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## **Stem cells and evolution: the teloblasts of the annelid Platynereis**

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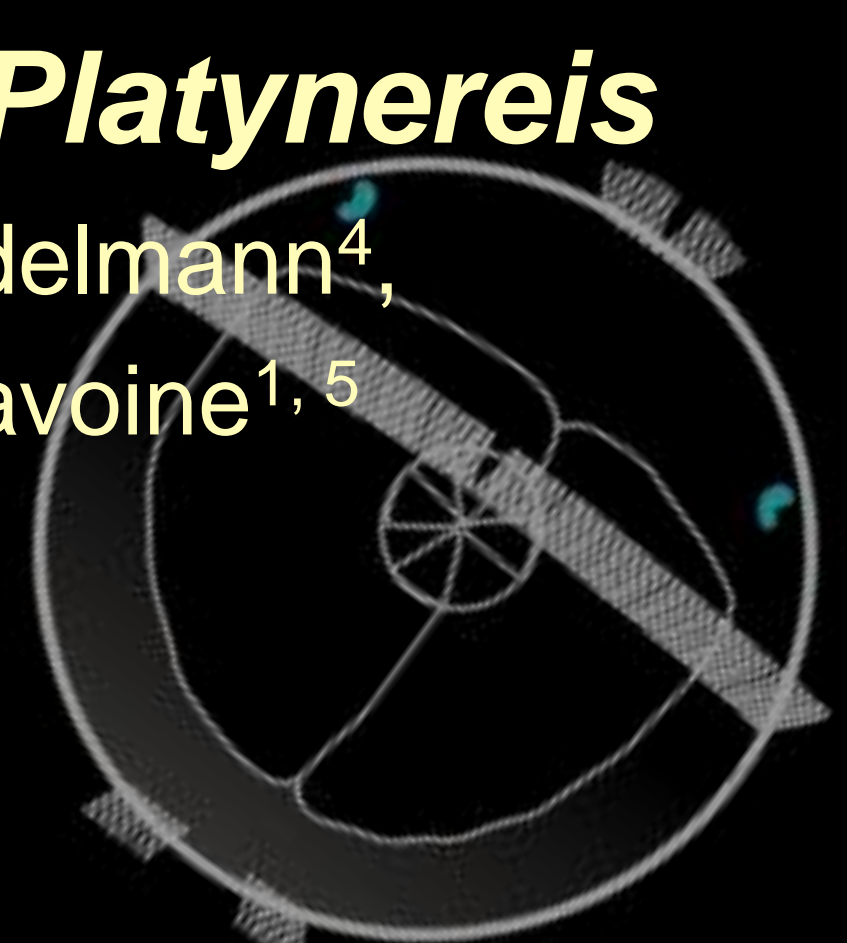
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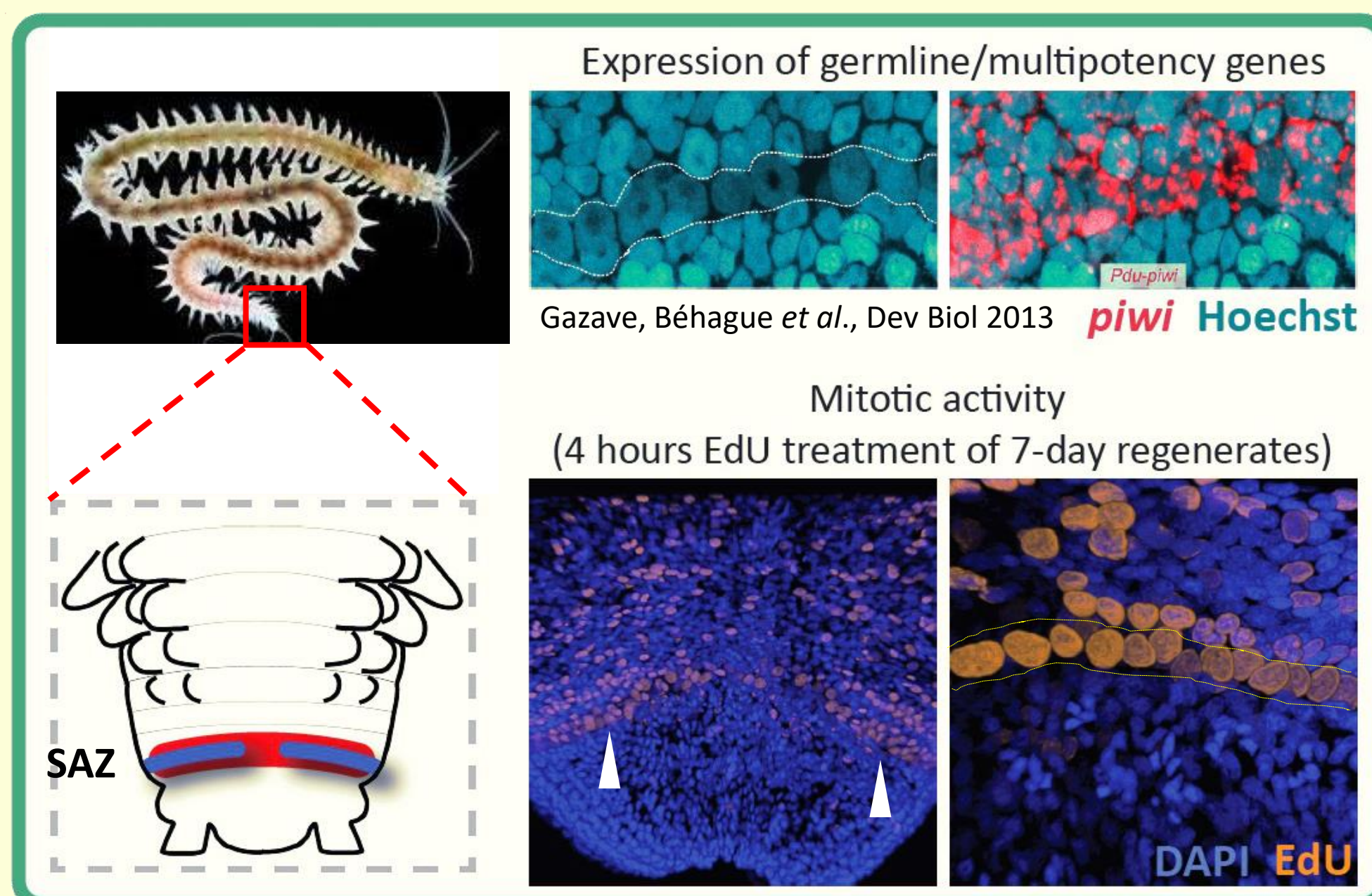
## Introduction

