Among many potential culprits of aging, changes in metabolic pathways and age-related chronic diseases due to low-grade inflammation seem to be a common occurrence.[4–7] A good example is insulin resistance (IR), which represents a major metabolic problem that is commonly observed in aged people.[8] Along with IR, major metabolic impairments including obesity, type 2 diabetes, fatty liver diseases, and atherosclerosis also increase with aging.[6,9,10] Although metabolic syndromes are associated with many biologic processes, including genetics and epigenetics, it has become clear that inflammation is a key feature.[11] The term "meta-inflammation" describes the importance of inflammation on the onset and progression of metabolic syndrome.[12,13] Collectively, these age-associated alterations in metabolism and inflammation are intricately involved and connected. The identification of signal pathways that control age-related metabolism dysfunction and dysregulate inflammation is therefore crucial for a better understanding of the factors involved in regulation of the aging process.

In this chapter, peroxisome proliferator-activated receptors (PPARs) will be highlighted as important transcriptional factors with substantial potential in the regulation of aging process. First, changes in inflammation and metabolism during aging will be described, especially focusing on their mutual relationship. Then functions of PPARs will be briefly reviewed in the context of metabolism and inflammation. Thus, the involvement of PPARs in aging and age-related diseases will be discussed based on the roles they play in metabolism and inflammation according to recent evidence. Furthermore, newly synthesized PPAR agonists will be suggested as anti-aging drugs with therapeutic potential.

16.2 Age-Related Changes in Inflammation and Their Role in Metabolic Diseases

16.2.1 Chronic Inflammation and Aging

Current aging research focuses on chronic inflammation as a potent casual mediator underlying the process of aging. This age-related, low grade inflammation is different from classical views on inflammation as traditional inflammation was defined as a part of the body's complex biological response to harmful stimuli, such as pathogens, damaged cells, or other irritants that may induce the acute phase response. The initial recognition of harmful stimuli in the body is mediated by receptors of the innate immune system, such as Toll-like receptor (TLRs) and NOD-like receptors. The most powerful players in this process are tissue resident macrophages, mast cells, and neutrophils.[14] They effectively cope with the initial injury or infection by production of various inflammatory mediators, including cytokines, chemokines, eicosanoids, and other physiologically active molecules.[14] A successful acute inflammatory response leads to elimination of the cause of inflammation by a resolution process. In this context, inflammation is a protective process that maintains the homeostasis of individuals.