epithelial cells by expression of a subset of β-defensins.[104] Accordingly, it is important to maintain proper activity of PPARγ by therapeutic or nutritional means to prevent colonic inflammation, which contributes to the progression of IBD. Although experimental evidence and precise mechanism studies are insufficient, PPARα agonist also showed anti-inflammatory effects in a colitis model. The deletion of PPARα or supply of exogenous PPARα ligands reduce the degree of colitis induced by dinitrobenzene sulfonic acid (DNBS) and dextran sulfate sodium (DSS).[109,110] The role of PPARβ/δ in colitis was controversial in mouse models of IBD, so additional studies are needed to fully address its exact roles.[111,112]

16.4.2 PPARs in Aging and Longevity

Increasing evidence demonstrates the PPARs' intimate involvement in the aging process. Whether or not associated with age-related inflammation, the decreased expression or activity of PPARs during aging is detected commonly in various tissues. In aged rat kidney, decreased PPARα and PPARγ expression were detected both in mRNA and protein levels.[113] Furthermore, binding activity of PPARs was also decreased during the aging process in the kidney.[113] Aged rat heart also showed decreased PPARα expression followed by target-gene reduction.[114] PPARγ expression during aging in metabolically important tissues (adipose tissue, muscle) also decreased in aged rodents, indicating possible association of PPARγ with insulin resistance during aging.[115,116] Interestingly, spleen PPARα levels were also decreased during aging, implying the possible relevance of the immune system and PPARs during aging.[117]

More direct evidence on the important role of PPARs in the aging process comes from observation of PPARα knockout mice. As explained in a previous chapter about the role of PPARα in lipid metabolism, PPARα null mice exhibited a number of defects in lipid metabolism and lipid accumulation in the liver.[35,36,118] In addition to altered lipid metabolism, Poynter and Daynes first reported a premature and enhanced age-dependent increase of oxidative stress and NF-κB activation in PPARα knockout mice.[53] The administration of PPARα ligands to aged mice restored cellular redox balance as well as highly activated inflammatory response, which was not detected in PPARα knockout mice.[53] These results suggested that PPARα plays an important role in maintaining proper levels of oxidative stress and inflammation during aging. Howroyd *et al.* further expanded the role of PPARα during aging. The authors showed that PPARα knockout mice had decreased longevity compared with wild type mice. Reduced longevity in PPARα-null mice was associated with increased levels of various non-neoplastic spontaneous aging lesions.[119] Although direct evidence for the link between PPARγ and longevity are lacking because of the lethality of PPARγ knockout mice during embryogenesis, various studies suggest the important role of PPARγ in aging. PPARγ variants were reported to have an essential role in aging in humans with low insulin resistance.[120,121] In addition, Klotho, which is a transmembrane protein that suppresses aging, is directly regulated by PPARγ, suggesting possible links