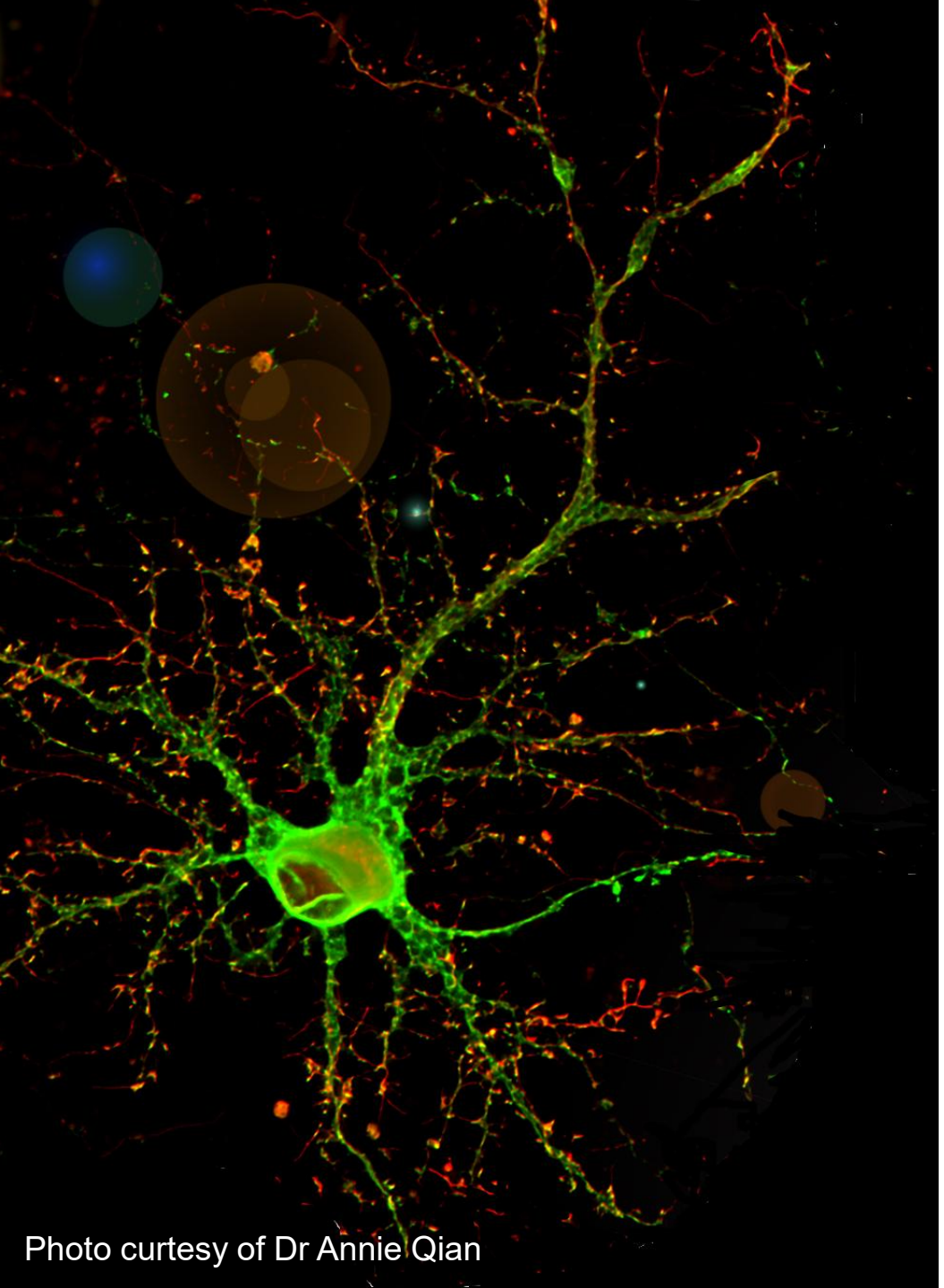


Photo curtesy of Dr Annie Qian

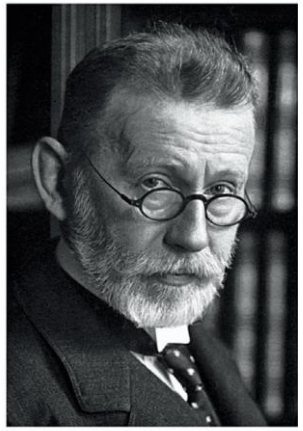
Beyond Sentinels: Dendritic Cells as Orchestrators of Immunity in Kidney Disease

