Chapter 16

Introduction

- model organisms: species easy to raise in a lab/use in experiments

*know the mechanisms that send cells down diverging genetic pathways to adopt different fates
*Stem cells are a powerful cell type that is key to the developmental process
*understand how flaws in gene expression result in cancer

Section 1: A program of differential gene expression leads to the different cell types in an organism

- cell division, cell differentiation, morphogenesis (why frogs go from tadpoles → frogs)
  - cell division would only result in a group of identical cells
  - differentiation: the process by which cells become specialized in structure/function
    - ↳ organized into tissues/organs
  - morphogenesis: the development of the form of an organism/its structures (shaping of an organism) → differentiation means different genes turned on in different cells
- different gene expression results from the genes being regulated differently
  - specific transcription factor activators - but where do the activators come from?
    - ↳ materials placed in the cell by maternal cells set up a program (specific genes expressed in any particular cell of a developing organism determines its path

2 sources of information tells a cell which genes to express at a given time during development

1) The egg's cytoplasm → contains RNA/proteins encoded by the mother's DNA
   - mRNAs, proteins, substances, organelles distributed unevenly
   - cytoplasmic determinants: maternal substances in the egg that influence the course of early development
     - ↳ during cell divisions, the zygote's cytoplasm is distributed into different cells, and the cells' nuclei is exposed to different determinants
2) The environment around a cell
   - signals conveyed to an embryonic cell from other nearby cells
   - induction: when signals recieved by zygotes from other zygotes cause changes in the target cell

- determination: the point at which an embryonic cell is irreversibly committed to becoming a particular cell type

*the outcome for determination is marked by the expression of genes for tissue-specific proteins - found only in a specific cell type/give the cell its structure/function

- differentiated cells are specialists at making tissue-specific proteins
  - liver cells specialize in making albumin

muscle cell determination:

- embryonic precursor cells grown, analyzed
- different genes isolated
- each expressed in a separate precursor cell
- watched for differentiation into mytoblasts/muscle cells
- discovered master regulatory genes → protein products commit the cells to becoming skeletal muscle cells
- in muscle cells, the molecular basis of determination is the expression of one+ regulatory genes
- some cells in developing organisms are programmed to die
- apoptosis: programmed cell death
  - cellular agents chop up DNA/fragment the organelles/other cytoplasmic components

-pattern formation: cytoplasmic determinants/inductive signals both contribute to setting up a spatial organization in which tissues/organs are in their correct places
-positional information: molecular cues that control pattern formation
-fruit flies have a head-tail axis, a back-belly axis, and a left-right axis
-Edward B. Lewis determines that genes direct the developmental processes
-homeotic genes: regulatory genes that control pattern formation
-embryonic lethals: mutations with death-causing phenotypes
-cytoplasmic determinants are the substances that establish axes
  ·called maternal effect genes (if mutant in the mother, mutant in the offspring)
  ↳ "egg polarity genes"
-bicoid: determines head structure
  ·if a mom has two mutant bicoid alleles the offspring has two back halves
-morphogen gradient hypothesis: gradients of substances called morphogens establish an embryo's axes and other features of its form
-bicoid research was groundbreaking:
1) led to the identification of a specific protein required for some of the earliest steps in pattern formation
2) increased understanding of the mother's critical role in the initial phases in embryonic development
3) a gradient of morphogens can determine polarity and position has been proved key to developmental concept

Section 7: cloning of organisms showed that differentiated cells can be reprogrammed → stem

-can cells express all of its genes
·"cloning": when a differentiated cell generates a whole organism w/o meiosis or fertilization (parent donates a single cell)
-stem cells: relatively unspecialized cells that can both reproduce themselves and differentiate into many different tissues
*differentiation does not necessarily involve irreversible changes in DNA
-totipotent: plant cells that can dedifferentiate and give rise to all the specialized cell types of the organism
*differentiated cells in animals generally don't divide in culture

Research
  ·remove nucleus from an egg
  ·replace it w/ a nucleus of a differentiated cell (somatic cell nuclear transfer)
  *older donor nucleus = lower percentage of normal tadpoles
  ↳-something in the nucleus does change as animal cells differentiate
  ·*sometimes clones are not identical

-clones have low efficiency and high incidence of abnormalities
1) in the nuclei of differentiated cells, a lil bit of genes are turned on and the rest of the genes aren't accepted
  ↳ ·result of changes in the chromatin (DNA in cells from cloned embryos often have more methyl groups)
-early animal embryos have stem cells that can make any differentiated cell
-adult bodies also have stem cells (replace non-reproducing specialized cells as needed)
-stems cells can be used to supply cells for the repair of damaged/diseased organs
-pluripotent: capable of differentiating into many different cell types
-scientist were able to turn differentiated cells back to stem cells
  ·called induced pluripotent stem cells (iPS)
  ·iPS different than normal stem cells

↳ cell division different
2 major used for iPS cells
1) cells from ppl w/ diseases have been made to iPS so they can be studied
2) a patient's cells can be used to replace nonfunctioning tissues
- genes can also reprogram a differentiated cell into another w/o it passing thru its pluripotent state

Section 3: Abnormal regulation of genes that affect the cell cycle can lead to cancer

- cancer cells avoid control mechanism
- oncogenes: cancer-causing genes
  - proto-oncogenes: code for proteins that stimulate normal cell growth/divison (normal versions of oncogenes
- ocogenes happen when a genetic change happens → increase either in the amount of proto-ocogene's protein product/in the intrinsic activity of each protein molecule

CHANGES OF PROTO-OCOGENES TO OCO-GENES

1) movement of DNA within the genome
2) amplification of a proto-oncogene itself
3) point mutations in a control element or the proto-oncogenes

- cancer cells have chromosomes that have broken and rejoined incorrectly
  - if a gene ends up near a promoter, it can become an oncogene
- amplification increases the number of copies of the proto-oncogene thru gene duplication
- changes in control elements causes an increase in a promoter/enhancer's expression
  - changes the gene's products to a more active protein or one that is more resistant to degredation
- tumor-suppressor genes: genes whose normal products inhibit cell division (proteins they encode help prevent uncontrolled cell growth
- functions of proteins made from tumor-suppressor genes:
  - repair damaged DNA (prevents cells from accumulating cancer-causing mutation)
  - control adhesion of cells to each other or to the extracellular matrix
- proteins function incorrectly in cancer cells
- two genes have mutations that commonly occur in cancer cells: ras proto-oncogene and p53 tumor-suppressor gene
- ras gene: encodes Ras protein
  - ras protein is a G protein that relays a signal from a growth factor receptor to a cascade of protein kinases
    - ↳ ultimately stimulates the cell cycle *normally doesn't operate unless triggered by appropriate growth factor
      - mutations can cause the Ras protein to stimulate cell cycle w/o growth factors
      - causes excessive cell division
- p53 gene: a tumor suppressor gene - the protein it encodes is a specific transcription factor that promotes synthesis of cell cycle-inhibiting proteins
  - a mutation that impacts this gene leads to increased cell division