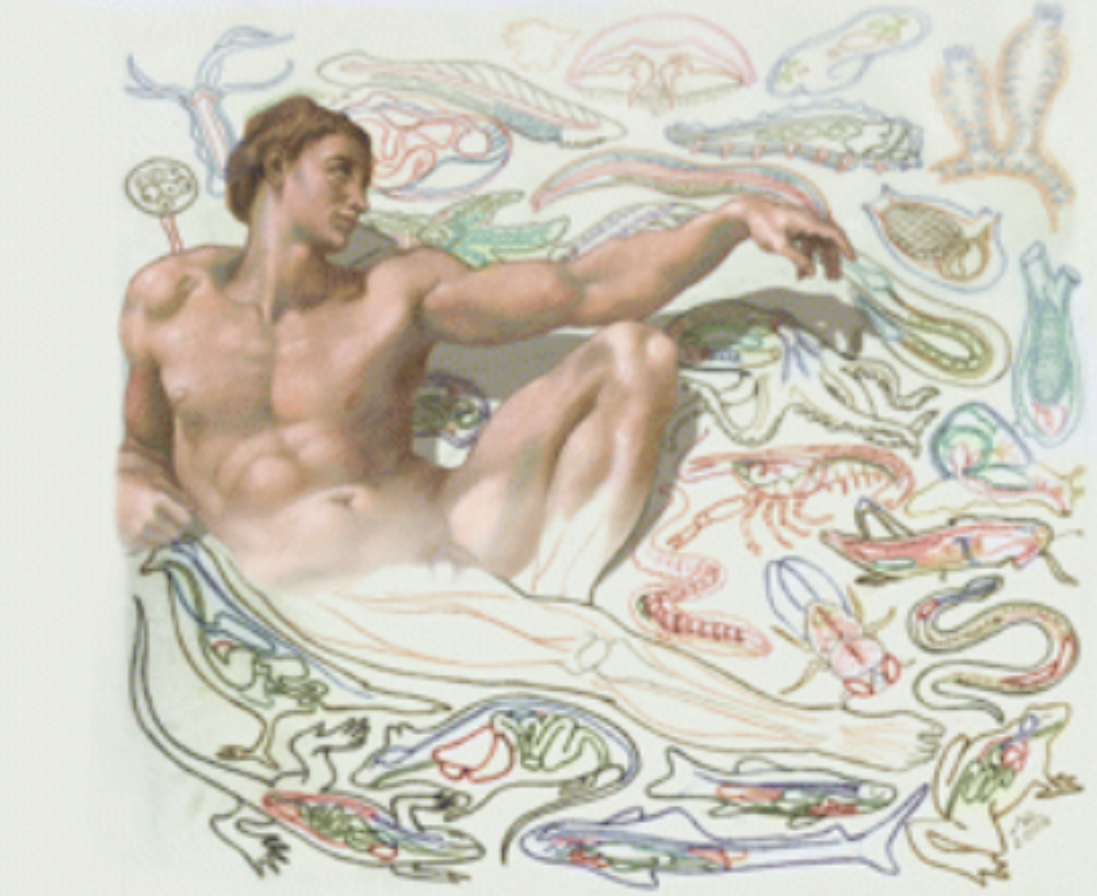
MGY460H

Molecular Genetics
UNIVERSITY OF TORONTO

Contemporary analysis of model organism development

Syllabus and course manual for Fall term 2021



Introduction

The path from a single cell to a complex organism requires a highly coordinated sequence of genetic and molecular events that encompass all known cellular and intercellular pathways and processes. Although there are many fail-safes to ensure that these processes occur accurately and reproducibly, when they do fail, major developmental defects occur, and if redeployed or disrupted later in life, all manner of diseases can occur. This course will provide insight into these pathways, how they are coordinated and how they compare in organisms that range from simple worms to humans. It will also cover past and current genetic and molecular methodologies that have and are being used in the major model organisms that are being used to understand these processes. Our objective is to provide students with an appreciation of the intricacies that underlie the amazingly reproducible patterning of a complex organism, and an ability to read and understand, not only the most recent research papers involving these model organisms, but also the classics. Students will also be able to appreciate current issues and areas of focus, as well to design effective approaches that can provide new answers.

LECTURE SCHEDULE

Introduction to development and major model organisms

Drs Spence, Protze, Krause- Lectures 1, 2

These lectures will explore the challenges faced by a single cell in order for it to produce a complex animal capable of repeating the cycle. You will be introduced to the invertebrate and vertebrate model organisms that have been chosen by scientists to study these processes, as well as why they were chosen, how they are manipulated and their various pros and cons. You will also be introduced to online tools for accessing experimental information.

Fundamental genetic approaches

Drs. Spence, - Lecture 3

We will review genetic approaches that have been crucial to unravelling the mechanisms directing development, including the design of mutant screens, transgenesis, and mosaic analysis.

