



STAGE DE RECHERCHE M2 ECOLOGIE EVOLUTION GENOMIQUE Rentrée 2017

An eco-evolutionary approach of telomeres length and dynamics among vertebrates

(Approche éco-évolutive de la longueur et dynamique des télomères chez les vertébrés)

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Background: Aging is a nearly ubiquitous biological process among vertebrates. Most species investigated so far show an increase in mortality rate (i.e. actuarial senescence) and a decrease in reproductive performance (i.e. reproductive senescence) with advancing age (Nussey et al. 2013). Among the different biological factors that could possibly underpin the evolution of both actuarial and reproductive senescence, the progressive attrition of telomeres in somatic cells has been repeatedly suggested in the last two decades (López-Otín et al. 2013).

Telomeres consist of short repeated DNA sequence ($[\text{TTAGGG}]_n$ in all vertebrates) that prevent the chromosome extremities from deterioration and fusion in most eukaryote cells. Telomeres are shortened during DNA replication (~25-200 bases are lost per chromosome at each cell division), until the chromosomes reaches a critical length below which they lose their proliferative capacities ('Hayflick limit'; Hayflick & Moorhead 1961). This telomere-base replicated senescence has been proposed to be a source of the dysregulation of many functions of the organism at old ages and a source of age-related diseases (Calado & Young 2009). To prevent from telomere erosion, a dedicated enzyme (i.e. telomerase) governs the telomere elongation through replication of these DNA sequences. Such telomerase is thus a key contributor of telomere maintenance. Interestingly, the telomerase is not universally expressed among taxa and its activity seems to be repressed in the somatic cells of many species (Gomes et al. 2010).

Telomere length and attrition have been suggested to be involved in the deterioration of the organism during the course of aging (López-Otín et al. 2013) and to be tightly associated with lifespan. For a long time, these questions have been mainly tested using laboratory organisms and within humans populations. It is only recently that telomere dynamics has focused the attention of evolutionary ecologists (Dantzer & Fletcher 2015). However, despite the growing descriptions of telomere dynamic in non-model organisms, little is known on the ecological factors shaping the diversity of telomere length and dynamics across vertebrate species with very contrasting life-histories. Overall this project will allow a better understanding of evolutionary causes and consequences of telomere length and dynamics in vertebrates and will shed a new light on the relationships between functional and demographic senescence, which currently constitutes a very important topic in both evolutionary biology and biogerontology.

Project: In the first part of her/his project, the student will perform an intensive literature survey to compile data on both absolute telomere length and pace of telomere attrition in vertebrates. Previous comparative analyses have revealed that these data have become available for many species (e.g. telomere length data for 61 mammalian species in Gomes et al. 2011) and the availability of such data for new species is currently rapidly increasing (e.g. Young et al. 2013 in birds; Yip et al. 2017 in fishes or Plot et al. 2012 in reptiles). Since telomere length or dynamics can be estimated from various biological tissues or with different molecular assays (Nussey et al. 2014), all relevant information on telomere length and dynamics will be recorded to test and control for any possible influence on the observed patterns of telomere attrition. Sex-specific estimations will be compiled in priority since there is good evidence that telomere length differs between males and females (Barrett & Richardson 2011). Finally, estimates of telomerase activity (i.e. an enzyme involved in the replication of the telomeres and known to be tissue- or species-specific) will also be compiled for these species.

In the second part of the project, the student will perform several phylogenetically- controlled comparative analyses (including path- analyses) to test several hypotheses (see below). She/he will take advantage of databases on demographic and life-history data already available in the laboratory (e.g. Lemaître & Gaillard 2013).

- i) Telomere length and dynamics predict both the age at the onset and the rate of actuarial senescence, independently of either body mass or of the species ranking along the slow-fast continuum of life histories. So far, most studies have exclusively focused on longevity (e.g. Gomes et al. 2011), which is a poor indicator of the species-specific aging trajectory.
- ii) In females, telomere length and dynamics predict both the age at the onset and the rate of reproductive senescence, independently of either body mass or the species ranking along the slow-fast continuum of life histories. This hypothesis has been suggested in humans (Aydos et al. 2005) but has never been investigated in other species.
- iii) The biological and ecological features of the species shape the pace of telomere attrition in vertebrates (e.g. species living in harsh and/or highly variable environmental conditions should show a faster pace of telomere attrition / in polygynous species males should show a faster pace of telomere attrition than females as a physiological cost of sexual competition).

References: Aydos et al. (2005). *Arch. Gynecol. Obstet.* 272:113-116. / Barrett & Richardson (2011). *Aging Cell* 10:913-921. / Calado & Young (2009) *N Engl J Med* 2009;361:2353-65. / Dantzer & Fletcher (2015). *Exp. Gerontol.* 71:38-47. / Gomes et al. (2010). *FEBS Letters* 584:3741-3751. / Gomes et al. (2011). *Aging Cell* 10:761-768. / Lemaître & Gaillard (2013). *Behavioral Ecology* 24:421-438. / López-Otín et al. (2013). *Cell* 153:1194-1217. / Hayflick & Moorhead (1961). 25:585-621. / Nussey et al. (2013) *Ageing Research Reviews* 12:214-225. / Nussey et al. (2014). *Methods in Ecology and Evolution* 5:299-310. / Plot et al. (2012). *PlosOne* 7(7):e40855. / Yip et al. (2017). *Marine Pollution Bulletin. In press.* / Young et al. (2013). *PlosOne* 8(9): e74931.