

# Disclosures

- None

# Dendritic cells mediate T cell activation in the kidney lymph node during hypertension

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# Dendritic cells (DCs) and hypertension

- Dendritic cells are potent antigen presenting cells that mediate T cell activation
- Adoptive transfer of DCs from hypertensive mice increased susceptibility to hypertension
- Preventing interactions between antigen presenting cells and T cells attenuated hypertension

Kirabo A, et al. *JCI*. 2014

Vinh A, et al. *Circulation*. 2010

Itani HA, et al. *Circ Res*. 2016

# T lymphocytes and hypertension

- T cells are adaptive immune cells that infiltrate the kidney during hypertension
- Pharmacological or genetic inhibition of T cells:
  - diminishes hypertension
  - Preserves renal sodium excretion after a hypertensive stimulus
- Inflammatory cytokines produced by mononuclear cells that infiltrate the hypertensive kidney:
  - Upregulate sodium transporter activity
  - Promote sodium retention by the kidney

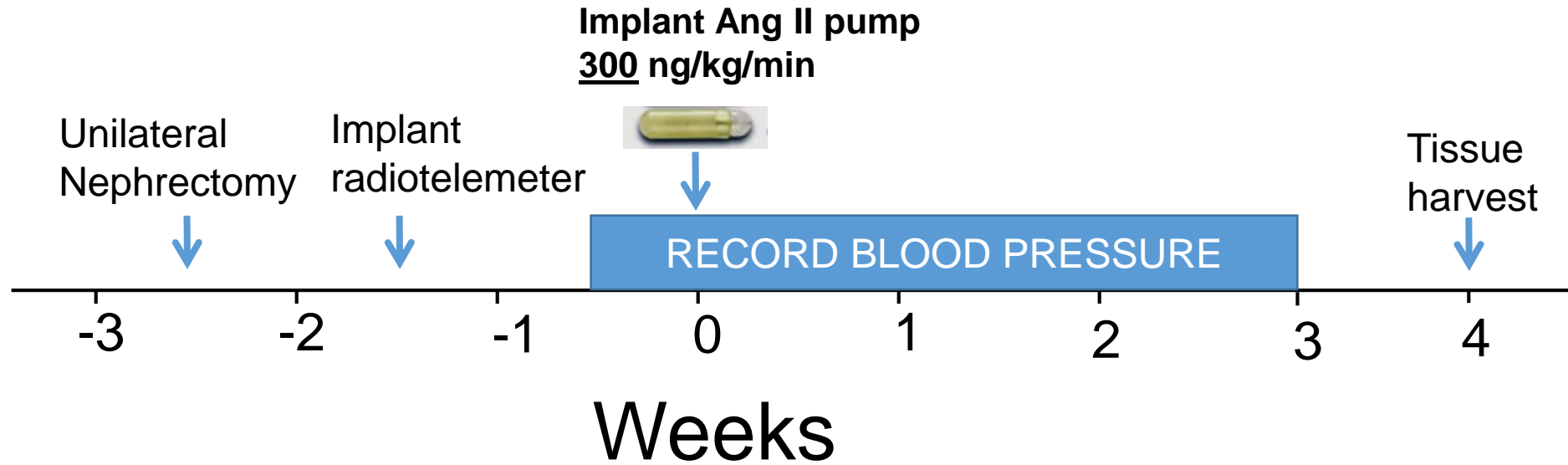
# Hypothesis

Dendritic cells activate T cells in the kidney lymph node during hypertension

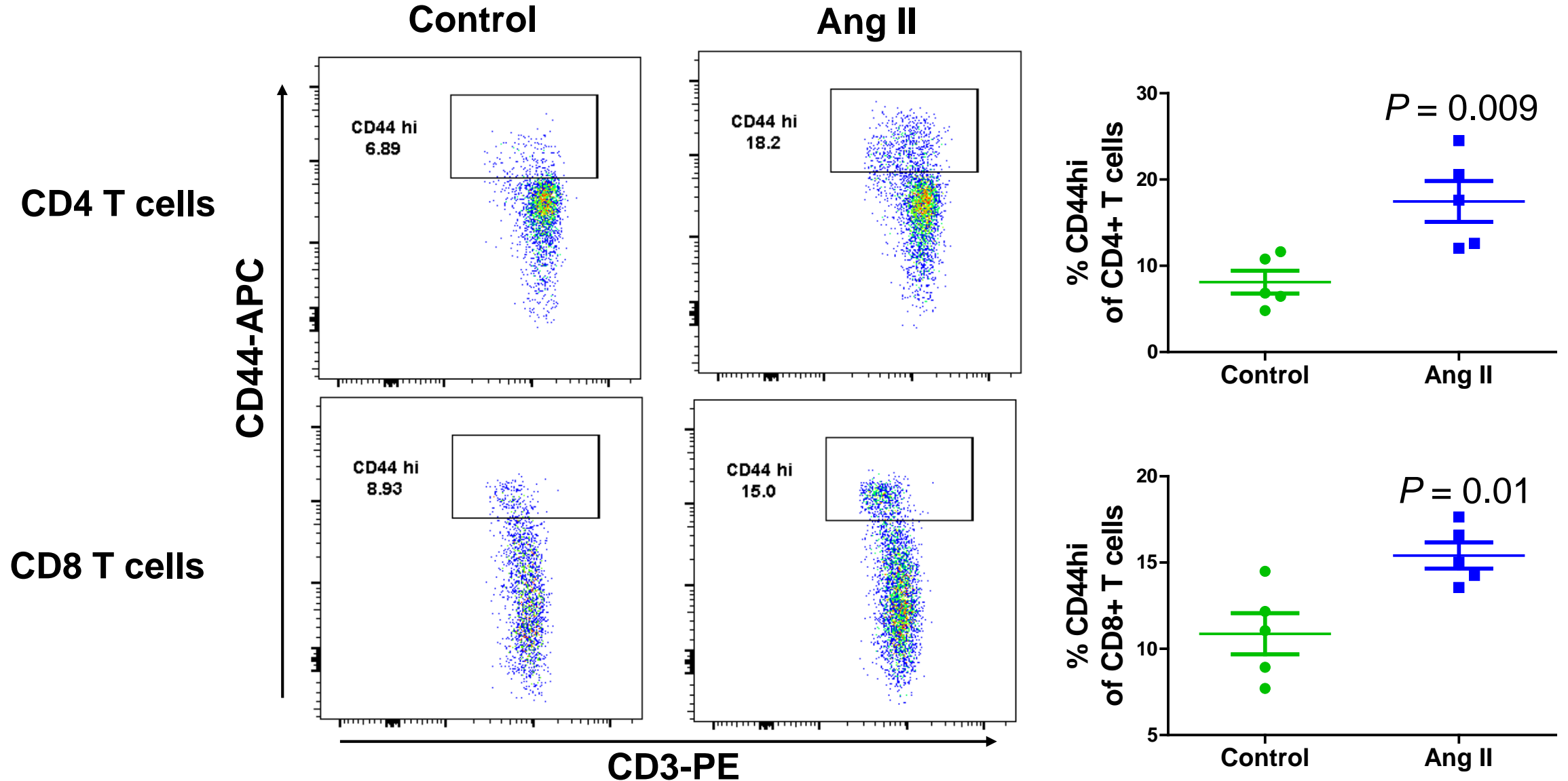
# Hypertensive model – chronic angiotensin II infusion



