Comparative RNA-seq for analysis of regeneration in axolotl

BMI/CS 776

www.biostat.wisc.edu/bmi776/

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Some motivation

James Thomson

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Axolotl

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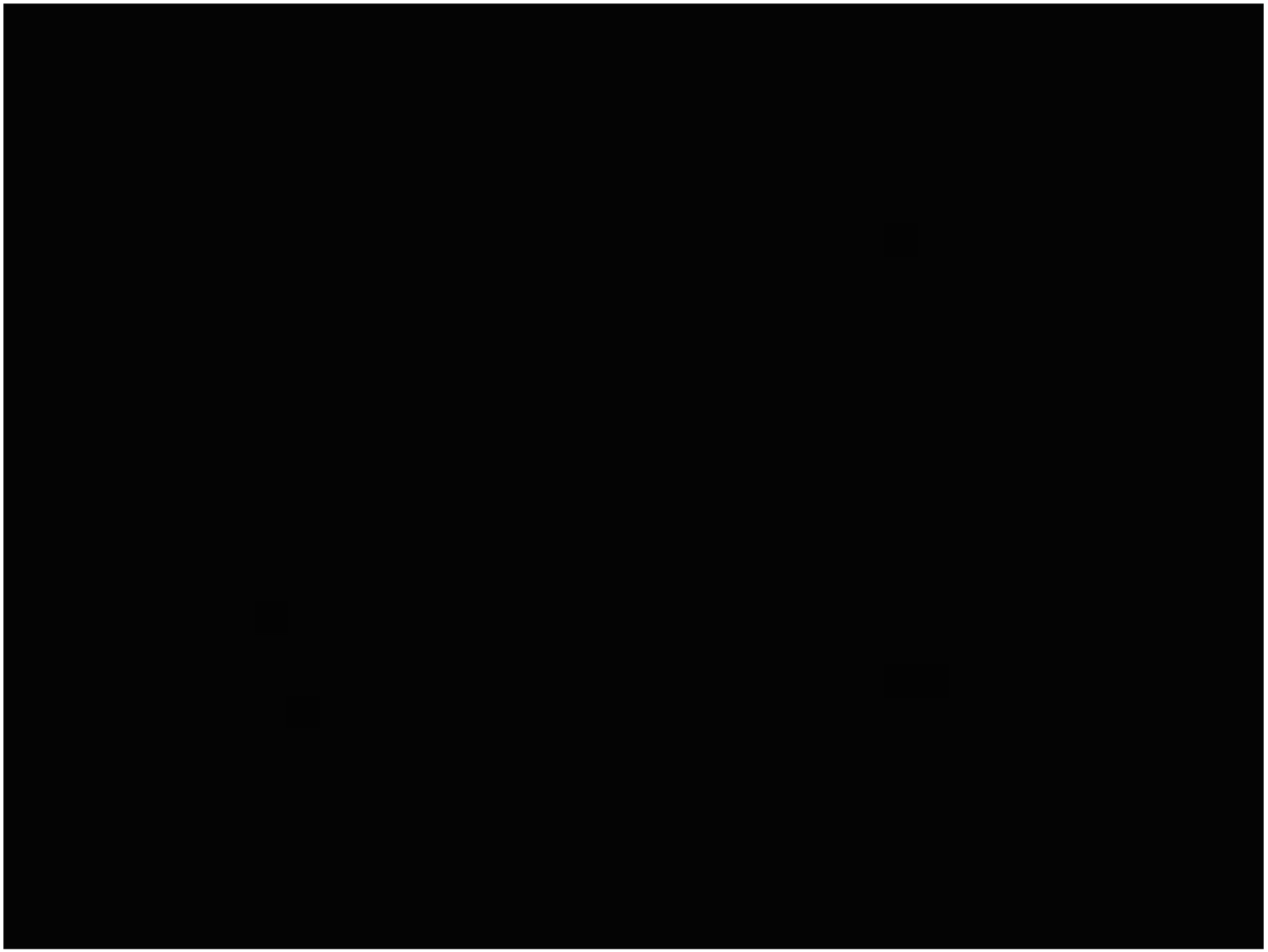
Axolotl limb regeneration



David Gardiner - HHMI-UCI

Goals

- What are the axolotl genes that are responsible for this remarkable regenerative ability?

