



Non-cell autonomous roles of telomere shortening in zebrafish

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Mariana M. GIL¹, Ahmed MAOUCHÉ², Naz SERIFOGLU², Margarida FIGUEIRA¹ and Miguel GODINHO FERREIRA ^{1,2}

¹ Instituto Gulbenkian de Ciência, 2781-901 Oeiras, Portugal Instituto de Medicina Molecular

² Institute for Research on Cancer and Aging of Nice (IRCAN), CNRS UMR7284 INSERM U1081 UNS, 06107 Nice, France.

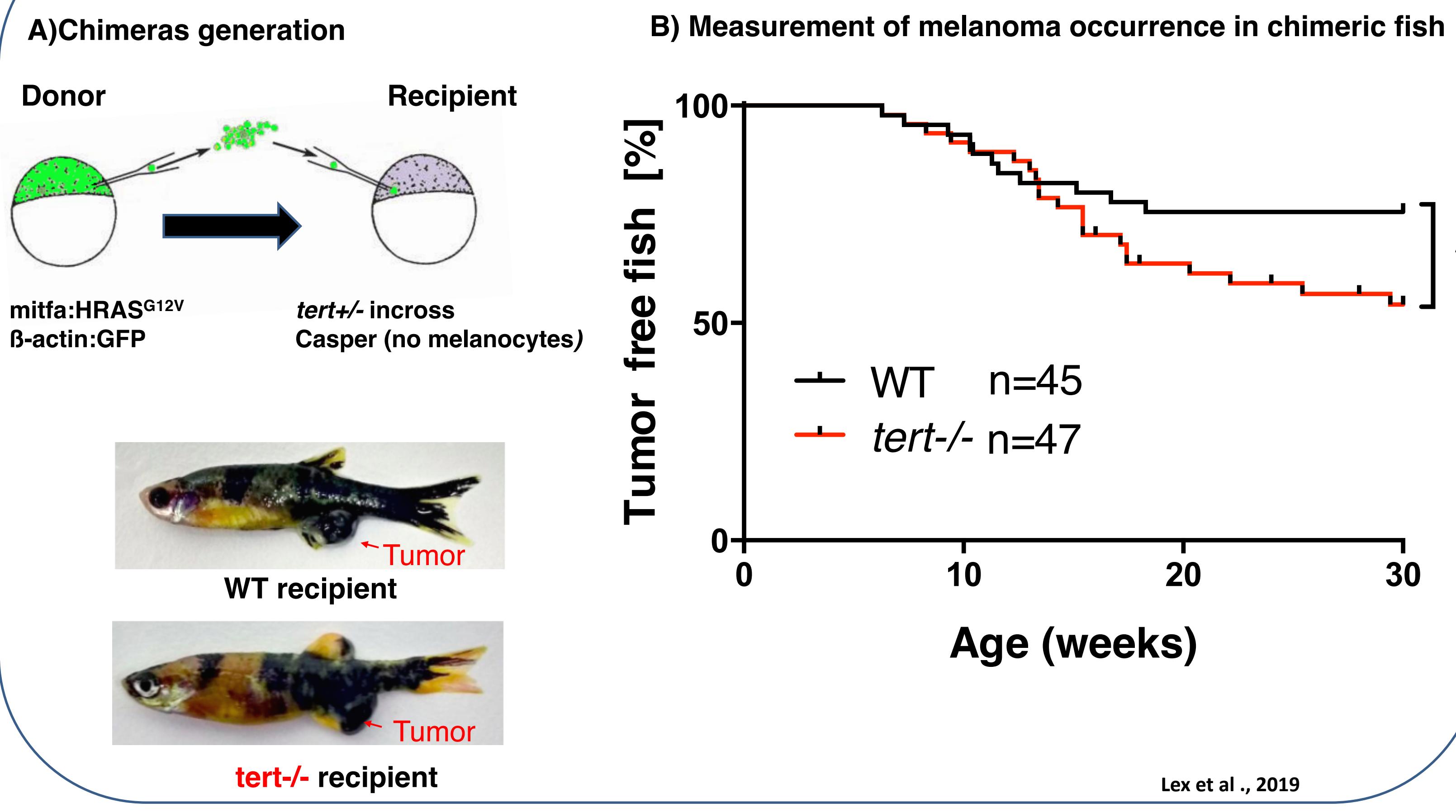
Background:

