Wnt – a new player in aging

Abstract
Aging is the process that the physiological functions necessary for survival and fertility of an organism are deteriorated. There are a variety of different mechanisms that are thought to participate in aging process. Recently, three papers show that wnt signaling pathway may also contribute to the aging.

One molecular characteristic of senescence in human cells is the formation of SAHF, and the formation of SAHF depends on the localization of HIRA to PML bodies. Based on the studies between HIRA and wnt2, Ye et al. showed that one of the downstream enzymes of wnt signaling-GSK3β can phosphorylate the HIRA and this phosphorylation is important for the localization of HIRA. Therefore, down regulation of wnt signalling triggered the cell senescence. In contrast, cell senescence was delayed by extracellular canonical wnt3 ligands.

A new gene termed Klotho has been identified to relate to the aging process. Through the studies of Klotho mice, Liu et al. found that Klotho could interact with wnt and inhibit the wnt signalling. The increased activity of wnt3 can accelerate cellular senescence both in vitro and in vivo. Therefore, Klotho appeared to be a wnt antagonist in mice. However, this inhibition does not affect the wnt canonical signaling, because Klotho did not affect the level of β-catenin, which is one of the downstream enzymes of wnt signalling. There may be other unknown signaling pathway involved in this interaction. At the same time, Andrew Brack et al. showed that wnt signaling was also involved in the change of muscle stem cells. Exposure old tissue to young systemic environment reduced the fibrotic response of old muscle. Conversely, young tissue in old environment has reduced progenitor proliferation. These changes can be blocked by wnt inhibitors or by reducing wnt in serum, which showed that wnt signaling is important for the conversion of muscle stem cells from myogenesis to fibrogenesis. Since fibrogenesis is one of the sign for tissue aging, it is suggested that augmented wnt can accelerate aging.

The discrepancies in these papers are difficult to understand. It may relate to the differences between mouse and human cells or different experiment conditions. Specificity of different isoforms of wnts or some unknown pathways may also be the reasons that the function of wnt signaling alters in aging process.

Reference