**Epigenetics and Development**

**Our Goals:**

* To build our own definition of “epigenetics”;
* To classify the major mechanisms of chromatin remodeling;
* To investigate how external environment/behaviour can trigger a completely different developmental fate
* To propose, and interpret some experiments that allow us to shed light on this phenomenon (in a specific case)

1. What could be the underlying mechanism driving the different developmental trajectory of the organisms studied in today’s class?

* queen produces hormones (juvenile) that prevents development of other queens
* random X inactivation
* the diet plays a huge role in the development trajectory
* initially, all larvae eat royal jelly 🡪 after a few days, most are switched to nectar/pollen 🡪 queen remains on royal jelly
* Jelly may have hormones or proteins present
* proteins in jelly may initiate signal cascade 🡪 gene expression profile changes (methylation/demethylation)

1. a) With one or two partners, take two minutes to come up with a definition of “epigenetics”:

* Epigenetics is a study of factors that affect gene expression without a direct change in the DNA sequence
* Epigenetics has to be heritable
* Inheritance of phenotype that can't be explained by differences in DNA sequences

b) After listening to other classmates’ ideas, provide a more complete (if necessary) definition of “epigenetics”:

* Epigenetics is a study of heritable factors that can regulate/alter gene expression without a direct change in the DNA sequence or structure.

1. a) What are different mechanisms that can affect developmental trajectory, and that could be affected/directed by an “outside factor”?

* If the diet is a strong methyl or acetyl group source, then you can effectively alter the methylation/acetylation profile of the genome, such that the gene expression profile is changed dramatically.
* Diet can change up enzymes involved in the process.

b) What are the mechanisms that can affect chromatin structure?

* DNA supercoiling
* methylation/acetylation of histone tails
* histone variance
* different/variant histone modifying enzymes
* factors involved with condensing chromosomes at mitosis
* chromatin remodelling factors (slide nucleosomes closer/further apart on DNA)

1. What would you predict about gene expression patterns in the two distinct developmental trajectoriesif epigenetics is driving the phenotype?

* worker bees have reproductive genes methylated
* growth, lifespan, behavior genes may be differentially expressed

1. Researchers (Grozinger et al., 2007) actually checked… what do you notice about the gene expression patterns in individuals following each of the two developmental trajectories?

* worker bees upregulate genes that are associated with foraging behaviors
* queen bees upregulate genes associated with reproduction and longetivity

1. What kind of protein/factor could be a key component of the epigenetic control of developmental trajectories? How would you test your hypothesis?

* DNA methylase/demethylase enzyme
* transcription factor (DNA-binding domain)
* DNA/histone methyltransferases
* Look at methylation status of larvae + royal jelly; larvae + nectar; larvae + royal jelly + DNMT3 K)

1. What did Kucharski and colleagues find, and what does their experiment suggest?

* honey bees have a fully functional DNA methylation system
* knock-down of DNMT3 greatly enhances the number of individuals which develop a queen-like phenotype. This suggests that DNA demethylation is important for queen bee development. It's possible that a component of royal jelly activates DNMT3.
* A lipid called 10HDA is the most abundant lipid in royal jelly. 10HDA treatment induces FAS activation. FAS is a gene involved in cell division.

1. a) What component of the food in question is most likely to affect gene regulation?

* Lipid called 10HDA activates transcriptionally silenced FAS gene.

1. How does the food in question activate a transcriptionally silenced gene?

* 10HDA treatment leads to an overall increase in acetylation of lysine residues on histones.

1. \*\*\*optional\*\*\* Using these pieces of data that we just discussed, construct a model of how consumption of the food in question leads to each of the developmental trajectories.

* 10HDA permeates cell membrane or activate a cell-surface receptor
* goes onto repress DNMT3
* this leads to a decrease in methylation, increase in acetylation of histone tails 🡪 there might also be prevention of methylation
* since acetylation of histone tails is transcriptionally permissive, FAS and other reproductive and growth genes are induced