A/Prof Titi Chen, The University of Sydney

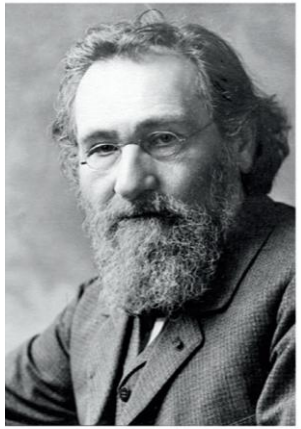
Titi.chen@sydney.edu.au

Asian Pacific Congress of Nephrology, Dec 2025

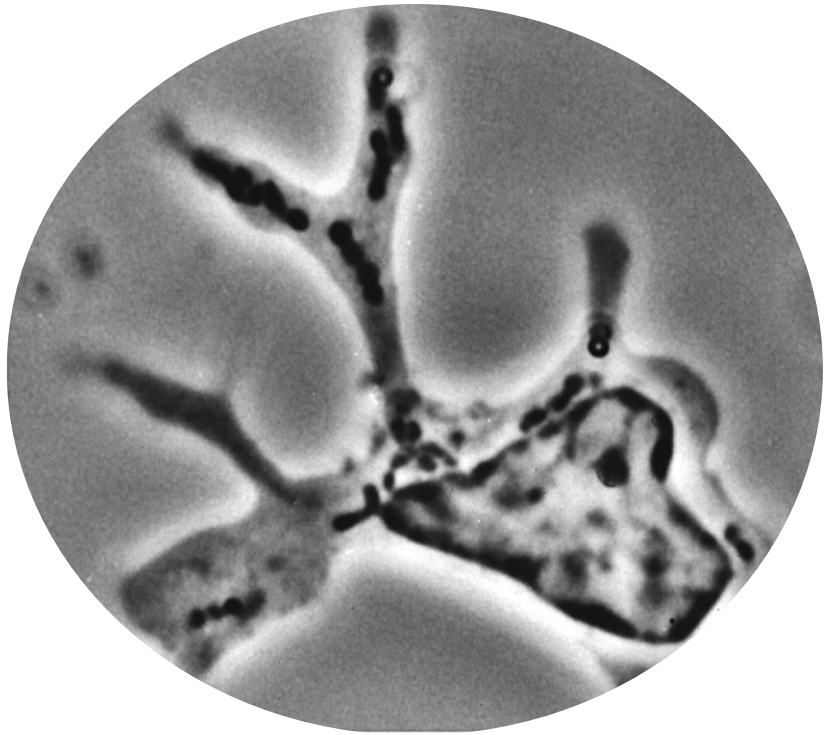
Historical Background

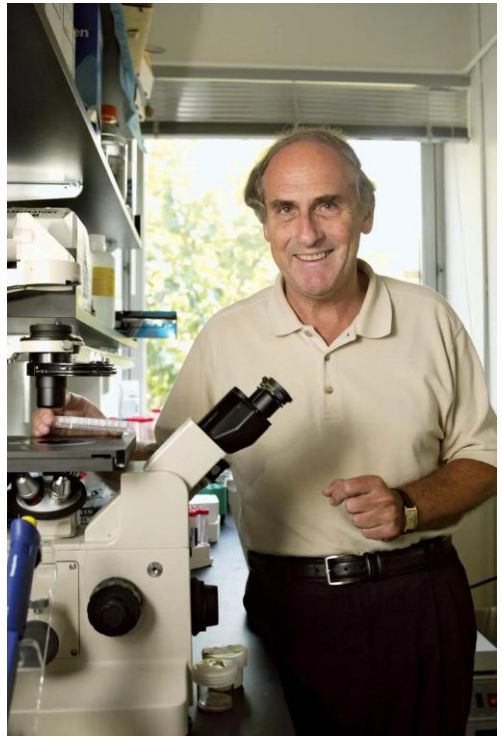


Paul Ehrlich
Adaptive Immunity

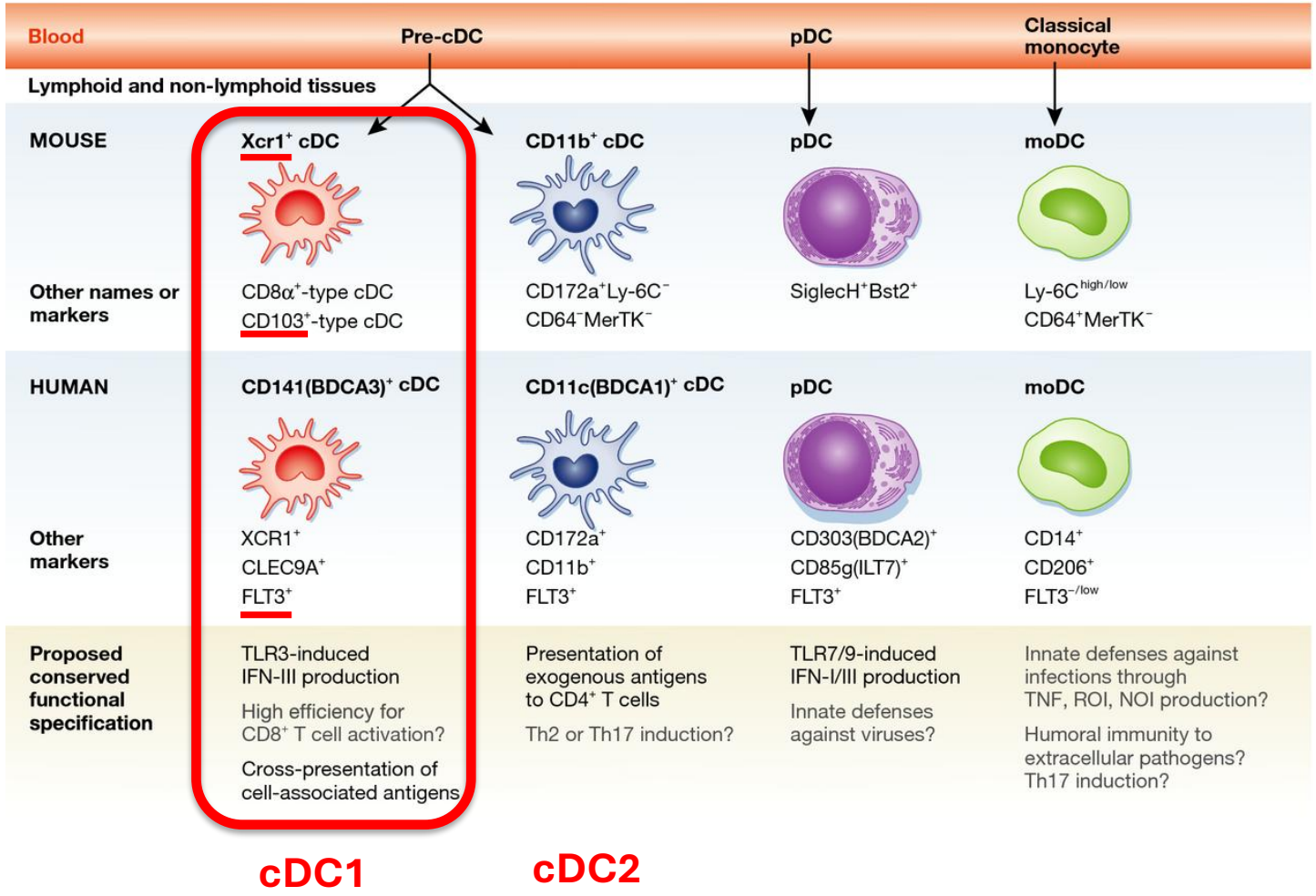


Ilya Ilyich Metchnikov
Innate Immunity





The Dendritic Cell Family



Dalod M, Chelbi R, Malissen B, Lawrence T. Dendritic cell maturation: functional specialization through signaling specificity and transcriptional programming. EMBO J. 2014 May 16;33(10):1104-16. doi: 10.1002/embj.201488027. Epub 2014 Apr 15. PMID: 24737868; PMCID: PMC4193918.

Dendritic Cell in Human Kidney Disease

Comparative Study > Front Immunol. 2021 May 12:12:635212.
doi: 10.3389/fimmu.2021.635212. eCollection 2021.

Conventional Type 1 Dendritic Cells (cDC1) in Human Kidney Diseases: Clinico-Pathological Correlations

Titi Chen [1 2 3], Qi Cao [1 2], Ruifeng Wang [2], Guoping Zheng [1 2], Farhana Azmi [1 2], Jeffery Wang [1 2], Vincent W Lee [1 2 3], Yuan Min Wang [4], Hong Yu [2], Manish Patel [1 5], Chow Heok P'ng [6], Stephen I Alexander [4], Natasha M Rogers [1 2 3], Yiping Wang [1 2], David C H Harris [1 2 3]

Affiliations + expand

PMID: 34054804 PMCID: PMC8149958 DOI: 10.3389/fimmu.2021.635212

Dendritic Cell in Human Kidney Disease

Main objective

To analyze the role of conventional dendritic cells (cDC1 and cDC2) in human kidney diseases and their clinical and their clinical pathological associations.

