

GETTING STARTED WITH THIS NETWORK DIAGRAM:

This symbolic diagram is not really a picture of a cell. It changes in scale from molecular events at the top, through whole cell activities in the middle, to tissue, organ, and whole body diseases at the bottom. Thick horizontal borders separate transitions in scale. Intracellular events are described on the top left. Extracellular matrix and blood are described on the top right. Colors have meaning, as indicated in the "Color Key". Shapes have meanings described in the "Shape Key". Refer to the Abbreviations table below.

Solid boxes represent physical materials. Slanted-roof boxes represent increase or decrease in quantities during aging. Hatched boxes represent activities or processes. Thin arrows represent causal sequences of events. Thick arrows represent physical transport or movement. A circle with an "X" inside represents inhibition of the indicated process; this might mark a candidate target for therapeutic intervention. Tags on the outsides represent environmental factors or external interventions.

ACKNOWLEDGEMENTS and CITATIONS:

This *Network Model of Human Senescence* was compiled and arranged by John D. Furber, based upon information in research reports from many scientists. References and links to more information about these topics may be found at:

- <http://LegendaryPharma.com/senescence.html>

Keywords may be searched at:

- PubMed
- scirus
- Google Scholar

A very good recent review of aging mechanisms was published in the journal, **Nature** by Jan Vijg & Judith Campisi. (2008) Puzzles, promises and a cure for ageing. *Nature*, 454, 1065-1071.

Special thanks go to the following scientists for their helpful suggestions on earlier versions of this network diagram, which were used to update it to its current form:

Alexandra Stolzing, Aubrey de Grey, Pat Langley, Ulf T. Brunk, Alexei Terman, Caleb Finch, George M. Martin, Mark A. Smith, Richard G. Cutler, Florian Muller, Robert Bradbury, James Joseph, Mark P. Mattson, Allen Herbst, Arthur Balin, Bill Vaughan, Juraj Dzifcak, Stanley Primmer, Stephen A. Racunas.

Abbreviations

| | | | |
|----------------------------|--|--------------|---|
| Aβ | = β -amyloid peptide 1-42 | LDL | = Low Density Lipoprotein |
| AGEs | = Advanced Glycation Endproducts | LF | = Lipofuscin or ceroid. Heterogeneous, crosslinked, indigestible material. |
| ALEs | = Advanced Lipoxidation Endproducts | Lysm | = Lysosome |
| Aggs | = Aggregated, crosslinked Junk molecules, including Lipofuscin & similar aggregated material | MSCs | = Mesenchymal Stem Cells, and derivatives, e.g. fibroblasts, osteoblasts. |
| BBB | = Blood-brain barrier | mito | = mitochondrion |
| BM | = Basement Membrane | mt | = mitochondrial |
| CMA | = Chaperone-mediated Autophagy | mtDNA | = mitochondrial DNA |
| CMV | = Cytomegalovirus | MMP | = matrix metalloproteinase |
| CR | = Calorie Restriction | nDNA | = nuclear DNA |
| COPD | = Chronic Obstructive Pulmonary Disease | Pb | = Lead |
| Cu | = Copper | PM | = Post Mitotic tissues, non-dividing cells, especially CNS neurons, skeletal muscle, and cardiac muscle |
| ECM | = Extracellular Matrix | RAGE | = Receptor of Advanced Glycation Endproducts |
| ETC | = Electron Transport Chain | RBCs | = Erythrocytes |
| exp | = Gene Expression | ROS | = Reactive Oxygen Species. Free radicals, such as superoxide, hydrogen peroxide, hydroxyl radical. |
| GPx | = Glutathione Peroxidase | TTR | = Transthyretin |
| HDACs | = Histone deacetylases | | |
| Hg | = Mercury | | |
| Ig | = Immunoglobulins | | |
| IMM | = Inner Mitochondrial Membrane | | |
| Junk | = Damaged Intracellular Structures, incl. oxidized proteins, lipid membranes, mitochondria, & proteasomes. | | |