Let’s change the question to

HOW Do We Age?

and talk about senescent cells and inflammation

Since the early 1800s, our life expectancy has increased from 40 years to 80 years.

In the wake of that, it has led to the #1 cause of dying: Aging!

Current average age at *global* level is 73.7 years

What do our cells do?

Normal cells have a limited capacity for cell division - about 50 times - before division is irreversibly stopped and the cells enter a state known as **cellular senescence**.

Life and division of various cells

Rapidly Dividing Cells

- **Skin cells**: Every few weeks
- **Intestinal lining cells**: Less than a week
- **Blood cells**: Live for 3 to 120 days (330 billion cells replaced *daily!*)

Moderately Dividing Cells

- **Fat cells (adipocytes)**: Replace at a rate of about 8% per year
- **Red blood cells**: Have a lifetime of about 4 months

Slowly Dividing Cells

- **Muscle cells**: 15 years
- **Fat cells**: Last an average of 12 years
- **Heart muscle cells**: Estimates vary, but replacement occurs at a slow rate of 0.5% to 30% per year

Non-Dividing Cells

- **Neurons in the central nervous system**
- **Lens cells in the eyes**

What do our cells do?

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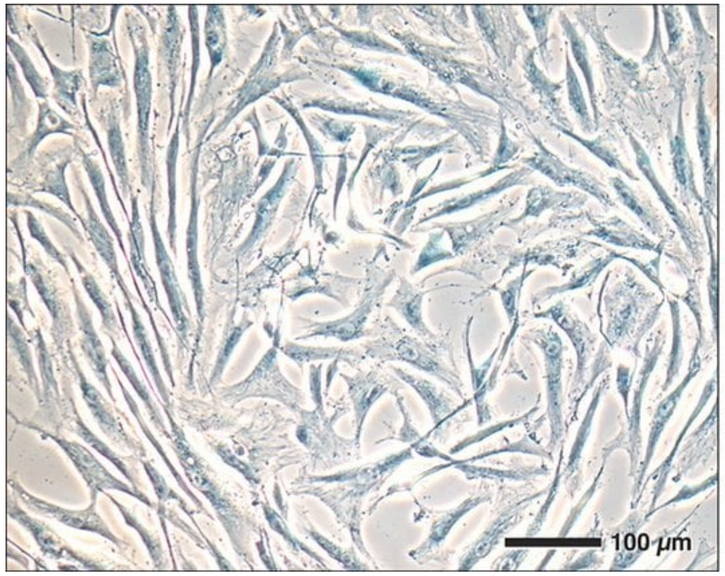
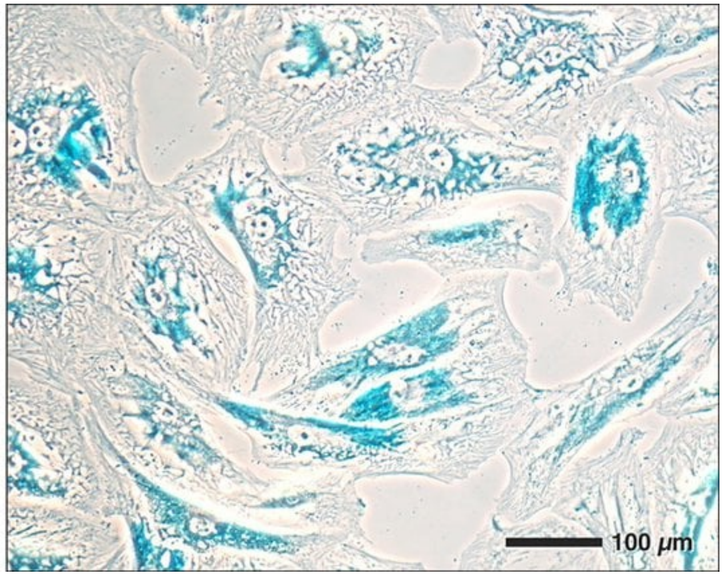
Senescent cells are in a kind of stasis and decline - *but they don't die*. They are still metabolically active BUT . . .
unlike young and healthy cells, they produce proteins that upregulate* immune responses in nearby tissues and distant organs.

*) increase the quantities of cellular components

Lab grown cells



Young cells



Older cells

When cells reach this state of senescence, they grow larger and start exhibiting a variety of genetic abnormalities.

