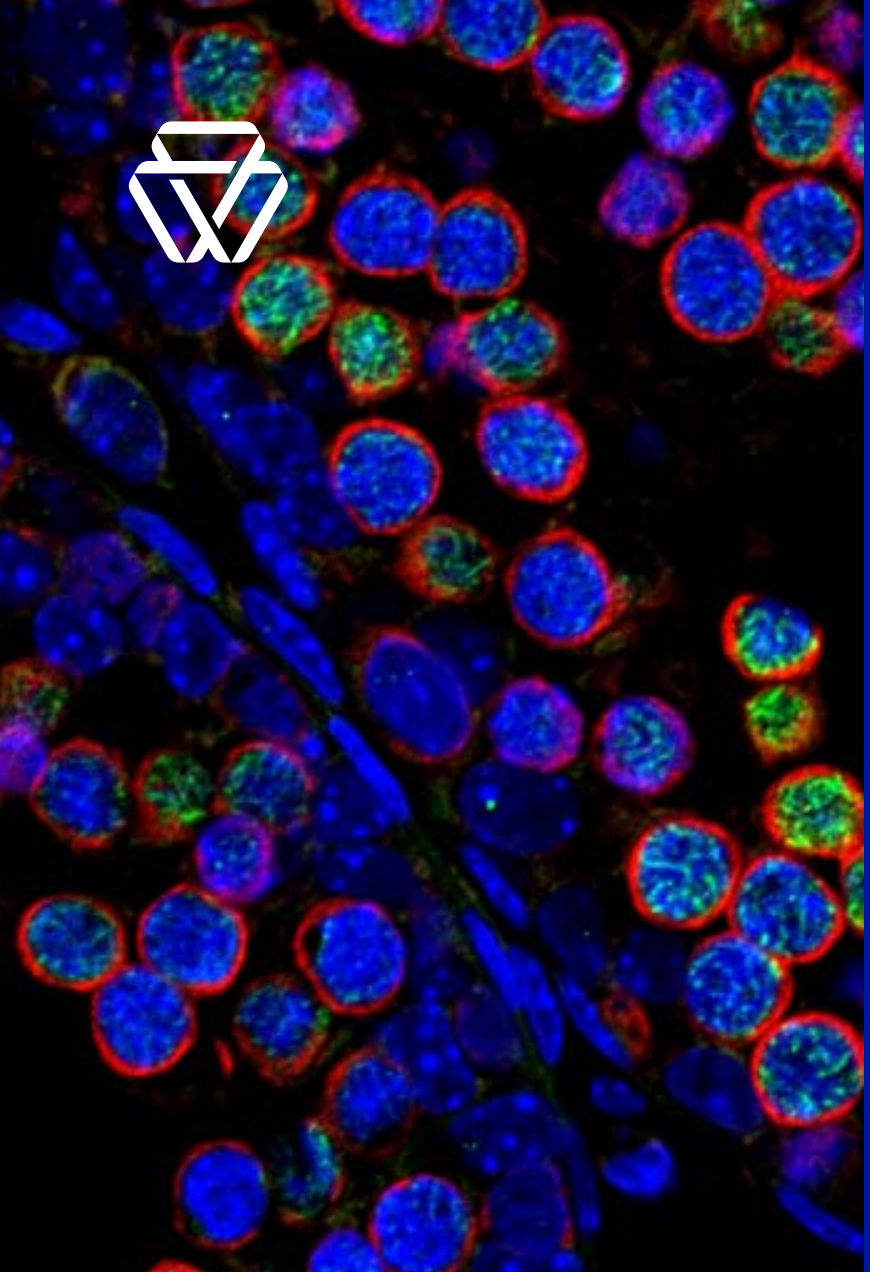

Rejuvenation and aging

As we age, our cells and tissues go through changes—such as losing the ability to repair themselves or make new cells—that underlie the changes we experience in our bodies. Whitehead Institute researchers are studying how cells change with age, work that may eventually lead to therapies that can mitigate some effects of aging. Our researchers also study cells that are unusually capable of rejuvenation, such as germ cells, the cells that become eggs and sperm. The lineage of these cells, the germline, is essentially immortal: a germ cell becomes an egg that becomes an individual containing germ cells, and then the cycle repeats: an unbroken line throughout the generations of dividing cells. Understanding how these cells replenish themselves indefinitely could provide insights into how to mitigate the effects of aging in other cells—as well as how to counter other immortal cell types, such as cancers.

Member **Iain Cheeseman** seeks to understand cell division, a process constantly occurring in our bodies to replenish cell populations. As our bodies age, the capacity to repair or replace damaged cells and tissues declines, in part due to limitations in the ability of aged cells to proliferate. Researchers in his lab have discovered key features that allow cells to persist in a state of proliferative hibernation, termed quiescence, to protect cells and rejuvenate aged tissues. For

example, they identified how female oocytes maintain their cell division machinery over years or even decades of disuse before resuming division—an essential task to preserve fertility during aging. Work in the Cheeseman lab also explores how cells regulate quality control checkpoints in cell division to minimize the chances of creating cancerous or diseased cells as we age.

Director and Member **Ruth Lehmann** studies germ cells throughout their lifecycle, from when they are first set aside from the rest of the body's cells early in embryonic development, through their migration across the embryo to reach the gonads, to their maintenance during maturity in order to preserve fertility. One area of interest to her lab's researchers is how the female germline passes on cellular contents such as mitochondria. Mitochondria have their own DNA that is prone to mutation and doesn't have some of the protections our other DNA has, so mitochondria must use different mechanisms to maintain genomic integrity over generations.

Member **Yukiko Yamashita** studies how germ cells maintain their immortality. One focus of her lab has been how the germline replenishes ribosomal DNA (rDNA). This is an essential type of DNA that contains the same sequence repeated many times in a row and is prone to losing repeats over time. Losing too many repeats would kill off the germline. The researchers have discovered many details of how the number of rDNA repeats is increased in germline stem cells when it gets too low in fruit flies, including how the organism selectively keeps cells with more rDNA repeats in the germline stem cell pool, while letting cells with fewer repeats differentiate and exit the pool. The germline's ability to replenish rDNA levels is essential to germ cell immortality—and may be relevant to understanding other immortal cells like cancer cells.

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