### What is the evolutionary origin of the different categories of stem cells?

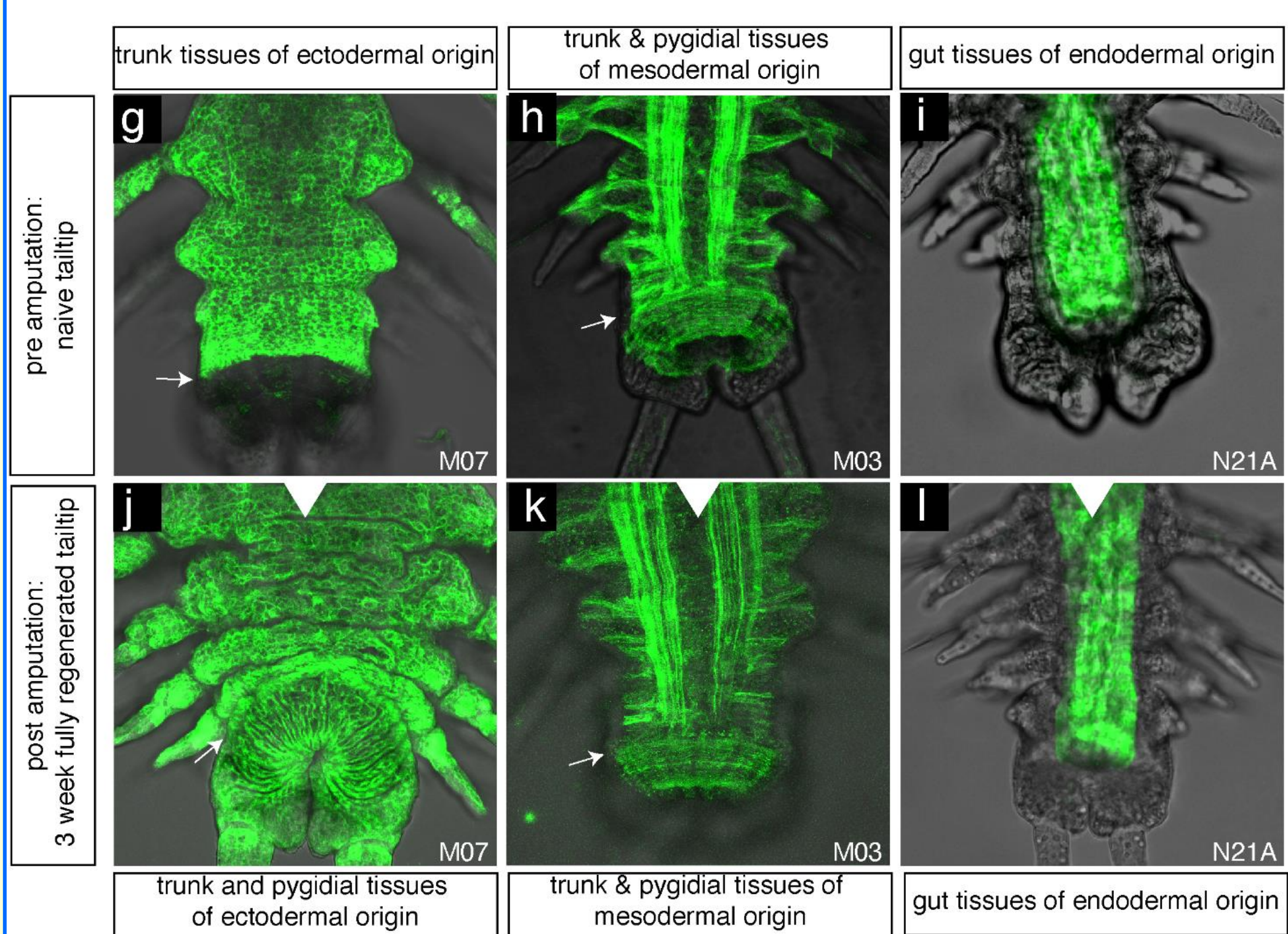
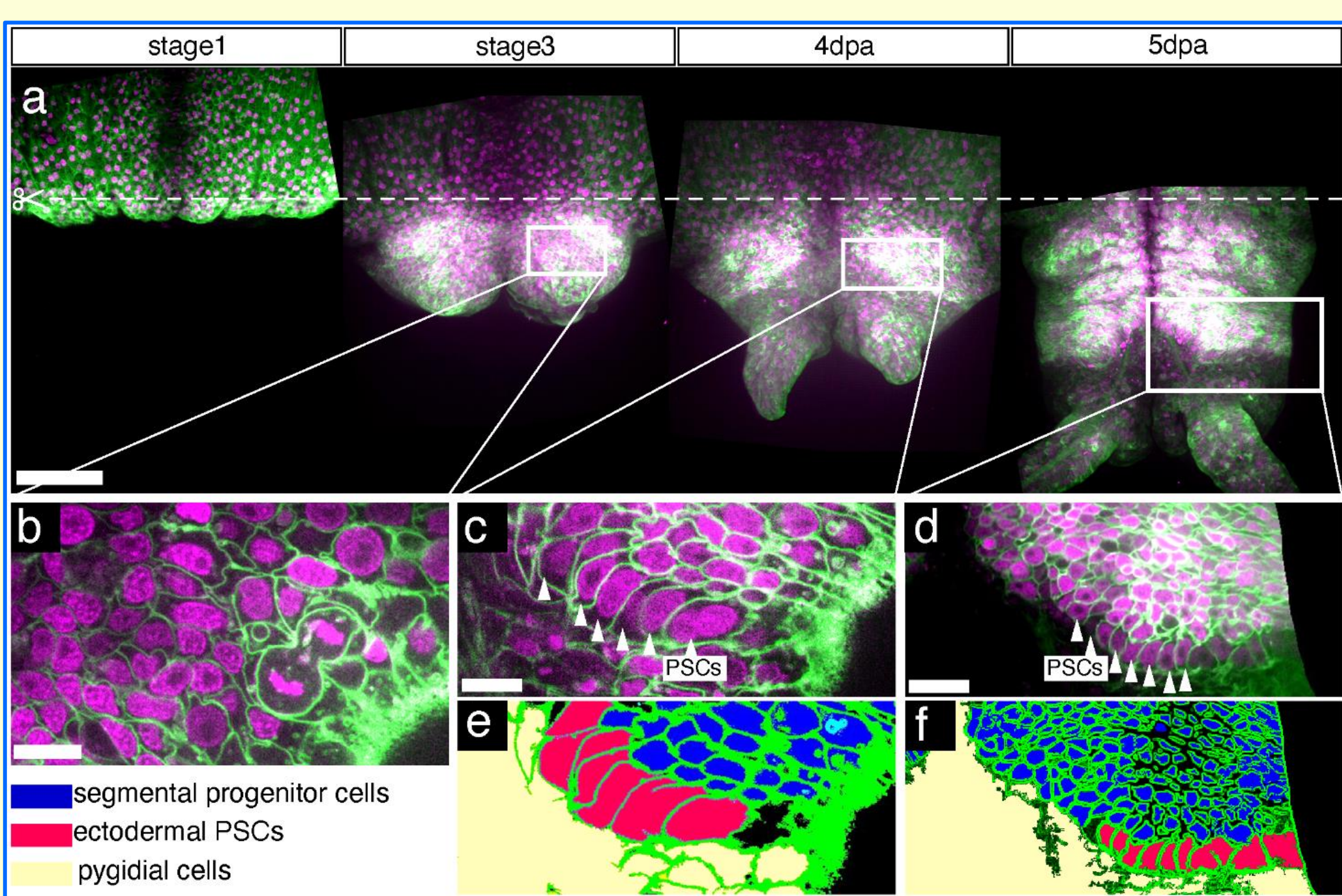
A variety of stem cells are present in the animal kingdom. However, the representation of stem cells in individual animal clades varies considerably from a total absence in some groups (nematodes) to the presence of a large contingent of pluripotent stem cells in constant activity (planarians). The different categories of natural stem cells (excluding mammalian cultured embryonic stem cells) are distinguished by their location and potency. Some groups display pluripotent stem cells crucial to their growth, tissue maintenance, regeneration and sometimes asexual reproduction. On the other hand, adult stem cells are niche- and fate-restricted in vertebrates and mammals in particular. What is the origin of stem cells and in what direction did they evolve along metazoan lineages?