Scientists have identified a dozen biological changes that correspond with aging.

All of them are associated with inflammation - the pillar of aging* . . .

*) And the latest research suggests that that's also the case with dementia

The link between

INFLAMMATION - DISEASES - **AGING**

is now called

INFLAMMAGING

The history of inflammation

- Acute inflammation - swelling, pain, heat, and redness - was described by Roman encyclopedist Aulus Celsus more than 2,000 years ago.

- In 1839 German scientists identified **leukocytes**, or white blood cells

- In 1882, Mechnikov described the way leukocytes consumed bacteria and dead cells (Nobel Prize in 1908).

- In 1927, Sir Thomas Lewis discovered that **histamines** play an important role in the response to bodily harm

- In 1980s, interleukine-1, the first of 11 inflammatory markers called **cytokines**, was identified

Before we despair . . .

Inflammation isn't inherently bad or good.

Depending on the situation,
we just need the “right amount” of it!

Inflammation is good

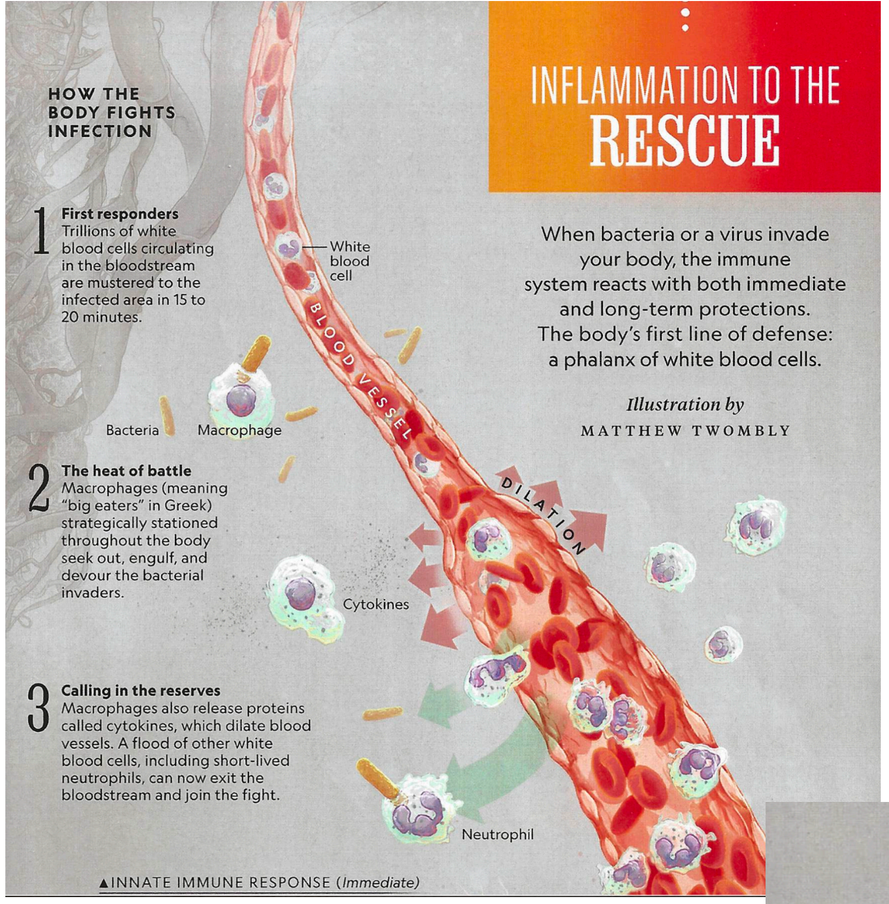
- You could never heal a wound or fight many diseases without it,
and
- If you have an infection and you don't have inflammation, you're going to die

The 5 steps of immune defence . . .

