BIO426 and BIO526 Genes and Cancer 2018

Instructor: Dr. Paul Cullen pjcullen@buffalo.edu

This is a 3-credit course for undergraduates (BIO426) and graduate students (BIO526).

Description:

The goal of the course is to understand the biology that underlies cancer and the scientific basis for studying and treating cancers. The course is topic-driven and discussion oriented. Every student in the class will present one topic in the field of cancer research. A significant portion of the student's grade (60%) is based on this presentation. Attendance in the class will be taken, which accounts for part of the student's grade for the course (20%). Class participation is also important (20%). Guest lectures may be presented by visiting faculty or postdoctoral students in the department.

Prerequisite: The prerequisite for the course is Genetics (BIO 319).

Class times: Tuesdays and Thursdays, 11AM-12:20 PM, Room: Clemens Hall 117, the course runs through most of the spring semester.

Course outline:

The goal of the course is to gain an understanding of how the study of aberrant protein function in cancer has helped us to gain insights into both their normal biological functions and role in disease. This will begin with an overview of our current understanding of the multistep events leading to cancer, hereditary predisposition and the two-hit hypothesis of pediatric cancers. ***The course will focus on the biology underlying normal cell progression and the basic biology underlying cancer.*** The classic examples of the major tumor suppressors and oncogenes that act through the genome, including: the role of the tumor suppressor p53 in the DNA damage response; the function of the Retinoblasoma tumor suppressor in the regulation of gene expression during the cell cycle; Viral and cellular oncogenes; The tumor suppressors and oncogenes

of the Wnt signaling pathway and their role in driving cell proliferation. The mechanisms of gene regulation by the oncogenes c-myc and NFκB.

Assessment:

In class oral presentation (60%) and class attendance (40%). Presentation is required for a passing grade in the course. Missing three presentations typically results in reduction by one letter grade. There is no extra credit for the course. Students who participate in the discussion, ask questions, and explore novel experimental approaches will do well in the course. Students who show independence in putting together their presentation will be successful. No tests or final exam.

Course outline BIO526:

BIO426 and BIO526 are graded on the same system. Graduate student will present during the first part of the course.

Syllabus:

This course is designed to discuss and learn about the genetic basis of cancer. The course will cover the latest breakthroughs and up-to-date treatments. It will discuss the current challenges and complexities will cancer therapies. Because different types of cancers (lung, skin, colon, pancreatic) typically result from mutations in the same genetic pathways, we will focus on the genetic pathways rather than individual cancer types.

Presentations will involve the following. Students will pick a topic. They will research that topic and present background material (1st half of the presentation) and experiments from a paper (2nd half of the presentation) that the student reads and evaluates. Topics and papers chosen by students will be approved by the instructor.

Breakdown of class attendance (40%):

Attending class…….……20%

Asking questions and participating in the discussion……...……20%

Breakdown of the oral presentation (60%):

Oral communication skills……10%

Comprehension of background material……..……...……5%

Presentation of background material……..……..……...……5%

Comprehension of the results and conclusions of the paper……10%

Presentation of the results and conclusions of the paper… ……10%

Comprehension of the experiments presented…….……..…5%

Presentation of the experimental techniques…….……5%

New experimental techniques or new topics…….....5 %

Independence in putting together the presentation……5%

Students choose a research topic. Each presentation covers a different topic. Focus on a unique aspect of cancer research and different experimental techniques. Each student leads one presentation. Class participation is graded. Students ask questions and can provide information about the background information. Active discussions occur around the scientific papers. Students read the papers and discuss them in class.

We want to understand what techniques scientists use to study cancer. What are the main problems in cancer research, and how are scientists trying to solve them? What techniques are being used, and how do the results lead scientists to a clearer understanding.

Here are a list of topics (in bold) and papers that are available for choosing.

mTOR

Jewell JL, Kim YC, Russell RC, Yu FX, Park HW, Plouffe SW, Tagliabracci VS, and Guan KL. Differential Regulation of mTORC1 by Leucine and Glutamine. Science 347, 194-198 (2015).

Zoncu R… Sabatini DM (2011). mTORC1 senses lysosomal amino acids through an inside-out mechanism that requires the vacuolar H ATPase.
Science 334: 678-683. PMCID: PMC3211112.

O-GlcNac modification

Bond, M. R. & Hanover, J. A. A little sugar goes a long way: the cell biology of O-GlcNAc. J. Cell Biol. 208,869–80 (2015).

Discovery of a nucleocytoplasmic O-mannose glycoproteome in yeast Adnan Halim

UNFOLDED PROTEIN RESPONSE

Chen X, Iliopoulos D, Zhang Q, Tang Q, Greenblatt MB, Hatziapostolou M, Lim E, Tam W, Ni M, Chen Y, Mai J, Shen H, Hu DZ, Adoro Z, Hu B, Song M, Landis MD, Ferrari M, Brown M, Chang JC, Liu XS, Glimcher LH. XBP1 promotes triple negative breast cancer by controlling the HIF1α pathway. Nature 2014; 508(7494):103-7.

Warburg effect

Tyrosine phosphorylation inhibits PKM2 to promote the Warburg effect and tumor growth. Sci Signal 2 (97) ra73

Vander Heiden, M. G., L. C. Cantley and C. B. Thompson (2009). "Understanding the Warburg effect: the metabolic requirements of cell proliferation." Science 324(5930): 1029-1033.

Schell JC, …Rutter J.
A role for the mitochondrial pyruvate carrier as a repressor of the warburg effect and colon cancer cell growth.
Mol Cell. 2014

HISTONE MODIFICATIONS

KAT2A coupled with the α-KGDH complex acts as a histone H3 succinyltransferase.
Nature. 2017 Dec 14;552(7684):273-277. doi: 10.1038/nature25003.

RAS ACTIVATION

Justilien V, Ali SA, Jamieson L, Yin N, Cox AD, Der CJ, Murray NR, Fields AP.Ect2-Dependent rRNA Synthesis Is Required for KRAS-TRP53-Driven Lung Adenocarcinoma.Cancer cell. 2017; 31(2):256-269.

Kanada, M., A. Nagasaki, and T.Q. Uyeda, Novel Functions of Ect2 in Polar Lamellipodia Formation and Polarity Maintenance during "Contractile Ring-Independent" Cytokinesis in Adherent Cells. Mol Biol Cell, 2008. 19(1): p. 8-16.

METABOLOMICS

Johnson CH,Ivanisevic J,Siuzdak G. Metabolomics: beyond biomarkers and towards mechanisms. Nat Rev Mol Cell Biol. 2016 Jul;17(7):451-9. PubMed PMID: 26979502.

AKT

Akt-mediated regulation of autophagy and tumorigenesis through Beclin 1 phosphorylation. Wang RC *Science*

PTEN

PTEN functions by recruitment to cytoplasmic vesicles. Naguib A, Bencze G, Cho H, Zheng W, Tocilj A, Elkayam E, Faehnle CR, Jaber N, Pratt CP, Chen M, Zong WX, Marks MS, Joshua-Tor L, Pappin DJ, **Trotman LC**. Mol Cell. 2015 Apr 16;58(2):255-68. doi: 10.1016/j.molcel.2015.03.011. Epub 2015 Apr 9.

FOXO

Zheng X, Zhai B, Koivunen P, Shin SJ, Lu G, Liu J, Geisen C, Chakraborty AA, Moslehi JJ, Smalley (2014). Prolyl hydroxylation by EglN2 destabilizes
FOXO3a by blocking its interaction with the USP9x deubiquitinase.
Genes & Development