

P037 Telomere instability and variation in the male germline
**Bethan Britt-Compton¹, Jan Rowson¹,
Nazar N. Amso², Linda Gregory³,
David Kipling¹ and Duncan M. Baird¹**

*¹Department of Pathology, ²Obstetrics and Gynaecology,
Cardiff University, Heath Park, Cardiff CF14 4XN, UK*

*³Cardiff Assisted Reproduction Unit, University Hospital of
Wales, Heath Park, Cardiff, CF14 4XW, UK*

Telomeres play a key role in upholding the integrity of the genome; telomerase expression in spermatogonial stem cells is considered to be responsible for the maintenance of telomere length for subsequent generations. We have previously described allelic variation in somatic cell telomere length, the ultimate source of which may be the germline. Here we describe an analysis of both genome-wide telomere length and single molecule analysis of specific chromosome ends in human sperm. We observed individual specific differences in genome-wide telomere length; this variation may result from genetic differences within the components that determine the telomere length setting of each individual. Furthermore we observed chromosome specific telomere lengths implying the existence of cis-acting determinants of telomere length. Superimposed on the genome-wide telomere length setting was a stochastic component of variation that generates germ-cells containing severely truncated telomeres. These human Telomere Rapid Deletion events (hTRD) may be mechanistically related to similar events observed in yeast. TRD in yeast is an intrachromatid process that is dependent upon the Mre11/RAD50/Xrs2 (MRX) complex and may involve the processing of holiday junction-like intermediates formed between the 3' terminus and the proximal regions of the telomere. The nature of these events is consistent with the known patterns of variation observed within telomeres and adjacent sequences that indicate that these sequences are subjected to intra-allelic mutation. We are investigating the mechanisms of this variation.