Cancer incidence increases with age. Due to the end-replicative problem, telomeres shorten with each cell division throughout our lives. Telomere shortening has consequences beyond the cellular level. As we age, cells approach replicative senescence and DNA damage emanating by short telomeres initiate a cascade of events that expands to the extracellular environment. Senescent cells were shown to release a set of molecules including inflammatory cytokines, termed senescence-associated secretory phenotype (SASP). Indeed, an inflammatory environment generates a pro-tumorigenic environment that supports tumor invasiveness.

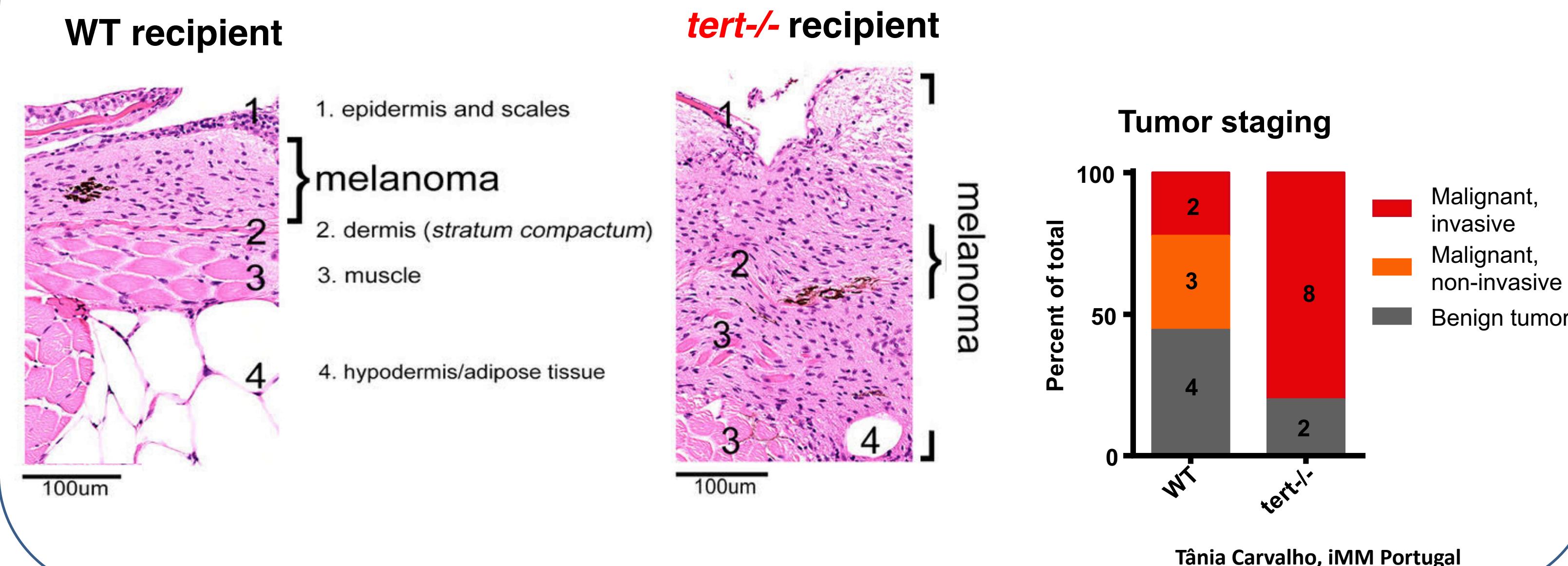
Aim of the study:

Investigate the causal relation between short telomeres and cancer incidence. Determine whether this effect has a non-cell autonomous component by using zebrafish embryo chimeras and tumor transplants.