Number

Location

Clinical Correlation

T cells

Dendritic Cell in Human Kidney Disease

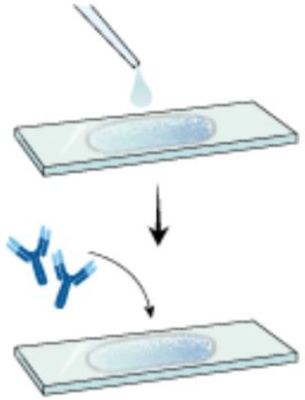
Material

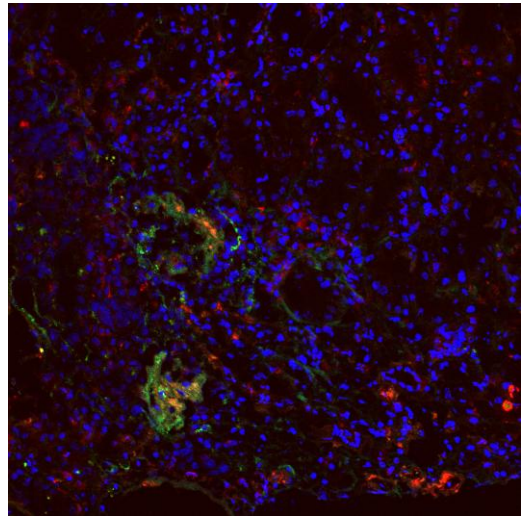
Disease 135, Control 7

Disease Category	Number
Non Glomerular disease (ATN, AIN)	32
Proliferative GN (IgA, Pauci-immune, Lupus, Anti-GBM)	72
Non Proliferative GN (MCD, Membranous)	10
Diabetic nephropathy	21

