Studying yeast to better understand male infertility

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Men and yeast have something in common: they use the same molecular process to ensure the integrity of their gene pool during reproduction. This is a recent finding by researchers from CNRS, Inserm and the Université Joseph Fourier in Grenoble. The scientists are therefore set on studying yeast in order to shed light on the numerous cases of male infertility related to the malfunction of this process during spermatogenesis.

Over the last fifty years, male fertility has declined steadily. Men are thought to have lost half their spermatozoa in half a century, probably because of pollutants. But the fragility of the remaining spermatozoa is also responsible for this situation. If the DNA borne by the spermatozoa is damaged, it prevents the development of a healthy embryo.

During their “voyage” towards the ovum in the female body, spermatozoa undergo changes in temperature and other chemical aggressions. In order to withstand these conditions, the DNA is compacted during spermatogenesis: it loses around 90% in volume. At the molecular level, this results in the loss of histones, the molecules around which the DNA is wound, to the profit of smaller molecules known as protamines. Defects in the compaction process are responsible for numerous cases of male infertility. Such defects have been highlighted in particular by the presence of histones, which remain in the DNA of spermatozoa.

The team headed by Saadi Khochbin, CNRS senior researcher at the

Institut Albert Bonniot (Inserm/Université Joseph Fourrier in Grenoble)1 has compared the molecular steps of compaction in mice to those that occur during sporulation (the dissemination of spores) in yeast, a unicellular fungus. Sporulation meets a need to protect the gene pool against environmental strains. From a functional point of view, it is comparable to the compaction that occurs during spermatogenesis. What the researchers have discovered is that it is also comparable from a molecular point of view. Before being replaced by protamines, the histones have already undergone a chemical alteration known as hyperacetylation, which triggers the compacting signal. The researchers have demonstrated the existence of such hyperacetylation in yeast and a similar molecular factor in yeast and men, which acts on the acetylated histones.

This study suggests that spermatogenesis may have evolved from the more simple process of sporulation, while at the same time retaining the same molecular principles. More important still: it will be possible to use sporulation in yeast, a simple system to study, as a model for elucidating spermatogenesis and studying human pathologies affecting male fertility.

Provided by Université Joseph Fourier in Grenoble