



**Figure 8:** Post-membrane effect of rhein (Novartis osteocerein brochure, n.d.)

First, once IL-1 binds to its receptor, a downstream signalling pathway is triggered which results in release of active NF-κB. Active NF-κB translocates to the nucleus and stimulates expression of numerous genes including cytokines, matrix metalloproteinases (MMPs) and nitric oxide (NO). Pro-IL-1 is cleaved by IL-1 converting enzyme (ICE) to release active IL-1 into the extracellular matrix.

Afterwards, rhein induces IL-1-induced. IκB-a degradation (possibly by inhibiting an upstream MEK/ERK signalling pathway), blocking NF-κB activation and translocation to