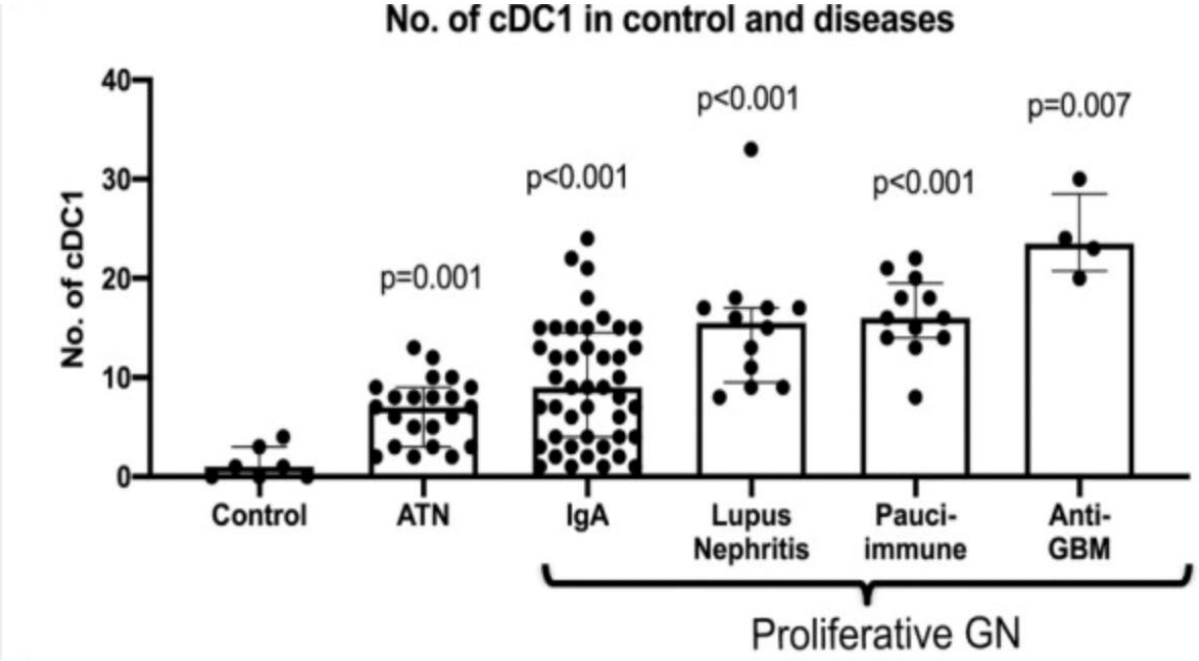
Method

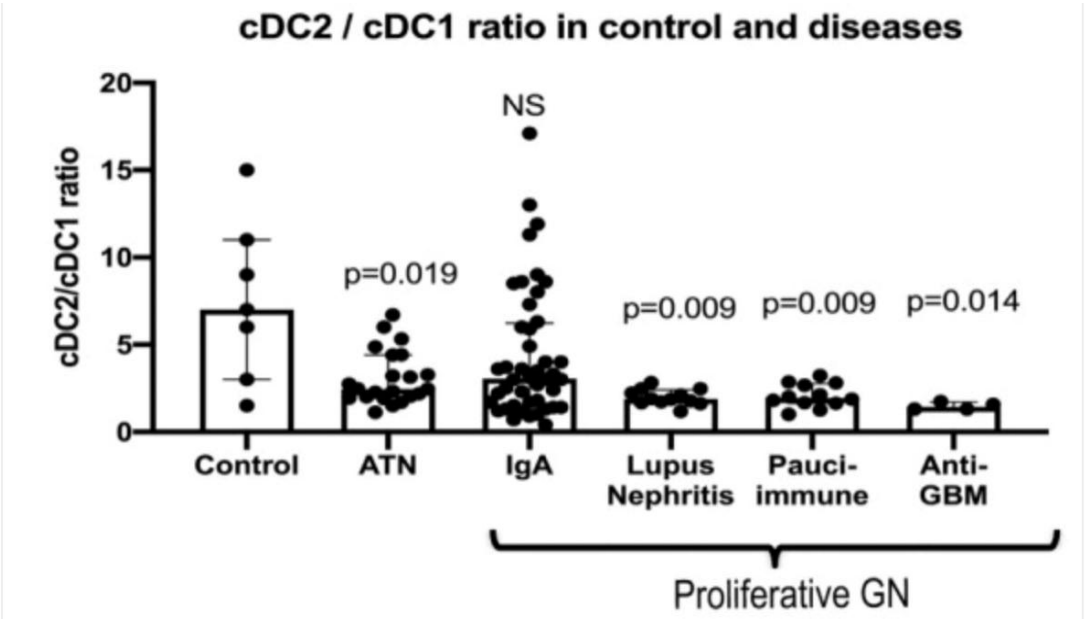
Immunofluorescence stain





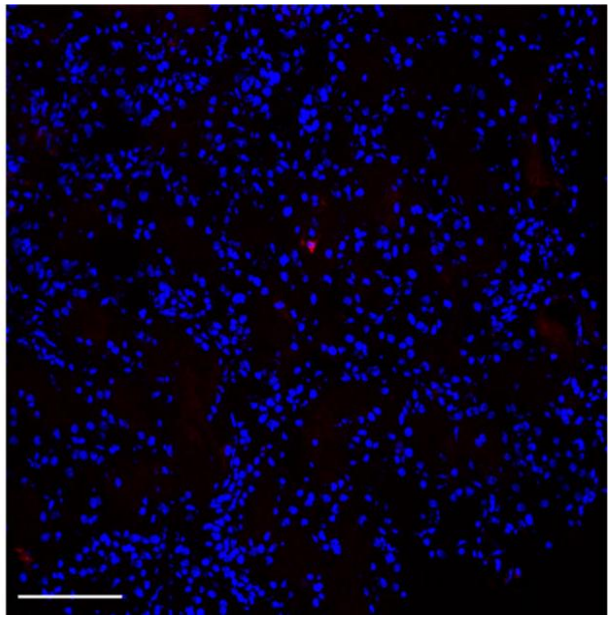
