

**P029** Recombination-like mutation events at telomeres in some cancers, is associated with instability at the human minisatellite, MS32

**Jennie N Jeyapalan, Aarón Méndez-Bermúdez, Clara Lopes Novo, Jenny L Foxon and Nicola J Royle**

*Department of Genetics, University of Leicester, University Road, Leicester, UK, LE1 7RH*

In cancer cells critically short telomeres are lengthened via telomere maintenance mechanisms (TMM). Telomere lengthening is mainly achieved by the activation of the reverse transcriptase, telomerase, but around 10-15% of tumours activate alternative pathways (ALT). Evidence shows that one ALT pathway utilises a recombination-like mechanism for telomere elongation, as ALT+ cells show higher levels of telomere-sister-chromatid exchange. In addition recombination-like events between telomeres or between telomeres and extra-chromosomal telomeric repeats have been detected. MS32 is a hypervariable human minisatellite that mutates by crossover and conversion processes in the germ-line. Surprisingly, the MS32 minisatellite is highly unstable in ALT+ cell lines but five other hypervariable minisatellites are not. The MS32 mutation frequency in 15 ALT+ cell-lines showed an average 55 fold increase compared to ALT- cell lines. Additionally, MS32 instability was detected in 38% (3/8) of ALT+ soft tissue sarcomas, showing that MS32 destabilisation is an *in vivo* effect of ALT activation. Here we have extended the study to investigate MS32 and telomere instability in other tumour types. Liposarcomas vary in the TMM used, with some showing telomerase activity, others are ALT+ and yet others have no detectable TMM. Provisional data showed no MS32 instability in telomerase+ tumours, but instability was identified in 30% of ALT+ and ~5% of tumours with unknown TMM. Further work on MS32 mutation frequencies and telomere mutations in the liposarcomas will be described.