggesting that fathers have a bigger part to play in epigenetic inheritance than previously thought. This has implications not only for understanding mechanisms of inheritance and development but also our susceptibility to obesity and diseases like diabetes."

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