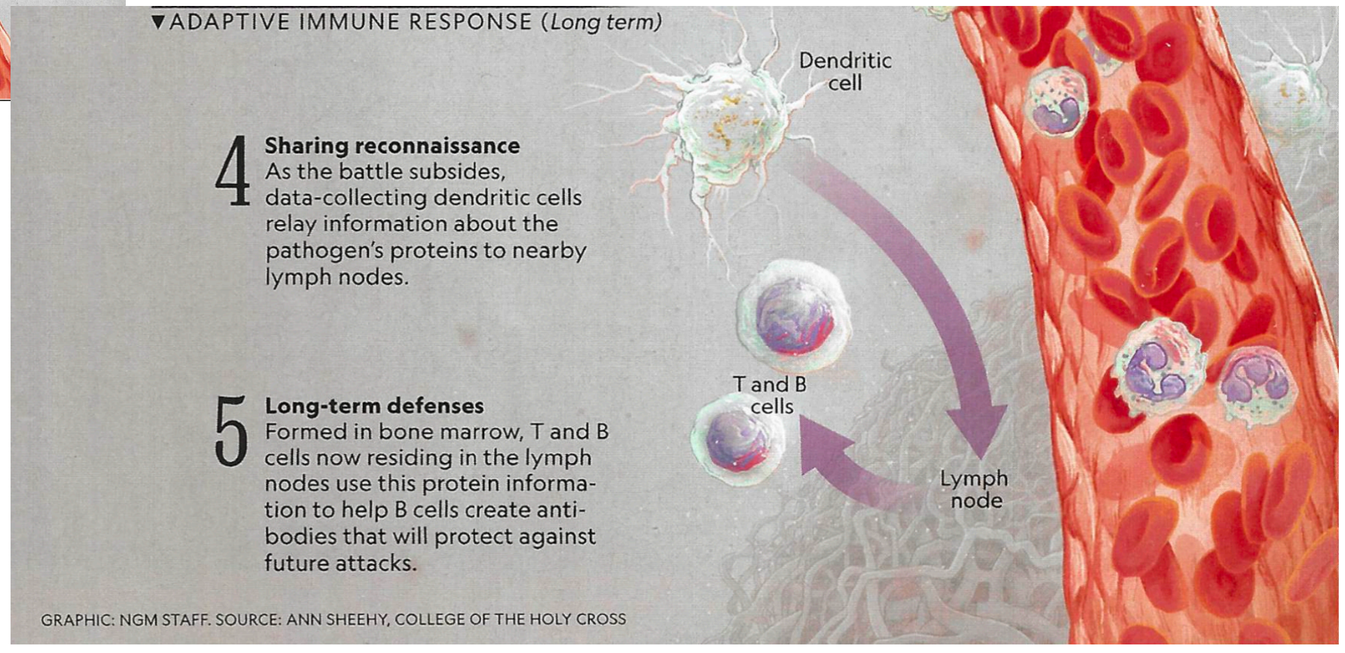
INFLAMMATION TO THE RESCUE

When bacteria or a virus invade your body, the immune system reacts with both immediate and long-term protections. The body's first line of defense: a phalanx of white blood cells.

