

**Potent Biology: Stem Cells, Cloning, and Regeneration**  
**2006 Holiday Lectures on Science**  
**Chapter List**

Lecture One

Understanding Embryonic Stem Cells

Douglas A. Melton, Ph.D.

1. Start of Lecture One
2. Welcome by HHMI President Dr. Thomas Cech
3. Dr. Melton in the lab
4. Introduction to stem cells
5. Development is growth and differentiation
6. The variety of cell types in the human body
7. Animation: Human embryonic development
8. Germ layer make specific tissues
9. Animation: Germ layers and cell fate
10. The pancreas: Structure and function
11. Function of specific pancreatic cells
12. Role of the pancreas in diabetes
13. Progressive development creates specialized cells
14. Demo: Using a DNA chip to study gene expression
15. Genes are turned on and off at each step of differentiation
16. Differentiation is like making life decisions
17. Cytoplasmic factors affect cell fate
18. Cell-cell interaction also affects cell fate
19. Q&A: How many genes are involved in differentiation?
20. Q&A: Does the ectoderm determine pigmentation?
21. Q&A: Does a cell respond to multiple growth factors?
22. Q&A: Can you change gene expression to change cell types?
23. Q&A: Can cells be changed in vitro with chemical factors?
24. Q&A: Do internal/external factors influence cells simultaneously?
25. Body maintenance and cell renewal
26. Different cell types have different renewal rates
27. Stem cells are responsible for maintenance and repair
28. Two essential properties of stem cells
29. Blood stem cells can replenish and differentiate
30. A single blood stem cell can replenish an entire animal
31. Some cell types replenish by division, not by stem cells
32. A pulse-chase experiment on pancreatic cell replacement
33. New pancreatic  $\beta$  cells are from division, not stem cells
34. In type I diabetes, no new  $\beta$  cells can be made
35. Embryonic stem (ES) cells and their traits
36. How are ES cells derived?
37. Animation: ES cell creation
38. Confirming that ES cells are totipotent
39. Deriving human ES cells and their potential usefulness
40. Video: Human ES cells differentiating into heart cells

41. Q&A: Would transplanted ES cells differentiate properly?
42. Q&A: What stimulates production of external/internal factors?
43. Closing remarks by HHMI President Dr. Thomas Cech

## Lecture Two

### Adult Stem Cells and Regeneration

Nadia Rosenthal, Ph.D.

1. Start of Lecture Two
2. Welcome by HHMI Vice President Dr. Peter Bruns
3. Dr. Rosenthal in the lab
4. Overview of differentiation
5. Replenishment and renewal of the body
6. Some cells replenish constantly
7. Replenishment vs. regeneration
8. The myth of Prometheus and liver regeneration
9. Is wound healing regeneration?
10. Stem cells are rare in adults
11. Some animals can regenerate body parts
12. Planaria regeneration and stem cells
13. Student experiments on planaria regeneration
14. Stem cells activated in regenerating planaria
15. Demo: The fire-bellied newt
16. Animation: Newt limb regeneration
17. Muscle cells contributed to skin in regenerating limb
18. Can humans regenerate body parts?
19. Q&A: Why can't the newt arm grow a new newt?
20. Q&A: Could you put newt stem cells into a human?
21. Q&A: What happens to muscle in limb lengthening?
22. Q&A: Can a newt regenerate its organs?
23. Q&A: How many times will the newt limb regenerate?
24. Q&A: What triggers cells to form the blastema?
25. Problems with mammalian regeneration
26. Dedifferentiation of cells during regeneration
27. Cancer and dedifferentiation are similar
28. Controlled cell proliferation in the newt
29. Are regenerative genes lost in higher organisms?
30. Identifying the signals that control limb regrowth
31. The CD59 protein may guide newt limb regrowth
32. Overexpressing CD59 causes malformation
33. Demo: Regeneration of deer antlers
34. Adult stem cells in bone marrow and muscle
35. Muscular dystrophy overwhelms stem cell capacity
36. Using bone marrow cells to repair dystrophic muscle
37. Growth factor IGF-1: Function and mechanism
38. IGF-1 improves bone marrow's ability to regrow muscle cells
39. Summary of regeneration schemes
40. Q&A: Could stem cells reverse the effects of liver cancer?
41. Q&A: Why do we age if we can regenerate cells?
42. Q&A: How far up a newt's limb can you cut?
43. Q&A: Are skin markings identical on the regrown newt limb?
44. Q&A: Can a newt regrow two limbs at once?
45. Closing remarks by HHMI Vice President Dr. Peter Bruns

Lecture Three  
Coaxing Embryonic Stem Cells  
Douglas A. Melton, Ph.D.

