

Conjoint Course 552 – Autumn Quarter

Title: **Metabolic Flexibility in Biology**

Course description:

This course will focus on small molecules and the ways that chemistry of these molecules facilitates life under changing conditions. It will include systems from microbiology to human physiology to understand aspects of cancer, aging, and animation. A combination of lecture and in class discussion will be used to explore topics including bioenergetics/metabolic flux, adaptation, and allometric scaling.

Requirements and Evaluation:

The course requires students to have taken undergraduate organic chemistry, and biochemistry. Evaluations will be made based on assigned problem sets.

Instructors:

Dan Gottschling (FHCRC / Genome Sciences Dept. Affiliate)

David Hockenbery (FHCRC/ Department of Medicine)

Mark Roth (FHCRC Biochemistry Dept. Affiliate)

Reference books:

Bacterial Metabolism (2nd Edition) by Gerhard Gottschalk

Microbial Physiology (2nd Edition) by Albert Moat & John Foster

Topics to be covered

1. Most microorganisms can utilize a constellation of small molecules for nutrition and energy. We will explore the inherent mechanisms by which this occurs in most organisms, and examine how these processes permit such adaptability. In addition, the ability of organisms to develop metabolic interdependence will also be presented.

Suggested Readings:

Blank LM, Kuepfer L, Sauer U. Large-scale ¹³C-flux analysis reveals mechanistic principles of metabolic network robustness to null mutations in yeast.

Genome Biol. 2005 6:R49.

2. Links between metabolism and aging: What do we “know”?

We will critically examine current topics that have been proposed to regulate organismal and cellular aging – including reactive oxygen species (ROS) and dietary restriction.

Suggested Readings:

Guarente L, Picard F. Calorie restriction--the SIR2 connection. Cell 2005 120:473-82.

Balaban RS, Nemoto S, Finkel T. Mitochondria, oxidants, and aging. Cell 2005 120:483-95.

3. Cell polarity and asymmetric cell divisions

a.Coffman JA et al, Dev Biol 273: 160-171, 2004 “Oral-aboral axis specification in the sea urchin embryo. II. Mitochondrial distribution and redox state contribute to establishing polarity in *Strongylocentrotus purpuratus*

4. Developmental arrest and nutrient supply

a.Jia K, et al., Development 131: 3897-906, 2004. “The TOR pathway interacts with the insulin signaling pathway to regulate *C. elegans* larval development, metabolism and life span.

5. Oxygen sensing, cell cycle and protein stability

a.Bemis et al., Genes Dev. 18: 739-744, 2004, “Distinct aerobic and hypoxic mechanisms of HIF-alpha regulation by CSN5”

6. Protein interaction networks and flux states

a.Almaas E et al., Nature 427: 839-43, 2004, “Global organization of metabolic fluxes in the bacterium *Escherichia coli*.”

7. Computational tools for network analysis (BioTapestry)

a.Longabaugh, WJR et al., Dev Biol in press “Computational representation of developmental genetic regulatory networks”