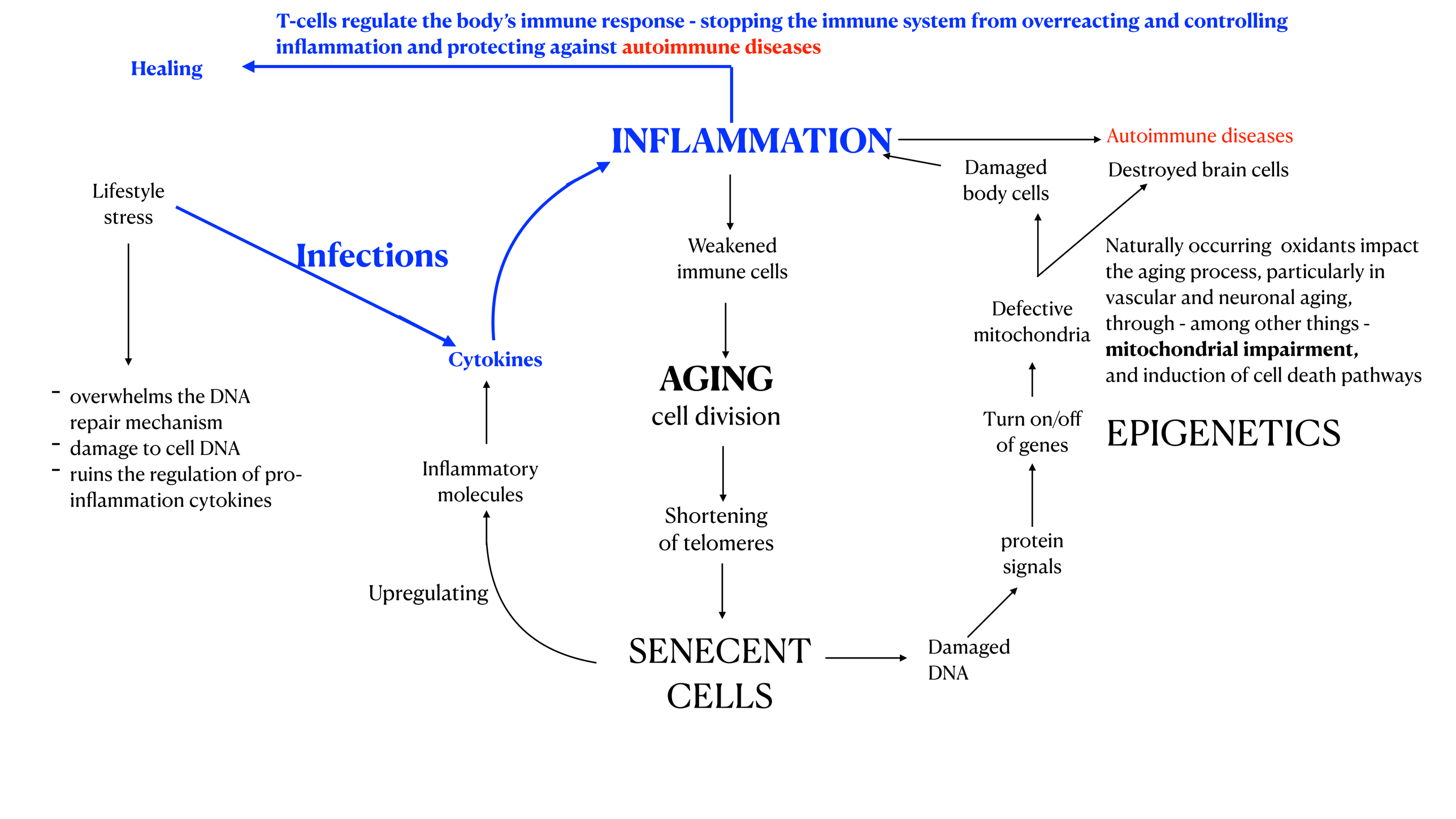
Illustration by
MATTHEW TWOMBLY



▲INNATE IMMUNE RESPONSE (*Immediate*)



GRAPHIC: NGM STAFF. SOURCE: ANN SHEEHY, COLLEGE OF THE HOLY CROSS


T-cells regulate the body's immune response - stopping the immune system from overreacting and controlling inflammation and protecting against autoimmune diseases
Healing
INFLAMMATION
Autoimmune diseases
Damaged body cells
Destroyed brain cells
Lifestyle stress
Infections
Weakened immune cells
Naturally occurring oxidants impact the aging process, particularly in vascular and neuronal aging, through - among other things - mitochondrial impairment, and induction of cell death pathways
Defective mitochondria
Cytokines
AGING
cell division
- overwhelms the DNA repair mechanism
- damage to cell DNA
- ruins the regulation of pro-inflammation cytokines
Turn on/off of genes
EPIGENETICS
Inflammatory molecules
Shortening of telomeres
protein signals
Upregulating
SENECENT CELLS
Damaged DNA

Time to despair . . .