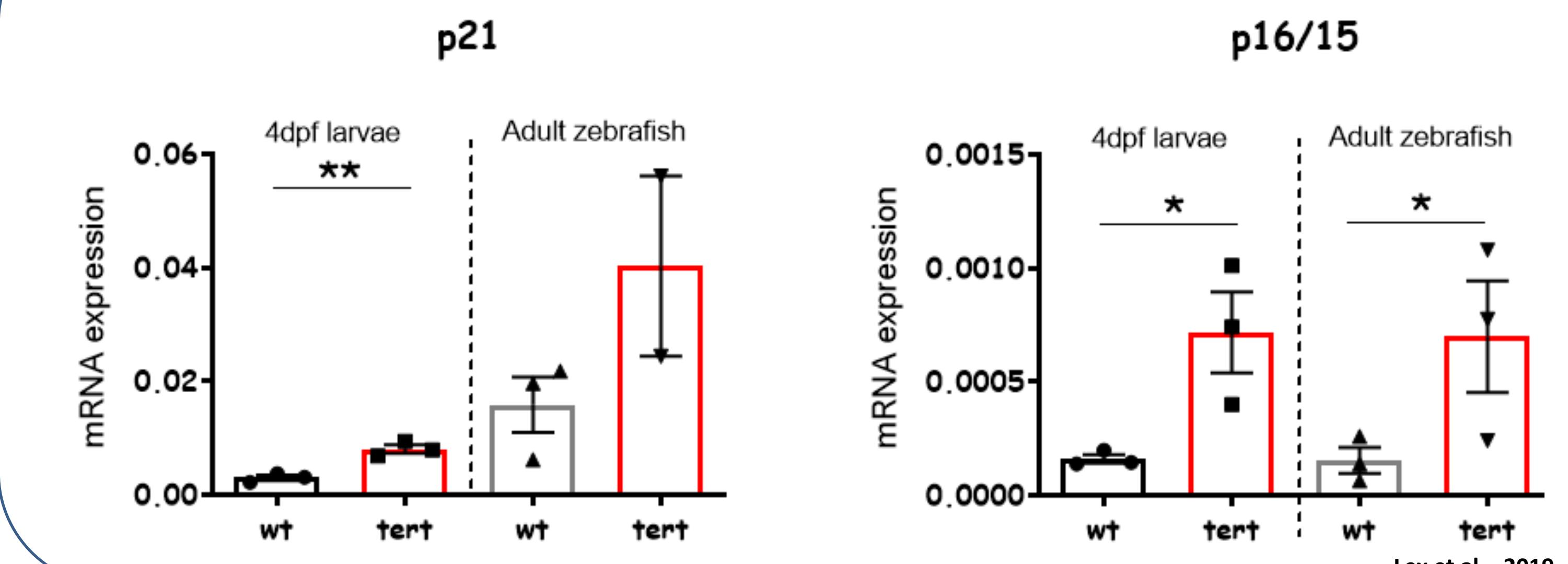
1. Short telomeres induce tumorigenesis in a non-cell autonomous manner