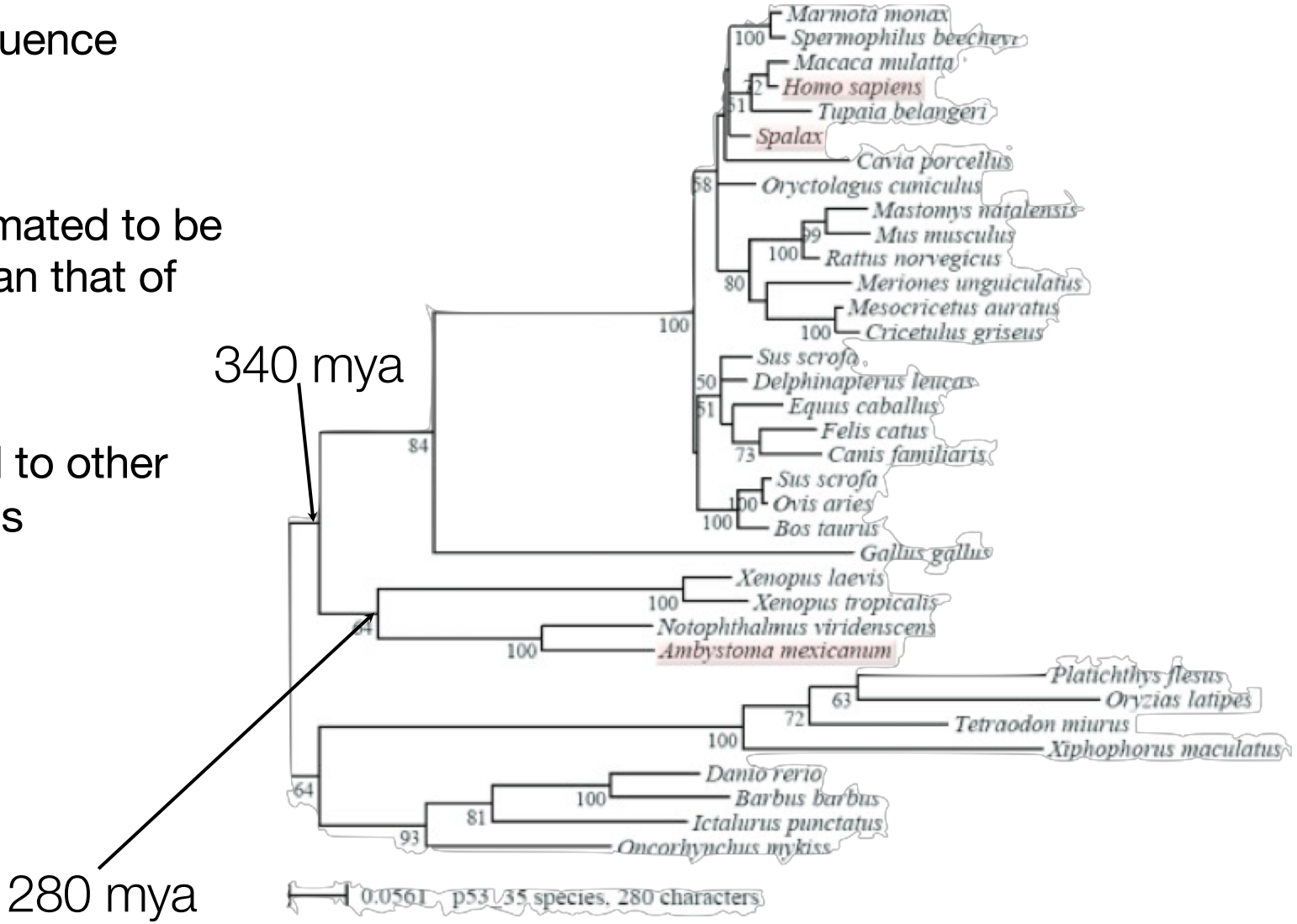
- Can this knowledge improve our medical treatments of severe wounds and tissue regeneration?

