

Response by Mobbs to de Grey's Rebuttal

Aubrey de Grey concedes the fatal flaw of SENS: that it treats symptoms rather than causes of senescence, when he states that SENS would target “damage” that is “in turn caused by metabolism itself”. He states that SENS focuses on (symptomatic) damage rather than (causal) metabolism even though no strategy proposed by SENS has been shown to increase lifespan, whereas inhibition of metabolism is in fact a robust approach to increasing lifespan, based on genome-wide screening (1, 2). Indeed, a simple antagonist of glucose metabolism mimics many of the protective effects of caloric restriction (3). This refutes his claim that “SENS is still probably closer to fruition than any alternative”. He attempts to mitigate this fatal flaw by comparing SENS with automobile maintenance, which analogy speaks for itself. The point of the diabetes analogy is that the SENS approach, which eschews basic research, would never have identified beta cell loss as the cause of diabetes to begin with, so would not have led to beta cell replacement. Instead SENS would attempt to “engineer” rehabilitation of (to use de Grey’s words) “downstream consequences” of beta cell deficiency, an absurd therapeutic strategy. In his rebuttal, de Grey systematically misrepresents the scientific literature: in fact oxidatively damaged proteins are in general not indigestible (4), long-term changes in gene expression (for example during development) do not in general entail epimutations (5), and no expert, much less many, believes that it will be possible to manipulate tissue-specific expression of the hundreds or thousands of genes required by SENS in adult humans within 2 decades. A SENS approach to polio would entail perfecting the iron lung; focusing on causes through basic research has historically proven a far more effective strategy to treat diseases than focusing on symptoms, and senescence should be no exception.

References

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