Maria Rosa Maduro, PhD

RECOMBINATION-DEFECTIVE ALLELE UNCOVERS REMARKABLE SEX DIFFERENCES

Genetic recombination is a key event in all organisms, as it is required for DNA damage repair, proper chromosome segregation during meiosis, and genetic diversification.

Our comprehension of meiotic recombination in mammals largely depends on studies of model organisms. In fact, many of the genes controlling meiotic recombination are extremely conserved, from bacteria and yeast to humans. Despite this, our understanding of the recombination process is far from complete, and continued research in the field does not cease to amaze us.

Such an example is the report by Bannister et al,[1] recently published in *PLoS Biology*, in which the authors describe the isolation of an allele of *Dmc1* and uncover remarkable sex-specific properties; the phenotype is very different from the null allele of the same gene. Specifically, Bannister and colleagues report the identification of a novel dominant mutation in the rodent *Dmc1* (*Dmc1*^{Mei11}) that causes male-specific infertility and a susceptibility to premature ovarian failure in females due to defects in meiosis.

Dmc1 is a meiosis-specific homolog of bacterial RecA and eukaryotic Rad51 believed to be required for recombinatorial repair of meiotic double-strand breaks since it is able to catalyze homologous DNA strand invasion and D-loop formation in vitro. In *Saccharomyces cerevisiae* and mice of both sexes, DMC1-deficient mutants arrest in late zygonema/early pachynema of meiotic prophase 1, with an accumulation of double-strand breaks and defective synaptonemal complex formation.

In the article, the authors are able to characterize a previously generated *Dmc1* mutant, *Dmc1*^{Mei11}, through a combination of genetic mapping, yeast 2-hybrid system, and gel shift analysis. Thus, *Dmc1*^{Mei11} is known to encode a missense mutation in the DNA binding domain of DMC1, which abolishes its strand invasion activity and therefore its capability to resolve double-strand breaks during recombination.

Using histological analyses and immunohistochemistry with antibodies directed against diagnostic markers of meiotic chromatin, Bannister et al show that meiosis in male *Dmc1*^{Mei11} heterozygotes arrests in pachynema and is characterized by incomplete chromosome synapsis and no crossing over. Unexpectedly, young *Dmc1*^{Mei11} heterozygous females are fertile and have normal litter sizes, despite having a high incidence of meiosis 1 abnormalities and a decreased oocyte pool, leading to a susceptibility to premature ovarian failure.

As such, *Dmc1*^{Mei11} interestingly reveals a sex difference in recombination; in contrast to the male, a significant proportion of female gametes can compensate for DMC1 deficiency to undergo crossing over and complete gametogenesis.

In sum, the study presented by Bannister and colleagues importantly identifies a dominant defective allele of *Dmc1* that is associated with male infertility and female premature ovarian failure, which may have profound implications for the evaluation of the human infertile patient. Moreover, it exposes sex differences in the meiotic recombination process, which may revolutionize our understanding of this fundamental mechanism. In addition, the data presented show that dominant alleles of meiosis can arise and propagate in populations, causing infertility and other reproductive consequences.

REFERENCE

1. Bannister LA, Pezza RJ, Donaldson JR, et al. A dominant, recombination-defective allele of *Dmc1* causing male-specific sterility. *PLoS Biol*. 2007;5(5):1016-1025.

IMPLANTATION OF THE EMBRYO: MYTHS AND FACTS

One of the main events occurring in the uterus during the implantation of the embryo is the proliferation and subsequent differentiation of the endometrial fibroblast-like cells into large decidual cells. This process, known as decidualization, results in the formation of a tissue usually referred to as the decidua.

Whether the conceptus plays a role in the decidualization process has been a matter of debate for some time. More conservative and generally accepted views have argued that molecular signals from the conceptus are not required for decidualization to occur, as the uterus can undergo a similar process in response to an artificial stimulus with

Reproductive Sciences Vol. 14 No. 5 July 2007 401-402
DOI. 10.1177/1933719107306748