This is a Work-in-Progress. I invite your collaborative suggestions of references and commentary regarding the numbered boxes, as well as pathways involving groups of boxes.

I also invite discussion regarding whether setting up an online Wiki, or database, or spreadsheet, or discussion thread might be more or less useful than a text document.

0xx Cytosolic or Intracellular Activities
1xx WHOLE CELL ACTIVITIES; populations of cells
2xx Extracellular spaces and ECM, blood, lymph
3xx Gene expression & repression. Intranuclear events
7xx External Intervention, Environmental Factors, Therapies, Drugs, Lifestyle, etc.
9xx TISSUE, ORGAN, & WHOLE BODY: PHYSIOLOGY & PATHOLOGY. Downstream effects of aging.

001 Lysosomes digest Junk, until they become filled with LF
002 ROS oxidize proteins & lipids
005 Ana Maria Cuervo.
027 Iron-Sulfur cluster assembly depends on membrane potential.
032 Clonal amplification of mutant mtDNA causes PM cell or skeletal muscle fiber segment to become anaerobic. Aubrey de Grey.
092, 093, 096, 923 With age, noradrenergic alpha2A receptors in pre-frontal cortex neurons decline, allowing cytoplasmic cAMP levels to increase. This opens K+ channels, which inhibits neurons from firing, thus reducing working memory, executive function, and clarity of thinking. Wang M, Gamo NJ, Yang Y, Jin LE, Wang XJ, Laubach M, Mazer JA,


Senolytic Drugs kill arrested cells to prevent spread of damage. Research includes quercetin, Dasatinib, and FOXO4-DRI (James Kirkland, Mayo Clinic)

Commanding neuroendocrine cell population in hypothalamus declines with age. Ulf Brunk.


TWC in Longevity Book 2015, p18.

Increased Wnt Signaling During Aging Alters Muscle Stem Cell Fate and Increases Fibrosis. Andrew S. Brack; Michael J. Conboy; Sudeep Roy; Mark Lee. Science. 2007. http://science.sciencemag.org/content/317/5839/807


Telomeres become oxidized and telomere length decreases in some cells.


Progerin and telomere dysfunction collaborate to trigger cellular senescence in normal human fibroblasts. Kan Cao, Cecilia D. Blair, Dina A. Faddah, Julia E. Kieckhaefer, Michelle Olive, Michael R. Erdos, Elizabeth G. Nabel, Francis S. Collins. J Clin Invest. 2011;121(7):2833-2844. doi:10.1172/JCI43578. "...progressive telomere damage during cellular senescence plays a causative role in activating progerin production. Progressive telomere damage was also found to lead to extensive changes in alternative splicing in multiple other genes. Interestingly, elevated progerin production was not seen during cellular senescence that does not entail telomere shortening."


Without the action of telomerase or ALT, each cell's telomeres get shorter with each subsequent mitosis.


Gonzalez-Suarez op.cit. 2009.

Kan Cao op.cit. 2011.

Methylation of histones.

Agmatine is a precursor of Spermadine.

Gene Editing, Genetic Engineering:

Increase expression of beneficial genes: eg TFAM, Lamp2a, hTERT, Lon Protease, Proteasome.


George Church. The Next Big Future. 16 Feb 2017

Genetically engineer more TFAM into cells. This allows them to increase their own NAD+/NADH ratio, so there is no need to take NMN. This upregulates ATP production. TFAM is a key regulatory protein that is in this pathway of NMN and NAD+. It allows cells to manufacture the NMN precursor on their own, so you don't have to manufacture it outside the cell and then try to get it into the cell from outside. Ideally, you don't want to have to take NMN for the rest of your life, you want to fix the body’s ability to make its own NMN and buy yourself rejuvenation for at least a few decades before you have to worry about NMN again. In order to accomplish this on a single cell level, they have used CRISPR to activate a TFAM activator, and they made it semi-permanent. With this technique, they were able to increase TFAM levels in the cell.
by 47-times. This resulted in restored ATP levels, increased NAD+, and an increased NAD+ / NADH ratio. It also increased total mitochondrial mass and reversed several other age-related changes.

TTR solubilizing drugs. Concept by JD Furber.

Stimulate or engineer super-fibroblasts or MSCs to be better and faster at repairing ECM, digesting bad ECM molecules; replacing them with good ones. Concept by John D. Furber. Chapter 19. The Future of Aging. (Springer 2010).


Telomeres shorten in response to psychological stress, as well as to other factors. (Rita Effros, Elissa Epel)

Sleep enhances clearance of amyloidβ. (Mendelsohn & Larrick book, ch 11)

Senolytic Drugs kill arrested cells to prevent spread of damage. Research includes quercetin, Dasatinib, and FOXO4-DRI (James Kirkland, Mayo Clinic). Also https://www.oisinbio.com/

Nano-scavenger therapy. (Lou Hawthorne, US Patent)

Induce Exocytosis to remove lipofuscin. Concept by JD Furber.

Gamma frequency 40 Hz flashing light stimulates glia to remove amyloidβ from brain. Li-Huei Tsai, Nature Dec 2016.


Minor surgery can remove bone depositions blocking the channels in the cribiform plate. A shunt is installed to allow natural circulation of cerebrospinal fluid. (Prof. Doug Ethell, UC Riverside and Leucadia Therapeutics)

Nature. 2015 Jul 30;523(7562):607-11. doi: 10.1038/nature14650. Epub 2015 Jul 22. Lanosterol reverses protein aggregation in cataracts. Zhao L(1), Chen X(2), Zhu J(3), Xi YB(2), Yang X(4), Hu LD(2), Ouyang H(5), Patel SH(6), Jin X(4), Lin D(6), Wu F(6), Flagg K(6), Cai H(7), Li G(8), Cao G(8), Lin Y(5), Chen D(6), Wen C(6), Chung C(6), Wang Y(9), Qiu A(10), Yeh E(6), Wang W(11), Hu X(8), Grob S(6), Abagyan R(12), Su Z(8), Tjondro HC(2), Zhao XJ(2), Luo H(6), Hou R(13), Jefferson J, Perry P(14), Gao W(15), Kozak I(16), Granet D(6), Li Y(4), Sun X(17), Wang J(4), Zhang L(15), Liu Y(9), Yan YB(18), Zhang K(19).

Macrophages digest LF - filled Exosomes


GnRH improves Cognition, muscle strength, skin, bone, neurogenesis, memory

Cardiac Hypertrophy

Body Plan Dysregulation

Failure to Regenerate

Prostate Hyperplasia