Inflammation is good -

You could never heal a wound or many diseases without it,

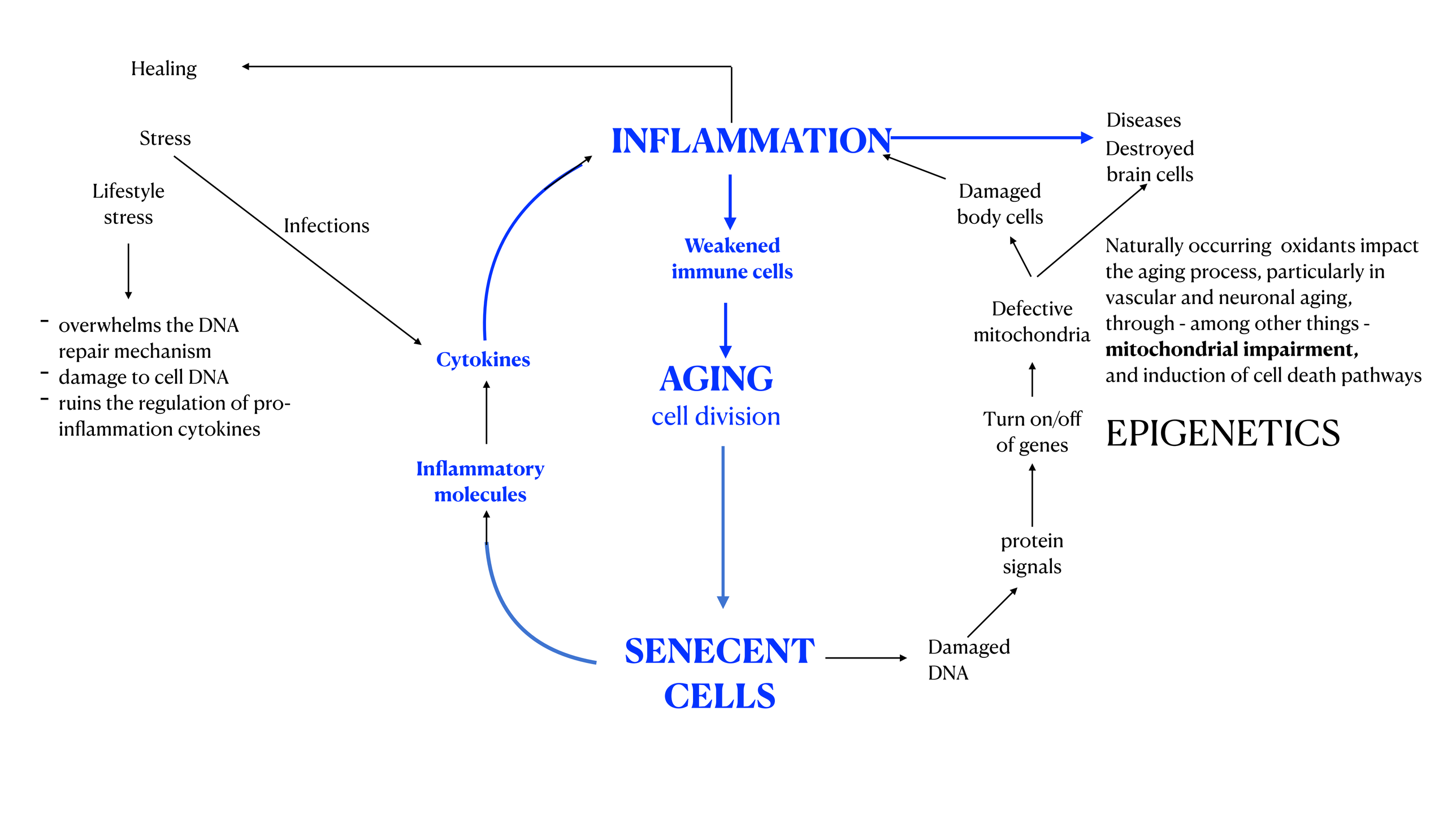
and

If you have an infection and you don't have inflammation, you're going to die

It's *losing control of inflammation that is bad* -

