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Small RNAs in Sperm, Affected by Diet, Transmit Information to Offspring

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A class of small RNAs derived from tRNAs has a distinct profile in mice fed unhealthy diets, suggests two new studies. These RNAs may be involved in the intergenerational inheritance of metabolic states.

Studies in the last several years have suggested that fathers can pass down metabolic information to offspring. For instance, male mice fed either a low-protein or high-fat diet produce offspring with metabolic abnormalities. In flies and worms, piRNAs—typically 25 to 33 nucleotides in length—have been implicated in transgenerational inheritance. But whether small RNAs have a similar role in mammals has been unclear.

Previous research found that a class of small RNAs is abundant in mouse sperm, tRNA-derived small RNAS (tsRNAS). tRNAs are derived mainly from the 5′ ends of tRNAs and have been suggested to have regulatory roles in various cell types. The new findings suggest that tsRNA profiles are different in sperm from males subjected to either a low-protein or high-fat diet.

In one study, Qi Zhou and colleagues [1] fed mice a high-fat diet and isolated small RNAs from their sperm including a 30- to 40-nucleotide fraction that consisted predominantly of tsRNAs. Injection of this RNA fraction into normal zygotes resulted in altered expression of numerous genes, including those involved in metabolic pathways; this RNA fraction also affected the metabolic phenotype of F1 offspring.

In a second study, Oliver Rando and colleagues [2] provide evidence that tsRNAs are delivered to sperm via epididymosomes: vesicles that fuse with sperm as they transit through the epididymis. A protein-restricted diet resulted in increased levels of glycine tsRNAs, which seem to have a regulatory role in the embryo—for instance, interfering with a glycine tsRNA-affected expression of a set of about 70 genes in embryonic stem cells. Curiously, these genes are highly expressed in the preimplantation embryos and are regulated by the same DNA element (the long terminal repeat of the murine endogenous retroelement, MERVL). Injection of a synthetic oligo of this tsRNA affected expression of a similar set of genes in the early embryo. Whether injection of this oligo affected the metabolic phenotype of the offspring was not tested.

The findings suggest that diet can affect tsRNAs in sperm and that these tsRNAs may have a role in intergenerational inheritance. But other factors may also come into play; for instance, other molecules were also altered in the sperm from males fed unhealthy diets, such as the let-7 small regulatory RNA. Another recent study in humans has suggested the piRNA profiles and DNA methylation in sperm is affected by diet [3].

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