C57BL/6



# Kidney Lymph Node - Hypertension enhances CD44 expression on T cells

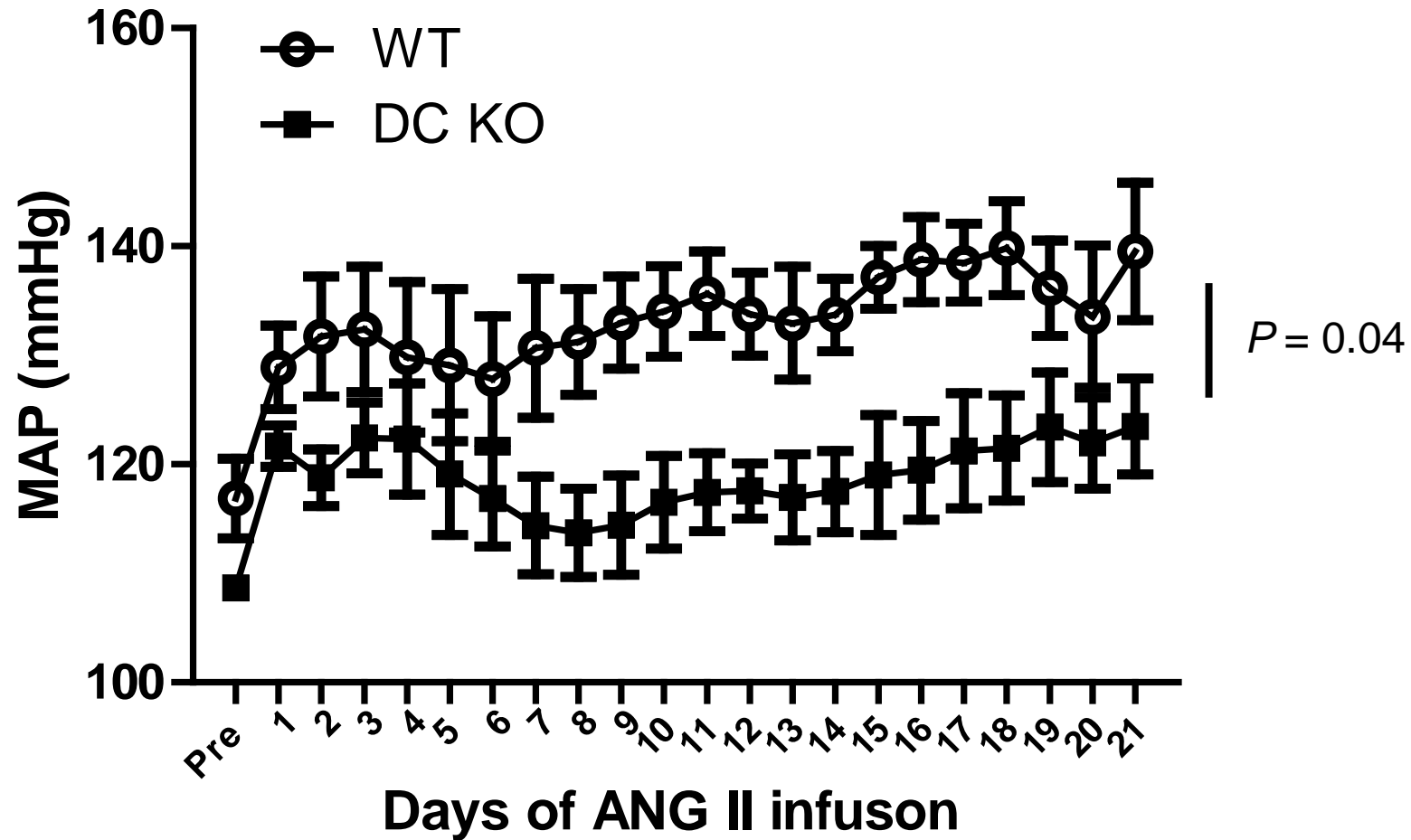


# Model of dendritic cell deficiency (FLT3L<sup>-/-</sup> = “DC KO”)

- FMS-like tyrosine kinase 3 ligand (FLT3L) is a cytokine important in the development and steady state regulation of dendritic cells
- Widely used model of DC deficiency
- T cell compartment is undisturbed