Embryo polarity and axis specification

Drs. Spence - Lectures 4, 5

Invertebrate and vertebrate organisms establish primary anterior-posterior, left-right, and dorsal-ventral axes early in development. The mechanisms used to control these fundamental

processes and their timing will be compared among organisms. A key learning objective will be to understand the molecular pathways that establish polarity in the embryo and determine the main body axes during development, and to recognize similarities and differences among organisms.

Metamerization

Dr. Krause - Lectures 6, 7

The bodies of most animals are divided along the anterior-posterior axis into repeating morphological units, such as the segments of insects or the backbones of vertebrates. This lecture will explore how fields of equivalent cells are divided into repeating units of equal size to generate the precursors of the metameric units.

Hox genes and epigenetic zippers

Dr. Krause - Lectures 8, 9

At the same time that metamerization is occurring, these evolving structures are also being provided with identities that are different from the units ahead and behind. This highly conserved process of anterior to posterior identity assignment is controlled by clusters of genes called 'homeotic' genes. Mutations in these genes cause transformations of one body part into another. These lectures will look at how these genes evolved, how they function and how they themselves are regulated.

Signaling

Dr. Spence - Lectures 10, 11

Communication between cells is a central feature of development in every animal group. Signals from one region, germ layer, or tissue may induce a change in the fate of neighbouring or distant cells. In other case, interactions between cells of equivalent developmental potential lead members of the group to adopt distinct fates. The pathways that mediate inductive and lateral interactions during development have been remarkably well conserved during evolution. We will review some of the experiments that revealed the existence of cell interactions important for development and the mechanisms mediating those interactions.

Compartments

Dr. Krause - Lectures 12, 13

Cellular differentiation can result in permanent borders between groups of cells that prevent subsequent mixing. These borders are often the sources of molecular signals that act to maintain the borders and promote differentiation in the adjacent compartment. These lectures will explore how compartments were discovered, how they originate and some of their primary uses.

Heart development and regeneration

Dr. Protze – Lectures 14-16

The formation of complex organs such as the heart requires precise control of signaling pathways. We will cover literature that identified the key signals required for heart development using classical animal models such as mouse and chicken. We will also explore the latest insights into human heart development gained by using human pluripotent stem cells as a model system. In the last lecture of this series we will take a look at heart regeneration across different species and study the genetic models used to study regeneration.

Germ line determination

Drs. Spence, Protze - Lectures 17, 18

Establishing the germ cells is a key feature of sexual reproduction. The essential characteristics of the germline are similar among organisms, yet how germ cells are established differs with respect to place, time and mechanism. How do the different organisms set aside and maintain cells that must be passed to the next generation? Do these cells differ between males and females? What are the consequences of disturbing germ cell development?

Sex determination

Drs. Spence, Protze - Lectures 19, 20

Sexual reproduction is almost universal among animals, and yet the mechanisms that determine sex are enormously diverse. We will examine what genetic analysis has taught us about sex determination mechanisms in worms, flies and mammals, and whether those mechanisms reveal signs of a common origin. How primary sex determination affects the development of tissues throughout the organism will be discussed.

Developmental timing

Dr. Krause - Lectures 21, 22

The developmental life cycle of an organism requires an ability to coordinate the rates of growth of various tissues with one another. It also requires coordination with external factors such as temperature, light and available nutrition. This topic will look at the molecular sensors and clocks that monitor and control these processes.

Marking scheme

This year's evaluations will include in class quizzes and take-home assignments with a currently planned weight of 30%, a midterm worth 30% and a final during the exam period worth 40%.

Further details will be provided in class.

***WE ASK THAT YOU INFORM US BEFORE THE MIDTERM IF YOU WILL BE TAKING TESTS THROUGH ACCESSIBILITY SERVICES.

Course Policies

TEXTBOOK: There will be no required textbook for this course. Today, most of this information is easy to find online, and primary references will be provided. There are also a number of helpful online resources, many of which will be explored in class.

LECTURE MATERIALS: Lecture materials (as ppt or pdf) will be provided ahead of each class on Quercus. Students should be aware that: (1) Faculty are not required to provide the postings and handouts; this is something we do to make the course easier to follow. (2) The lecture itself is the primary conduit of information. (3) Lectures may not follow the posted materials or handouts exactly and are likely to contain information that cannot be gained from the slides alone or the assigned reading material. (4) Exams may include information that is not found on handouts and postings.

Students should also be aware that the lecture materials are the Intellectual Property of the lecturers. Access to this material and to the lectures (and lecturers), who have unique, special, up-to-date expertise in the course topics, is something you have earned through your previous efforts that got you into this course, and is also a significant component of what you are paying for with your tuition. Further distribution of the lecture materials (e.g. on other web sites, in computer or paper files accessible by other students or the public, or by giving paper copies to others not registered in the course) without permission constitutes an academic offence, and the instructors have the right to pursue disciplinary action.

The same principles apply to recordings of the lectures, which will be provided after each lecture. The distribution of such recordings without permission constitutes an academic offence.

Your Instructors

Dr. Henry Krause (course organizer)
Dr. Andrew Spence
Dr. Stephanie Protze