LANDRY
CANCER BIOLOGY
CONSORTIUM

A Harvard Interdisciplinary Graduate Consortium

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Nanocourse:

Genomic Instability and Cancer

Lecturers:
Andrew Murray, PhD; David Pellman, MD; David Nelson, PhD

Schedule:
First Session (open to all at Harvard without registration):
Tuesday, November 10, 3 – 6 PM
Location: Emerson Hall, Room 210

Second Session (limited to registered grad students, register by Nov 2):
Thursday, November 12, 3 – 5 PM
Location: Memorial Hall, Room 28

This nanocourse will begin by exploring the history of two lines of research and the intersection between them that informs modern cancer biology. The first are studies of genetic instability in model organisms, starting with the work of Boveri and ending with the discovery and analysis of DNA repair pathways and cell cycle checkpoints. The second is the gradual appreciation that genetic instability plays a major role in cancer, beginning with the realization that cancer required multiple mutations, moving on to Nowell's seminal work on cancer progression, and finishing with a description of the biology of tumor suppressor genes. We will continue with a discussion of the mechanisms leading to the evolution of karyotypes with implications for cancer, congenital disease, and likely organismal evolution. The focus will be on newly discovered mutational processes that can generate massive chromosome rearrangements "all-at-once" and are curiously localized to one or occasionally a few chromosomes. A review of recent technical progress in combining cellular imaging with single cell genomics, enabling mechanistic studies of these phenomena, will be included. Finally, we will explore the interplay between evolutionary and spatial dynamics at the surfaces of evolving three-dimensional cell masses, such as tumors. A crucial aspect is the effect of "inflation" on gene fixation at the frontier of expanding tumors. Key dimensionless parameters controlling the survival probability in the limit of small selective advantage will be identified, showing that inflating spherical cell masses can enhance mutant survival probabilities by factors of 100 or more, compared to cell masses which are merely "treadmilling", i.e. those where the radius remains constant in time.

FOR MORE INFORMATION: https://nanosandothercourses.hms.harvard.edu/node/398
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