Number

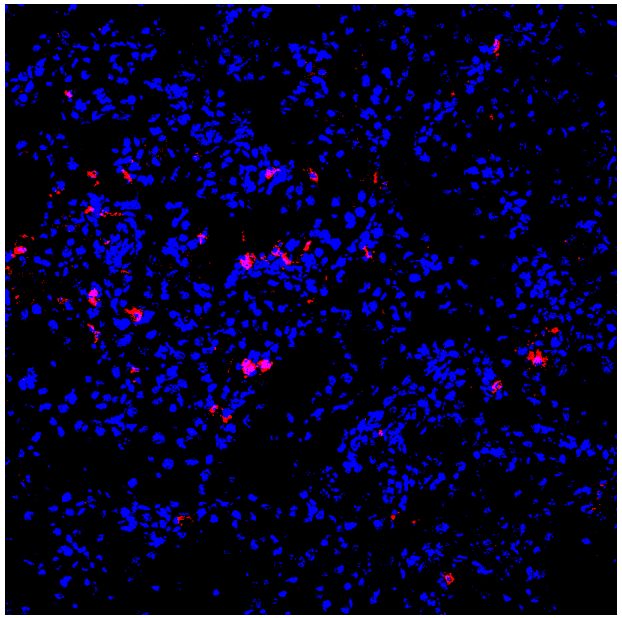


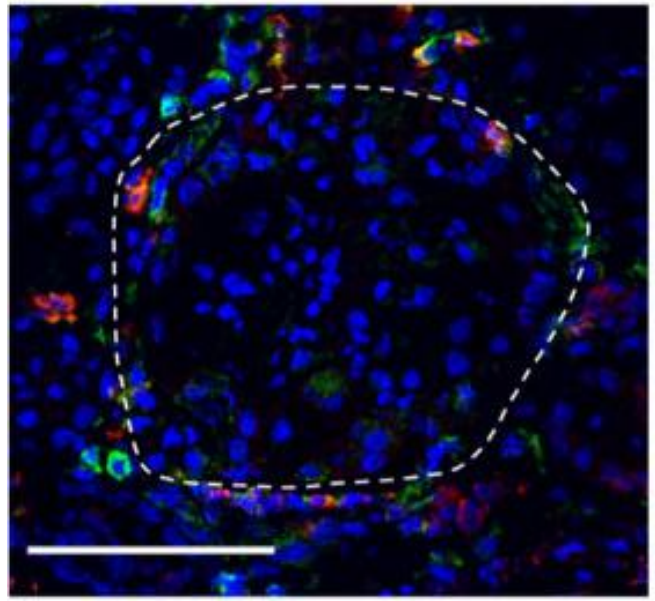


Human cDC1s increase in ATN & proliferative GN, more than other cDC subsets

