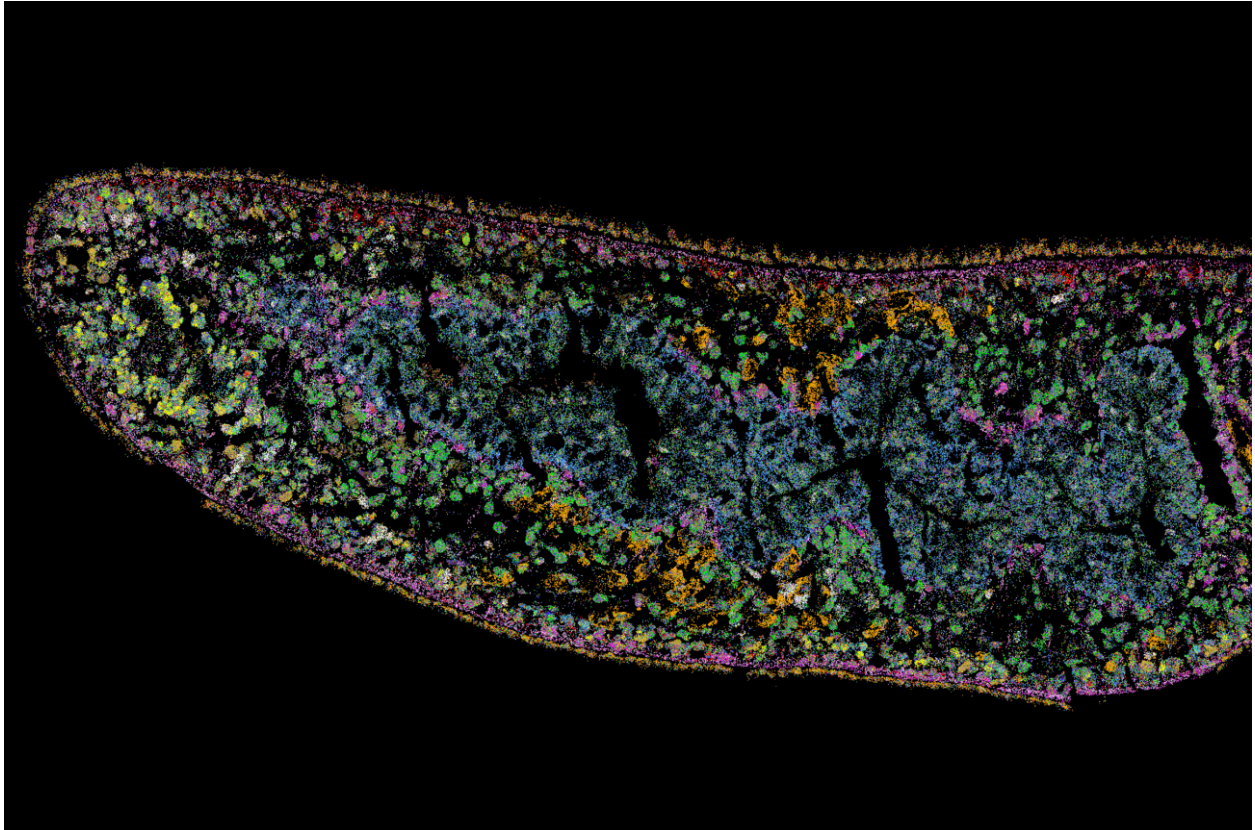


What is the role of Calcium Signaling in Planarian Regeneration?

Aakanksha Roy



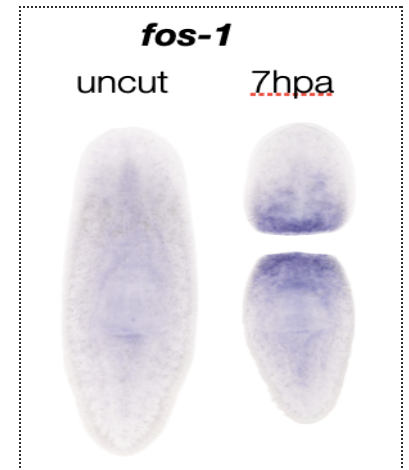
Introduction

Calcium signaling is very crucial for the process of tissue regeneration in planarians. Additionally, calcium ions are used for DNA synthesis in plant cells, containing several genes that affect the early stages of regeneration and the activity of the stem cells. The genes associated with chemical signaling and regeneration are the Fos-1 gene, Hadrian, the Pim-3 gene, and others that are not discussed in this article. These genes all correlate with the process of neoblast proliferation for planarians to have high activity levels of gene expression.

