Developmental Biology Exam 1 Name
Feb. 5, 2010

1. (15 pts) Since we know that all cells have the same genetic information encoded by DNA, give examples of molecular mechanisms at different levels of gene regulation that allow differentiated cells to exhibit specialized functions. Make sure to describe **how** each mechanism would function to regulate gene expression.

Transcriptional level – (1) Promoters/ (2) enhancers (temporal and/or tissue specific), (3) DNA Imprinting and (4) developmental DNA methylation, (5) transcription factor regulatory networks, (6) chromatin modification. Translational level – (7) mRNA processing and (8) translation, (9)RNAi. Protein level – (10)post-translational modification (i.e. protein stability). Multiple levels - (11) intracellular signaling

2. (15 pts) What is the role of the dorsal lip of the blastopore during development? What classical experiment was done to identify and test this role? Explain how this fits with the model of **mosaic** and **regulative** development.

It is a cell-organizing center that influences the fate of surrounding cells. Transplantation of the dorsal lip blastopore from a donor embryo to the opposite side of a recipient embryo lead to a duplicated body axis. Cells fated to become ventral cells changed fates in the presence of the transplanted dorsal lip blastopore. Dorsal lip fate is fixed (mosaic development), while the fate of host tissue regulates in response to inductive signal from dorsal lip.

3. (15 pts) Draw a diagram of a positive "gene" feedback loop and a negative "gene" feedback loop. Describe the expected spatial and temporal expression pattern of the genes in each case and suggest how these genetic interactions could be used during development.

Positive feedback – gene 1 activates expression of gene 2, gene 2 then feeds back on gene 1 continuing its expression. Thus, once initiated both genes activate the other gene. Negative feedback – gene 1 activates expression of gene 2, gene2 then feeds back on gene 1 preventing the expression of gene 1. Once gene 2 reaches peak expression, gene 1 is turned off and gene 2 is subsequently turn off due to loss of activation by gene 1.

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4. (10 pts) What is the gold standard experiment to prove the potency of a mammalian stem cell, eg., iPS cell? Describe results supporting totipotency and results supporting pluripotency.

Transplant a potential mammalian stem cell into the inner cell mass. Totipotent stem cells give rise to all tissues of the developing embryo. Pluripotent stem cells give rise to a subset of lineages in the embryo.

5. (10 pts) Name at least 3 ways cells can communicate with each other and describe why cell-cell communication is important in the developing embryo.

Secretion and diffusion of signaling molecules, direct contact of cell (1) Secretion and diffusion of ligand from one cell to a membrane or nuclear receptor, (2) direct contact of cell surface ligands and receptors on adjacent cells, (3) cytoplastic sharing via gap junctions and (4) mechanical/physical contact. Cell-cell communication always for induction, cell relay positional information and influences each other in order to facilitate the development of complex tissues.

6. (15 pts) Briefly explain or diagram positive-negative selection used to identify those rare cells in which homologous recombination has occurred in a gene knock out (or knock in) in a mammalian ES cell line.

On the genetically engineered piece of DNA there are 2 transgenes used for selection, 1 positive and 1 negative. The positive selection marker is within the region of homology (within an intron for a knock-in and within the coding sequence followed by a stop codon for a knock-out). The negative selection marker is outside the region of homology. The positive selection marker selects for cells in which the transgene has been incorporated into the genome. The negative marker selects against cells that have random integration since it is outside the region of homology and thus will not be incorporated at the target site.

7. (10 pts) What is the main cause of non-spontaneous embryonic lethality and name one relatively common birth defect that is associated with this.

Aneuploidy or non-disjunction, trisomy-21 (Down Syndrome). Accepted chromosomal deletions and angelman/prader-willi syndrome.

8. (10 pts) Describe the novel approach Ian Wilmot took to reproductive cloning that allowed him to be successful at cloning Dolly, when his predecessors had failed. Explain the cell biologic mechanism thought to explain his success.

He used a somatic nucleus from a non-dividing cell (mammary) instead of one from a rapidly dividing cell. He also starved these cells, which caused them to arrest in the G_0 stage. This allowed a longer time for the egg to reprogram the somatic nucleus to a totipotent state before beginning the development program.