Axolotl background

- *Ambystoma mexicanum*
- Natural habitats
  - Lake Xochimilco (canals)
  - Lake Chalco (drained)
  - Endangered
- Commonly sold as pets
- Neotenous
- Regenerative abilities
  - Limbs
  - Portions of Heart
  - Portions of Brain
  - Tail and spinal cord

Challenges with genomic studies of Axolotl

- No genome sequence available
  - genome estimated to be 10x larger than that of human
- Distantly related to other model organisms



Villiard et al. 2007

Prior gene expression studies in Axolotl

- Microarrays
  - Exist, but not very complete
  - Limited amount of mRNA sequence data from Axolotl
  - No genome, so can’t use predicted gene sequences

Axolotl experimental setup

Samples

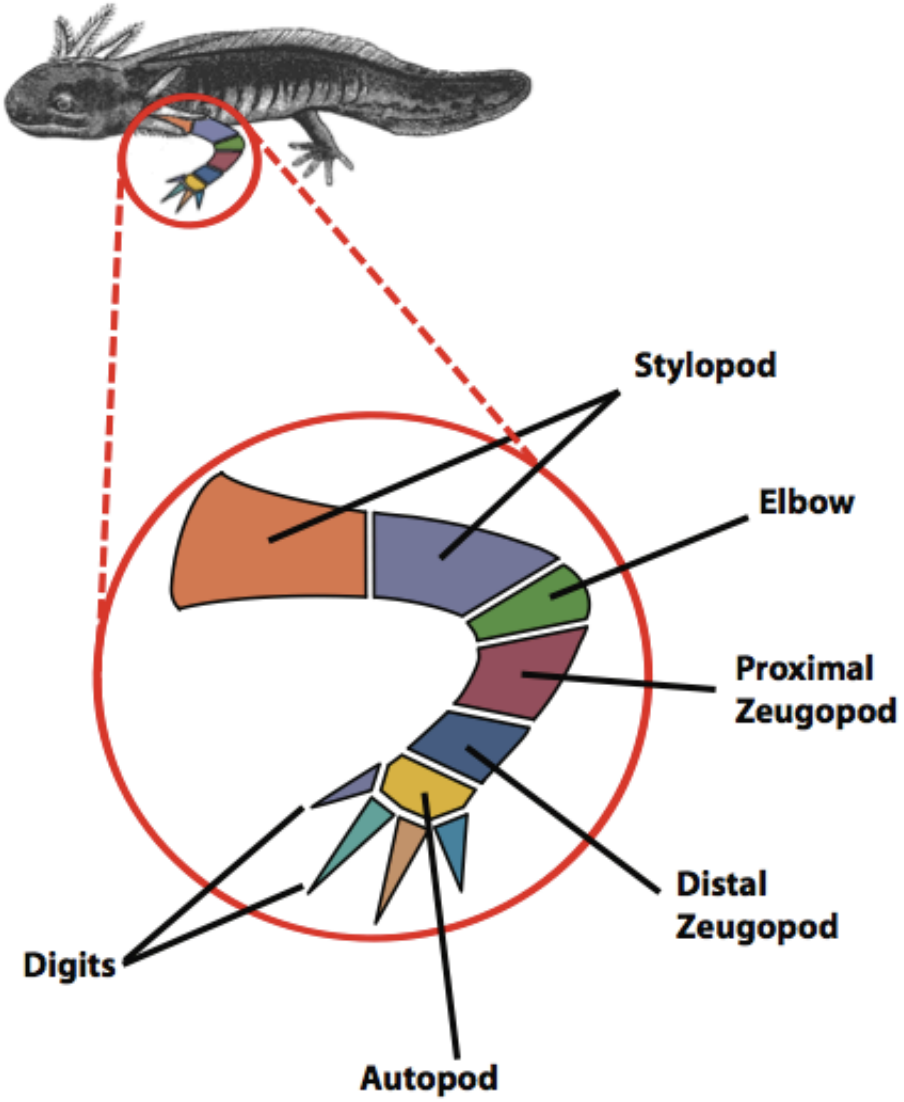
Stylopod (upper arm) (3)

