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

Araos P.		
Prado C.		
Lozano M.		
Figueroa S.		
Espinoza A.		
Berger T.		
Mak T.W.		
Jaisser F.		
Pacheco R.		
Michea L.		
Amador C.A.		

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. © 2019 Wolters Kluwer Health, Inc. All rights reserved.

cardiovascular fibrosis

dendritic cells

inflammation

mineralocorticoid receptor

neutrophil gelatinase-associated lipocalin

aldosterone

APC protein

brain natriuretic peptide

CD3 antigen

CD11b antigen

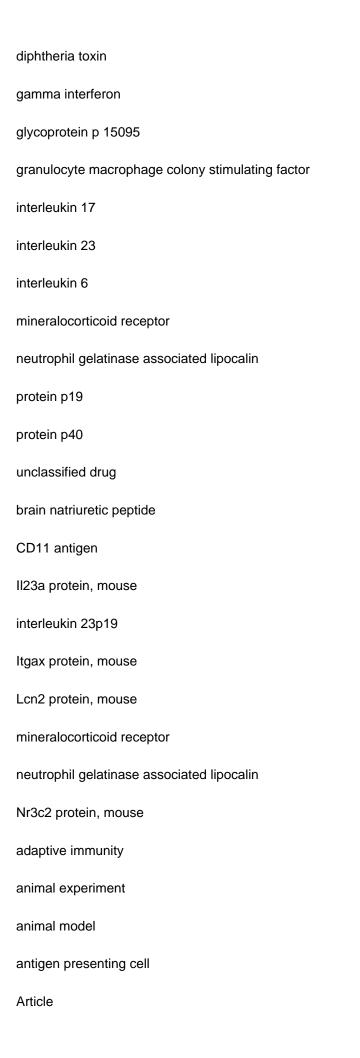
CD4 antibody

CD4 antigen

collagen

collagen 1a1

connective tissue growth factor



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
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Animals
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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		