Immunological, vascular and metabolic actions of androgens

Akademisk avhandling

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Avhandlingen baseras på följande delarbeten


SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR MEDICIN
Immunological, vascular and metabolic actions of androgens

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Abstract

Men have higher prevalence of cardiovascular disease (CVD) but lower risk of autoimmune disorders than women. The actions of sex steroids may be involved in the sexual dimorphism of these diseases. Although testosterone, the main androgen, seems to protect against autoimmunity, its role in CVD is contradictory and disease-dependent. Androgens, acting mainly via the ubiquitously expressed androgen receptor (AR), regulate multiple physiological processes (e.g. reproduction, immunity, and energy homeostasis) and are potent anabolic hormones. However, the target cells and mechanisms involved in these effects remain poorly defined. The aim of this thesis was to define effects, target cells and mechanisms involved in the actions of androgens on splenic B cell numbers, atherosclerosis, abdominal aortic aneurysms and brown fat activity in male mice.

The main findings were that androgens/AR: 1) control splenic B cell numbers via nervous regulation of splenic stroma and the cytokine BAFF, 2) protect against atherosclerosis in a T cell-dependent manner and that thymic epithelial cells is a likely AR target for atheroprotection, 3) increase angiotensin II-induced aortic neutrophil infiltration and abdominal aortic aneurysms by targeting bone marrow mesenchymal/stromal cells, and 4) reduce brown fat activity and core body temperature in male mice.

In conclusion, our studies support that many immunological actions of androgens are mediated by targeting the stroma of lymphoid organs. Further, these immunological actions contribute to beneficial (atherosclerosis) as well as deleterious (abdominal aortic aneurysms) effects on vascular pathology. We also show that androgens are important regulators of brown adipose tissue thermogenesis in male mice. These findings elucidate androgen actions of potential importance for cardio-metabolic and immunological diseases and may have implications for future development of selective AR modulators.

Keywords: androgens, androgen receptor, immune system, atherosclerosis, abdominal aortic aneurysm, brown fat, mice.