**Discovering Epigenetics – Ageing in *C. Elegans* Fact Sheet**

**Background on ageing**

What is it?

* Growing old
* Time-dependent decline in physiological function
* Exponential increase in mortality

Who is ageing?

* Every living thing (animals, plants)

What are features of ageing?

* Frailer
* Organ function declines (muscle, eyes, lungs, brain etc.)
* Wrinkled skin
* Spine curvature
* Muscle wastage
* Infection
* Cataracts
* Cancer
* Alzheimer’s
* Sleeping problems

Why do we need model organisms to study ageing?

* It’s a complex process – need to be able to simplify it down to understand it better first
* It takes a long time for us to age – model organisms live for shorter amounts of time

**Background on *C. Elegans***

*C. (Caenorhabditis) Elegans* worms are small, 1-2mm, nematode worms. They feed on bacteria that grow on rotting plants and live all over the world. There is a saying that you are never more than a few yards away from a *C. Elegans* worm!

The worms have a short lifespan of 2-3 weeks, depending on the conditions they live in. 99.9% of the worms are hermaphrodites and 0.1% are males. As hermaphrodites they can selfreplicate and lay 200-300 eggs during their short lifespan.

**Why use *C. Elegans* in research?**

*C. Elegans* worms can easily be bred in the laboratory. They prefer a temperature of 15-25°C. In the lab they tend to be fed on *E. Coli* bacteria, though the food source might be altered for certain experiments. As C. elegans can easily be grown inside petri dishes, there are many opportunities for scientists to change their environment to better understand how things affect the worm.

The *C. Elegans* has a short lifespan. This is most helpful i.e. for ageing studies, as you won’t have to wait months or years for the organism to grow old and to see the results of the experiment, but just a few weeks.

As many worms are hermaphrodites, the offspring are clones of the adult worm. This is great for research as you easily can have access to large numbers of model organisms with the same genetic traits.

The *C. Elegans* is well characterised, which makes it a great organism for genetic studies. Their full genome was sequenced in 1998, the first multi cellular organism whose genome was fully known! Scientists also know that the worm tends to exist of 959 somatic cells. Having all this detailed information on the *C. Elegans* ensures that researchers can understand and manipulate the worms on a molecular level.

Humans and *C. Elegans* used to have the same ancestor 500-600 million years ago, and some genes are still similar between humans and these nematode worms. There are many obvious differences between human and *C. Elegans*. However, when looking at ageing there are some similar patterns of physiological decline. Overall, the *C. Elegans* worm is used as a proof of concept model, to understand the mechanisms of how something affect an organism. Once it is fully understood in worms, the theory can be tested in more complex organisms with more similarities to humans that the *C. Elegans*.

**In short**

Advantages:

* Small
* Short lifespan
* Rapid reproduction
* Hermaphrodites which means they are clones of the adult worms

Disadvantages:

* Evolutionarily not very close to humans, so can only look at basic things and can’t extrapolate too much into humans

**Background on the challenge**

Besides their short lifespan and the ability to easily change their environment, *C. Elegans* are a great model organism for ageing studies as they also give visual clues on how the worm is ageing.

By clicking the video/text, you will see a video with 4 screens, 2 screens with worms in their early life (left), which is their 4th day of adulthood, and 2 screens with worms in their late life (right), which is their 10th day of adulthood.

The worms in the upper two screens have been grown under normal conditions (normal temperature and large amount of E. Coli bacteria to eat). The worms in the two lower screens have been put on a restricted diet to study how that influences the ageing process. The restricted diet was created by treating the *E. Coli* bacteria (the worms’ food source) with a weak antibiotic (sulfamethoxazole). Because of this the bacteria don’t grow/ multiply anymore, restricting the food available over time to the worms. It is expected this could raise to a 30% food reduction.

The worms used in this video have a temperature-sensitive mutation which renders them sterile. This makes them much easier to grow to old ages (plates overpopulate rapidly otherwise!) and is the reason there will not be eggs visible on the plates.

Young vs. Old answers

The following differences could be seen between the early and late life worms:

* Movement speed of the worms decreases with age
* The worms become more transparent with age
* The worms’ intestines start to look damaged with age and the walls become thinner
* Older worms have a straighter body posture (young worms seem more curled compared to older worms)
* Young worms tend to move their whole body, whereas older worms just mostly move their heads and tails

All in all there are quite some visual clues that the researchers get to see whether the worm is ageing and in what stage of ageing the worm is.

Some of these differences might not have been fully visible on the recording as they might require a trained eye and a different type of microscope

Normal vs. Restricted diet

There are no noticeable differences in early life between worms on a dietary restriction and normal C. Elegans worms.

However, the worms show visual differences when they are at the late life stage. Remember that both are 10 days old. However, those on a restricted diet appear to be moving fast, slightly less transparent and have a more curved body and use more of their body when moving compared to normal worms of 10 days. These differences imply that the C. Elegans worm ages slower when it is on a dietary restriction.

What exactly slows down the ageing process when the worms are dietary restricted is not fully understood. With more research into how a dietary restriction slows down ageing in model organisms such as worms, researchers hope to understand the mechanisms of this process and in the future be able to slow down the ageing process in humans as well, without them having to restrict a large percentage of their diets.