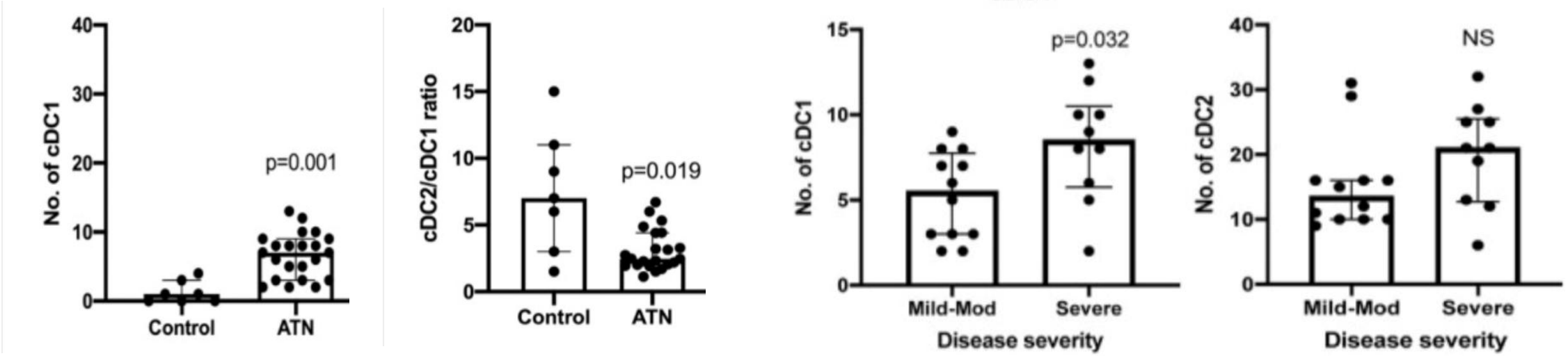
Location





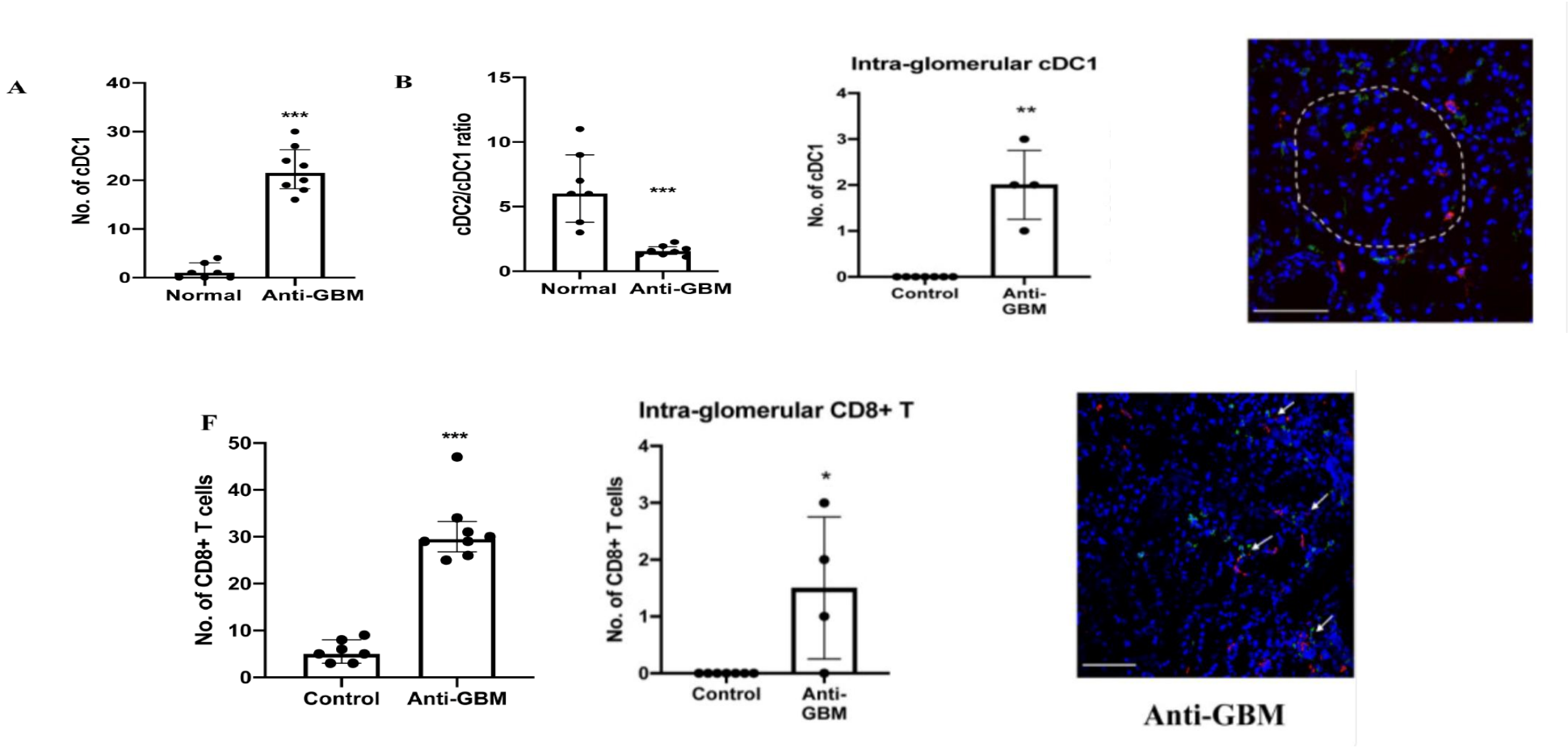


Clinical Correlation and T Cell (ATN)