Inflammation accelerates aging and disseases. The key mechanism is **Cytokines**

> age 50: some cytokines> age 65: a lot of cytokines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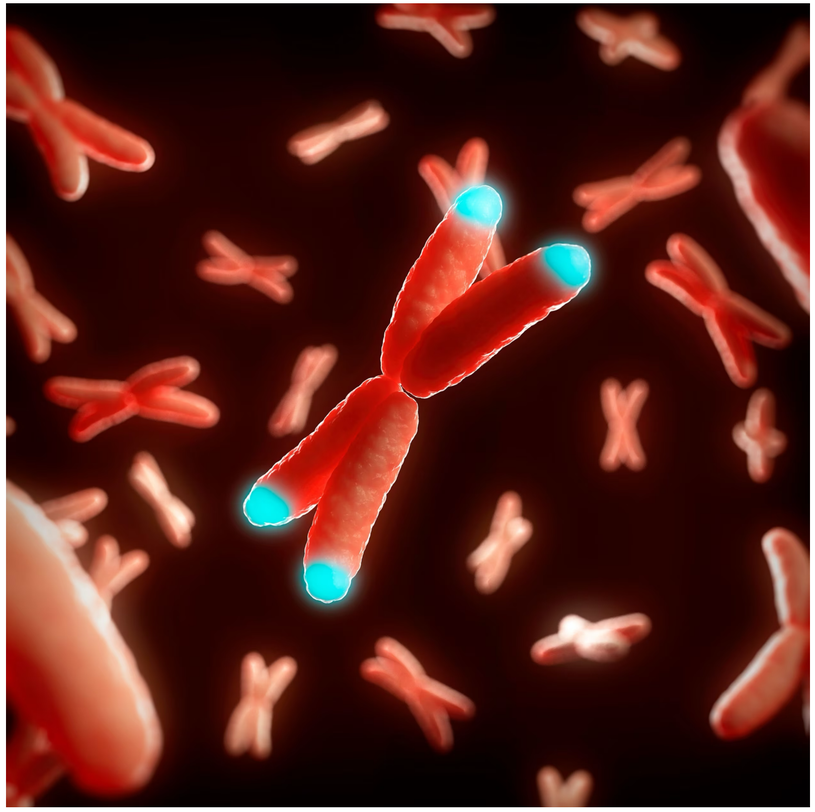
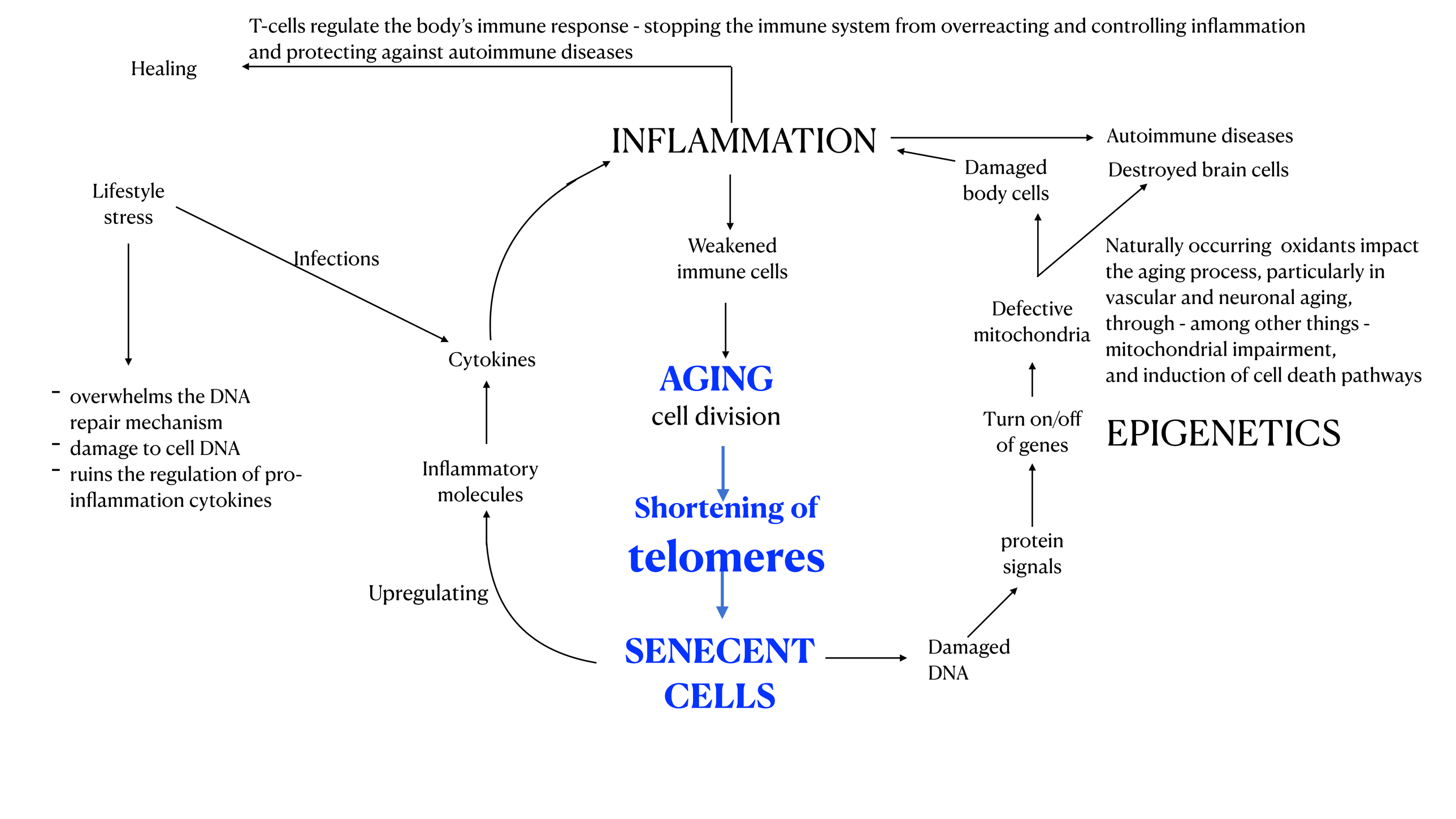
EPIGENETICS

