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IS40. DOPİNG AGENTS: MOLECULAR UNDERSTANDİNG OF THE İMMUNOMODULATORY EFFECTS OF ANABOLİC STEROİDS

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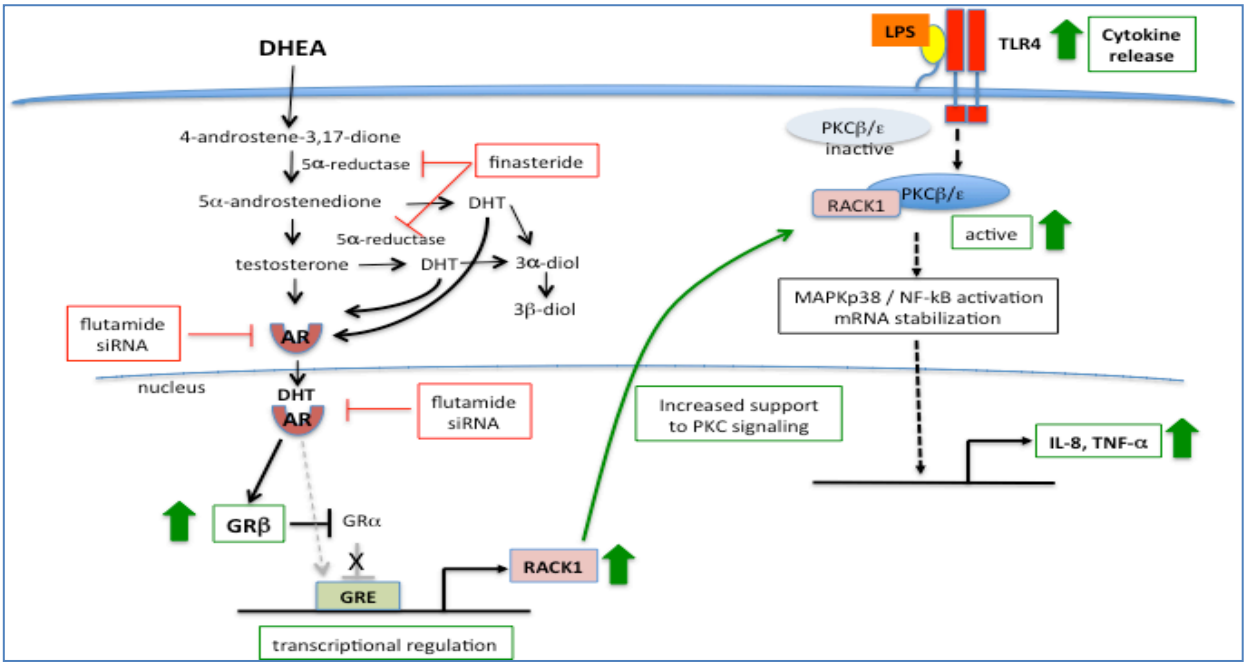
Anabolic drugs or anabolic steroids are molecules chemically related to testosterone, and with similar effects in the body. Hormones have an important role in homeostasis and function of the immune system, including sex hormones, which appear to have distinctive and exclusive roles in the development of the immune system and in shaping the immune responses. Evidence is accumulating on the existence of bidirectional interactions among oxidative stress, immune and endocrine systems and concern is warranted.



RACK1 is the acronym for receptor for activated C kinase 1, encoded by a gene known as GNB2L1, guanine nucleotide-binding protein subunit beta-2-like-1. RACK1 is involved in embryonic development, immune response, neuronal activity and addiction, and in circadian rhythm. At the cellular level, RACK1 is involved in a variety of signaling pathways and different aspects of cell regulation. Due to its plethora of interaction partners, RACK1 appears to be the fulcrum of cellular homeostasis, controlling essential cellular processes such as transcription, epigenetics and translation, cell proliferation and growth as well as cell spreading and cell-cell interactions. We previously demonstrated that RACK1 gene expression is negatively regulated by glucocorticoids, and dehydroepiandrosterone (DHEA, an endogenous anabolic androgenic steroid) has opposite effects on RACK1 expression and on the regulation of protein kinase C (PKC) activity involved in immune cells activation.

DHEA seems to antagonize the effect of glucocorticoids by inducing a dose-related up-regulation of the negative dominant glucocorticoid receptor-β (GRβ). More recently (manuscript submitted), we demonstrated that androstenedione, testosterone, dihydrotestosterone (DHT), in analogy to DHEA, induced an increase in RACK1 expression (both mRNA and protein) and in LPS-induced IL-8 and TNF-α production. Furthermore, we demonstrated that by blocking the androgen receptor (AR), DHEA-induced GRβ and RACK1 expression could be completely prevented, posing AR at the center of the action of DHEA, further supporting the ability of steroid hormones to modulate RACK1 expression and immune cell activation.

We suggest that any changes in steroid hormones ratio may lead to an imbalance between the actions of these hormones, which eventually become relevant for the expression of proteins in the signal transduction machinery involved in key elements of the immune response. This evidence will be used to highlights the immunomodulatory effects of anabolic drugs.

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