

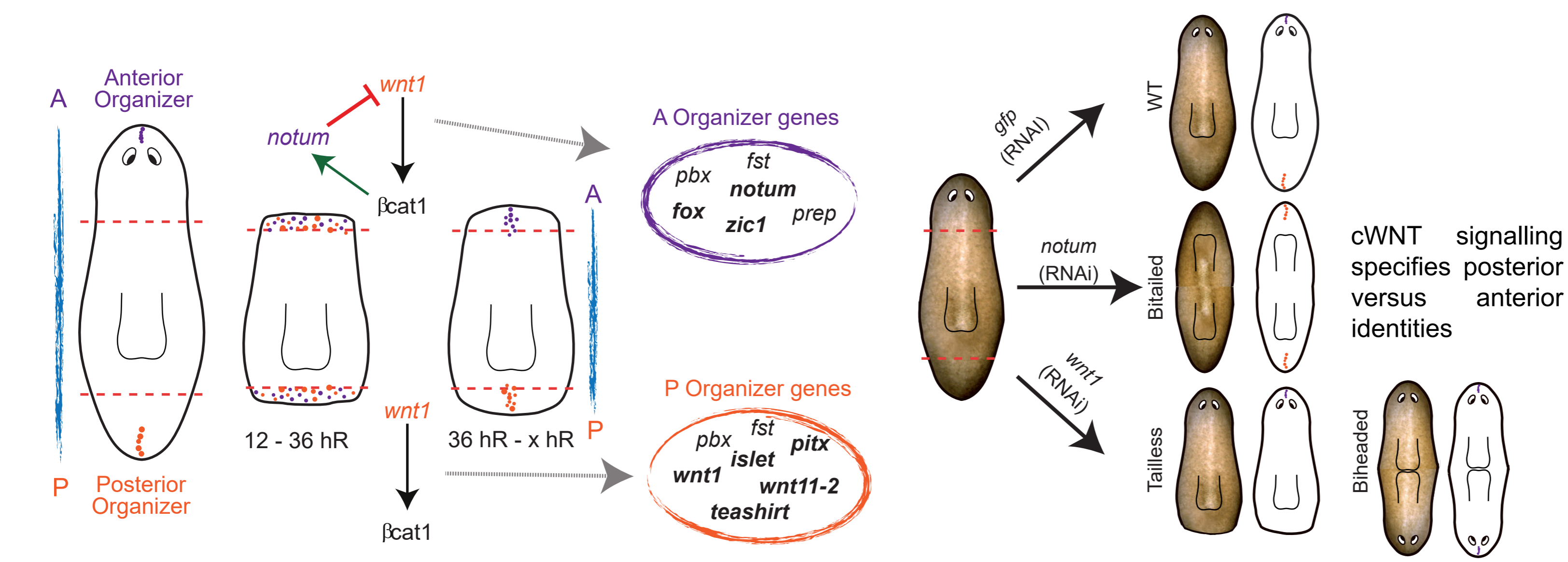
ATAC-seq and RNA-seq analysis reveal new elements of planarian posterior organizer

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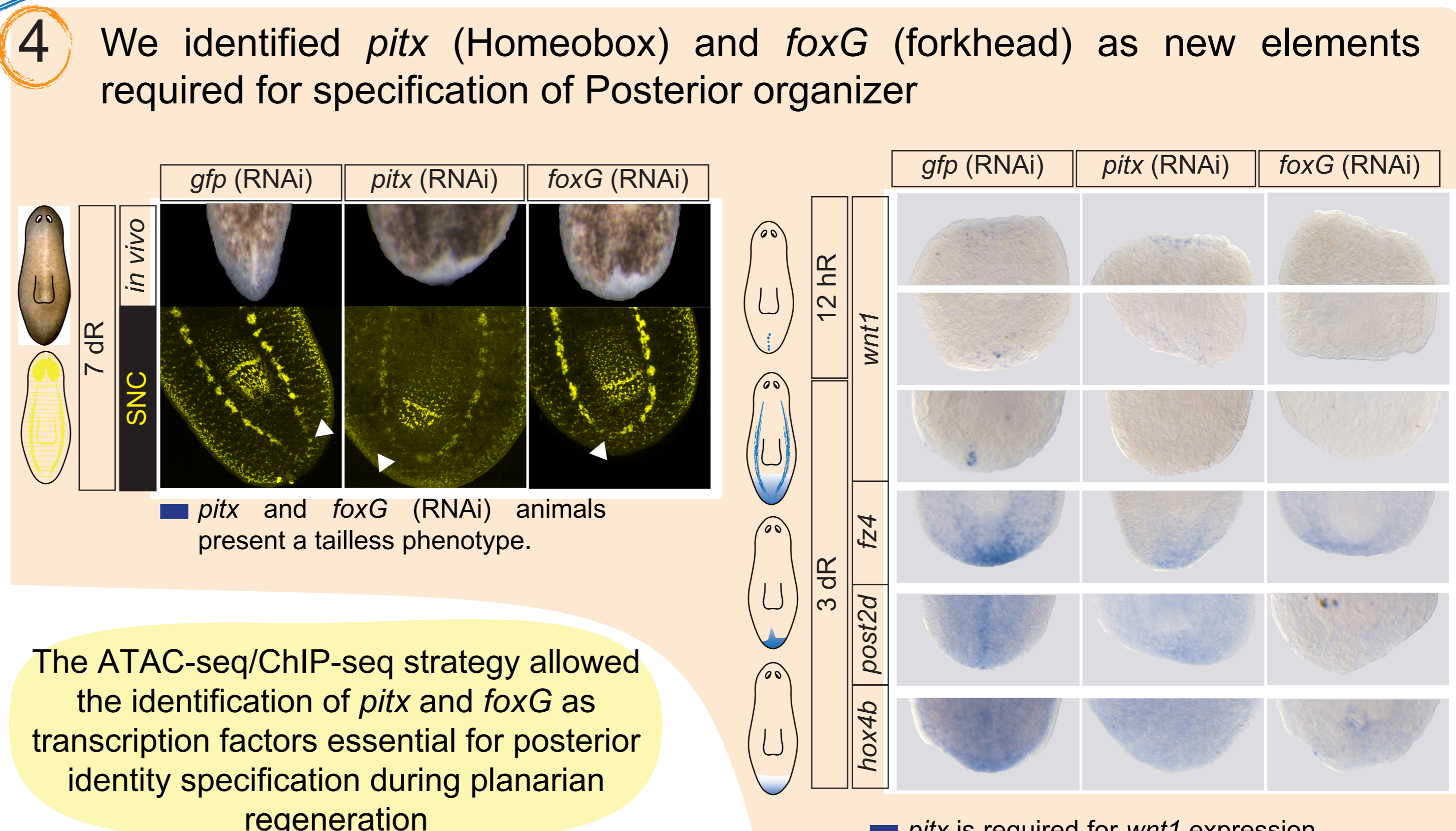
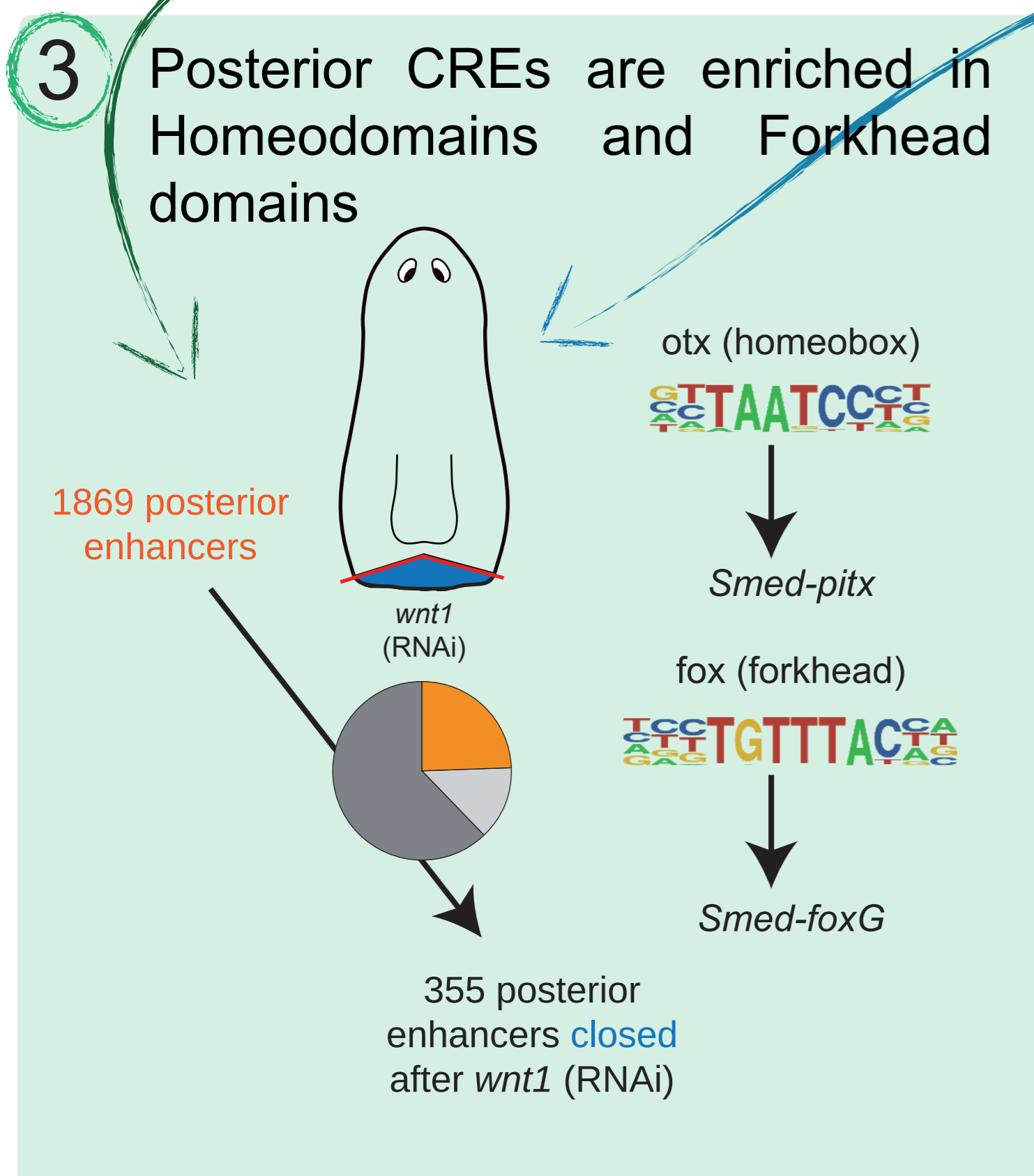
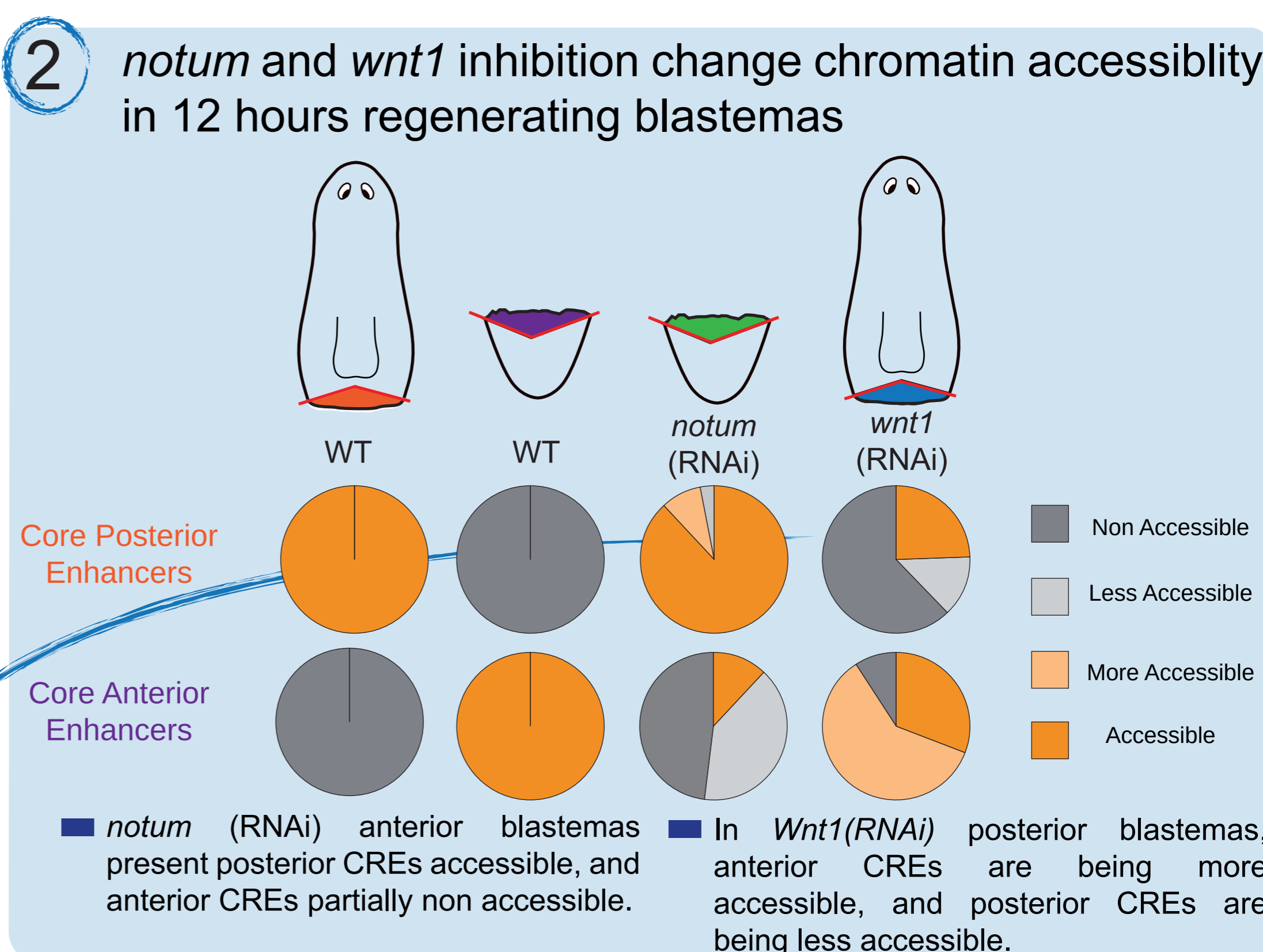
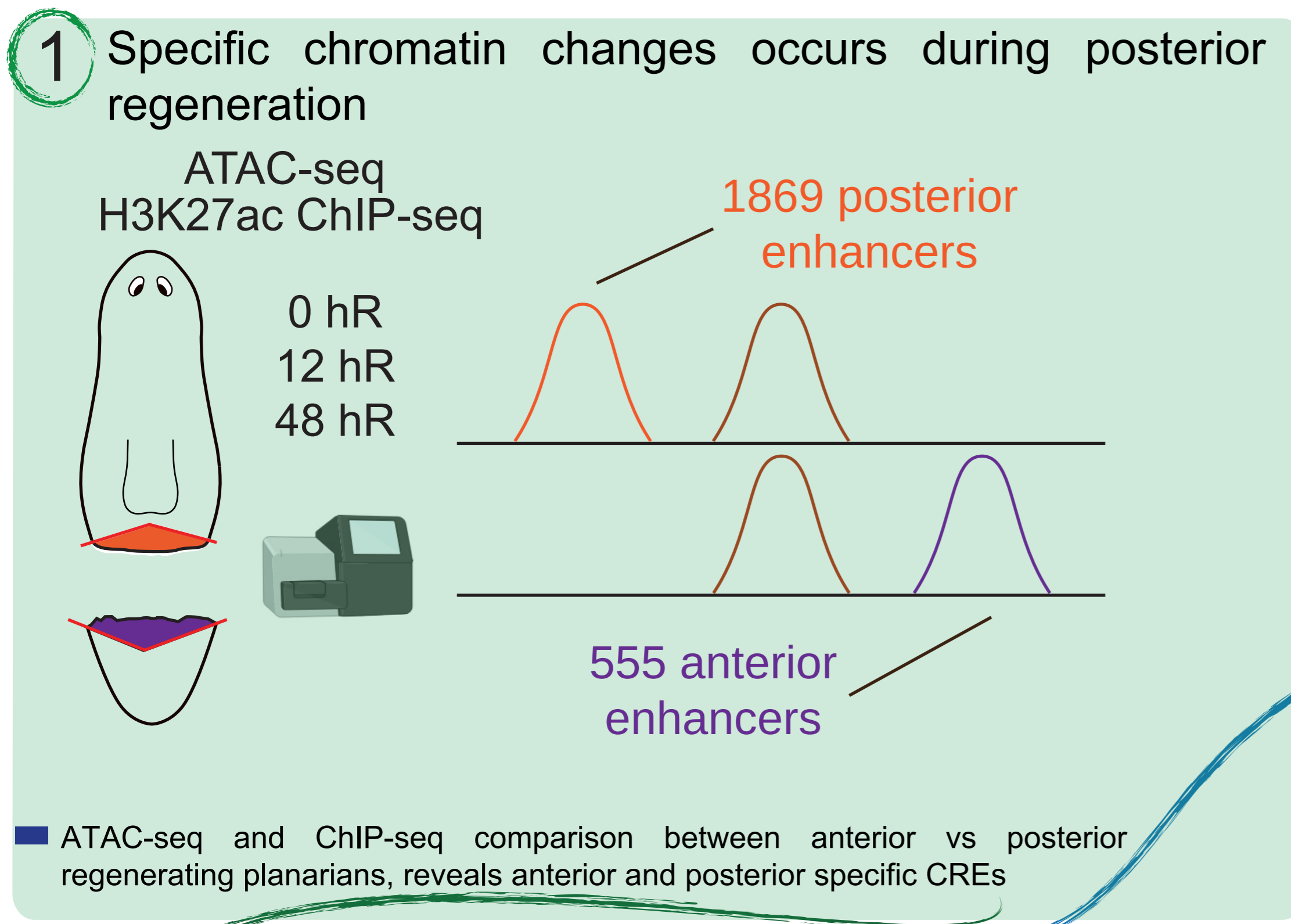
Organizers or signaling centers are a group of cells with the ability to specify the fate of adjacent cells, allowing a patterned growth. Although organizers are mainly studied during embryogenesis, their