Ideally, these genes correlate towards chemical signaling in a way that they influence the wound responses, blastoma formations, and the regeneration of tissues within planaria as well.

FOS-1 Gene (SMED30013808)

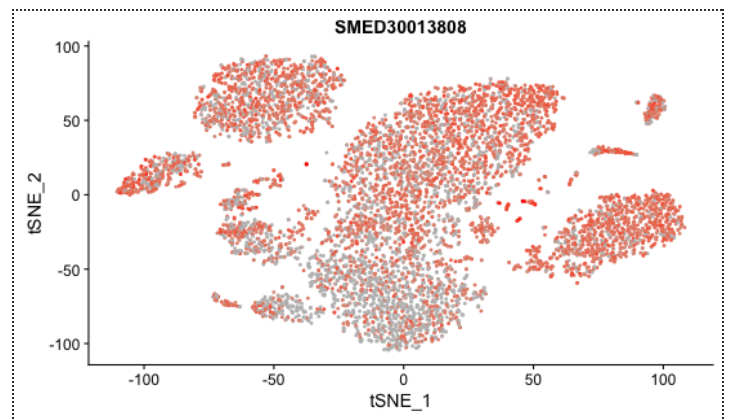
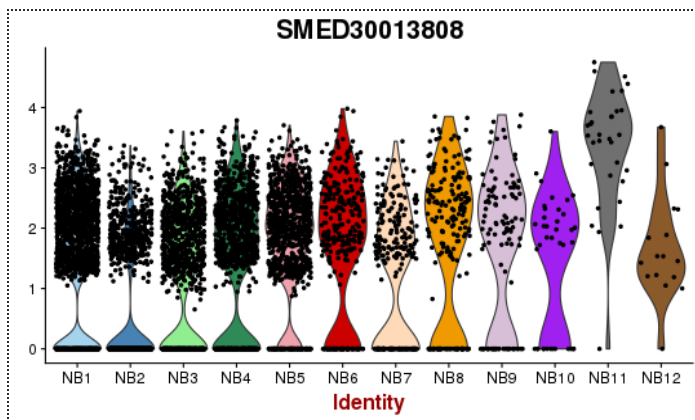
This gene is referred to as the FOS-1 Gene, and its smed ID is known as the SMED30013808 with a length of 1713 base pairs. The picture beside shows the *fos-1* gene in planaria when it's cut and after 7 hours post-amputation. It shows its regeneration process in planarians.



This gene is known as a component of the activator protein-1 (AP-1), regulates changes in metabolism, and assists in the cholesterol synthesis in Human Perioovulatory Granulosa Cells. It is also known that it is represented as an important group of basic region leucine zipper (bZIP) transcription factors, and it encodes for their proteins that can dimerize with JUN proteins. Additionally, they are recognized for development, differentiation, stress responses, and apoptosis in mammals.

Neoblast Stem Cell Population Within the FOS-1 Gene

The neoblast (stem cell) cluster is found under the epidermal progenitor 2 (Nb1), cNeoblasts (Nb2), epidermal progenitor 1 (Nb3), muscle progenitor (Nb4), and gut progenitor (Nb5) clusters. It's mostly found under the Nb1 and Nb4 clusters; however, the Nb1-Nb5 neoblast regions show a strong, significant distribution of gene expression levels of the Fos-1 in cells, as shown in the charts below.



Sub-Lethal Irradiated Surviving X1 and X2 Cell Population of FOS-1 Gene

The Fos-1 is found mostly within the regions of the muscle (SL1) and the neural (SL2) of the sub-lethal irradiated surviving X1 and X2 cells. It is not very well represented within the other areas of the epidermal, gut precursors, or the parapharyngeal regions, which are expressed in the SL4 through SL10 cells.

Tissue Expression of the FOS-1 Gene

The tissues that this gene is expressed in are primarily the epidermal tissue, muscle cells, pharynx, nervous system tissue, cephalic ganglia, neoblasts, and parenchymal cells. In planarian anatomy, it's mostly found within the pharynx, neurons, muscle cell tissues, and parenchymal cells.

