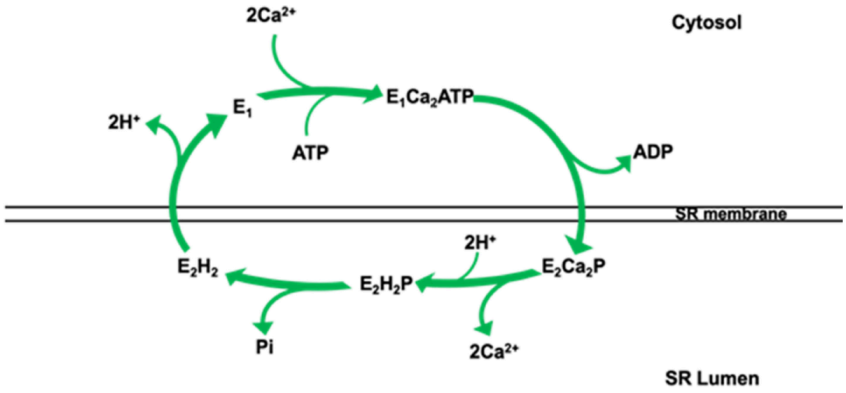
EC Planarian Research

Lauren Langer

What is the role of calcium signaling in planarian regeneration?

I would like to research and investigate the role of calcium signaling on the SERCA, FOS-1, and Pim-1 genes in planarians. Calcium signaling is the use of calcium ions as a second messenger to transmit signals within cells, triggering various cellular responses. In planarians, calcium signaling is believed to play a crucial role in regeneration. Calcium signaling is highly associated with the development of the nervous system, activity of stem cells, and regeneration of the anterior-posterior axis.



The SERCA gene's smed_id is SMED30029216. SERCA is named the Calcium-transporting ATPase. The SERCA gene helps with the regulation of calcium levels within cells. It is a protein that serves as a pump to transport calcium from the cytoplasm to the sarcoplasmic reticulum. Studies have shown that neoblasts expressing SERCA genes are present in multiple clusters, and are not found in a single, isolated cluster. Again, the SERCA gene in planarians is not directly related to a specific sub-lethal irradiated surviving X1 and X2 cell populations. The SERCA gene however is heavily expressed in muscle cells of planaria. It is therefore known to be highly associated with muscle relaxation and calcium homeostasis within the cell, aiding in the process of regeneration.

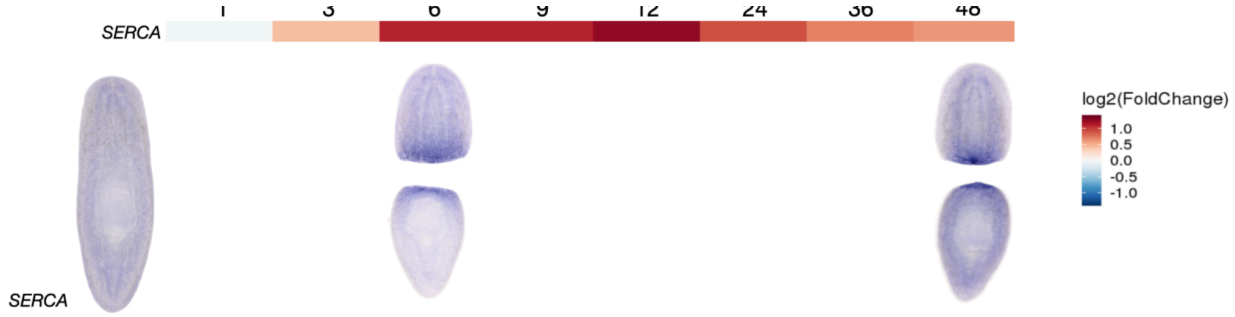
The molecular physiology of the SERCA pump in planarian is made up of fast-twitch skeletal muscle.

Wuytack, F., Raeymaekers, L., & Missiaen, L. (2002). Molecular physiology of the SERCA and SPCA pumps. *Cell Calcium*, 32(5-6), 279–305. https://doi.org/10.1016/s0143416002001847

The SERCA gene is strictly correlated with the movement of CA^{2+} across the cell membrane.

Abou-El-Naga, I. F. (2020). Schistosoma mansoni sarco/endoplasmic reticulum Ca2+ ATPases (SERCA): role in reduced sensitivity to praziquantel. *Journal of Bioenergetics and Biomembranes*. https://doi.org/10.1007/s10863-020-09843-7

Does SERCA gene use active or passive transport when moving calcium through the cell?



