

2005 NETWORK DIAGRAM OF THE BIOLOGY OF AGING

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The many observable signs and symptoms of human senescence have been hypothesized by various researchers to result from several primary causes. Close inspection of the biochemical and physiological pathways associated with age-related diseases and with each of the hypothesized causes reveals several parallel cascades of events with multiple interactions and feedback loops among them. As an aid to keeping track of the many processes and interactions, a network diagram is presented. Promising intervention points for the development of new therapeutics are also highlighted on the flow chart. The mechanisms which are included in this network diagram range from the molecular to the whole-body level. Important pathways include: Glycation, oxidation, and crosslinking of extracellular proteins; Mitochondrial DNA mutation; Chromatin alterations change gene expression; Reactive, crosslinked material accumulates in lysosomes, and leaks into cytoplasm; Increased redox poise alters signaling and enzyme activities; Stiffer blood vessels promote stroke and heart disease; Loss of stem cells; Cell death leads to tissue wasting, neurodegeneration, and organ malfunction; Degradation of neuroendocrine and immune systems; Impaired repair & turnover of macromolecules & organelles; Inflammatory cascades promoted by damaged molecules and sick cells. Theoretically powerful targets for the development of new interventions include: Removing lipofuscin from lysosomes; Breaking AGE crosslinks in extracellular proteins; Preventing proliferation of mutant mitochondrial DNA; Enhancing turnover of damaged macromolecules and organelles. This flow chart is continuously maintained on the Web as a reference to researchers, [www.LegendaryPharma.com/senescence.html#Mechanisms] and is updated as new information comes to light.