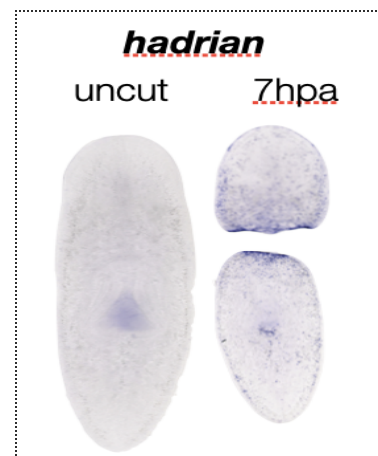
How does this correlate with Planarian Regeneration? (Interesting Facts)

It plays a significant role in wound response, including remodeling of the tissue, healing the wound, and aiding in the organization of the regeneration process with transcription and signaling pathways. Its involvement in the regeneration process is shown because it begins to get activated and upregulated in the area of the pharynx after amputation. Additionally, studies have shown that RNA interference is used to prevent the expression of fos-1 in the regeneration of the pharynx in planaria.

Now, there's a rising question about what specific pathways interact with it during the initial stages of planarian regeneration and how these interactions influence stem cell differentiation in wound responses.

Hadrian Gene (SMED30003738)

This gene is referred to as the Hadrian Gene, and its smed ID is known as the SMED30003738, with a length of 651 base pairs. The picture beside shows the Hadrian gene in planaria when it's cut and after 7 hours post-amputation.

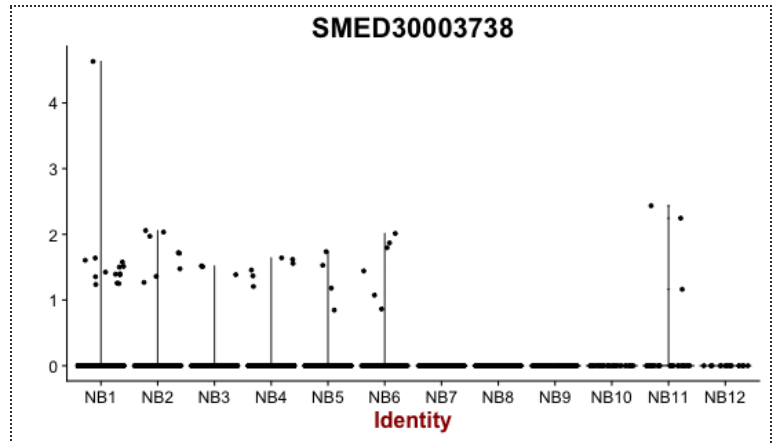


It is known that this gene is a W3 gene that is decentralized in the epidermis, where it assists in the co-expression of wound-induced genes in injured animals' muscle cells. Additionally, it is

expressed in a novel protein around the peripheral area of injured pieces of a wounded site in a cell.

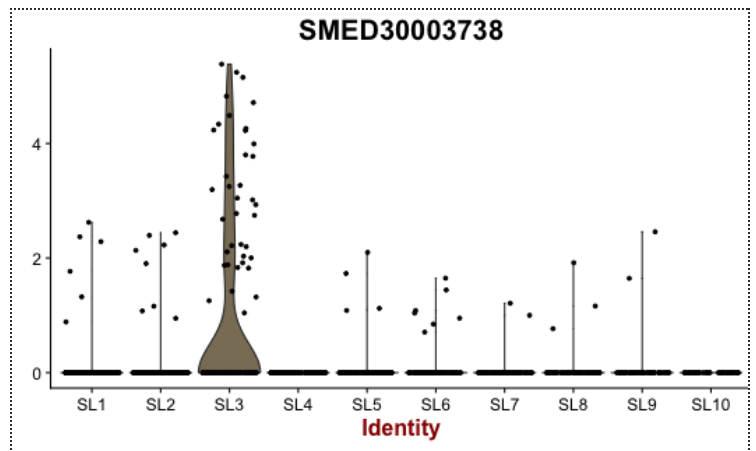
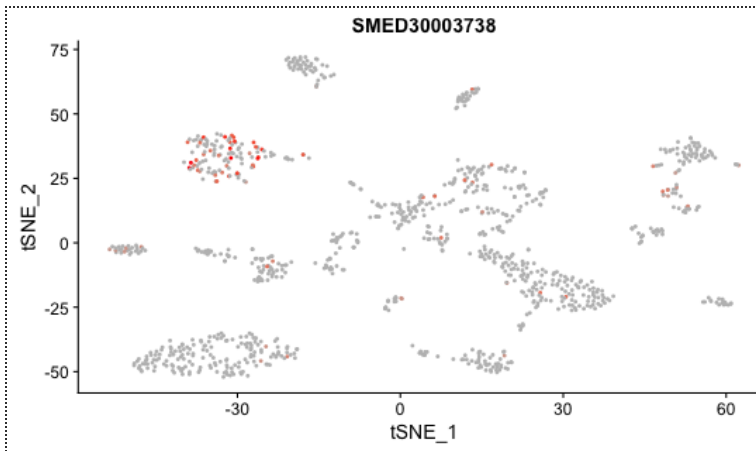
Neoblast Stem Cell Population Within the Hadrian Gene