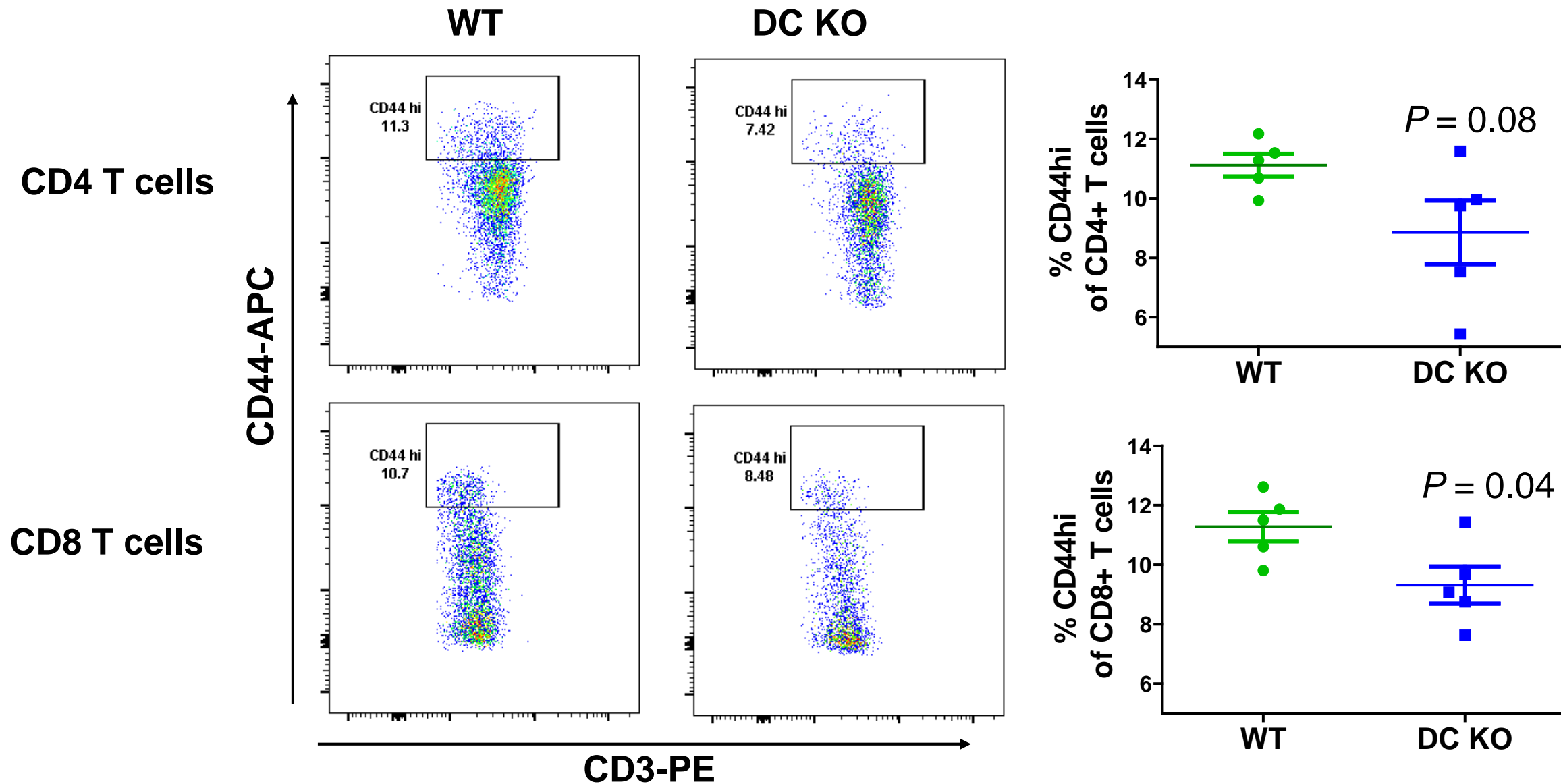


# DC KO mice have attenuated hypertension

