Dendritic cells are crucial for cardiovascular remodeling and modulate neutrophil gelatinase-associated lipocalin expression upon mineralocorticoid receptor activation

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Background:Adaptive immunity is crucial in cardiovascular and renal inflammation/fibrosis upon hyperactivation of mineralocorticoid receptor. We have previously demonstrated that dendritic cells can respond to mineralocorticoid receptor activation, and the neutrophil gelatinase-associated lipocalin (NGAL) in dendritic cells is highly increased during aldosterone (Aldo)/mineralocorticoid receptor-dependent cardiovascular damage. However, the interrelationship among dendritic cells, target organs inflammation/fibrosis induced by mineralocorticoid receptor, and NGAL-dependence remains unknown.Objective:We studied the role of dendritic cells in mineralocorticoid receptor-dependent tissue remodeling and whether NGAL can modulate the inflammatory response of dendritic cells after mineralocorticoid receptor activation.Methods:Cardiovascular and renal remodeling induced by Aldo and high-salt diet [nephrectomy-Aldo-salt (NAS) model] were analyzed in CD11c.DOG mice, a model which allows dendritic cells ablation by using diphtheria toxin. In addition, in-vitro studies in NGAL-knock out dendritic cells were performed to determine the

immunomodulatory role of NGAL upon Aldo treatment.Results:The ablation of dendritic cells prevented the development of cardiac hypertrophy, perivascular fibrosis, and the overexpression of NGAL, brain natriuretic peptide, and two profibrotic factors induced by NAS: collagen 1A1 and connective tissue growth factor. We determined that dendritic cells were not required to prevent renal hypertrophy/fibrosis induced by NAS. Between different immune cells analyzed, we observed that NGAL abundance was higher in antigen-presenting cells, while in-vitro studies showed that mineralocorticoid receptor stimulation in dendritic cells favored NGAL and IL-23 expression (p19 and p40 subunits), which are involved in the development of fibrosis and the Th17-driven response, respectively.Conclusion:NGAL produced by dendritic cells may play a pivotal role in the activation of adaptive immunity that leads to cardiovascular fibrosis during mineralocorticoids excess.

cardiovascular fibrosis

dendritic cells

inflammation

mineralocorticoid receptor

neutrophil gelatinase-associated lipocalin

aldosterone

APC protein

brain natriuretic peptide

CD11b antigen

CD3 antigen

CD4 antibody

CD4 antigen

collagen

collagen 1a1

connective tissue growth factor

diphtheria toxin

gamma interferon

glycoprotein p 15095

granulocyte macrophage colony stimulating factor

interleukin 17

interleukin 23

interleukin 6

mineralocorticoid receptor

neutrophil gelatinase associated lipocalin

protein p19

protein p40

unclassified drug

brain natriuretic peptide

CD11 antigen

Il23a protein, mouse

interleukin 23p19

Itgax protein, mouse

Lcn2 protein, mouse

mineralocorticoid receptor

neutrophil gelatinase associated lipocalin

Nr3c2 protein, mouse

adaptive immunity

animal experiment

animal model

antigen presenting cell

Article

cardiovascular disease

controlled study

dendritic cell

enzyme activation

female

gene overexpression

heart muscle fibrosis

heart ventricle hypertrophy

high salt diet

immunocompetent cell

immunomodulation

in vitro study

inflammation

kidney disease

kidney fibrosis

kidney hypertrophy

male

mouse

nephrectomy

nonhuman

priority journal

protein expression

target organ

Th17 cell

vascular fibrosis

animal

C57BL mouse

cardiomegaly

cardiovascular system

coculture

cytology

dendritic cell

fibrosis

genetics

hyperaldosteronism

kidney

knockout mouse

lymphocyte activation

metabolism

salt intake

T lymphocyte

Aldosterone

Animals

Cardiomegaly

Cardiovascular System

CD11 Antigens

Coculture Techniques

Dendritic Cells

Female

Fibrosis

Hyperaldosteronism

Inflammation

Interleukin-23 Subunit p19

Kidney

Lipocalin-2

Lymphocyte Activation

Male

Mice

Mice, Inbred C57BL

Mice, Knockout

Natriuretic Peptide, Brain

Receptors, Mineralocorticoid

Sodium Chloride, Dietary

T-Lymphocytes