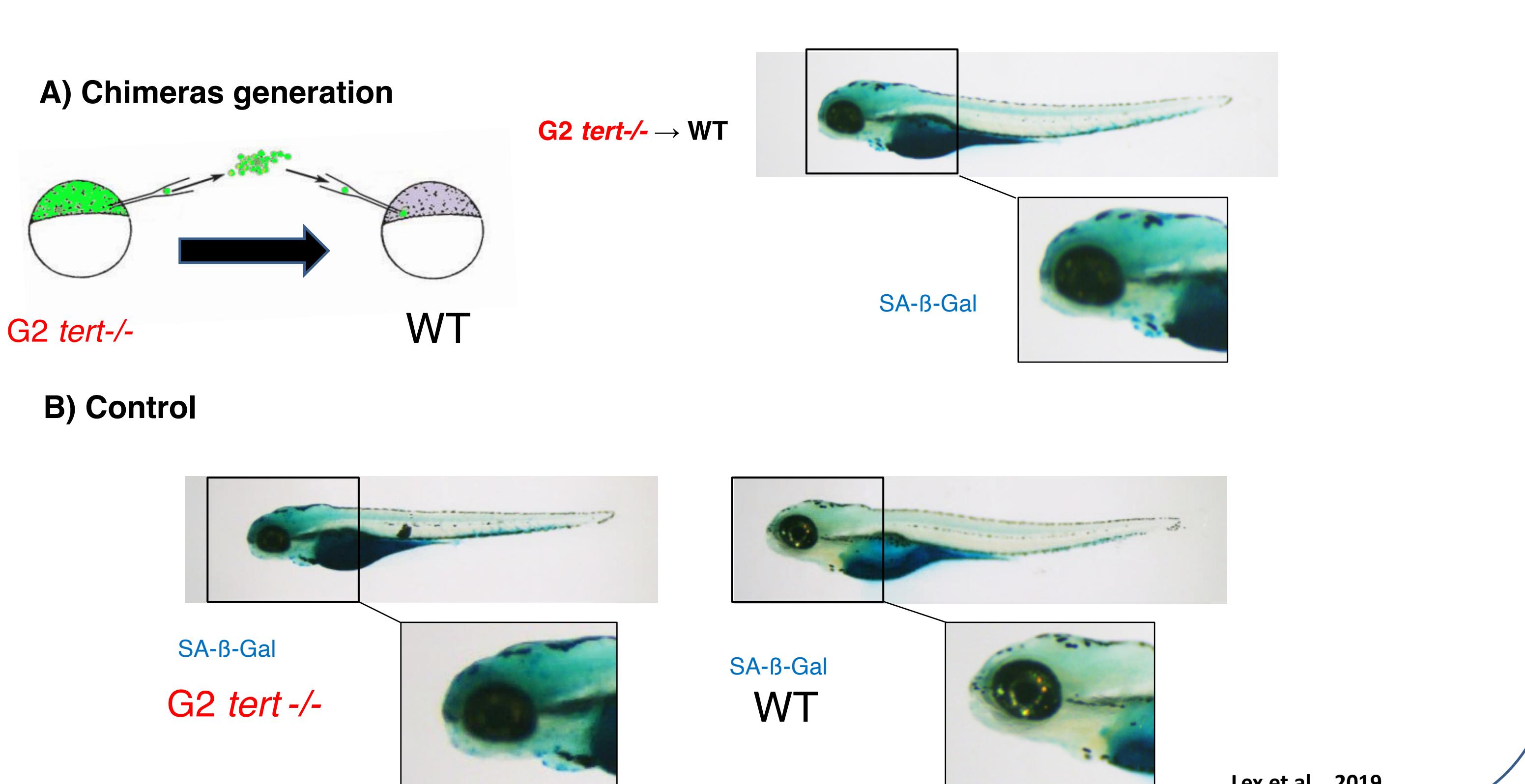
2. Melanoma is more invasive in an environment with short telomeres



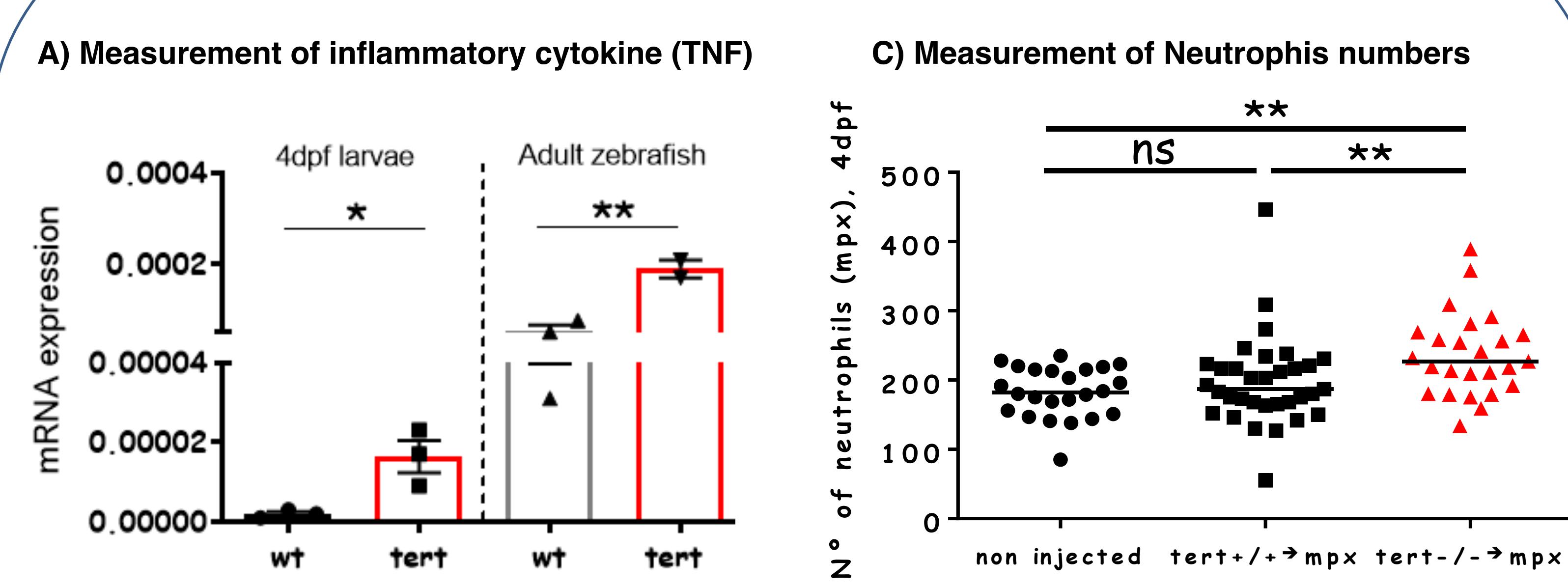
3. Telomerase deficient tissues present higher levels of senescence



