

CHAPTER 12

- 1) See Fig. 12.1 and also the glossary for definition. Include cell proliferation, cell enlargement, accretionary growth, and the pathways controlling cell size and cell number.
- 2) Include control of entry into the cell cycle, cell cycle checkpoints, timing mechanisms — cyclins and cyclin-dependent kinases.
- 3) Early cell cycles in *Drosophila* create the syncytial blastoderm – see also Chapter 2 – and there are virtually no G phases. Include discussion of distinct domains in the blastoderm at the 14th cell cycle with different cell-cycle times and the function of String and Twine.
- 4) Outline experiments in which organ precursor cells are specifically destroyed. Include details of methodology using transgenic mice and the results of the experiments. Need to explain how the conclusions are drawn.
- 5) Refer to Hippo pathway in Box 12A. Regulation of *bantam* expression is one of the outputs of the pathway.
- 6) See also definition in the glossary. Include pituitary, growth hormone-releasing hormone, somatostatin, insulin-like growth factors.
- 7) See also definitions in the glossary of tumour-suppressor gene and proto-oncogene. Include genes encoding Wnt and Hedgehog signals and components of their intracellular signaling pathways.
- 8) Need to take into account the feedback loops that normally control production of thyroid hormones in the tadpole and also the effects of thyroid hormones on different tissues. There are also practical considerations for the experiments. Is thyroxine likely to penetrate the skin? How long will it remain active when simply added to the water in which the frog tadpole is reared?
- 9) Include senescence – see also glossary for definition, life-spans in different animals, effects of insulin/IGF signaling pathway on life span in *C. elegans* and *Drosophila*, Werner syndrome, cell doublings of cultured fibroblasts.
- 10) Include requirement for nerves for salamander limb regeneration, anterior gradient protein and experiments that show that this is the essential growth factor. Which cells express anterior gradient protein can explain why limbs that have never been innervated can regenerate.
- 11) The experiment investigates why distal structures normally regenerate when a salamander limb is amputated. Include discussion of different models that could explain how this happens and how the experimental results obtained distinguish between them.
- 12) Include the nature of the Prod1 protein, expression levels of Prod1 along the proximo-distal axis of the salamander limb, stimulation of Prod1 expression by retinoic acid, experiments on the behaviour of explants of limb blastemas when confronted in culture and effects of treatment with blocking antibodies to Prod1, the identity of the ligand for Prod1.
- 13) Retinoic acid has a proximalizing effect on a salamander limb blastema. See morphology of regenerated limb in Fig. 12.33. Might also mention effects of retinoic acid treatment on tail regeneration in frog tadpoles.
- 14) You should be able to work this out by using the numbers 1-5 shown on the figure indicating the postulated positional values along the proximo-distal axis of the cockroach leg tibia.
- 15) Understanding how the heart regenerates in zebrafish might lead in the long term to devising new treatments for heart disease. Outline knowledge about the ability of cardiomyocytes (cardiac muscle cells) of adult zebrafish heart to dedifferentiate and proliferate and the signals that promote these cell activities. Include interactions between the different layers of the heart – also see Chapter 10 for how the heart develops. How likely is it that this knowledge gained from investigations on regeneration of the zebrafish heart can be applied to the mammalian heart? Include investigations on regenerative ability of the heart in newborn mice.

- 16) Outline the hypothesis that tissue/organ size is regulated by negative feedback. What is the evidence for negative feedback regulating muscle size? Include myostatin and genetic evidence for its function in regulating the amount of muscle—both mouse knock-out experiments and ‘double-muscled’ domestic animals. Is negative feedback likely to be involved in controlling the size of other tissues and organs?
- 17) Consider the information in section 12.19 and Box 12E. Is it simply a question of finding an appropriate cocktail of growth factors to apply to an injured limb or are there fundamental differences between mammalian and amphibian limbs in terms of their regenerative ability?