MEIOTIC RECOMBINATION AND ANEUPLOIDY

The relationship between reduced meiotic crossover and aneuploidies in females is well known. Carioscia et al., in a paper published in Nature (1), investigated this relationship in a very large PGT study, comprising over 139,000 IVF embryos, a scale that allows the study of inviable aneuploidies that never reach live birth and provides statistical power unavailable to earlier work.

The central new contribution is demonstrating that common genetic variants shape both recombination rate and aneuploidy risk simultaneously. The strongest signal is a haplotype spanning SMC1B, encoding a meiotic cohesin subunit, where a promoter-proximate SNP reduces ATF1 transcription factor binding and lowers SMC1B expression, a non-coding regulatory mechanism validated experimentally with an electrophoretic mobility shift assay. Transcriptome-wide analyses additionally implicate C14orf39, CCNB1IP1, and RNF212 in aneuploidy risk. These genes were previously connected only to recombination phenotypes.

The paper also shows that several of these same variants associate with age at menarche and menopause, suggesting a shared genetic logic linking meiotic fidelity and female reproductive lifespan. Finally, the authors tackle an evolutionary paradox: if these alleles reduce fitness, why are they common? Their modelling argues that the loose connection between embryo euploidy and realized fitness — mediated by environment, behaviour, and parental care — is sufficient to let risk alleles drift to intermediate frequencies despite negative selection pressure.

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