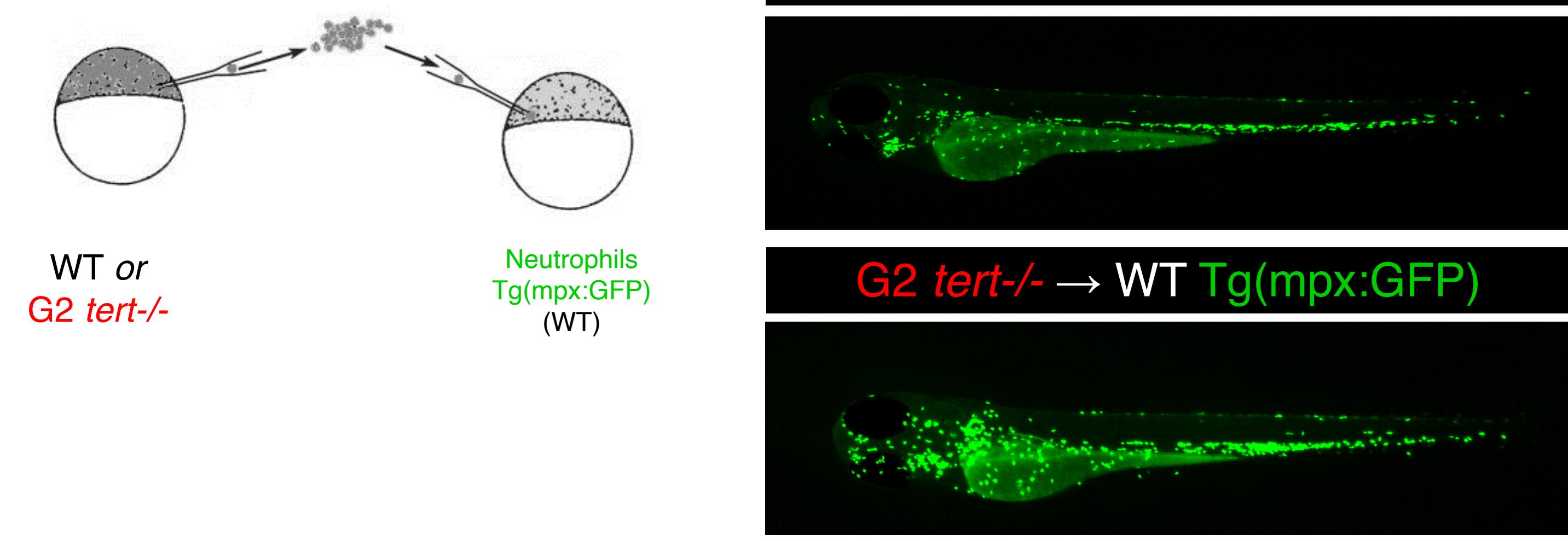
4. Short telomeres influences neighbour tissues



