Abstract


Aromatase and regulation of the estrogen-to-androgen ratio in synovial tissue inflammation: common pathway in both sexes.

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BACKGROUND: Sex hormones play an active role in inflammatory responses, with androgens being anti-inflammatory, whereas estrogens have both pro- and anti-inflammatory effects.

FINDINGS: In rheumatoid arthritis (RA) patients, low levels of androgens and high levels of estrone are found in the synovial fluid. Aromatase is the key enzyme for the conversion of androgens into estrogens. Proinflammatory cytokines stimulate aromatase activity so that the inflammatory milieu can induce conversion of androgens to estrogens. Moreover, testosterone inhibits aromatase activity. As local androgen levels are low in RA, this can contribute to high aromatase activity in the synovium. Importantly, aromatase-converted estrogens are converted into proproliferative and proinflammatory 16-hydroxylated estrogens. A hormone involved in aromatase activity is vitamin D, which downregulates aromatase in human RA macrophages.

CONCLUSIONS: Collectively, evidence suggests a key role of aromatase in sex hormone balance during chronic inflammation and points to the importance of vitamin D as a possible new tool for aromatase modulation.

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