The FOS-1 gene's smed_id is SMED30013808. FOS-1 gene is a wound gene that is associated with the early stage of planarian regeneration following an incision. FOS-1 is expressed within 30 minutes of wounding. It, like SERCA, is not associated with a specific neoblast cluster. Additionally, the surviving X1 and X2 cell population after sublethal irradiation in planarians does not include the FOS-1 gene. FOS-1 belongs to the AP-1 transcription factor family and aids in the process of muscle relaxation and movement. In planarian, FOS-1 is found in muscle cells, neurons, parenchymal cells, and in the pharynx. It is known for aiding the healing process of the outer epithelium after a trauma wound.

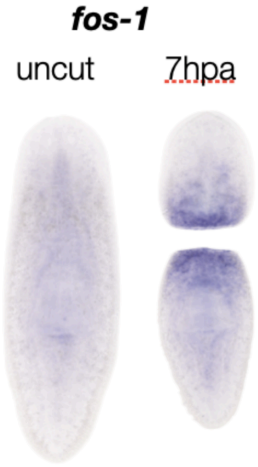
RNA interference experiments have shown that suppressing FOS-1 expression can disrupt planarian regeneration.

Scimone, M. L., Lapan, S. W., & Reddien, P. W. (2014). A forkhead Transcription Factor Is Wound-Induced at the Planarian Midline and Required for Anterior Pole Regeneration. *PLoS Genetics*, 10(1), e1003999. https://doi.org/10.1371/journal.pgen.1003999

The FOS-1 gene is involved in a calcium-dependent signaling pathway that regulates transcription in cells.

Morgan, J. I., & Curran, T. (1988). Calcium as a modulator of the immediate-early gene cascade in neurons. *Cell Calcium*, 9(5-6), 303–311. https://doi.org/10.1016/0143-4160(88)90011-5

Is there a factor that naturally suppresses or mutates the FOS-1 gene resulting in the inability to regenerate and death of that affected planarian?



The Pim-1 genes' smed_id is SMED30025671. The Pim-1 gene in palarian aids in cell growth, cell cycle regulation, and apoptosis. The Pim-1 gene is expressed in the epidermis, muscle tissue, in neurons, and parenchymal cells. Again, the Pim-1 gene is not expressed in a

specific neoblast cluster. Pim-1 is highly expressed though at sites of tissue damage. In planaria, the X1 cells are enriched in Pim-1 high expression, while X2 cells have Pim-1 low expression. The direct link to planarian calcium and Pim-1 gene is not yet established. In humans however, it is believed that Pim-1 expression in the heart can increase the calcium dynamics promoting cardiomyocyte survival and proliferation. Although planaria have no heart, calcium signaling may aid Pim-1 in planarian regeneration.

