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## Reversal of epigenetic aging and immunosenescent trends in humans

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### Abstract

Epigenetic "clocks" can now surpass chronological age in accuracy for estimating biological age. Here, we use four such age estimators to show that epigenetic aging can be reversed in humans. Using a protocol intended to regenerate the thymus, we observed protective immunological changes, improved risk indices for many age-related diseases, and a mean epigenetic age approximately 1.5 years less than baseline after 1 year of treatment (-2.5-year change compared to no treatment at the end of the study). The rate of epigenetic aging reversal relative to chronological age accelerated from -1.6 year/year from 0-9 month to -6.5 year/year from 9-12 month. The GrimAge predictor of human morbidity and mortality showed a 2-year decrease in epigenetic vs. chronological age that persisted six months after discontinuing treatment. This is to our knowledge the first report of an increase, based on an epigenetic age estimator, in predicted human lifespan by means of a currently accessible aging intervention.

**Keywords:** PD-1; PSA; c-reactive protein; lymphocyte-to-monocyte ratio; naive T cells; thymic regeneration.

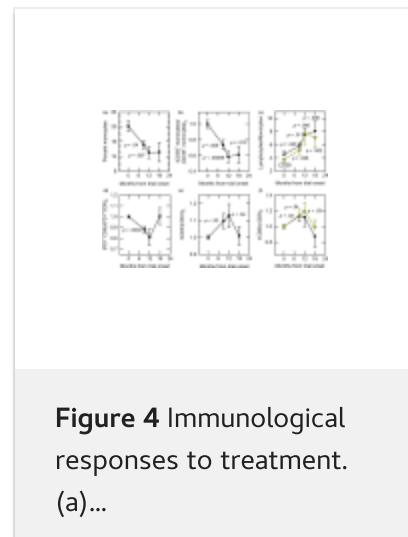
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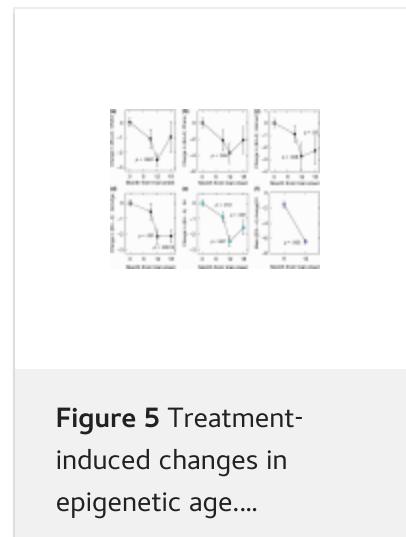
### Conflict of interest statement

GMF, RTB, JPW, and SH are shareholders in or have options to purchase shares in Intervene Immune, Inc., GMF and RTB are officers of Intervene Immune and are named in a related Intervene Immune patent application. All other authors declare no competing interests.

### Figures



**Figure 1** Treatment safety indices. In this...



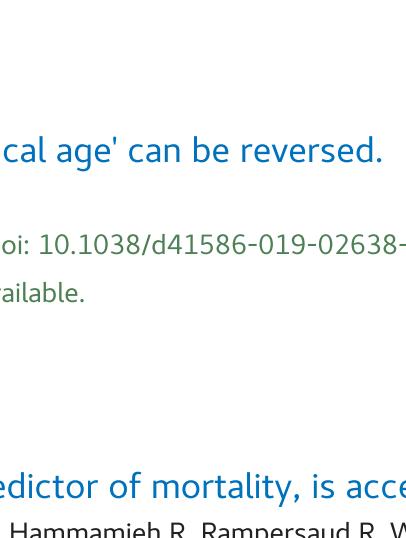
**Figure 2** Example of treatment-induced change in...



**Figure 3** Quantitative MRI-based regeneration outcomes. Like...



**Figure 4** Immunological responses to treatment. (a)...



**Figure 5** Treatment-induced changes in epigenetic age....

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