Zeugopod (lower arm) (3)

Autopod (hand) (3)

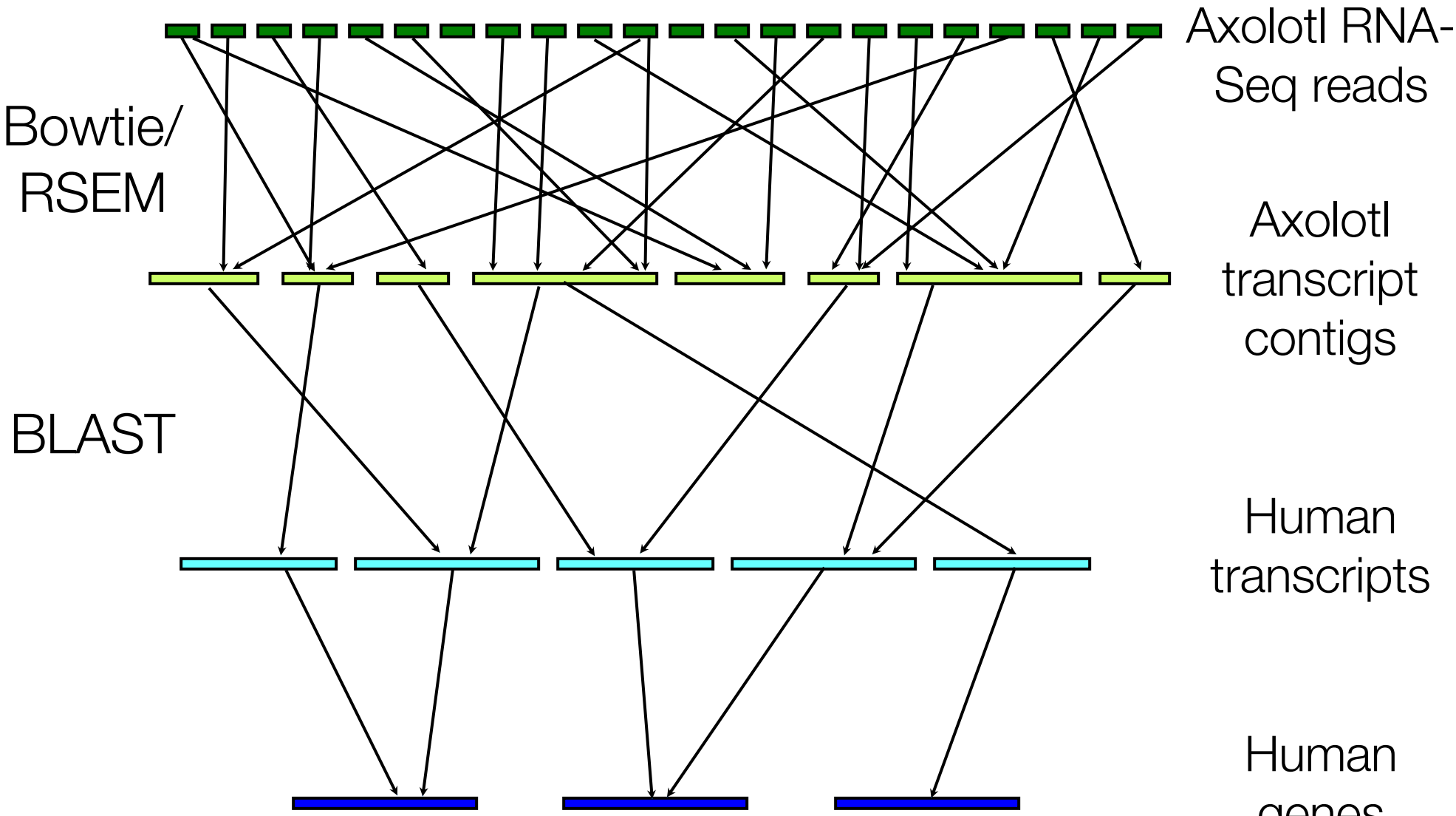
Digits (3)

