low-density lipoprotein (LDL) particles, a contributing factor to heart disease, by scavenging free radicals and chelating copper.[109,146] Second, resveratrol thins the blood and prevents excessive platelet aggregation, which can result in thrombus formation leading to ischemia, infarction, or stroke.[109,146] This property is thought to be due to its ability to inhibit COX1.[147] Third, resveratrol increases expression levels of both endothelial and inducible nitric oxide synthetase (eNOS and iNOS), and acts as a vasodilator to relax arteries and decrease blood pressure.[148] Another mechanism by which it appears to protect endothelial cells is *via* SIRT1-mediated activation of the transcription factor KLF2.[149] Finally, resveratrol has been shown to reduce the formation of atherosclerotic plaques in rabbits fed a high-cholesterol diet,[150] and it may lower serum cholesterol and triglyceride levels *via* SIRT1-independent regulation of the bile acid transporter ASBT.[151]

Synthetic STACs that are structurally unrelated to resveratrol will prove to be a useful tool in dissecting which of the cardioprotective effects of resveratrol are due to activation of SIRT1 and which are caused by ancillary effects on other enzymes. While synthetic STACs have not been extensively studied in the context of cardiovascular disease, a few reports have suggested that they might impart protective effects. For example, administration of SRT1720 reduces myocardial infarction in mice[152] and reverses vascular endothelial dysfunction in aging mice.[153] Moreover, SRT1720 has been shown to reduce vascular inflammation in an angiotensin II apoE-knockout mouse model of atherosclerosis,[154] and SRT3025 also provides protection in this model.[155] In humans, SRT2104 has been shown to improve the serum lipid profile of otherwise healthy cigarette smokers by reducing LDL, cholesterol, and triglyceride levels,[156] in a manner similar to resveratrol studies in mice.[151] However, analysis of these patients also revealed that SRT2104 had no effect on vascular or platelet function,[156] or arterial stiffness.[120] Thus, the effectiveness of STACs in improving a patient's cardiovascular health could depend on a number of factors, including diet, age, and pre-existing medical conditions.

11.4.6 Inflammation and Immunity

Many diseases of aging, as well as autoimmune diseases, are influenced by inflammation. In general, STACs are thought to control inflammation through activation of SIRT1 and subsequent deacetylation of NF-kB, a transcription factor that acts as a central mediator for the immune response.[15] However, in the case of resveratrol, its effects on immunity are likely multifaceted due its antioxidant and antiviral properties, and its ability to regulate a number of other enzymes involved in inflammation and immunity (*e.g.* COX1, COX2).[15,109] Resveratrol decreases inflammation in autoimmune models of Crohn's disease,[157] psoriasis,[158] and inflammatory arthiritis[159] in rats, mice, and rabbits, respectively. In addition to acting as a natural antibacterial and antiviral agent (especially against HSV1 and HSV2),[109,160] resveratrol decreases inflammation in response to pathogen infection by *Listeria monocytogenes*[161] and reduces levels of inflammatory cytokines in