Plant mutations, beyond the clichés

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The popular perception of plants as inferior forms of life as compared to animals, despite their central functional and environmental roles (a.k.a. plant blindness, e.g. Jose et al. 2019) has a pervasive downstream symptom in science. By default, functional and evolutionary processes are assumed to be less complex in plants than in their animal counterparts. Mutation rates in plants are for instance generally assumed to scale with the number of cell divisions in the tissues, the UV exposure, as well as several other weakly supported general hypotheses (Schmitt et al. 2023). Recently, Akiko Satake from the Kyushu University, Japan and her collaborators in Asia and Europe reported fascinating counter-intuitive evidence - at first sight - for aging, rather than number of cell divisions, as a major driver of de novo mutation accumulation in plants (Satake et al. 2023).

In animals, the origin of mutations was initially assumed to occur predominantly due to DNA replication errors and therefore to accumulate linearly, as the product of the number of cell divisions and the mutation rate per cell division. Detailed investigations over the last decade have however shown that germline mutations accumulate with age, rather than with the number of cell divisions. This has typically been observed through the significant contribution of maternal age at conception on the number of de novo mutations passed to the progeny (Goldmann et al. 2016, Jónsson et al. 2017, Fig. 1). Since then, it is now widely accepted that animal mutation rates are mostly replication-independent, driven by unrepaired damage-induced mutations. These DNA repair errors in turn explain many mutational biases, including the abundance of cytosine-to-thymine mutations at CpG sites (Gao et al. 2019).

Unlike in animals, the plant germline is generally assumed to be set aside late in development (but see Lanfear, 2018), leading to the general expectation that plants could pass to the progeny the somatic mutations accumulated along growth. Recent empirical evidence indeed found support for the intergenerational transmission of somatic mutations in plants, at least in trees (Plomion et al. 2018, Wang et al. 2019, Schmitt et al. 2023). As a consequence, somatic mutations can have an evolutionary fate in plants. This plant specificity has contributed to attract further interest for investigating the accumulation of somatic mutations along tree growth in order to dissect the link between growth, aging and mutation rates.

Satake and collaborators sequenced and assembled the genomes of two hardwood species of the Dipterocarpaceae botanical family living in central Borneo, Indonesia. These two species have notable differences in growth rates, with *Shorea leprosula* growing more than three times faster than *S. laevis*. The authors then extracted DNA from leaves at the ends of several branches and compared them to identify within-individual somatic mutations. They replicated this experiment in two individuals per species from trees of similar heights. Consequently, the investigated trees had different ages, 256 and 66 years on average for the slow and fast-growing species, respectively. Overall, Satake et al. identified far more mutations in the slow growing species (962 vs. 174), which represents a 3.7-fold higher

mutation rate per meter of growth after considering the physical distance between branch tips.

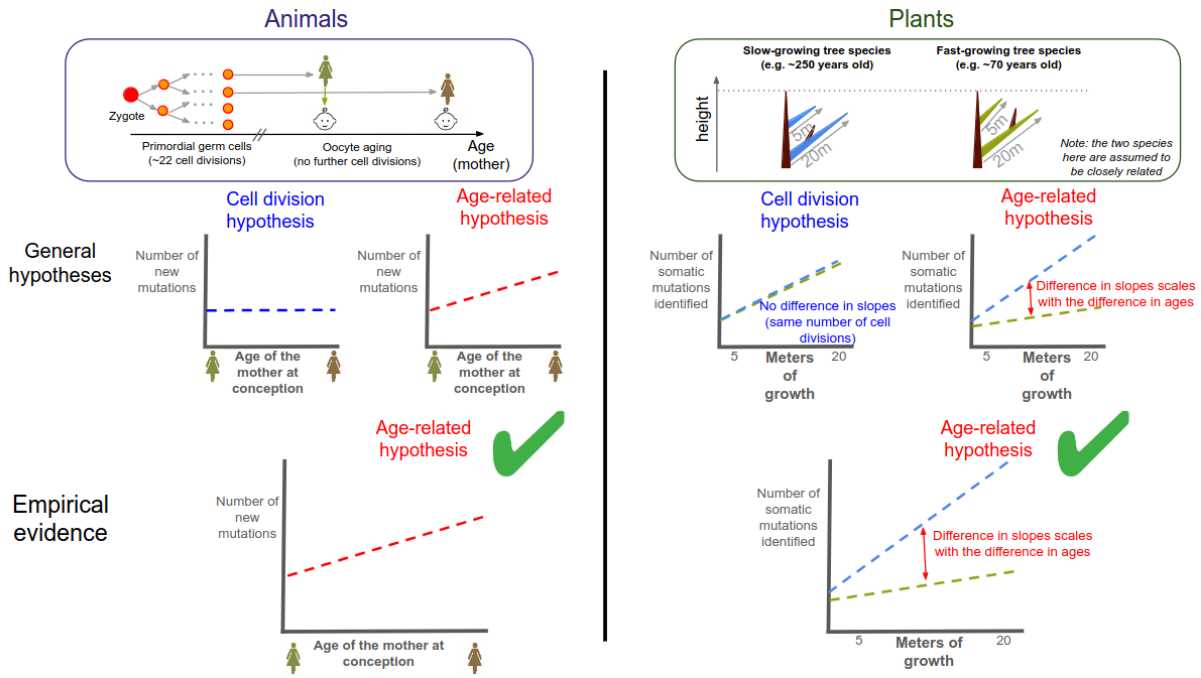

Figure 1: Simplified scheme highlighting how cell division (replication-associated mutations) and age-related hypotheses (unrepaired damage-induced mutations) have been tested in animals (left) or in plants (right). The references considered for the empirical evidence are data from Goldmann et al. 2016 and Jónsson et al. 2017 (among others) in humans for animals and Satake et al. 2023 for plants. Note that the animal model especially concerns mammals and that all animals are not expected to strictly follow the so-called animal scenario. Additional plant studies are also needed.

Why is this remarkable? Despite the fact that the authors used an experimental design allowing to only identify high frequency mutations, likely representing a small part of the total number of somatic mutations (Schmitt et al. 2022; 2023), their design and results are sufficient to reject the hypothesis of cell division as the main driver of mutation in plants. According to the cell division hypothesis one would expect similar mutation rates per meter of growth, at least after making a series of reasonable assumptions for two evolutionary related species (Fig. 1). Instead, the observed 3.7-fold difference in the somatic mutation rates is remarkably consistent with the average difference in age between the trees (256/66=3.9, Satake et al. 2023). Their main interpretation is therefore that somatic mutations accumulate with absolute time, not with the number of cell divisions (Fig. 1).

This result suggests that somatic mutations in plants could mostly be driven by unrepaired damage-induced rather than replication-associated mutations, representing an interesting parallel with animals. Satake and collaborator's work lends additional support to such a parallel, sometimes confirming previous reports, including similar enrichments of cytosine-to-thymine substitutions at CpG sites, or shared mutation signatures with human cancers. From a more methodological perspective, methods initially developed for cancer have been demonstrated to perform better for the discovery of somatic mutations in plants (Schmitt et al. 2022). All together, this suggests that the mutational processes in plants and

animals are largely conserved. Recognizing this, scientists interested in mutation seem to have much to gain from a closer collaboration between plant and animal research communities in the future.

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