aged rat kidneys. An age-related decrease in PPAR binding activity was also slowed by CR in aged rat kidneys. To further examine the possible role of PPARα and PPARγ in age-related inflammation, lipopolysaccharide (LPS) treatments were administered to young and aged rats. Treatment with LPS deceased the levels of both PPARs in young and aged rat kidneys, but the extent of this decrease was greater in aged rat kidneys.[113] The authors further compared the effect of the PPARγ agonist with CR on the aging process of rat kidneys.[143] PPARγ activation by its agonist suppressed age-related oxidative stress and inflammation through inhibiting the NF-κB signaling, just like the CR effects. Collectively, the authors concluded that down-regulation of PPARs in the aged rat kidneys might be related to age-related oxidative stress and inflammation, and those conditions could be reversed by CR or PPAR activation.

16.7 Conclusion

PPARs have been extensively investigated since their discovery as ligand-dependent nuclear transcriptional receptors. The roles of PPARs are also well characterized. Because PPARs control patterns of gene expression involved in a broad spectrum of biological processes, including metabolism and inflammation, the PPAR family has been proposed to be an attractive target for various pharmacological interventions. Through continued efforts, several PPAR agonists (fibrates for PPARα, TZDs for PPARγ) have been developed and used for the treatment of metabolic diseases.

More recently, PPARs have been shown to be associated with aging in many aspects. In the aging process, increased low-grade chronic inflammation is commonly observed and its association with various age-related diseases is well documented. In particular, an age-related increase in inflammation is strongly associated with progressive deterioration of metabolic function. Recent evidence also strongly suggests PPARs as key modulatory transcription factors responsible for the suppression of inflammation through regulation of NF-κB. The anti-inflammatory actions of PPARs were further verified by *in vitro* and *in vivo* studies that indicate the importance of PPARs as major players in the pathogenesis of many inflammatory diseases. Furthermore, more recent studies suggest that PPARs agonists can directly reduce age-related inflammation and thereby modulate the pathophysiology of aging. Because currently available PPAR agonists have unwanted adverse effects, great efforts are being made to develop more selective PPAR agonists without adverse effects. In addition, balanced activation of PPARs through dual- or pan-agonists provides a better strategy in controlling age-related diseases. Concluding, it can be assumed that better understanding the association between aging and PPARs can further lead to the development of new therapeutic agents (including PPAR agonists) that modulate aging and age-associated diseases (Figure 16.2).