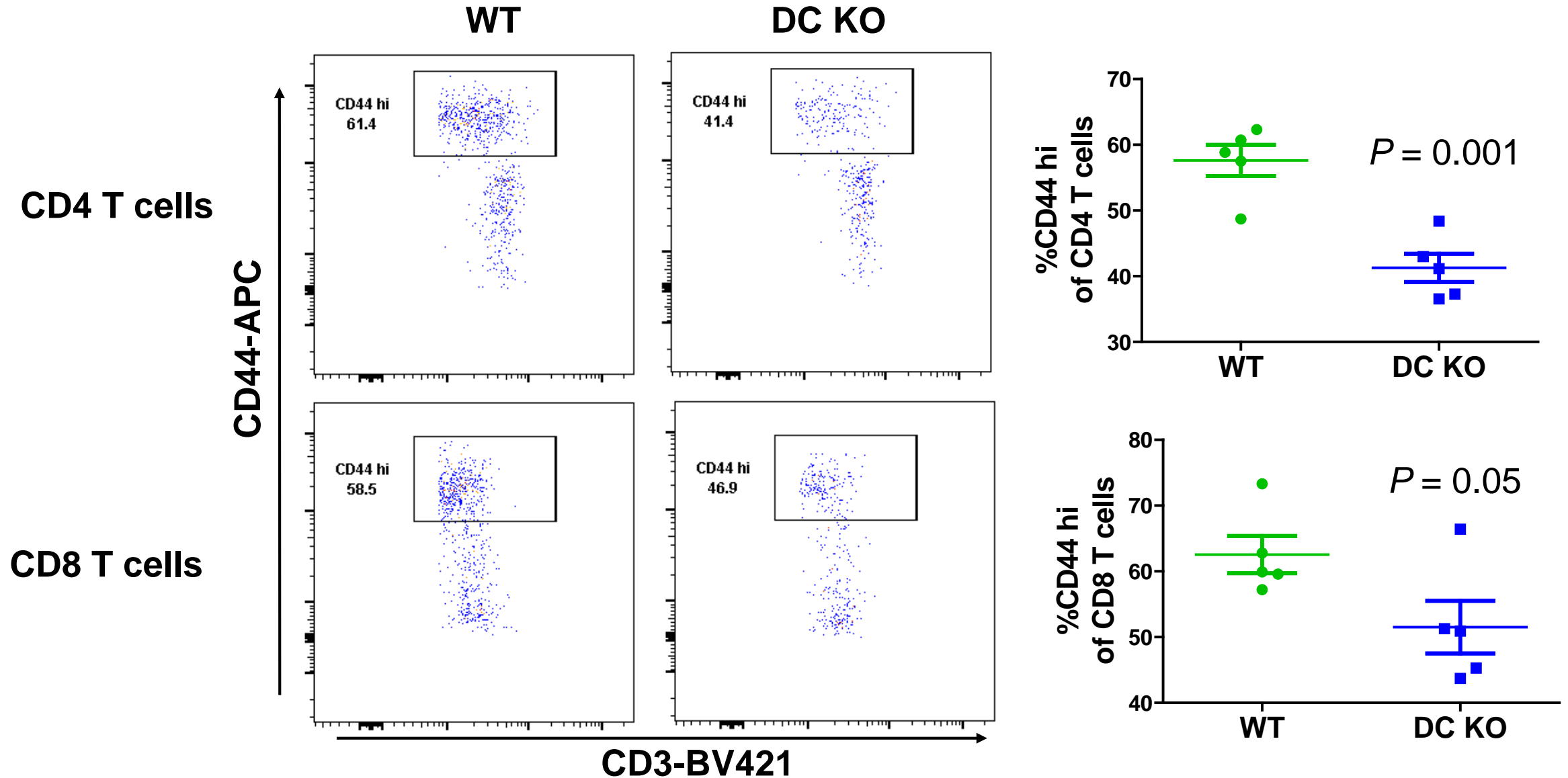


n = 4-5/group

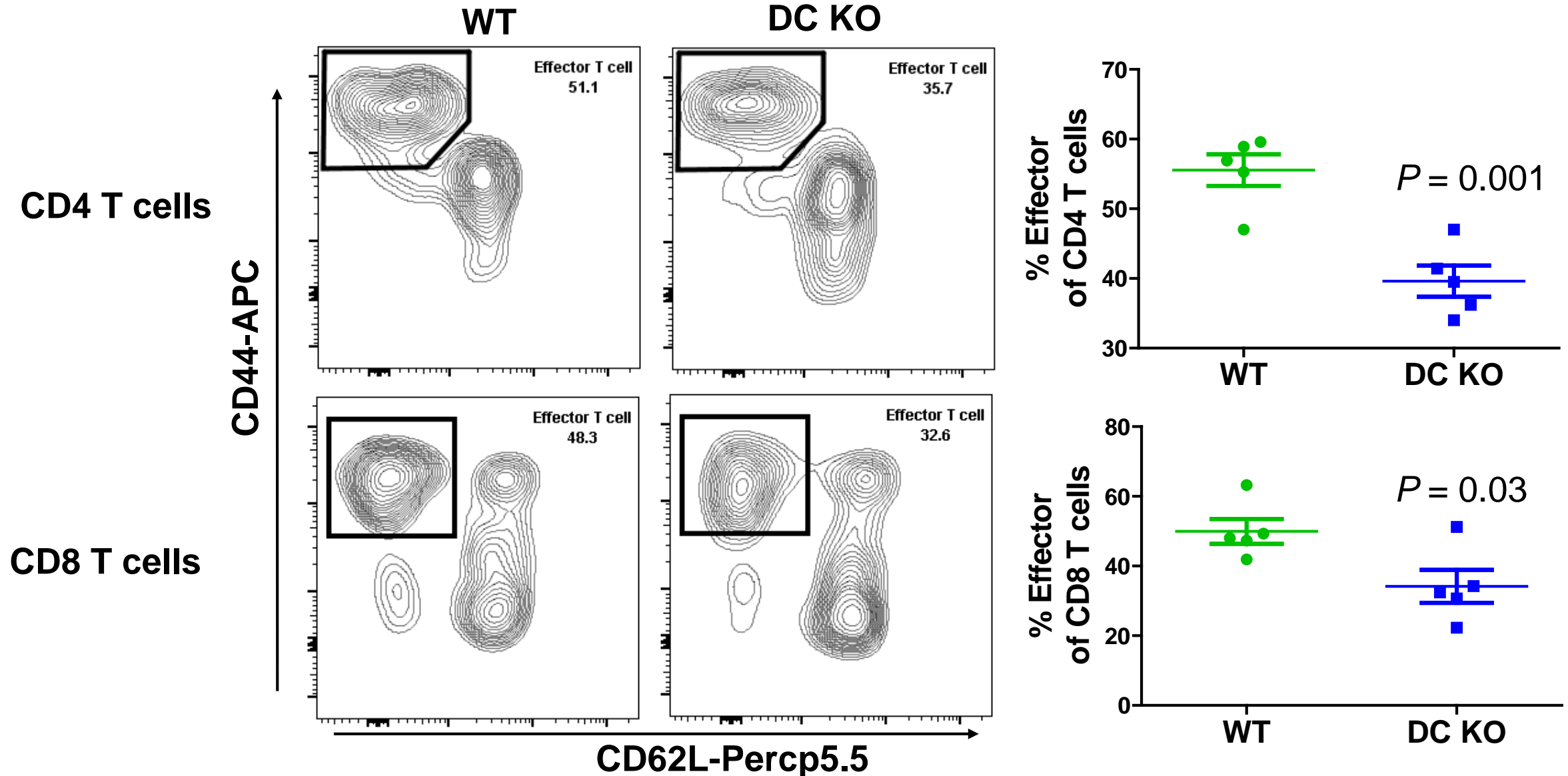
# Kidney Lymph Node - DC deficiency blunts accumulation of CD44<sup>hi</sup> T cells during hypertension



