Lipofuscin, the toxic waste of aging

As we and other organisms age, the means of dealing with intracellular junk decline. Autophagy, for instance, is a prime method that cells have of ridding themselves of and recycling structures and proteins that have passed their expiration date. Aging organisms lose the ability to activate autophagy as strongly as they could when younger. One consequence of this is the accumulation of lipofuscin, the toxic waste of aging.

To explain what lipofuscin is, one could do no better than to quote from an article in Science:

Lipofuscin is membrane-bound cellular waste that can be neither degraded nor ejected from the cell but can only be diluted through cell division and subsequent growth. The fate of postmitotic cells is to accumulate lipofuscin, which as an “aging pigment” has been considered a reliable biomarker for the age of cells such as neurons and, by extension, their hosts. In the aging human brain, deposits of lipofuscin are not uniformly distributed but are concentrated in specific regions of functional interest. The prevailing thought is that the major source of lipofuscin is incomplete lysosomal degradation of damaged mitochondria. Accumulating evidence suggests that lipofuscin is not benign but can impair the functioning of seemingly unrelated cellular systems, including the ubiquitin/proteasome pathway. A damaging feedback loop of lysosomal and proteasomal inhibition may occur as lipofuscin accumulates, leading to what has been appropriately named a “garbage catastrophe.” Reversing this catastrophe presents a formidable challenge.(1)

It seems clear enough that preventing the accumulation of lipofuscin ought to be a target for anti-aging strategies. How can that be done?

First, let’s take a closer look at how lipofuscin accumulates. Decreased autophagy is a major cause, and lipofuscin in turn limits autophagy in a descending spiral.(2)
Iron is key in the formation of lipofuscin

It will not by now come as a surprise that iron is involved in the accumulation of lipofuscin, and in fact iron forms a major part of this toxic waste.(3)

Key points from this last citation:

- Iron accumulates in lysosomes (autophagic vessels)
- Hydrogen peroxide reacts with iron to form hydroxyl radicals to form lipofuscin
- Lipofuscin is not degradable
- Formation rate of lipofuscin is inversely related to species lifespan
- Lipofuscin degrades autophagic capacity
- This causes declining removal of damaged structures and proteins

Iron is key in the formation of lipofuscin.

Free iron, which is iron not locked down by ferritin or other iron storage molecules, is the kind that does damage. But the amount of free iron appears to be a function of the amount of total iron, so the less iron in the system altogether, the lower the rate of lipofuscin formation.

Lipofuscin and the iron in it is a major source of oxidants and can lead to cells becoming senescent.(4) This is probably why the presence of senescent cells causes a system-wide increase in oxidative stress.

How to prevent/remove lipofuscin, the toxic waste of aging

There seems to be a very limited number of ways to deal with it.

Long-term treatment with acetylcarnitine (ALCAR) significantly reduced the amount of lipofuscin in the brains of old rats.(5)

Zinc deficiency leads to lipofuscin accumulation.(6) Zinc supplementation would presumably help.

Revving up the autphagic mechanism may be of help, and intermittent fasting as well as intermittent fasting enhancers will do this.

Finally, and to my mind the most important method of avoiding the accumulation of lipofuscin, keep iron levels low; this can be done with blood donation, iron chelators, and inhibition of iron absorption with tea, coffee, and red wine, as well as a low-iron diet rich in plant polyphenols.