## The annelid *Platynereis* posterior stem cells

- Platynereis dumerilii* is a segmented marine worm (annelid).
- As most annelids, *Platynereis* adds new segments through most of its life at the level of a sub-terminal "segment addition zone" (SAZ)
- The SAZ harbors stem cells called « teloblasts »
- Teloblasts express germline/multipotency genes such as *piwi*, *vasa* and *nanos*
- Teloblasts display coordinate mitotic activity



## *Platynereis* regeneration involves lineage-restricted precursors

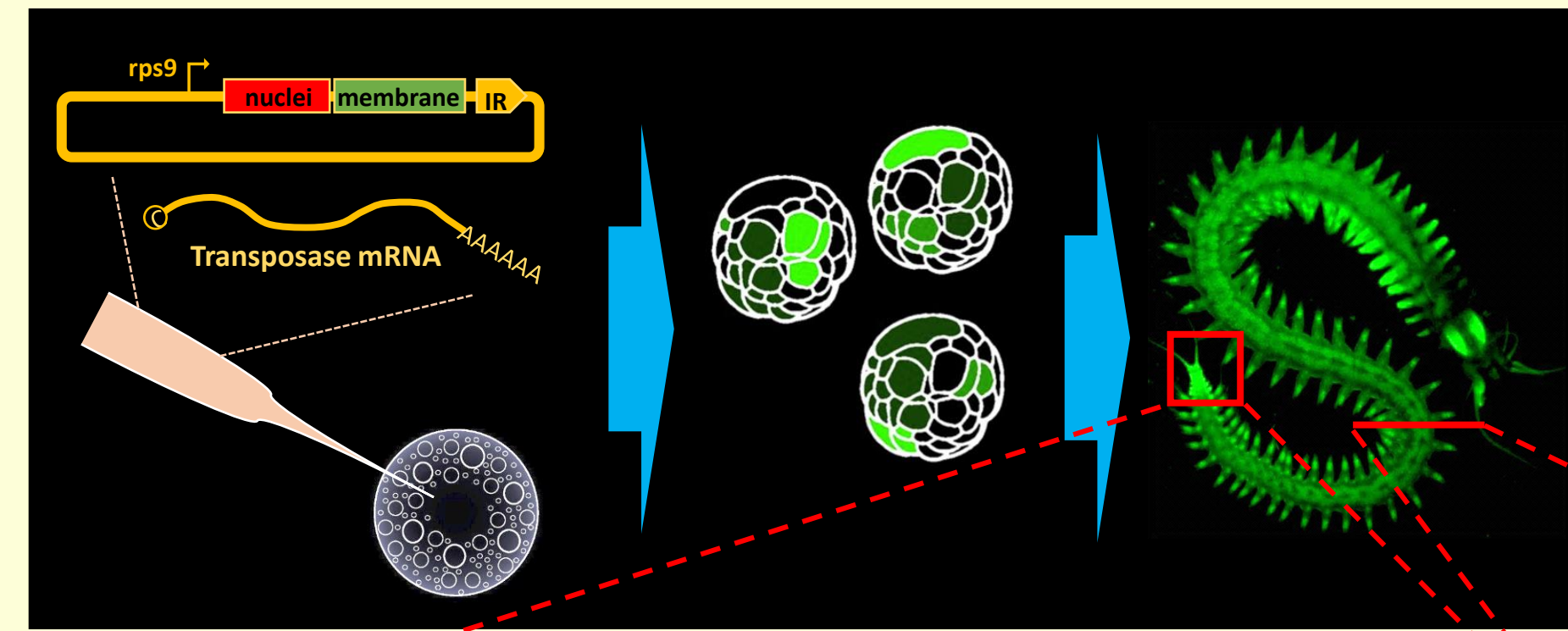


Worms clonally transgenic in various tissues were cut in mid-body and left to regenerate posteriorly. (A-F) Stages of regeneration of an ectoderm-labelled worm (B-F) Progressive reestablishment of the ectodermal teloblasts. (G-H) Worms labelled respectively in the ectoderm (G, J), in the mesoderm (H, K) and the endoderm (I-L) were cut mid-body and left to regenerate for three weeks. (J, K, L) Fully regenerated posterior parts showing strict fate restriction to the germ layer of origin.

