A Brief Critique of SENS

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A hoary joke, passed down by medical residents through the ages, pertains to the therapeutic principles of dermatology: if it's dry, wet it; if it's wet, dry it; if it's cold, heat it; if it's hot, cool it; and use steroids. The joke, of course (funny at least to sleep-deprived non-dermatological residents), is that treating symptoms, rather than causes, is about the most brain-dead therapeutic approach imaginable. Should a patient, dissatisfied with the progress of his condition, overhear this joke, take it literally, and develop a web-based campaign to promote treating symptoms rather than causes of disease, physicians would not likely take time away from treating patients to publish a detailed critique of the joke. Unless, of course, the patient develops a following large enough to land him in the pages of Technology Review. Then attention must be paid.

So it is with SENS. The SENS strategy to treat symptoms rather than causes of aging has obvious and numerous flaws, any one of which would doom the strategy to failure; subject to a limit of 750 words, only a few of these flaws are indicated below.

The conceptual foundation of the SENS approach is that there are seven major categories of age-related impairments that contribute to senescence, and "there are no more to be found" (*1*). This is wrong: even though these categories are sometimes so general as to be almost meaningless, they still omit many age-related changes that contribute to senescence, including age-related increases in oxidative damage and changes in gene expression. Oxidative damage to proteins increases with age (*2*) and has been shown to impair function (*3*). Indeed, the specific activity of many proteins has been shown to decrease with age, probably due to age-related increases in oxidative damage. Furthermore, many studies, including high-throughput microarray studies (*4*), have demonstrated that the expression of hundreds, possibly thousands, of genes changes with age. Reversing specific age-related impairments without reversing ubiquitous age-related changes in protein oxidation and gene expression will not reverse senescence.

The practical rationale for the SENS approach is that correction of the seven forms of damage can be accomplished "by techniques that… can (with adequate funding) probably be implemented in mice within a decade or so (1)." However, the major categories of damage each entail a multitude of specific impairments. Furthermore, it is not known which of these age-related changes actually predispose to functional impairments and which may be benign. Therefore SENS would require an impractically large number of interventions. Finally, even if it were possible in some way to target the vast number of changes that occur during aging, at the moment, and indeed for the foreseeable future, the available technologies do not allow even one such modification to be carried out, much less the vast number necessary.

The fundamental flaws of the SENS approach may be illustrated by an example. SENS is so simple as to be equally applicable to any disease: say, “Strategies to Engineer Negligible Diabetes”. Like aging, untreated Type I diabetes is associated with a vast number of impairments, including many in categories enumerated by SENS: cell loss and atrophy, mitochondrial abnormalities, course AGE-mediated extracellular crosslinking, and, of course, death. To treat Type I diabetes by a SENS-like approach of treating symptoms (e.g., using stem cells and growth factors to increase muscle volume and repair diabetic neuropathy) would be fatal. Instead, Type I diabetes is successfully treated by targeting the cause of the disease: replacing the missing insulin. Even better would be to replace the destroyed pancreatic beta cells with similar cells resistant to autoimmune destruction. Insulin therapy was developed, and beta cell replacement will be developed, not through the engineering-like approach advocated by SENS, but through basic research disdained by SENS. Even more damning, though, is that it has not yet been possible to develop a practical way to replace even this single cell type (*5*). The technical challenges entailed by SENS, including whole-body delivery of genes for somatic gene therapy, dwarf those posed by simple replacement of a single endocrine cell type. Multiply so-far unresolved problems posed by a single simple disease, by the vast number of age-related changes enumerated by SENS and the age-related changes not enumerated by SENS, and it is clear why SENS is not taken seriously.

References

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