Neutrophil Gelatinase-Associated Lipocalin from immune cells is mandatory for aldosterone-induced cardiac remodeling and inflammation

Buonafine M.

Martínez-Martínez E.

Amador C.

Gravez B.

Ibarrola J.

Fernández-Celis A.

El Moghrabi S.

Rossignol P.

López-Andrés N.

Jaisser F.

Immune system activation is involved in cardiovascular (CV) inflammation and fibrosis, following activation of the mineralocorticoid receptor (MR). We previously showed that Neutrophil Gelatinase-Associated Lipocalin (NGAL) is a novel target of MR signaling in CV tissue and plays a critical role in aldosterone/MR-dependent hypertension and fibrosis. We hypothesized that the production of NGAL by immune cells may play an important part in the mediation of these deleterious mineralocorticoid-induced effects. We analyzed the effect of aldosterone on immune cell recruitment and NGAL expression in vivo. We then studied the role of NGAL produced by immune cells in aldosterone-mediated cardiac inflammation and remodeling using mice depleted for NGAL in their immune cells by bone marrow transplantation and subjected to mineralocorticoid challenge NAS (Nephrectomy, Aldosterone 200 ?g/kg/day, Salt 1%). NAS treatment induced the recruitment of various immune cell populations to lymph nodes (granulocytes, B lymphocytes, activated CD8 + T lymphocytes) and the induction of NGAL expression in macrophages, dendritic cells, and PBMCs. Mice depleted for NGAL in their immune cells were protected against NAS-induced cardiac remodeling and inflammation. We conclude that NGAL produced by immune cells plays a pivotal

role in cardiac damage under mineralocorticoid excess. Our data further stressed a pathogenic role of NGAL in cardiac damages, besides its relevance as a biomarker of renal injury. © 2017

Aldosterone

Cardiovascular

Fibrosis

Inflammation

MR

NGAL

aldosterone

mineralocorticoid

neutrophil gelatinase associated lipocalin

aldosterone

neutrophil gelatinase associated lipocalin

animal cell

animal experiment

animal model

animal tissue

Article

B lymphocyte

bone marrow transplantation

carditis

CD8+ T lymphocyte

cell selection

controlled study

dendritic cell

fibroblast

flow cytometry

granulocyte

heart injury

heart muscle fibrosis

heart ventricle remodeling

immunocompetent cell

in vivo study

kidney injury

lymph node

macrophage

male

mouse

nephrectomy

nonhuman

peripheral blood mononuclear cell

priority journal

protein expression

protein function

animal

C57BL mouse

cardiac muscle

cell culture

cell proliferation

fibrosis

heart atrium remodeling

human

inflammation

knockout mouse

leukocyte

metabolism

oxidative stress

pathology

Aldosterone

Animals

Atrial Remodeling

Cell Proliferation

Cells, Cultured

Fibroblasts

Fibrosis

Humans

Inflammation

Leukocytes

Lipocalin-2

Male

Mice, Inbred C57BL

Mice, Knockout

Myocardium

Nephrectomy

Oxidative Stress