The neoblast (stem cell) cluster is rarely found within the neoblast stem cell population. As shown in the chart, there is a low distribution of gene expression levels for Hadrian. However, it is shown that the epidermal progenitor (Nb1) has a weak distribution of expression levels.



Sub-Lethal Irradiated Surviving X1 and X2 Cell Population of Hadrian Gene

The Hadrian gene is found significantly in the epidermal region of the surviving X1 and X2 cells. This is represented in the chart as it shows the red spots being present only in that area which proves that the muscle, neural, gut precursor, neoblasts, and parapharyngeal regions do not contain the Hadrian gene within them.



Tissue Expression of the Hadrian Gene

The tissues that this gene is expressed in are primarily the head region, pharynx, epidermis, ciliated epithelial cells, and non-ciliated epidermis. In planarian anatomy, the expression of this gene is within these regions as well.

How does this correlate with Planarian Regeneration? (Interesting Facts)

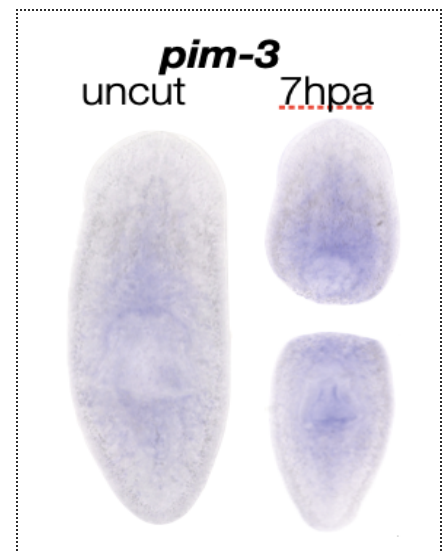
It plays a significant role in regeneration because it is significantly expressed at the wounded site of a planaria between 6 and 12 hours post amputation. It is involved in the regeneration process of the molecular wound response since it is activated by injury and is responsible for maintaining homeostasis for the tissues. It plays a role in calcium signaling during regeneration because it affects the anterior-posterior region of the tissue. As stated before, it assists with the maintenance of the anterior and posterior domains during early post-regeneration.

A question that could be answered with further research is what other genes might Hadrian genes influence that could assist neoblasts in effectively regenerating the wounded site?

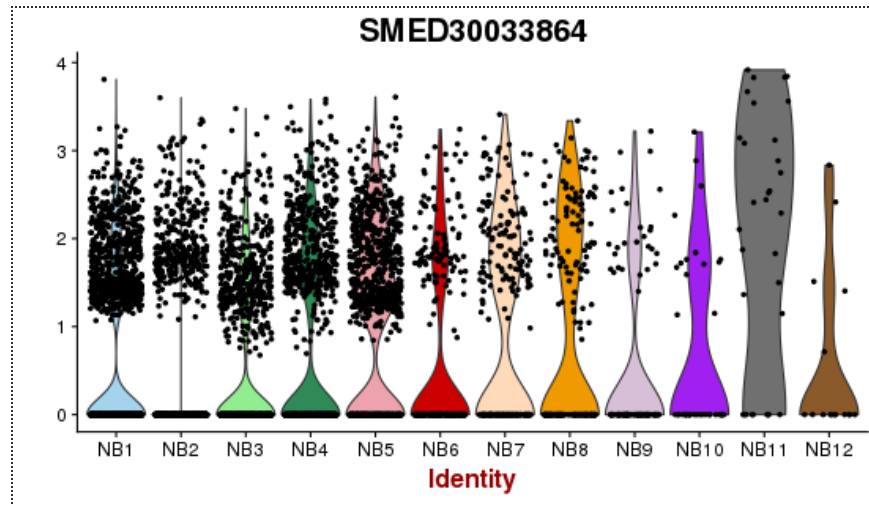
Pim-3 Gene (SMED30033864)

This gene is referred to as the Pim-3 Gene, and its smed ID is known as the SMED30033864 with a length of 1467 base pairs. The picture beside shows the Pim-3 gene in planaria when it's cut and after 7 hours post-amputation. It shows its regeneration process in planarias.

