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EPIGENETICS

Methylation from mother

There is increasing interest in discovering what epigenetic information is passed from parent to offspring and how it influences development. Two studies of mouse embryogenesis now show that transmission of DNA methylation from gametes is predominantly maternal.

Borgel and colleagues optimized methyl-CpG immunoprecipitation for very small numbers of cells to map DNA methylation in early mouse embryos. Consistent with previous immunofluorescence data, they found that at embryonic day (E)3.5 the genome is hypomethylated and substantial *de novo* methylation occurs during implantation. Surprisingly, however, the authors found 215 genes with methylated promoters before implantation. This group included known imprinted genes, as expected, but also many others that are not imprinted (they do not maintain allele-specific methylation later in embryogenesis). Some of the non-imprinted promoters show methylated alleles at E2.5 and in gametes: this strongly suggests that the methylation is passed from parent to embryo and that inheritance of methylation is more widespread than expected. Intriguingly, for the few genes analysed, this epigenetic transmission was restricted to maternal alleles.

Schulz *et al.* explored the functional impact of maternally and paternally inherited methylation at known imprinted genes. Using mice deficient for a DNA methyltransferase involved in imprinting, DNMT3L, they generated embryos without maternal imprints or with no imprinting. Both sets of embryos ceased development at E8.5; additional absence of paternal imprints did not exacerbate the defects caused by lack of maternal imprints alone, suggesting functional dominance of maternal imprints at this stage. The authors found that maternally imprinted genes are enriched in functional categories associated with the fetal–maternal interface, which is established at E8.5, thus providing a likely explanation for this observation. This impact of maternal imprinted methylation also fits with models of the co-evolution of imprinting and placentation.

It will be interesting to explore whether similar mechanisms maintain the imprinted and non-imprinted methylation passed on from the mother.

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ORIGINAL RESEARCH PAPERS Borgel, J. *et al.* Targets and dynamics of promoter DNA methylation during early mouse development. *Nature Genet.* **42**, 1093–1100 (2010) | Schulz, R. *et al.* The parental non-equivalence of imprinting control regions during mammalian development and evolution. *PLoS Genet.* **6**, e1001214 (2010)

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