Osteoarthritis (OA) is an autoimmune disease defined as bone damage in joints. Angiogenesis (new blood vessel formation) is involved in the pathogenesis of OA. A factor called VEGF promotes new blood vessel formation. Specific mechanism controlling induction of VEGF in OA is not clear. In the pathogenic condition of OA, a factor called SAF-1 is abundantly present in the diseased joint tissues. This study uses several molecular techniques to determine if SAF-1 regulates VEGF expression and the mechanisms by which inflammatory cytokines mediate joint damage. The results showed that SAF-1 regulate VEGF expression in a dose dependent manner. SAF-1 plays an important role in VEGF expression induced by inflammatory cytokines. Dysfunction of SAF-1 completely abolishes the expression of VEGF induced by inflammatory cytokines. The function of SAF-1 is also regulated by an other factor. Together these results indicate that the abundance of SAF-1 induced by inflammatory cytokines promote VEGF expression, leading to the damage of joint tissues. Therefore, SAF-1 could be a potential therapeutic target to design novel drug for the treatment of OA patients.