30 day blastema (5)

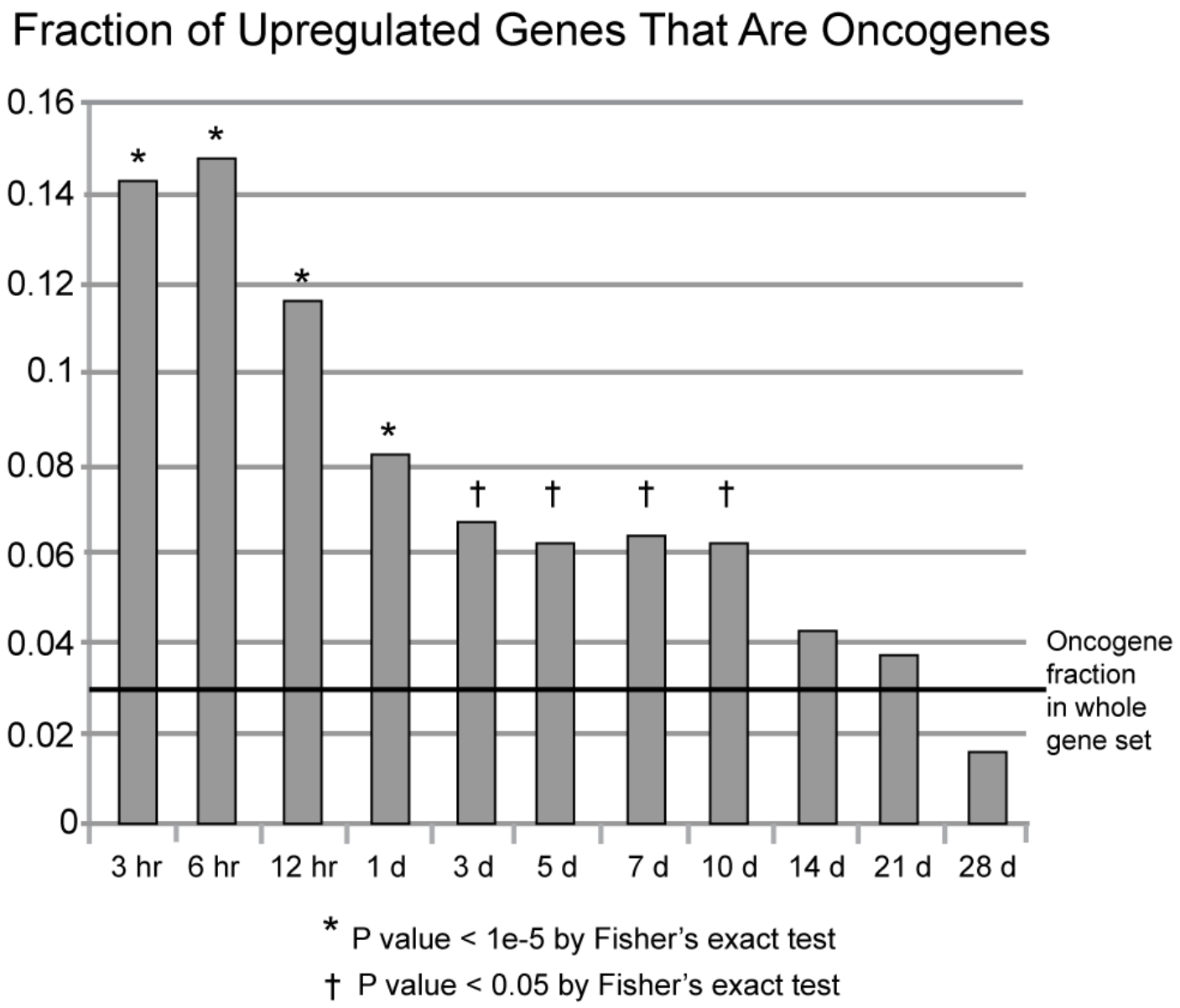


Comparative RNA-seq analysis in the unsequenced axolotl: The oncogene burst highlights early gene expression in the blastema
R. Stewart, C. Rascón, S. Tian, J. Nie, C. Barry, L. Chu, R. Wagner, M. Probasco, J. Bolin, N. Leng, S. Sengupta, M. Volkmer, B. Habermann, E. Tanaka, J. Thomson, and C. Dewey
PLoS Computational Biology. 9(3): e1002936. 2013.

Human-based analysis of axolotl transcription



The oncogene burst