# Kidney - DC deficiency attenuates accumulation of CD44<sup>hi</sup> T cells in the hypertensive kidney

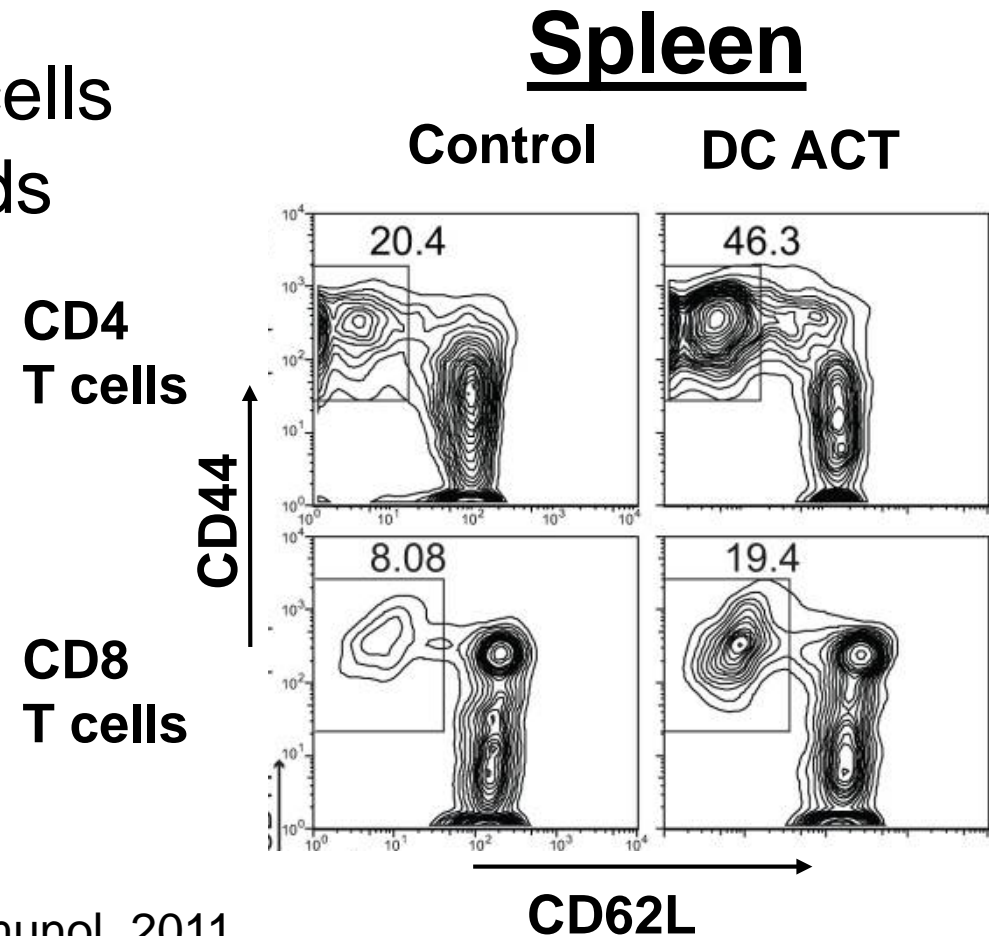


# Kidney - DC deficiency attenuates accumulation of CD44<sup>hi</sup> Effector T cells in the hypertensive kidney

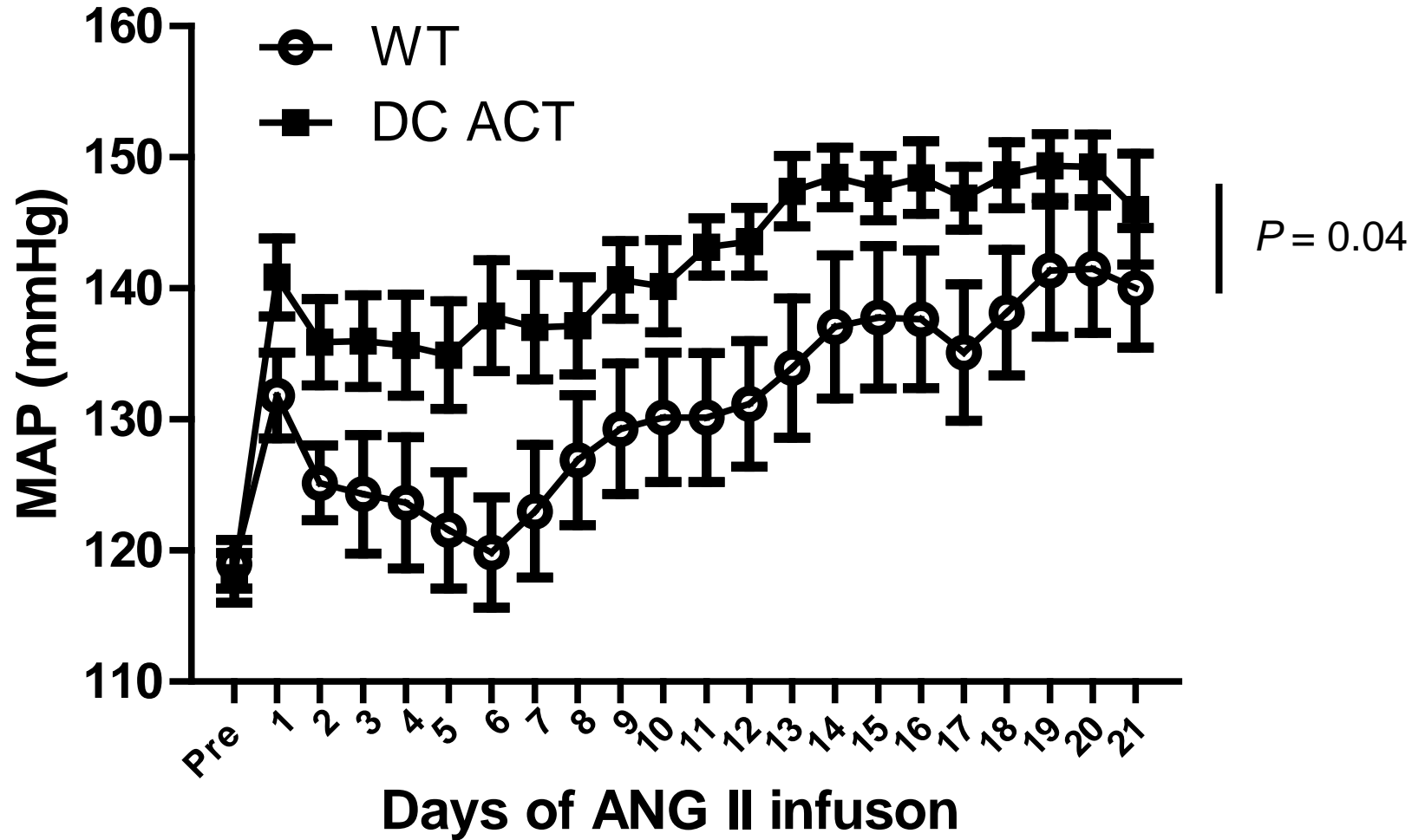


# Model of spontaneous dendritic cell activation (*CD11c-Cre A20<sup>flox/wt</sup>* = “DC ACT”)

- A20 is a ubiquitin-editing protein that prevents NF- $\kappa$ B-mediated DC maturation
- CD11c is a widely used Cre for dendritic cells
- Heterozygous deletion of A20 in DCs yields mice that:
  - are phenotypically normal at baseline
  - have enhanced T cell activation