On top of all this, we have . . .

the telomeres

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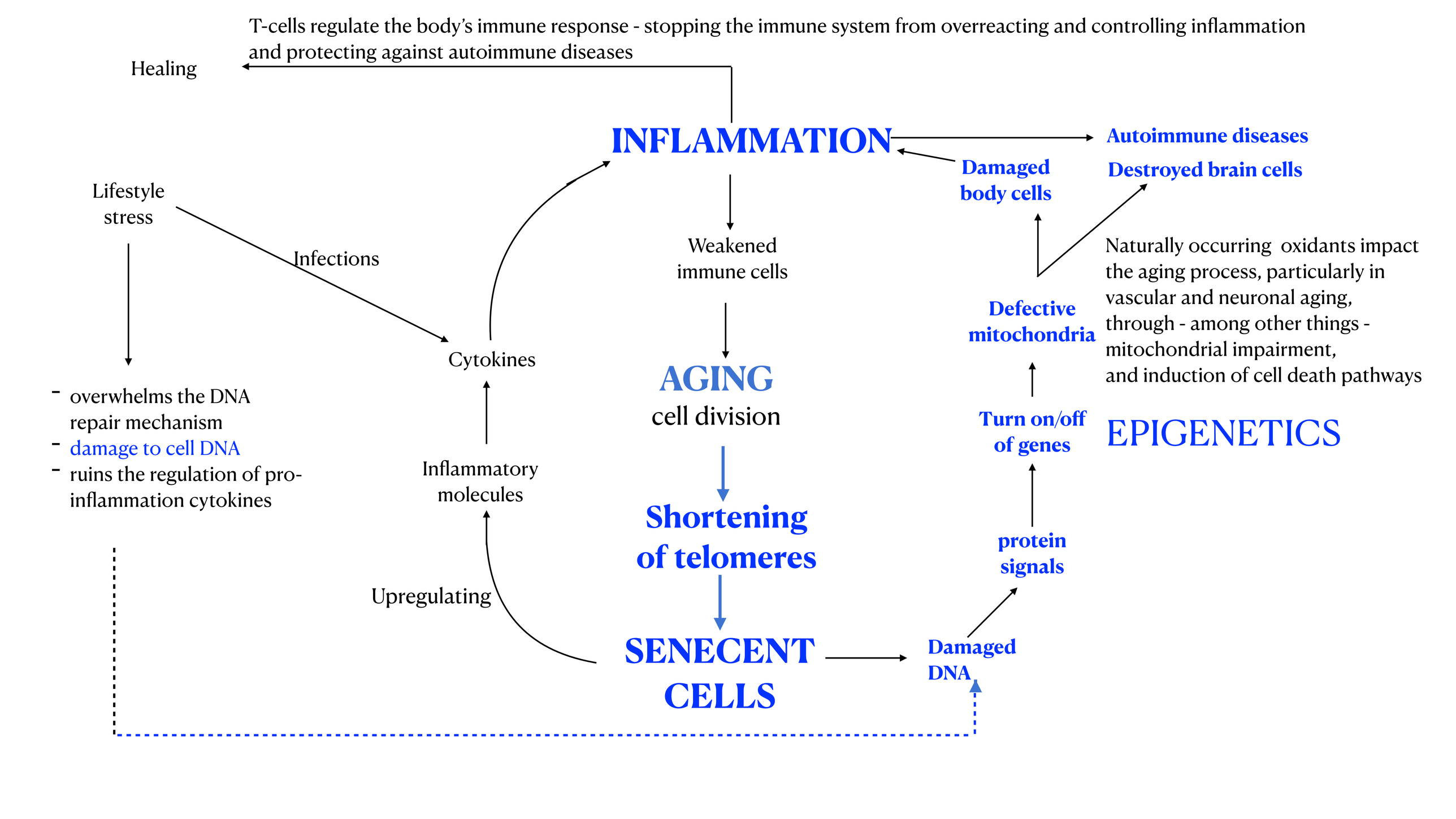
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. . . still, it's not all bad - senecent cells are important

There's *more to senescence than just cells running out of steam*.

