

Functional characterization of *pendolino*, a *Drosophila* gene required for telomere protection and DNA replication

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*Drosophila* telomeres are sequence-independent structures that are maintained by transposition to chromosome ends of specialized retroelements rather than telomerase activity. Fly telomeres are capped by the terminin complex that localizes and function exclusively at telomeres and by a number of non-terminin proteins that do not serve telomere-specific functions. *pendolino* (*peo*), encodes a non-terminin protein homologous to the E2 variant ubiquitin-conjugating enzymes. Null *peo* mutants exhibit ~ 5 telomeric fusions (TFs) per cell. We have recently identified a viable hypomorphic allele of *peo* (*peo<sup>h</sup>*) that causes ~ 1 TF/cell; more that 90% of the TFs observed in this allele involve the heterochromatic telomeres (the Y, XR and 4th chromosome telomeres), a TF pattern never observed in the telomere capping mutants so far characterized, where all telomeres fuse with comparable frequencies. This suggests that heterochromatic telomeres are preferentially affected by *Peo* reduction and that this effect is masked in null mutants in which most telomeres are fused. The preferential fusion of the heterochromatic telomeres in *peo* mutants is likely to reflect a defect in late DNA replication, as *peo* mutants are defective in DNA replication and PCNA recruitment. We also found that *Su(var)3-9/+; peo<sup>h</sup>/peo<sup>h</sup>* and *Su(var)205/+; peo<sup>h</sup>/peo<sup>h</sup>* larvae exhibit a strong increase in the TF frequency compared to *peo<sup>h</sup>/peo<sup>h</sup>; +/+* larvae, while mutations in the Jil-1 kinase coding gene partially rescue the *peo* TFs phenotype. These results show for the first time that “heterochromatic” (Y, XR and 4<sup>th</sup>) and “euchromatic” (XL, 2L, 2R, 3L and 3R) telomeres have different fusigenic properties and that these properties are modified by downregulation of genes that control the structure and function of *Drosophila* heterochromatin.