A number of stress factors including oxidative stress, aging and compromised energy supply can disrupt the function of endoplasmic reticulum (ER), leading to a condition termed, ER stress, whereby, unfolded or misfolded proteins accumulate inside the ER lumen. The ER responds to the accumulated unfolded proteins in its lumen by activating intracellular signal transduction pathways known as the unfolded protein response (UPR). The UPR pathways tightly monitor the condition in the ER to maintain cellular homeostasis or to induce apoptosis under persistent ER stress as a protective mechanism. Takada et al. (2011) showed that in human osteoarthritis (OA) cartilage samples, ER stress increases with the progression of cartilage degeneration as indicated by increased expression of ER stress markers: pPERK, Ubiquitin, CHOP and CCASP3, a marker of chondrocyte apoptosis. Cellular senescence plays an important role in the loss of ability of the chondrocytes to maintain and restore the articular homeostasis, as well as limiting cartilage repair leading to cartilage degeneration. The premature senescence phenotype of chondrocytes expresses elevated level of p53, p16 and p21 cell cycle proteins. ER stress in synoviocytes has been linked to the induction of apoptosis but its role in senescence remains to be investigated. Here, the role of senescence in synoviocytes, particularly on the involvement of ER stress will be discussed. The outcomes of this study will contribute further insights into the influences of the synovium on the wellbeing of chondrocytes.