Acute Tubular Necrosis

Clinical Correlation and T Cell (Anti-GBM)



Anti-GBM

Dendritic Cells in Animal Models

Adriamycin Nephropathy

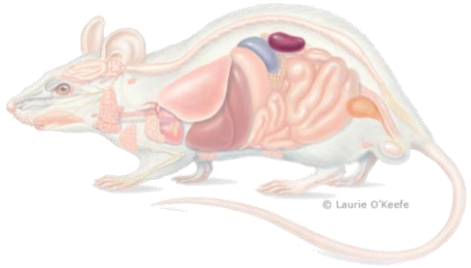
J Am Soc Nephrol. 2015 Sep 16;27(5):1344–1360. doi: 10.1681/ASN.2015030229

CD103+ Dendritic Cells Elicit CD8+ T Cell Responses to Accelerate Kidney Injury in Adriamycin Nephropathy

Qi Cao *,✉, Junyu Lu †, Qing Li *, Changqi Wang *, Xin Maggie Wang ‡, Vincent WS Lee *, Chengshi Wang *, Hanh Nguyen *, Guoping Zheng *, Ye Zhao *, Stephen I Alexander §, Yiping Wang *, David CH Harris *

Author information · Article notes · Copyright and License information

PMCID: PMC4849820 PMID: 26376858



Nephrol Dial Transplant. 2019 Nov 1;34(11):1853–1863. doi: 10.1093/ndt/gfy385.

Flt3 inhibition alleviates chronic kidney disease by suppressing CD103+ dendritic cell–mediated T cell activation

Ruifeng Wang [1,2], Titi Chen [1], Chengshi Wang [1], Zhiqiang Zhang [1], Xin Maggie Wang [3], Qing Li [1], Vincent W S Lee [1], Yuan Min Wang [4], Guoping Zheng [1], Stephen I Alexander [4], Yiping Wang [1], David C H Harris [1], Qi Cao [1]

Affiliations + expand

PMID: 30590794 DOI: 10.1093/ndt/gfy385

Anti-GBM disease

Clin Immunol. 2023 May:250:109295. doi: 10.1016/j.clim.2023.109295. Epub 2023 Mar 16.

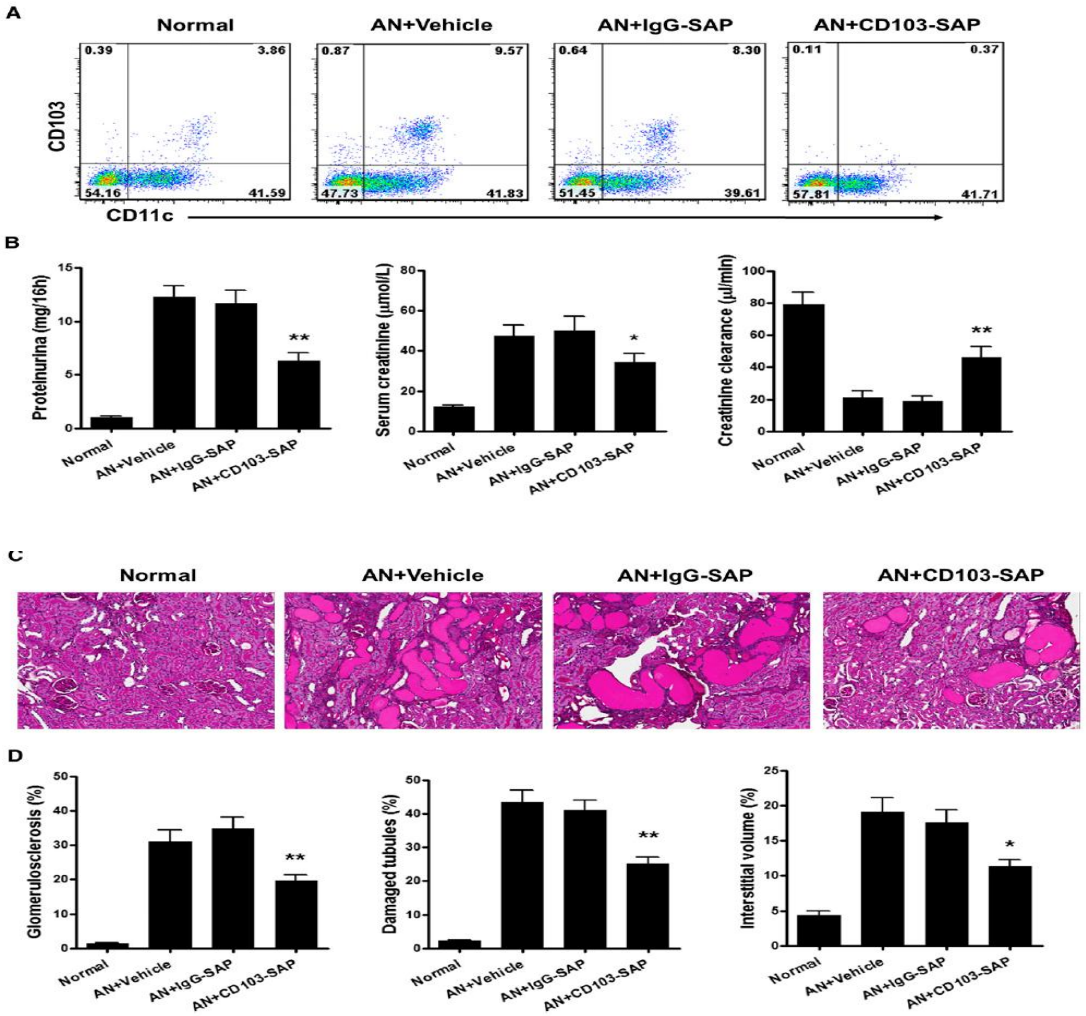
Attenuation of renal injury by depleting cDC1 and by repurposing Flt3 inhibitor in anti-GBM disease

