

CH 16.1

①

MODEL ORGANISM)

• "in situ"

- ① Cell division
- ② Cell differentiation
- ③ Morphogenesis.

↗ D. Differentiation GENE EXPRESSION results from the genes being regulated differently in each cell type

Cytoplasmic Determinants

- material substance in the egg that influence the course of early development.

Inductive Signals

- signaling molecule from one cell are conveyed by cell surface receptors to induce changes in gene expression through a signal transduction pathway.

Cell Differentiation

- transcription is the principal regulatory point for maintaining appropriate gene expression.

↳ making tissue-specific proteins

i.e. Liver cells Lens cells
↓
albumin crystallin

Example - muscle cells

↳ multiple nuclei
high concentration of contractile proteins myosin & actin
↳ membrane receptor proteins.

embryonic precursor
of myoblasts

Determination

↓
mature, elongated, multinucleate skeletal muscle cells

master regulatory gene controls determination

Mfod - master regulatory gene

↓
Mfod protein - a transcription factor

↓
Binds to enhancer
of target gene

↓
expression

APOTOSIS

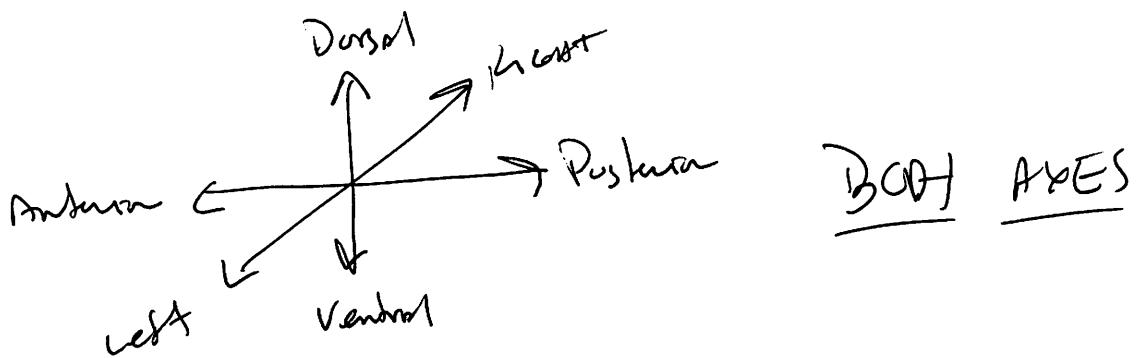
→ programmed cell death

→ "blebbing" → forming (lube)
that get engulfed by scavenger cells.

- C. elegans

- triggered by scavenger receptor pathway
"APOTOTIC PROTEIN"

⇒ the BUD PUP must be superimposed
on the Differentiation Process



Positional Information controls Pattern Formation

(cytoplasmic determinants
&
inductive signals)

Homeotic Genes (Edward Lewis)

- control pattern formation in the late embryo,
larva, and adult

Christiane Nüsslein-Volhard 1995 Nobel Prize

↳ identified 120 genes necessary for normal
segmentation

Maternal EFFECT GENES (e.g. POU-PROTEIN GENES)

↳ cytoplasmic determinants.

↳ mutations are embryonic lethals

Bicoid Gene - "two tail" effect

- essential for setting up the anterior end of the fly.

Maternal mRNA's are crucial during
development of many species

"EVO-DEVO"

16.2

(4)

CLONING

Totipotent - a mature cell that can "de-differentiate" and give rise to all the specialized cell types of an organism.
(plants)

Nuclear transplantation - "Dolly"

Stem Cells - unspecialized cells that can reproduce themselves indefinitely and differentiate into specialized cells of one or more types

ES cells - embryonic stem cells
- from the blastula (blastocyst) stage

Adult stem cells - serve to replace non-reproducing specialized cells as needed

→ Pluripotent → capable of differentiating into many different cell types.

iPS cells - 2007
induced pluripotent stem cells
reverted to stem cell stage by retrovirus
carrying cloned copies of master regulatory genes

||
oo

16.3 Cancer

(5)

Proto-oncogene



- (1) movement of DNA (translocation or transport)
- (2) amplification of proto-oncogene
- (3) point mutation in control element or proto-oncogene

oncogene

(promote excess cell growth)

- tumor -suppressor gene

- mutations that decrease their normal activities may lead to cancer.

→ stimulating growth through the absence of suppression

TS - gene

- (1) repair damaged DNA
- (2) control adhesion to other cells
- (3) produce proteins for cell signalling pathways.

Ras gene - proto-oncogene - 30% human cancer

- G protein
→ growth factor activates it
→ mutation can cause it to signal "growth" without growth factor.

P53 gene - tumor suppressor gene

- 50% human cancer

- 53,000 amu m.w. protein product

↳ p53 protein → transcription factor
that promotes synthesis of cell cycle inhibiting proteins.

- p53 - "guardian angel of the genome"
- ▷ many functions ▷
- miRNA's probably participate in cancer development.

Multi-step Model of Cancer Development

▷ - more than one somatic mutation is usually needed to produce cancer

Hence - cancer increases with age

- colon cancer - 6 changes
- $\text{ras} + \text{p53}$

oncogen - dominant gene
T-S gene - recessive \Rightarrow both must be mutated

▷ - the order matters

Pre-disposition to defective cancer because of inherited mutated genes

BRCA-1 - breast cancer gene T-S gene
BRCA-2

VIRUSES - can cause cancer.
- 15%