# Exposure to cold increases life expectancy

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*A study shows that exposure to cold temperatures activates a system specialized in the elimination of protein aggregates involved in cell aging.*

It has been known for several years that a moderate reduction in body temperature is associated with greater longevity. This is particularly striking in cold-blooded animals (poikilotherms) such as certain species of fish whose exposure to a low temperature (15°C) remarkably increases longevity.

This phenomenon is also observed in homeotherms (warm-blooded animals) such as rodents: when mice are exposed to cold to reduce their body temperature by 0.5°C, their lifespan is extended, while it decreases if we increase the temperature by 0.5°C.

It is also possible that slight cooling of the body is beneficial for human health: for example, although it has long been assumed that our normal body temperature is 37°C (with variations in fractions of degrees during the day), recent data suggests that this temperature has decreased by about 0.03°C per decade since the industrial revolution and is now around 36.6°C.

It has been proposed that this decline, which possibly reflects a decrease in chronic inflammation through better treatment of infections and the use of anti-inflammatory drugs, could contribute to the increase in longevity observed over the 150 last years (1).

## CELLULAR AGING

To better understand how cold can improve longevity; German researchers looked at the protein aggregates that accumulate inside cells during aging.

These aggregates, caused by defects in the three-dimensional configuration of proteins that make them insoluble, are very toxic to the cell and over time cause loss of function of the affected organs (2).

This is particularly striking for neurodegenerative diseases such as Alzheimer's disease, Huntington's disease or amyotrophic lateral sclerosis (ALS) (known as Lou Gehrig's disease or Charcot disease) which are all caused by the accumulation of abnormal clusters of certain proteins.

Since cells contain an enzymatic system specialized in eliminating these aggregates (the proteasome), they wanted to see if cold activated this proteasome and made it possible to eliminate these aggregates to protect the cell from their toxicity.

It appears that this is indeed the case (3).

In an animal model which contains the typical aggregates of Huntington's disease or ALS, lowering the temperature from 20 to 15°C causes activation of the proteasome and a complete elimination of these aggregates which is correlated with a increased longevity.

An identical phenomenon is observed when human cells derived from an ALS patient are subjected to a temperature of 36°C, suggesting that the mechanism for eliminating defective proteins that can be activated by cold is very ancient and has been preserved during evolution.

## CLEAN THE CELL

Human body temperature is kept constant by an extremely sophisticated control system and so it is obviously not possible to lower our body temperature over long periods of time.

On the other hand, an interesting observation from the study is that it would be possible to circumvent this limitation: the researchers have in fact observed that even at normal temperature (37°C), we can stimulate the elimination of toxic aggregates by increasing the levels of a protein (called PSME3) involved in proteasome activation.

By developing therapies that manage to recreate this phenomenon, we could not only slow down a central process involved in biological aging, but above all make it possible to cleanse the cell of toxic aggregates responsible for several serious diseases, particularly at the neurological level.

(1) Protsiv M et al. Decreasing human body temperature in the United States since the industrial revolution. Elife 2020: 9: e49555.

(2) Cuanalo-Contreras K et al. Extensive accumulation of misfolded protein aggregates during natural aging and senescence. Front. Aging Neurosci. 2022 ; 14 : 1090109.

(3) Lee HJ et al. Cold temperature extends longevity and prevents disease-related protein aggregation through PA28γ-induced proteasomes. Nat Aging 2023; 3: 546-566.

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