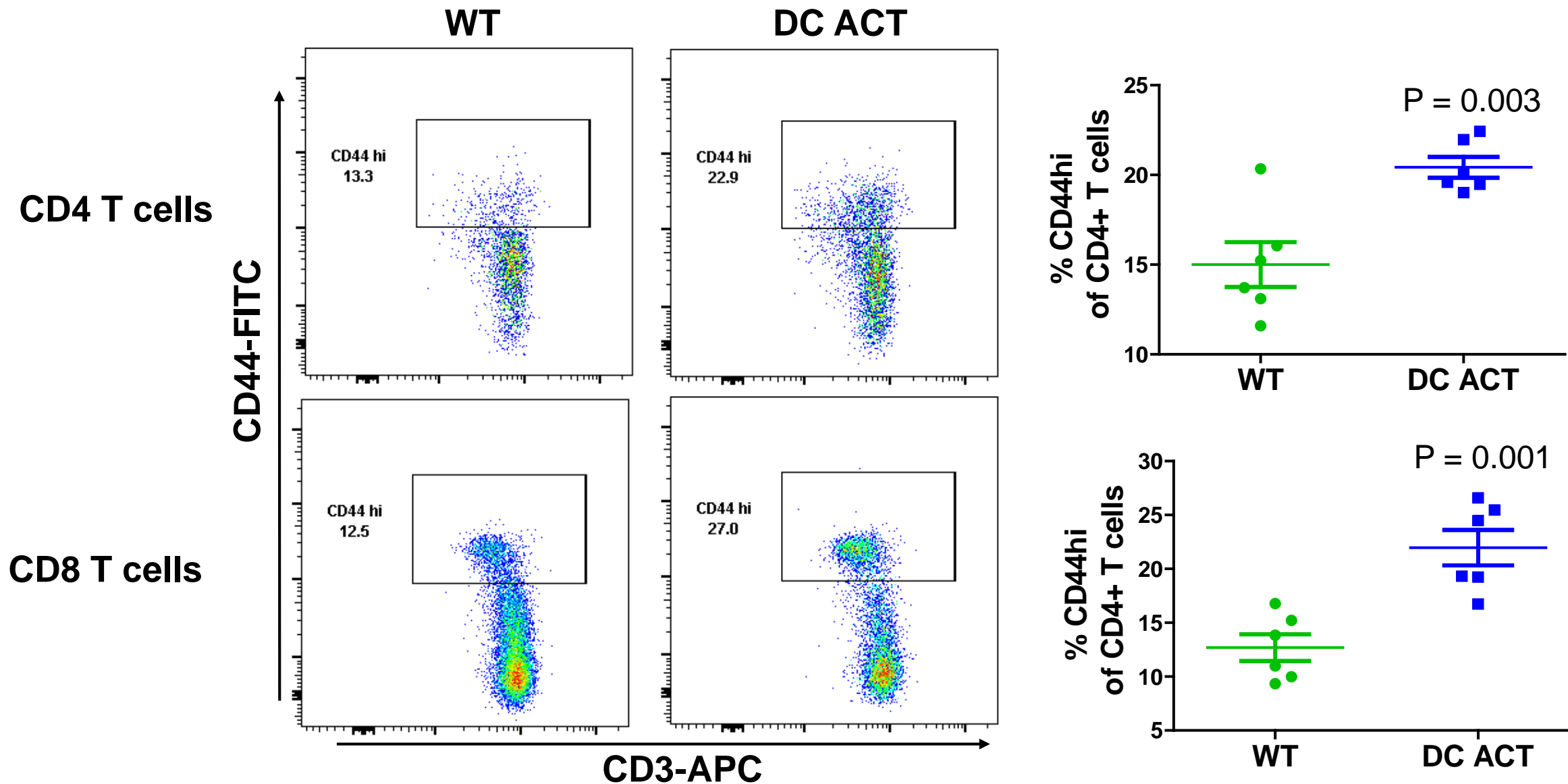


# DC ACT have augmented Ang II-induced hypertension



n = 8/group

# Kidney Lymph Node - DC ACT have greater proportion CD44<sup>hi</sup> T cells during hypertension



# Summary

- Dendritic cell deficiency attenuates hypertension and blunts T cell activation in the kidney and its draining lymph node during hypertension.
- Spontaneous dendritic cell activation augments blood pressure elevation and T cell activation in the kidney lymph node during hypertension.



# Perspectives and clinical relevance

- Dendritic cells make a key contribution to blood pressure elevation during renin-angiotensin system activation.
- Further analysis of activated T cells in the kidney and its draining lymph node should reveal mechanisms through which DCs exacerbate hypertension.
- Investigating proximal mechanisms of immune activation in hypertension should lead to novel immunomodulatory therapies to reduce blood pressure and target organ damage.

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