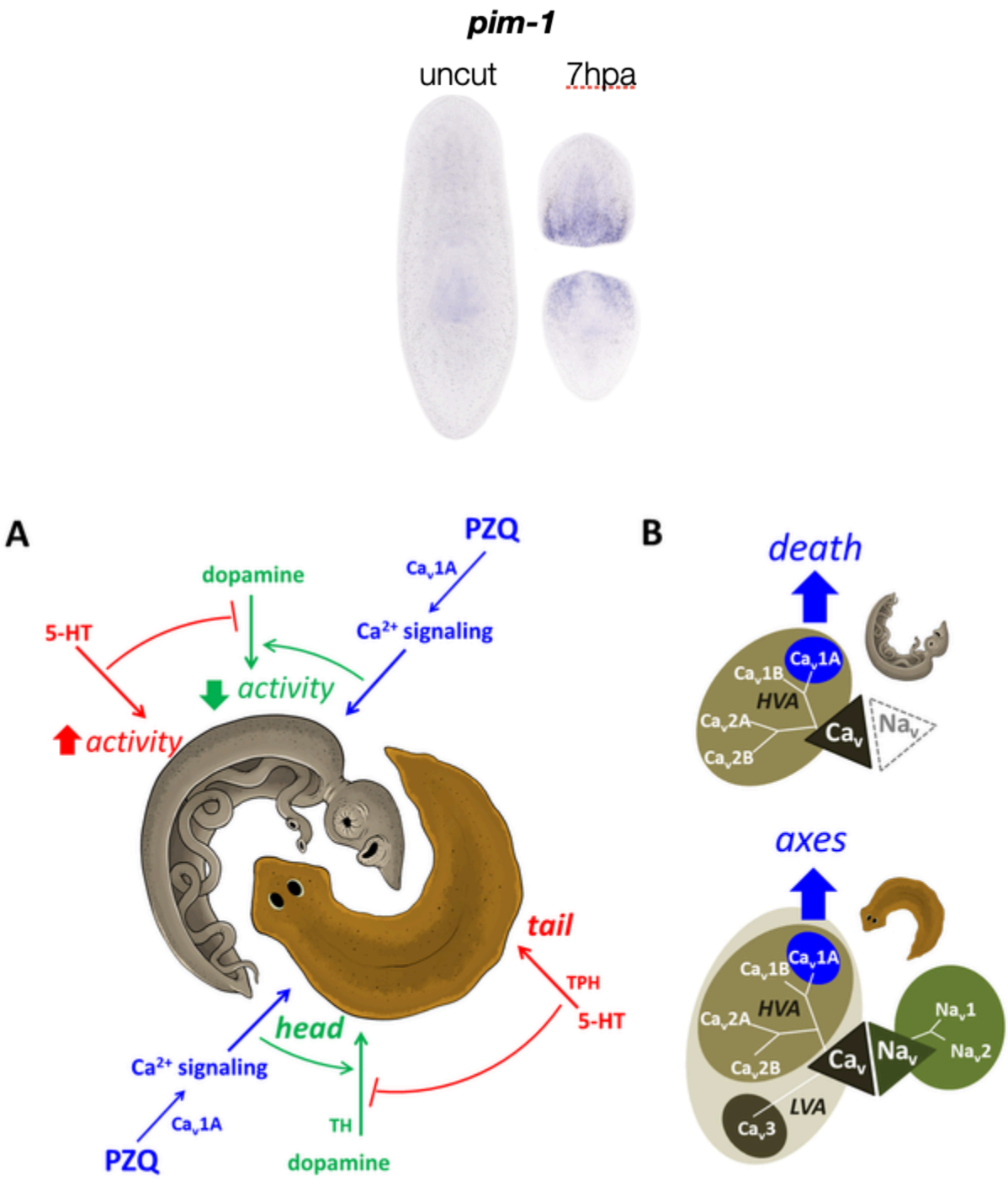
Research has shown that the Pim-1 gene is oftentimes overexpressed in stem cells after injury.

Zeng, A., Li, H., Guo, L., Gao, X., McKinney, S., Wang, Y., Yu, Z., Park, J., Semerad, C., Ross, E., Cheng, L.-C., Davies, E., Lei, K., Wang, W., Perera, A., Hall, K., Peak, A., Box, A., & Sánchez Alvarado, A. (2018). Prospectively Isolated Tetraspanin+ Neoblasts Are Adult Pluripotent Stem Cells Underlying Planaria Regeneration. *Cell, 173(7), 1593-1608.e20*. https://doi.org/10.1016/j.cell.2018.05.006

Pim-1 genes are shown to be upregulated in neoblasts following injury, suggesting a role in the regenerative response.

***PIM1 Pim-1 proto-oncogene, serine/threonine kinase [Homo sapiens (human)] - Gene - NCBI. (n.d.).* Www.ncbi.nlm.nih.gov. https://www.ncbi.nlm.nih.gov/gene/5292**

Could we implement planarian regeneration techniques associated with the Pim-1 gene in genetic technology techniques (such as CRISPR), to use for possible human regenerative processes (such as curing cancer or regenerating a limb)?


pim-1
uncut
7hpa
A
PZQ
Ca$_v$1A
dopamine
5-HT
Ca^{2+} signaling
activity
activity
tail
TPH
5-HT
head
Ca^{2+} signaling
Ca$_v$1A
PZQ
TH
dopamine
B
death
Ca$_v$1A
Ca$_v$1B
HVA
Ca$_v$2A
Ca$_v$2B
Ca$_v$
Na$_v$
axes
Ca$_v$1A
Ca$_v$1B
HVA
Ca$_v$2A
Ca$_v$2B
Ca$_v$
Na$_v$
Na$_v$1
Na$_v$2
LVA
Ca$_v$3