Juan Nicolas Malagon

EPITHELIAL DEVELOPMENT AND CANCER BIOLOGY

Goal: To familiarize students with key topics in cancer biology. In particular, I will show how deviation from normal epithelial morphogenesis can lead to cancer progression.

Why: Most types of cancer have an epithelial origin (70-90%) and as a result, understanding how epithelia retain constant numbers is fundamental to diagnose and treat different types of cancer.

Approach: This course will have both theoretical and practical components. By using data already collected in the last decade, students will develop a research project. At the end of the course, students will submit a final project, following the format of the journal article. Depending on their findings, I will encourage students to publish their work in an undergraduate research journal or to be part peer review scientific publication.

1. WHAT STUDENTS WILL LEARN:

Imaging software packages: Students will learn to process confocal images and time-lapse movies including measuring various cell parameters such as apical cell area and cell trajectories.
Examples of imaging software packages including LSM Browser, Image J, and Imaris.

Statistical tests: Various basic statistical tools such as average, standard deviation, t-test, Anova.

2. POTENTIAL SYLLABUS

Week	Topics	Teaching goals
1	***Introduction:*** • What is? • Types of cancer • Stages: Primary tumors Angiogenesis, Metastasis	Describe the six hallmarks of cancer and different types and stages of cancer
2	***Genetic basis of cancer:*** • Growth factors & oncogenes • RAS • WNT • ERK • MYC	Explain the types of gene mutations possible and how these mutations can contribute to cancer formation Describe an oncogene and why it is important in cancer development
3	***Epithelia development and cancer 1:*** • Epithelial development • Cell Competition	Is cell competition relevant to cancer? Mechanisms of cell competition: Themes and variations
4	***Epithelia development and cancer 2:*** • Coordination between proliferation and cell death	

		Different cellular mechanisms involved in regulation cell turnover: 1) mechanical forces and 2) Genetic components
5	***Cell extrusion and other diseases***	Potential new treatments of different epithelial pathologies such as asthma and inflammatory diseases

3. EXAMPLES OF ASSIGNMENTS

- **Theoretical components:** Students will present key papers or book chapters of cancer biology and epithelial development. Examples can be seen in the reference section.
- **Experimental component:** Students will test hypothesis by doing different measurement in developing and adults fruit fly legs. Students are expected to write a final project, which can be submitted a publication to an undergraduate research journal. Example of projects can be seen in the potential project section.

4. GRADING

Final grades will be based on the following:

1. First presentation……. ……....15%
2. Second presentation...……..……...15%
3. Capstone project proposal...…….20%
4. Capstone project final report……...30%
5. Attendance……...20%

Total……..……..……... 100%

5. REFERENCES

Introduction:

Hallmarks of Cancer: The Next Generation: http://www.cell.com/abstract/S0092-8674%2811%2900127-9

Genetic basis of cancer:

RAS oncogenes: weaving a tumorigenic web:
http://www.nature.com/nrc/journal/v11/n11/full/nrc3106.html

Epithelia development and cancer 1:

Marinari, E., Mehonic, A., Curran S., J Gale J., T Duke T., and Baum B. 2012. Live-cell delamination counterbalances epithelial growth to limit tissue overcrowding. Nature. Vol 484, pp 542–545. https://www.nature.com/nature/journal/v484/n7395/full/nature10984.html

Epithelia development and cancer 2:

Bringing balance by force: live cell extrusion controls epithelial cell numbers. Eisenhoffer GT, Rosenblatt J. Trends Cell Biol 2013 Apr;23(4):185-92. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3615095/

Cell extrusion and diseases

Epithelial cell extrusion: Pathways and pathologies. Gudipaty SA, Rosenblatt J. Semin Cell Dev Biol. 2016 May 19. pii: S1084-9521(16)30136-7. doi: 10.1016/j.semcdb.2016.05.010. http://www.sciencedirect.com/science/article/pii/S1084952116301367?via%3Dihub

6. POTENTIAL PROJECTS

6.1 PROJECT: MECHANISM REGULATING EPITHELIA TISSUE CROWDING

Question: Is there common cell dynamics to regulate epithelial cell density?
Importance: Misregulation of cell turnover is likely at the heart of cancer formation, but the mechanisms that coordinately regulate cell loss and division to control overall numbers within epithelia are just beginning to be understood.

System to study: Using long term live image to study various epithelial systems in fruit fly pupae including sternum and various leg structures (joints, tarsal segments, sex comb region).

Aims:

To test whether epithelia share common cell dynamics to regulate cell dynamics, my research will focus on three main aims:

Aim 1. Test whether epithelial systems share a common cell dynamic to relieve tissue crowding.
Aim 2. Aim 2. Determine cellular effects of perturbing tissue crowding.
Aim 3. Test the evolutionary implications of this mechanism to relieve tissue crowding:

Data: Information already collected, but analysis of section1, 2, and 3 is in progress. Long term live imaging movies of various fruit fly lines.

What students will learn:

Laboratory skills:

Model organisms: basic genetic techniques such as mutations, UAS-GAL4 systems

Imaging software: Processing of confocal images, measure various cell parameters such as apical cell area and cell trajectories

Examples of imaging software including LSM Browser, Image J, and Imaris.

Statistical tests: Various basic statistical tools such as average, standard deviation, t-test, Anova.

Academic topics:

Cancer biology: Cell competition, colonization, metastasis, among others

Developmental biology: Epithelial morphogenesis, cell proliferation and death,

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6.2 PROJECT: IMAGING CANCER DEVELOPMENT IN FRUIT FLIES

Question: Could pupal epithelial a good system to image cancer development?
Importance: .

System to study: Using long term live image to study various epithelial systems in fruit fly pupae including sternum and various leg structures (joints, tarsal segments, sex comb region).

Aims:

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