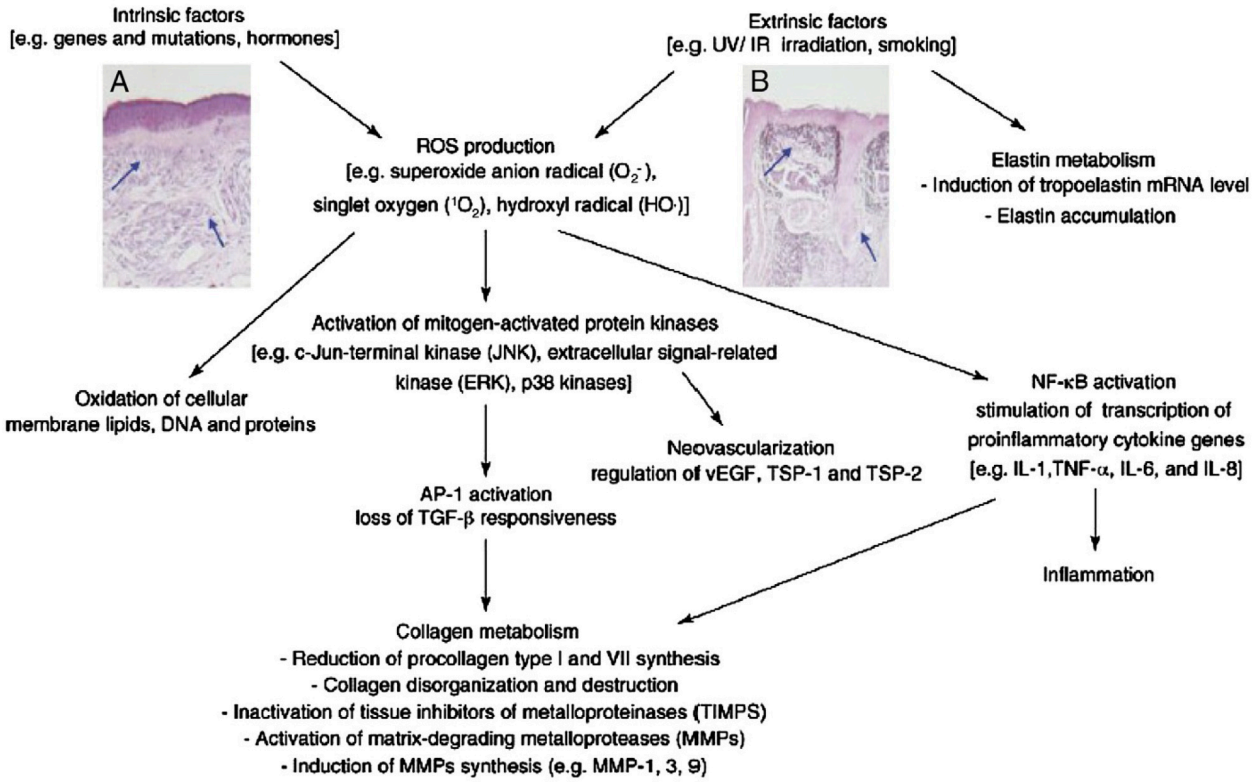

A schematic overview of major biochemical changes and signaling pathways involved in the generation of intrinsically and extrinsically aged skin. (A) Intrinsically and (B) extrinsically aged skin obtained from the (A) inner side of the upper arm of an 83-year-old and (B) the face of a 75-year-old woman. In the (B) sun-exposed skin sample, the typical histologic characteristics with accumulation of disoriented elastic tissue (blue arrows) in the dermis can be visualized after elastica staining. By contrast, (A) sun-protected skin shows only moderate histologic changes. In aged skin, mitogen-activated protein (MAP) kinase signal transduction pathways are important in regulating a variety of cellular functions. Downstream effectors of the MAP kinases include several transcription factors, including the c-Jun and c-Fos, which heterodimerize to form the activator protein 1 (AP-1) complex. AP-1 is a key regulator of skin aging, because it induces the expression of the MMP family and inhibits type I procollagen gene expression through interference with TGF-β signaling pathway. It has been postulated that MAP kinases may be activated by excess production of reactive oxygen species (ROS) that occurs with advanced age and may be superimposed by extrinsic factors such as ultraviolet irradiation. Excess ROS production also leads to accumulation of cellular damage, which includes oxidation of DNA resulting in mutations, oxidation of proteins leading to reduced function, and oxidation of membrane lipids resulting in reduced transport efficiency and altered transmembrane signalling. IL, interleukin; NF-κB, nuclear factor-κB; TGF-β, transforming growth factor-β; TSP-1, thrombospondin-1; TSP-2, thrombospondin-2; VEGF, vascular endothelial growth factor.

Copied from Zouboulis (2011, p 10)[7]