RECOMBINATION FAILURE IN HUMAN OOCITES

Meiotic errors are a hallmark of human gametogenesis, leading to an extraordinary high level of aneuploidies in conceptuses as compared to most other species. Specific maternal-age associated increase in aneuploidy rate is the only well described risk factor which has justified numerous studies to understand the molecular basis for this phenomenon. A second pathway to aneuploidy was revealed by previous studies on recombination during meiosis showing a link between altered crossing over and non-disjunction of homologues: almost 50% of trisomy 21 children had no crossing over between the two chromosomes 21 that failed to disjoin during meiosis.

In a paper which appeared in Am J Hum Genet, the team of Terry Hassold and Patricia Hunt addresses the question of how important is the absence of exchange between homologues in human meiosis. For the first time, they were able to analyze a large population of female meiotic cells, 7396 oocytes from 160 fetal ovaries, and showed a very high level of “exchangeless” chromosomes, up to 7%-10% of all analyzed cells. In line with previous observations on cell division check points in female versus male meiosis, the authors observed a ten-fold increase in the incidence of exchangeless chromosomes in oocytes versus spermatocytes.

As expected, their results show that most events of absence of crossing over are concentrated on small G group chromosomes. However, in contrast to previous studies, the authors did not observe a direct correlation between genome-wide size of the synaptonemal complex and the risk of exchangeless chromosomes, leading to the conclusion that the size of the synaptonemal complex may not be the main determinant for absence of crossing over. Rather, the large inter-individual variation in the frequency of exchangeless chromosome seems to be associated with overall level of meiotic recombination.

Exploring the reasons for inter-individual variation in recombination rate, the authors did observe a surprising correlation between maternal age and the number of recombination foci in the oocytes of the female fetuses; they suggest the existence of a grandmaternal effect on recombination where the age of a pregnant woman affects the recombination profile of her daughter’s oocytes.