It is known as the Proto-Oncogene, which can lead to developing cancer and the overexpression of epithelial and hematological tumors as well. Additionally, it encodes a kinase with serine and threonine that is involved with survival, proliferation, apoptosis, differentiation, and tumor growth within cells.



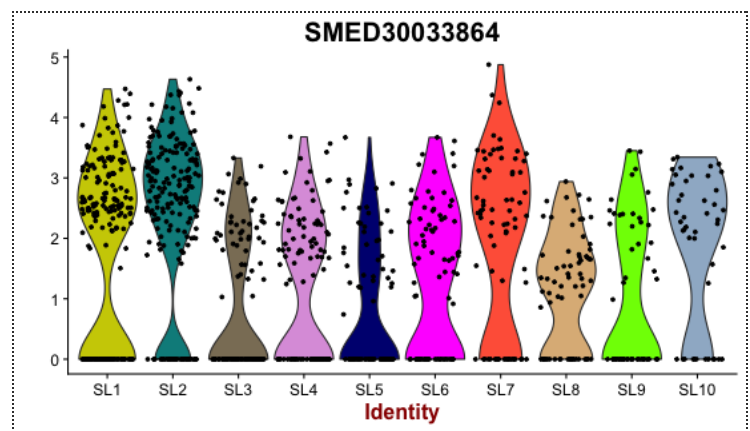
Neoblast Stem Cell Population Within the Pim-3 Gene



The neoblast (stem cell) cluster is found mostly within the epidermal progenitor 2 (Nb1), muscle progenitor (Nb4), and gut progenitor region (Nb5). It is shown that the red dots represent the expression of pim-3 t-SNE clustered cells, which proves that even there is activity in the pharynx progenitor (Nb8) and the anterior pole progenitor (Nb6); however, the regions previously stated tend to have an increased level of gene expression than the others.

Sub-Lethal Irradiated Surviving X1 and X2 Cell Population of Pim-3 Gene

The Pim-3 gene is massively found within the muscle (SL1), neural (SL2), epidermal (SL3), and gut precursor 2 (SL7) regions of the sub-lethal irradiated cell groups.



Tissue Expression of the Pim-3 Gene

The tissues that this gene is expressed in are primarily the pharynx, nervous system, muscle cells, parenchymal cells, and epidermis. It is also found within neurons in the anatomy of planarians.

How does this correlate with Planarian Regeneration? (Interesting Facts)

It plays a significant role in the PI3K signaling pathway, which allows for tissue regeneration to happen and with wound responses in the planaria. Additionally, it is essential for the regrowth of blastema and the regular cellular response to the amputation when regeneration occurs. It can influence the activity of genes involved in regeneration, such as the behavior of stem cells.

A question that arises from all this research is how the Pim-3 gene impacts the interaction between surrounding tissues and stem cells during the early stages of regeneration.

APA Citations of Papers & Websites

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Hadrian Gene:

Wenemoser, D., Lapan, S. W., Wilkinson, A. W., Bell, G. W., & Reddien, P. W. (2012). A molecular wound response program associated with regeneration initiation in planarians. *Genes & Development*, 26(9), 988–1002. <https://doi.org/10.1101/gad.187377.112>

Zaleena Akheralie, Scidmore, T. J., & Pearson, B. J. (2023). *aristaless-like homeobox-3* is wound induced and promotes a low-Wnt environment required for planarian head regeneration. *Development*, 150(18). <https://doi.org/10.1242/dev.201777>

Pim-3 Gene:

Database, G. (2025). *PIM3 Gene - GeneCards | PIM3 Protein | PIM3 Antibody*. Genecards.org. <https://www.genecards.org/cgi-bin/carddisp.pl?gene=PIM3>

Koike, A., Becker, F., Sennhenn, P., Kim, J., Zhang, J., Hannus, S., & Brehm, K. (2022). Targeting *Echinococcus multilocularis* PIM kinase for improving anti-parasitic chemotherapy. *PLOS Neglected Tropical Diseases*, 16(10), e0010483. <https://doi.org/10.1371/journal.pntd.0010483>

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