Dissecting the senescence regulatory network

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Aging is the single most important risk factor for various chronic human diseases, including cancer, metabolic syndrome, and neurodegenerative diseases. Therefore, targeting aging itself may be an alternative or even better strategy than targeting each chronic disease individually to improve human health. Recent advances indicate that cellular senescence is a fundamental process of aging and a driver of many age-related pathologies. Senescence exerts these pro-aging effects through two independent but not mutually exclusive mechanisms: (1) stem cell exhaustion and (2) the senescence-associated secretory phenotype (SASP), which causes chronic inflammation and tissue dysfunction. Recently, many efforts have been made to therapeutically target the detrimental effects of senescence, termed "senotherapy", including selective elimination of senescent cells (senolytics) and modulation of a proinflammatory senescent secretome (senostatics or senomorphics). Here, I discuss the current progress and limitations in the development and application of senotherapy and how to improve these crucial strategies by dissecting the senescence regulatory network for healthy aging.