1. Start of Lecture Three
2. Welcome by HHMI Program Director Dr. Dennis Liu
3. Dr. Douglas Melton on teaching
4. Stem cells and cloning
5. Cloning animals depends on reprogramming cells
6. Plants: The original cloned organism
7. Cloning frogs by nuclear transplantation
8. Frogs were the first adult cloned animal
9. The very first cloned mammal: Dolly the sheep
10. Video: Cloning by somatic cell nuclear transfer (SCNT)
11. Many types of animals have been cloned
12. Cloning shows that differentiation can be reversed
13. Q&A: Is the clone's surrogate mother different on purpose?
14. Q&A: Do clones have any deformities?
15. Q&A: Do clones have a greater risk of cancer?
16. Q&A: Why did the cloned cows have different markings?
17. Q&A: In SCNT, why doesn't the nucleus change the cell?
18. Q&A: Do cloned animals have similar personalities?
19. Combining cloning and stem cells for studying disease
20. Characteristics of degenerative diseases
21. Specific cells affected by degenerative diseases
22. Pancreatic  $\beta$  cells and type I diabetes
23. Can cultured ES cells differentiate to pancreatic  $\beta$  cells?
24. Interactions between different cells affect differentiation
25. Blood vessel proximity and pancreatic  $\beta$  cells
26. Molecular signals for each differentiation step are unknown
27. Deriving motor neurons from ES cells
28. Motor neurons derived from ES cells are functional
29. Challenges in studying degenerative diseases
30. Animation: Combining SCNT and ES cells
31. Creating ALS-diseased cells by SCNT for research
32. Using ES cells to study ALS development
33. Using ES cells to screen for effective treatments
34. Two approaches to using ES cells to study diseases
35. Q&A: Can lack of diversity in cloned cows cause problems?
36. Q&A: Are there cells that can't be used for cloning?
37. Q&A: How do you treat prion-based degenerative diseases?
38. Q&A: Only two factors for motor neuron differentiation?
39. Q&A: Why didn't the chick embryo reject mouse neurons?
40. Q&A: How would you deliver ES cells to an adult patient?
41. Q&A: Degenerative diseases that affect two cell types?
42. Q&A: Could cells be reprogrammed to prevent cancer?
43. Closing remarks by HHMI Program Director Dr. Dennis Liu

Lecture Four  
Stem Cells and the End of Aging  
Nadia Rosenthal, Ph.D.

1. Start of Lecture Four
2. Welcome by HHMI President Dr. Thomas Cech
3. Dr. Nadia Rosenthal on teaching
4. Physiological characteristics of aging
5. The stem cell pool and ability to regenerate tissue
6. Three ways stem cells could affect aging
7. Capacity to rebuild muscle decreases with age
8. Older muscle has fewer satellite cells
9. Satellite cells from aging muscle are still potent
10. Aging reduces satellite cell signaling
11. The Notch-Delta molecular signaling pathway
12. Notch-Delta response differs in young and old muscle
13. Changing Notch levels affects muscle repair
14. Does the stem cell's environment change during aging?
15. Response of old mouse stem cells to young mouse environment
16. Young-old "pairing" improves repairing ability of old muscle
17. Serum factors can activate Notch pathway in old cells
18. Old muscle revival is due to young molecules, not young cells
19. Summary of factors involved in aging and stem cell response
20. Q&A: How do muscle cells "know" that they are injured?
21. Q&A: High regeneration tissues have medium stem cell numbers?
22. Q&A: Old stem cells revert if young environment is removed?
23. Q&A: In rapid aging diseases, do stem cells appear old or young?
24. Can we improve the heart's ability to regenerate?
25. Animation: Heart structure and function
26. Heart function is crucial, but the heart is a poor regenerator
27. Demo: Cause and effect of a heart attack
28. After a heart attack, cardiac tissue is lost
29. Other organisms can regenerate heart muscle
30. Animation: Zebrafish heart regeneration
31. Potential cell therapy for heart failure
32. Evidence that the heart can incorporate circulating cells
33. Using bone marrow stem cells to rebuild heart tissue
34. In recent trial, stem cell heart therapy had mixed results
35. Using an IGF-1 mouse to see if heart muscle can make new cells
36. Damage to cardiac tissue heals in the IGF-1 mouse
37. Cellular basis of IGF-1's role in cardiac tissue regeneration
38. IGF-1 animals express signaling factors that aid in regrowth
39. T $\beta$ 4 found to reduce scarring in heart damage
40. T $\beta$ 4 and FGF create a response similar to zebrafish regeneration
41. Stem cells for potential heart repair
42. Acknowledgements
43. Q&A: Are blood types a factor in heart transplants?
44. Dr. Thomas Cech announces speakers for next Holiday Lectures