P032 Distinct effects of DNA-PKcs and Artemis inactivation on blunt DNA ends repair *in vivo*

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DNA double strand breaks generated by exogenous agents or under physiological conditions during V(D)J recombination of immune receptor genes can be extremely deleterious. In resting cells, they are repaired by non homologous end joining (NHEJ), which requires the sequential recruitment and activation onto DNA ends of several proteins, including the DNA-dependent protein kinase (DNA-PK) and the nuclease Artemis. Artemis activity, triggered by the DNA-PK, is required to remove complex lesions before ends are ligated. During V(D)J recombination, Artemis is essential for the resolution of the hairpin-sealed coding ends but appears dispensable for rejoining the reciprocal phosphorylated, blunt-ended signal ends. DNA-PK is however present on signal ends; therefore Artemis can potentially be recruited and activated during signal joint formation. To determine whether Artemis plays a role in DNA blunt ends repair, we analyzed the structure of signal joints generated in thymocytes during the V(D)J recombination of T cell receptor genes in mice mutated for NHEJ factors. We found a reduced level of junctional diversity and an absence of deletions in Artemis-deficient mice. This profile is qualitatively and quantitatively different than those found in wild type or DNA-PKcs mutated mice. These data indicate that Artemis participates in the repair of blunt ended DNA ends *in vivo,* in a physiological setting, and suggest that Artemis is the nuclease responsible for nucleotide loss from signal ends during the repair process.