In contrast, unresolved low-grade inflammation is different from acute inflammation in several aspects. When acute inflammation is not resolved, the inflammatory process persists and acquires new characteristics. Infiltration of macrophages and T cells replaces the neutrophils in the acute phase inflammation.[15] If these secondary immune cells fail to eliminate the cause of inflammation, a chronic inflammatory state continues with the formation of massive lymphoid infiltrate-like structures, such as granulomas. Although the general processes and mechanisms of chronic inflammation are not fully understood, its consequences are generally associated with many pathological conditions including autoimmunity problems, inflammatory tissue damage, fibrosis, metaplasia, and other tissue degenerative diseases.[16]

Recent studies have revealed the importance of inflammation as a major risk factor of aging. Our lab has proposed the molecular inflammation hypothesis and presented evidence supporting that the inflammatory process may play a major role in the aging process.[17] Accumulated data strongly suggest that continuous up-regulation of pro-inflammatory mediators is induced during the aging process.[18,19] These increases of inflammatory mediators and accumulation of pro-inflammatory tissue damages may result from multiple reasons, such as enhanced activation of the NF-κB transcriptional factor, the failure of the immune system to effectively clear pathogens or dysfunctional host cells (immunosenescence), the propensity of senescent cells to secrete pro-inflammatory cytokines, and other homeostatic unbalances.[7,20–23] Furthermore, these chronic inflammatory conditions are significantly associated with increased mortality and morbidity in elderly people.[24] Thus, importantly, the molecular inflammation hypothesis of aging may serve not only as a molecular basis for a link between normal aging and age-related pathological processes, but also aid in the identification of pathways that control age-related inflammation.

16.2.2 Roles of Inflammation in Metabolic Diseases During Aging

Aging is undoubtedly the most potent contributor to the etiologies of metabolic diseases.[9] Especially in industrialized and westernized society, it is easy to acquire various metabolic diseases from the current life style, like overnutrition and lack of exercise. These metabolic diseases include type 2 diabetes, cardiovascular diseases, and stroke. Along with these metabolic syndromes (MS), IR represents a major component of aging.[11] Persistence of these metabolic alterations leads to impairments of metabolic organs, including de-regulated hepatic gluconeogenesis, adipose lipogenesis, and defective glucose uptake and glycogen synthesis in skeletal muscle. These age-related alterations were once thought to be passive players in the aging process, now they are considered active participants in a vicious cycle that can accelerate the aging process.[10]