Terminal heterocyst differentiation in the *Anabaena patA* mutant as a result of post-transcriptional modifications and molecular leakage

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The *Anabaena* genus is a model organism of filamentous cyanobacteria whose vegetative cells can differentiate under nitrogen-limited conditions into a type of cell called heterocyst. These heterocysts lose the possibility to divide and are necessary for the colony because they can fix and share environmental nitrogen. In order to distribute the nitrogen efficiently, heterocysts are arranged to form a quasi-regular pattern whose features are maintained as the filament grows. Recent efforts have allowed advances in the understanding of the interactions and genetic mechanisms underlying this dynamic pattern. However, the main role of the *patA* and *hetF* genes are yet to be clarified; in particular, the *patA* mutant forms heterocysts almost exclusively in the terminal cells of the filament. In this work [1], we investigate the function of these genes and provide a theoretical model (Fig.1) that explains how they interact within the broader genetic network, reproducing their knock-out phenotypes in several genetic backgrounds, including a nearly uniform concentration of HetR along the filament for the *patA* mutant. Our results suggest a role of *hetF* and *patA* in a post-transcriptional modification of HetR which is essential for its regulatory function. In addition, the existence of molecular leakage out of the filament in its boundary cells is enough to explain the preferential appearance of terminal heterocysts, without any need for a distinct regulatory pathway (Fig.2).

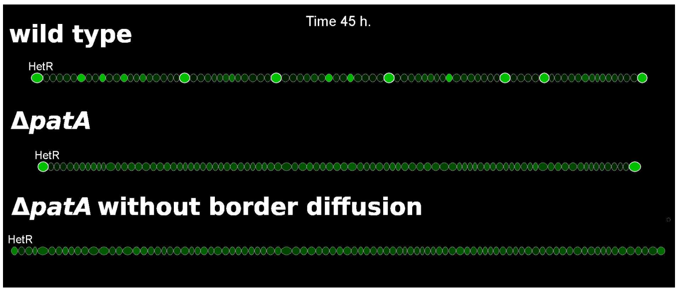

Fig. 2. Computational HetR profiles in filaments of wild-type, patA, and patA with no inhibitor leakage from the terminal cells.

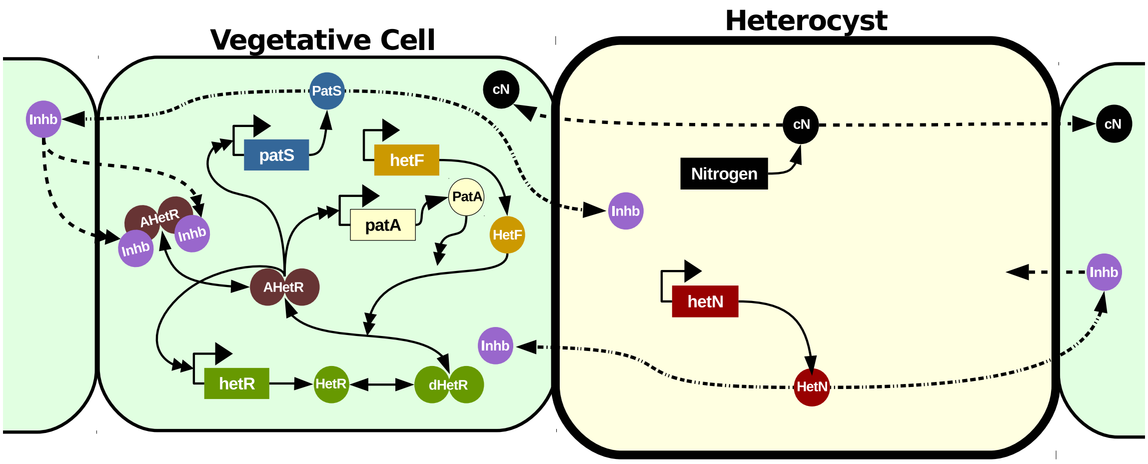

Fig. 1. **Mechanistic Model.** The vegetative cells are represented with a soft green background while the heterocyst has a soft yellow background and a thicker cell wall. Genes are represented in rectangles and proteic elements with circles. The dimers are represented with two attached circles and can be inactivated (in green), activated (in brown), and activated and inhibited (in brown with two attached purple inhibitors). Solid lines represent production (with only one simple arrowhead), transformations (with a simple arrowhead in both ends), and interactions (with a double arrowhead). Dashed lines represent inter-cellular traffic and dashed-doted lines represent a transformation when exported to a neighboring cell.

[1] P. Casanova-Ferrer, S. Ares, J. Muñoz-Garca. *Terminal heterocyst differentiation in the Anabaena patA mutant as a result of post-transcriptional modifications and molecular leakage*. bioRxiv, doi:10.1101/2021.12.20.473559 (2021).