Paternal components in fruit flies, humans may contribute to fertilization, embryonic development

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(PhysOrg.com) -- It had long been assumed that the human sperm cell's mission in life ended once it had transferred its freight of parental DNA to the egg. More recently however, other components of sperm have been implicated in fertilization, and perhaps even in subsequent embryonic development.

In a new study appearing in the *Proceedings of the Royal Society*, Timothy Karr, a researcher at Arizona State University's Biodesign Institute, along with colleagues from the Universities of Cambridge and Bath, England, examine messenger RNA (mRNA) transcripts present in the sperm of both fruitflies (Drosophila melanogaster) and humans.

The new report characterizes the complement of mRNA carried by Drosophila sperm cells, representing the first description of an invertebrate spermatozoal transcriptome. A close correlation is observed between fly and human mRNAs and in both cases, transcripts were delivered to the egg during fertilization.

"The observed evolutionary conservation between human and insect sperm mRNA suggests that Drosophila may present a useful alternative model organism to study the functions of these molecules," Karr says.

In addition to strengthening the case for sperm's enhanced responsibility in the reproductive process, the research may eventually lead to improved diagnosis and treatment of male factor infertility and inform new reproductive technologies. (Comparisons between sperm from fertile and infertile males have already implicated RNA transcripts as an essential ingredient for proper sperm function and highlighted their diagnostic potential.)

Until recently, the male genome was assumed to be the only vital information transferred to the egg during the process of fertilization. The discovery that mammalian sperm also delivers a centrosome and a soluble factor that activates the egg was therefore a revelatory advance and pointed to the possibility that other components found in sperm may play an as-yet unrecognized role.

Sperm are highly specialized cells, which undergo a dramatic transformation in the course of what is known as spermiogenesis. The once-spherical spermatogonium cell undergoes a process of mitosis to produce spermatocytes, followed by a first and second division through meiosis to produce spermatids. It is these spermatids that will eventually elongate, grow a tail and assume the characteristic shape and function of mature sperm cells or spermatozoa.

Mature sperm cells are often said to be 'transcriptionally silent,' meaning that the process of copying segments of a cell's DNA into the RNA templates necessary for protein synthesis has been shut down. Mature spermatozoa nevertheless have been found to contain a complex population of mRNA transcripts, at first presenting a conundrum to researchers.

The common assumption was that these transcripts represent remnants of mRNA produced prior to the shutdown of transcription and stored for use during the process of differentiation of sperm into their mature form. The approximate similarity of the mRNAs present in mature sperm to those found in immature sperm in the testis gave some support to the idea.

The new research however, strongly suggests that at least some of the mRNA transcripts in mature sperm are neither remnants strictly related to sperm development and maturation nor contaminants from nearby somatic cells contained in accessory glands, leaving the function of these transcripts an open question.

Previous studies have shown that mature mammalian spermatozoa carry a population of these mRNA molecules, which are transferred to the egg at the time of fertilization, though the function of these transcripts, if any, has remained obscure. Karr's team investigated the evolutionary conservation of this aspect of sperm biology by analyzing highly purified populations of mature sperm from the fruitfly.

Using DNA microarray analysis, Karr and his group analyzed isolated sperm samples for their RNA content. The highly purified samples were obtained from dissected seminal vesicles, which are almost entirely composed of mature sperm. By labeling three particular mRNA transcripts in fruitfly sperm, Karr and his colleagues demonstrated that they are indeed transferred to the egg at fertilization and can be detected before, and at least until, the onset of gene expression by the egg.

Additionally, the team found that 35 functional annotations – pertinent information added to the genome database – were conserved between human and fly mRNAs. In particular, mRNAs coding for ribosomal proteins were found in high proportions in both the human and fruitfly spermatozoal samples.

Comparison of mRNA transcripts from the testes and accessory gland confirmed that the majority of mRNA transcripts found in mature sperm were distinct and not the result of sample contamination. Further, it was found that 33 percent of mRNA transcripts from mature sperm encode components of ribosomes, compared with genes in the testis/accessory gland transcriptome, which are instead involved primarily in hormone activity.

Karr stresses that the high degree of functional coherence observed between human and fruitfly mRNAs may permit the use of Drosophila genetics to further probe the implications of such mRNA transcripts to the developing egg after fertilization: “The observed evolutionary conservation raises the exciting possibility that Drosophila can be used as an effective model organism for elucidating the function of sperm-derived mRNAs in both fertilization and early embryonic development .”

The current study demonstrates for the first time that non-mammalian sperm also deliver mRNA transcripts to the egg during fertilization, possibly sending signals of some type to the developing embryo. Whatever the precise role of these paternal mRNA transcripts, their remarkable evolutionary conservation between human and insect implies a practical importance requiring further inquiry. Additionally, the functional correspondence with human sperm suggests that the powerful tools of fly genetics may be brought to bear to further investigate the contributions of these transcripts to reproductive biology.

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