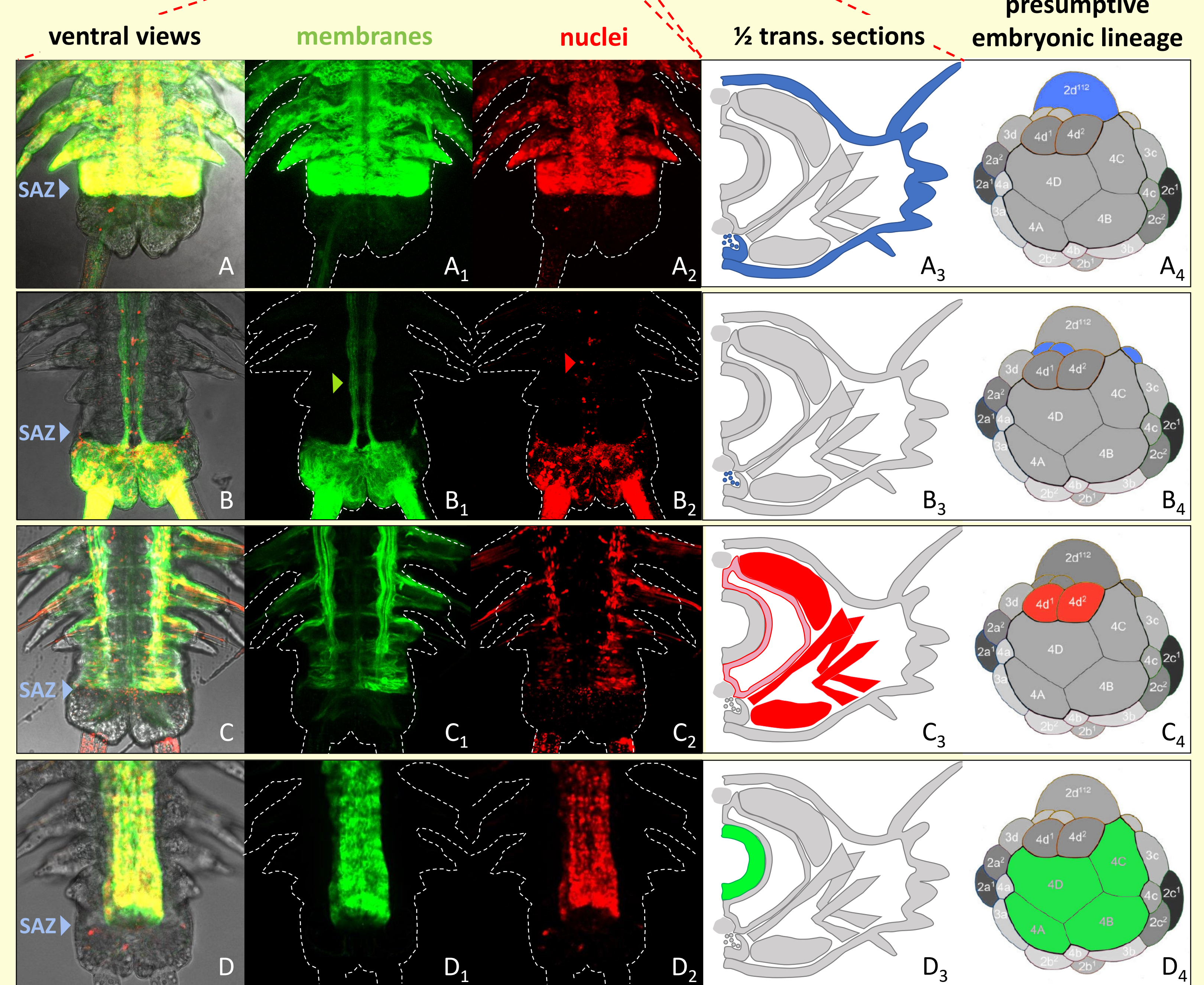
## Acknowledgements

## The annelid *Platynereis* posterior stem cells are lineage-restricted

*Platynereis* eggs undergo spiral cleavage, and embryonic development is highly stereotyped. Blastomere 2d contributes to the larval trunk ectoderm, blastomere 4d gives rise to the larval trunk mesoderm, and the macromeres 4A-D provide the larval endoderm. However, it was not known whether lineage restriction persisted during post-larval elongation as the worm continuously adds segments. To test this idea, we used clonal analysis through embryonic mosaicism transgenesis.

