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Hox genes limit adult body size in the planaria Schmidtea mediterranea

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Animals with nearly identical body plans exist in a wide range of sizes, and proper control of body size and allometry is essential for survival and propagation. Previous work has identified early developmental roles for the insulin, mTOR, and Hippo pathways in regulating the rate and duration of growth across cells and organs. However, specific control mechanisms ensuring animals grow to their characteristic adult size and no further remain poorly understood. We have identified a role for Hox genes, evolutionarily conserved transcription factors underlying body patterning and development, in body size restriction in the planaria, Schmidtea mediterranea. Knockdown of the planarian Hox gene Post2b removes this size restriction, resulting in viable adult animals that grow five times beyond their natural size limit. Morphometric analysis of Post2b RNAi worms revealed differential effects on growth duration across body parts, resulting in divergent allometric scaling following size delimitation. Furthermore, once Post2b RNAi animals eclipsed their natural size limit, they exhibited gradual tissue degeneration. Simultaneous knockdown of Post2b with the inflammatory pathway mediators JunD, MKK6, or p38 rescued the Post2b RNAi phenotype to different extents, countering both tissue degeneration and size expansion. Our findings indicate that Post2b is required to limit planarian body size via the activity of JunD/MKK6/p38. Altogether, our study reveals a novel role for Hox genes in determining final animal size and allometry. The NIGMS of the NIH supported this research under award number R35GM154889.

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