Researchers have found that senescent cells in adult mice participate in wound healing. . .

During normal wound healing, fibroblasts* cells turn senescent, fill in a wound, and release compounds that promote repair of the tissue and *then* call in immune cells to destroy them. . .

*) connective-tissue cells

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There's *more to senescence than just cells running out of steam*.

The problem is if scenecent cells hang around for *too* long!

As we age, the immune system isn't up to the task of eliminating senescent cells *before* they start producing a harmful cocktail of molecules that damage surrounding tissues.

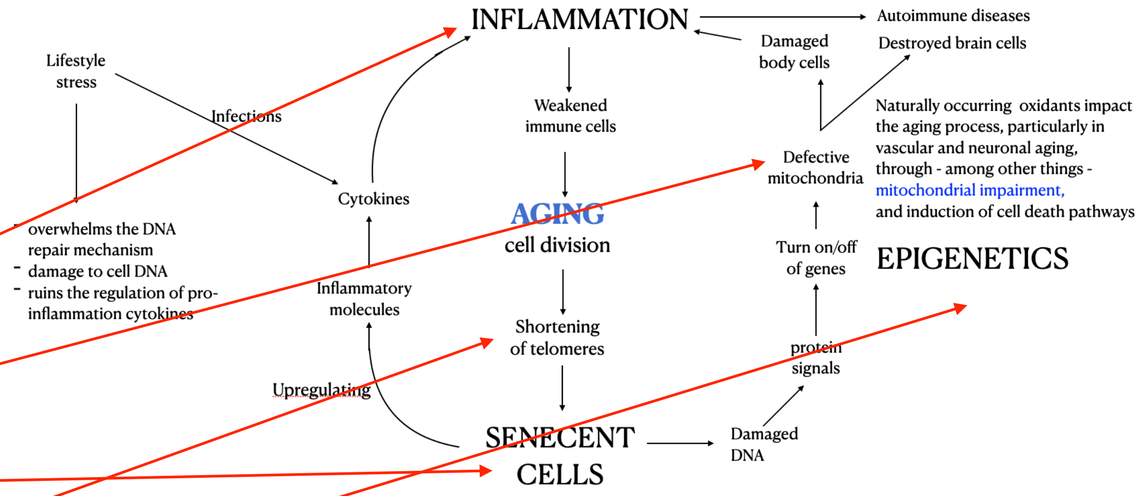
Also: To selectively induce senescence in cancer cells (so far only test tube research)

So, what can be done about aging?

1. Research makes progress
2. WE can do something

So, what can be done about aging?

Scientists are working on . . .



- Interfering in all the pathways in the chart . . . . . .

- Interventions that target inflammation

- Apply **senolytics** (agents, like enzymes) to kill senescent cells

- Enhance **mitochondria** - products like NAD+ (Nicotinamide Adenine Dinucleotide) is a crucial **coenzyme** found in all living cells that plays a central role in aging and in most cellular processes.

- Restore telomeres by using telomerase reverse transcriptase (TERT), an **enzyme** that helps **synthesize and extend telomeres**. TERT levels - important for the life of and forming of neurons - are reduced as we age!

- Erase a cell's identity and revert it back to a **stem-cell-**like state

So, what can be done about aging?

WE can improve our life style

Lifestyle factors → **INFLAMMATION** → **Autoimmune diseases**

- diet (microbiome)
- exercise
- sleep (light pollution)
- hearing/vision
- reduced stress
- infections

So, what can be done about aging?

About diets/supplements, see:

Resveratrol: https://www.healthline.com/nutrition/resveratrol

https://www.nationalgeographic.com/premium/article/food-diet-inflammation

Bryan Johnson, the guy who's trying to "Don't Die"
https://www.youtube.com/watch?v=6BP6V6wIvqY

So, what can be done about aging?

Food for thought:

The bioethical question is
. . . what would it mean for society to continually rewind the clock on aging?

Thank You

for your attention