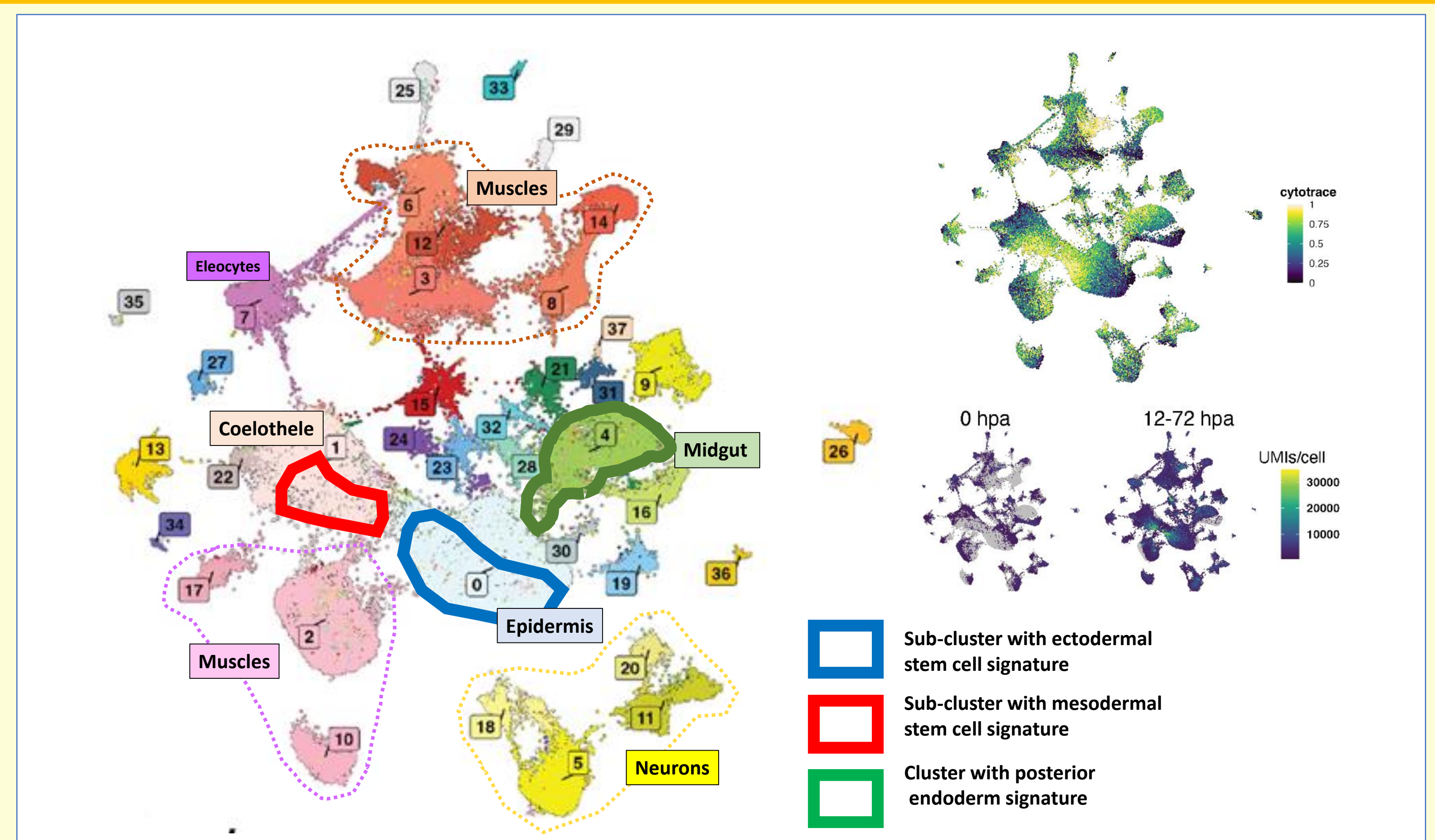


*Platynereis* eggs were injected with a transgene based on the DNA transposon Tol2. The mRNA encoded transposase is active only during early embryogenesis, resulting in mosaic transgenic individuals. Some worms have transgenic teloblast cells, labelling large clones of their specific progeny along the trunk.



Worms were screened for clones at 6 weeks, revealing a variety of clonal domains. Only the most striking individuals are shown here (A-D). All pictures are ventral confocal views of live immobilized specimens (A) is transgenic in the ring of ectodermal teloblasts and therefore in all ectodermal trunk tissues (epidermis, nervous system,...). (B) the pygidial ectoderm cells are labelled. These cells mostly do not contribute to the building of the trunk except for sensory nerves (green arrowhead) and a few glial cells (red arrowhead). (C) the mesodermal teloblasts are labelled, giving all trunk muscles, mesoepithelia and vessels. (D) is labelled in all gut endoderm but whether specific endodermal teloblasts exist is yet unknown.

## Single cell transcriptomics identifies three independent pools of blastemal progenitors, matching those detected with transgenics



Cells from regenerating posterior parts of various stages (0 hour post-amputation up to 3 days) were dissociated and analysed by Genomics 10x. Cytotrace analysis helps distinguishing undifferentiated progenitors and differentiated cell types. UMIs analysis detects cells with hypertranscriptomic activity, characteristic of fast proliferating progenitors. Molecular signatures identify three distinct pools of undifferentiated cells, inserted in the epidermis, coelothele and gut respectively that represents pools of blastemal progenitors.

## Conclusion

Somatic stem cells must have been present from the onset of metazoan evolution. However, the current picture of their locations, potencies, and relations to the germ line in various taxa suggests a complex evolutionary history. Two scenarios are possible: 1 – the presence in the last common ancestor of metazoans, and later of bilaterians, of pluripotent (including germ line) cells spread throughout the body, which either persisted in extant taxa or evolved into pools of localized fate-restricted somatic stem cells, sometimes correlating with reduced regeneration capabilities. In some cases, stem cells were completely lost in the entire lineage. 2 – the independent evolution of fate-restricted pools of somatic stem cells, possibly through the recruitment of the germline multipotency program (GMP), later evolving in some lineages into a general pool of pluripotent stem cells.