function is also required in adults, for instance during regeneration. To better understand the formation and function of adult organizers, we study planarians, flatworms that are able to regenerate any missing body part. In planarians the anterior and posterior tips of the body behave as organizers, being defined by the expression of *notum* (a secreted Wnt inhibitor) and *wnt1*, respectively. The inhibition of any of those elements leads to a shift in polarity. Interestingly, during the first hours of regeneration both *notum* and *wnt1* are expressed in both poles, and it's around 36 hours that their expression becomes restricted to their respective tip. To decipher the molecular interactions that restrict the expression of *wnt1* to the posterior tip and confer the organizing activity we used genome wide approaches. ATAC-seq and RNA-seq analysis of regenerating wild-type and *wnt1* (RNAi) planarians allowed the identification of specific Cis-Regulatory Elements (CREs) of posterior regeneration. We found that already at 12 hours of regeneration the accessible CREs in posterior and anterior blastemas have essentially changed, indicating that specific posterior chromatin changes induced by amputation occur much earlier than the formation of the organizers. Furthermore, we have identified specific transcription factors of the Otx and Fox families, which are enriched in posterior CREs and are essential for the specification of the posterior *wnt1*+ cells.

Anteriposterior axis establishment and WNT signalling pathways in planarians



How is cWNT pathway affecting the planarian epigenome during the formation of posterior organizer?

We have performed ATAC-seq, ChIP-seq and RNA-seq during posterior regenerating.



The ATAC-seq/ChIP-seq strategy allowed the identification of *pitx* and *foxG* as transcription factors essential for posterior identity specification during planarian regeneration

■ 355 out of 1869 enhancers associated with posterior regeneration were none or less accessible in *wnt1* (RNAi) animals. Homeodomains and forkheads motifs were highly represented, suggesting their putative role in normal posterior regeneration.