Regeneration as controlled cancer

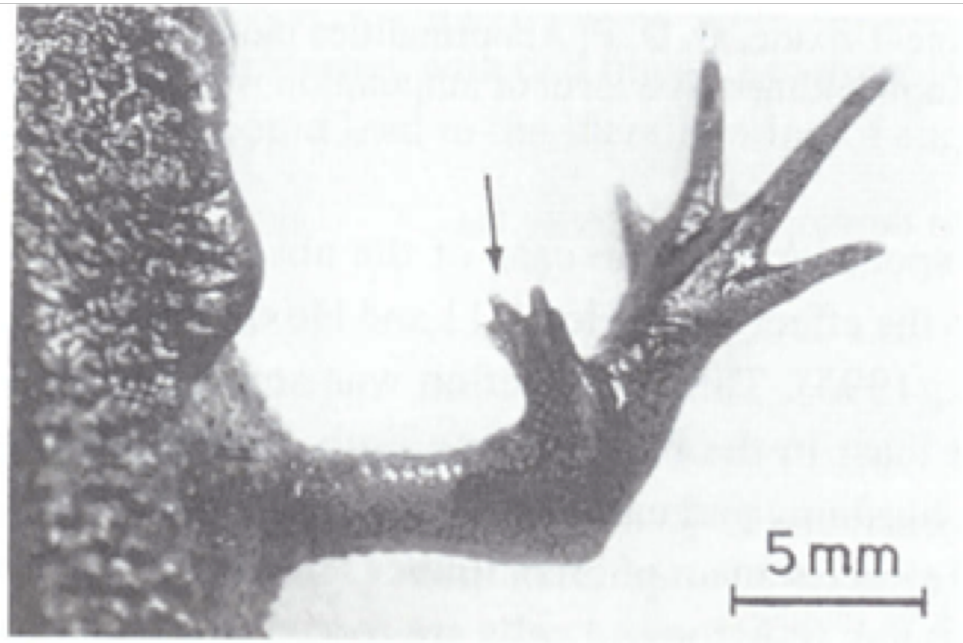


Figure 11.1 Induction of supernumerary limb formation in the Japanese newt Cynops pyrrhogaster by carcinogen treatment. The carcinogen used was N-methyl-N'-nitro-N-nitrosoguanidine.

P Tsonis, Limb Regeneration, 1996, Cambridge University Press

Limb Regeneration -- Oncogenes and tumor suppressors
"Controlled Cancer" --> development and differentiation
Salamanders very resistant to tumorigenesis by carcinogens