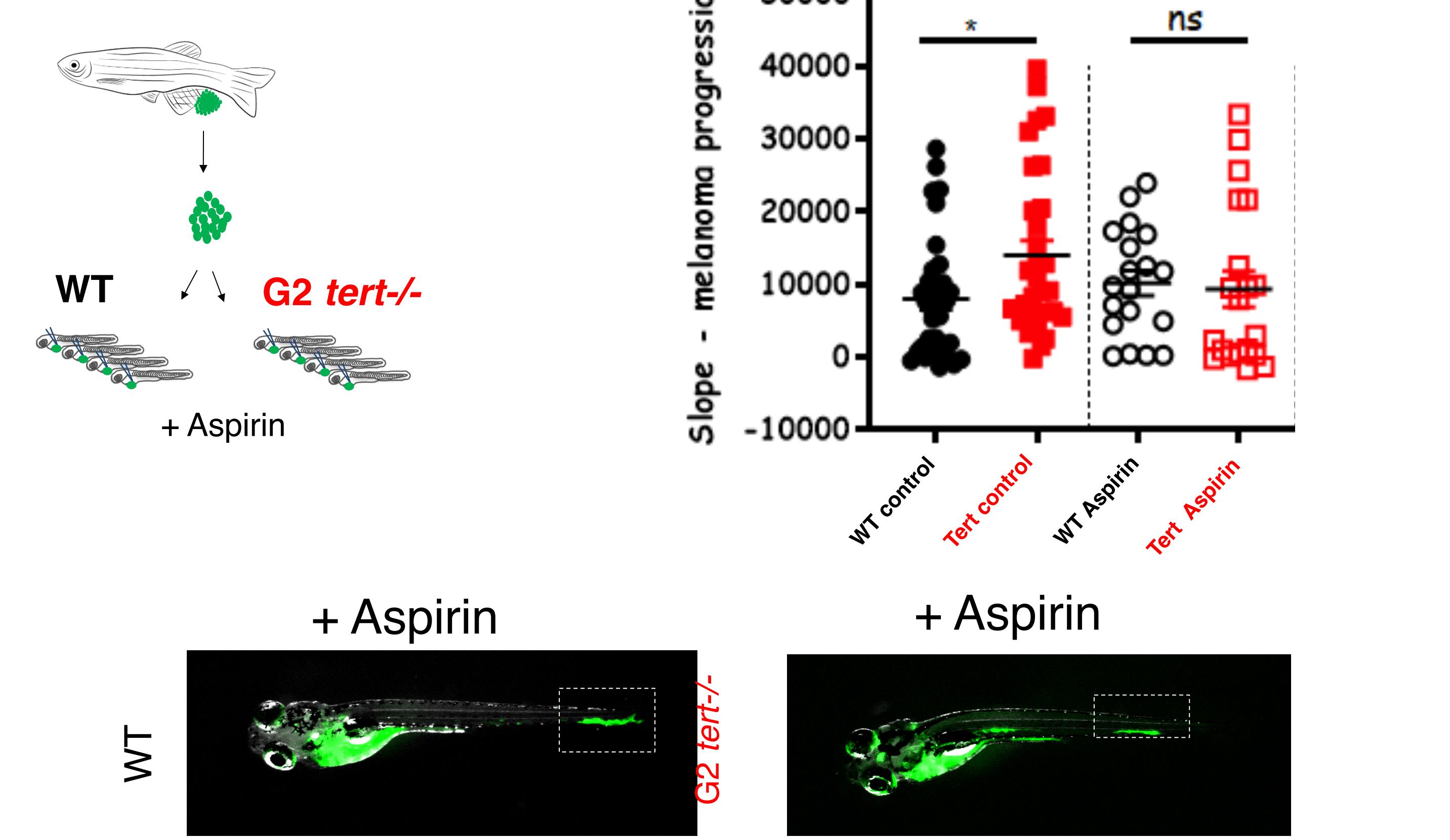
5. Telomerase deficient tissues present higher level of inflammation



B) Chimeras generation



6. Increased tumor invasiveness in G2 tert-/- larvae is rescued by inhibiting inflammation.



7. Conclusion

Wildtype ≈ normal telomeres

