BIOE219/DBIO219
Special Topics in Development and Cancer: Quantitative and Evolutionary Perspectives
Class meets @ 3-4:20p, M&W, Winter, Shriram 054.
Office hour: 5-7p F, Shriram 084.

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Learning goals
This class will be a guided tour at the intersection between development, cancer, evolution, and physics. Instead of focusing on what we know, the goal of this course is for students to trace how we know, and how we should ask questions for the future. In my opinion, the most important scientific problems are often left unresolved not for lack of adequate information, but for lack of insights to specify the questions that require explanation. Therefore, in this class, we will work together to search for important questions in the area, by reconstructing historical and controversial ideas, dissecting classic literature, formulating our own questions, and debating to test our answers. This class is a tour, as there is no intention for it to be comprehensive; students will be treated as my future colleagues and provided by a taste of science – you should progress in your own way, at your own pace that matches your ambition in learning. Therefore, I expect the class to be interactive and even provocative, and the students to be willing to read beyond the class as active reading is essential to succeed in this course.

Logistics
Contents: 6 lectures, 8 discussions, 2 debates.
Your responsibility: 16 homework, 1 debate, 1 term paper.

6 learning topics (Discussion 3-8) to be selected by students, from the Nature Milestones of Development and Cancer (attached).

Homework A: due by Tuesday @ midnight. Q on the discussion paper.
Homework B: due by Sunday @ midnight. Q&A near-topic.
Homework is submitted through google doc. Commenting on each other's homework is strongly encouraged.

Grades: class discussion 20%, homework 40% (5% each week), debate 20% (10% each), term paper 20%.

Schedule
Wk1

1/8 (M) **Lecture 1: From Weismann to Spemann**
Background: Alejandro Sánchez Alvarado, To solve old problems, study new species, https://www.ted.com/talks/alejandro_sanchez_alvarado_to_solve_old_problems_study_new_species
Further reading: Laland K. et al. Does evolutionary theory need a rethink? *Nature* 514, 161–164 (2014)

1/10 (W) **Lecture 2: von Baer's law and the clock of evolution**
Further reading: Sasai, Y. et al. Regulation of neural induction by the Chd and Bmp-4 antagonistic patterning signals in *Xenopus*. *Nature* 376, 333–336 (1996)
Streit, A. et al. Initiation of neural induction by FGF signalling before gastrulation. *Nature* 406, 74–78 (2000)

Wk2

1/15 (M) Holiday. no class

1/16 (T) *HW 1A due*

1/17 (W) **Discussion 1: Morphogen gradients**
Driever, W. & Nüsslein-Volhard, C. The bicoid protein determines position in the *Drosophila* embryo in a concentration-dependent manner. *Cell* 54, 95–104 (1988)
Background: Eric Wieschaus, Finding genes that control development, https://www.youtube.com/watch?v=FooMfVazCXM

Further reading: Nobel lecture: Nüsslein-Volhard, C. (1995)
Each volunteer explains one figure and answers associated questions brought up in HW 1A.
Votes for learning topics & and signup for debates due
1/21 (S) *HW 1B due*

Wk3
1/22 (M) **Lecture 3: What causes cancer, bad luck or bad genes?**
Further reading: Weissman, I. Stem cells are units of natural selection for tissue formation, for germline development, and in cancer development. *PNAS* 112, 8922-8928 (2015).
Panel discussion to select the learning topics
1/23 (T) *HW 2A due*
1/24 (W) **Discussion 2: Development and cancer**
Simon, M.A. et al. Ras1 and a putative guanine nucleotide exchange factor perform crucial steps in signaling by the sevenless protein tyrosine kinase. *Cell* 67, 701–716 (1991)
Further reading: Nobel lecture: Morgan, T.H. (1934)
1/28 (S) *HW 2B due*

Wk4
1/29 (M) **Lecture 4: Diffusion, noise, and morphogen.**
Further reading: Garcia, G.H. et al. Quantitative imaging of transcription in living Drosophila embryos links polymerase activity to patterning. *Current Biology* 23, 2140-2145 (2013).
1/30 (T) *HW 3A due*
1/31 (W) Discussion 3
2/4 (S) *HW 3B due*

Wk5
2/5 (M) **Debate 1: What is the unit of natural selection, selfish genes or selfish cells?**
2/6 (T) *HW 4A due*
2/7 (W) Discussion 4
2/11 (S) *HW 4B due*

Wk6
2/12 (M) **Lecture 5: Entropy, information, and lineage.**
2/13 (T) *HW 5A due*
2/14 (W) Discussion 5
2/18 (S) *HW 5B due*

Wk7
2/19 (M) Holiday, no class.
2/20 (T) *HW 6A due*
2/21 (W) Discussion 6
2/25 (S) *HW 6B due*

Wk8
2/26 (M) **Debate 2: Is aging stoppable?**
2/27 (T) *HW 7A due*
2/28 (W) Discussion 7
3/4 (S) *HW 7B due*

Wk9
Writing week, no class
3/11 (S) *Term paper due*
Write about a scientist, live or dead. Reconstruct the evolution of his/her work.

Wk10
3/12 (M) **Lecture 6: Probability, distribution, and evolution.**

3/13 (T) *HW 8A due*
3/14 (W) Discussion 8
3/18 (S) *HW 8B due*

Nature Milestones in Developmental and Cancer
Backgrounds are available:
http://www.nature.com/milestones/development/milestones/index.html
http://www.nature.com/milestones/milecancer/timeline.html

Note: I selected 10 from each to minimize the overlap with the lectures, and to weigh on topics that may lead to interesting open-ended discussions. Please select three of each, and submit your selection by 1/17.

Development
3. Notch signaling and lateral inhibition (1937)
6. Limb outgrowth and patterning (1957)
7. Sperry's chemoaffinity hypothesis (1963)
11. Homeotic genes and collinearity (1977)
15. Programmed cell death (1986)
18. Asymmetric cell division (1988)
20. Biology of the sex chromosomes (1990)
21. The floor plate and hedgehog (1991)
23. Left-right patterning (1995)
24. Somitogenesis and molecular clocks (1997)

Cancer
3. Immune surveillance (1909)
5. Hormone and cancer (1915)
6. Cancer stem cells (1937)
11. Tumour suppressor genes (1971)
13. Tumour microenvironment (1975)
14. Clonal evolution and multi-step tumourigenesis (1976)
19. Cancer epigenetics (1983)
20. Cell cycle and DNA damage checkpoints (1989)
21. Genetic basis for cancer predisposition (1990)
22. Mechanisms of genetic instability in cancer (1990)