

**P048** Ectopic meiotic recombination in the  $\beta$ -globin gene cluster  
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Meiotic recombination is of fundamental importance in maintaining diversity in the human genome and, through ectopic recombination between repeat sequences, can sometimes create duplications and deletions often with pathological consequences. However, the relationship between allelic and ectopic recombination in humans remains unclear. We have therefore characterised the  $\beta$ -globin allelic recombination hotspot at high resolution. Exchanges in this hotspot just extend into a homology block shared between the  $\delta$ - and  $\beta$ -globin genes within which ectopic exchanges can generate Hb Lepore deletions and anti-Lepore duplications. We have developed new methods to recover very rare *de novo* sperm deletions in the  $\delta$ -,  $\beta$ -globin gene region, and have used these to determine whether the allelic recombination hotspot is able to trigger Lepore-type ectopic exchanges and other types of deletion. Lepore-type deletions proved to be extremely rare in sperm, with breakpoints displaced away from the hotspot. Other rare, non-Lepore, deletions were also detected and likewise showed breakpoints that avoided the  $\beta$ -globin hotspot. This suggests that, despite its intense activity, the hotspot shows great fidelity and does not play a role in triggering ectopic exchanges or other deletions within the  $\beta$ -globin gene region. This study also establishes that rare deletion events can be detected and quantified in the human germline, and points to a possible deletion-controlling element in the  $\beta$ -globin gene separate from the crossover hotspot.