Titi Chen [1], Qi Cao [2], Ruifeng Wang [3], Guoping Zheng [2], Farhana Azmi [2], Vincent W Lee [4], Yuan Ming Wang [5], Hongqi Li [6], Di Yu [7], Natasha M Rogers [4], Stephen I Alexander [5], David C H Harris [4], Yiping Wang [2]

Affiliations + expand

PMID: 36933629 DOI: 10.1016/j.clim.2023.109295

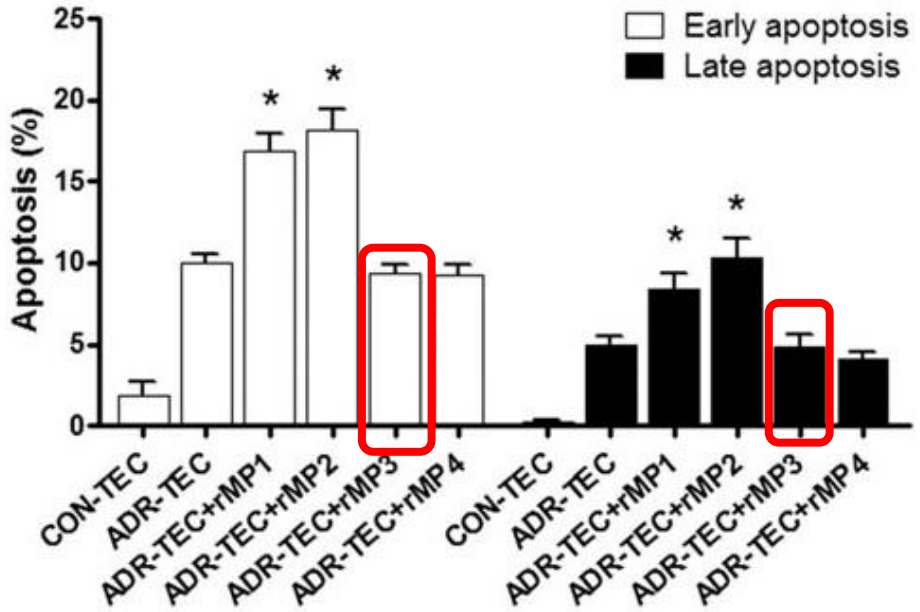
Dendritic Cells in Adriamycin Nephropathy



cDC1 is pathogenic in Adriamycin Nephropathy

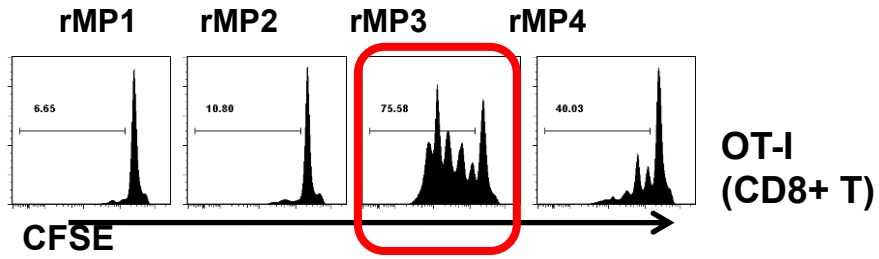
Mechanism: The cDC1 - CD8+ Axis

1. cDC1 do not directly induce kidney tubular cell damage

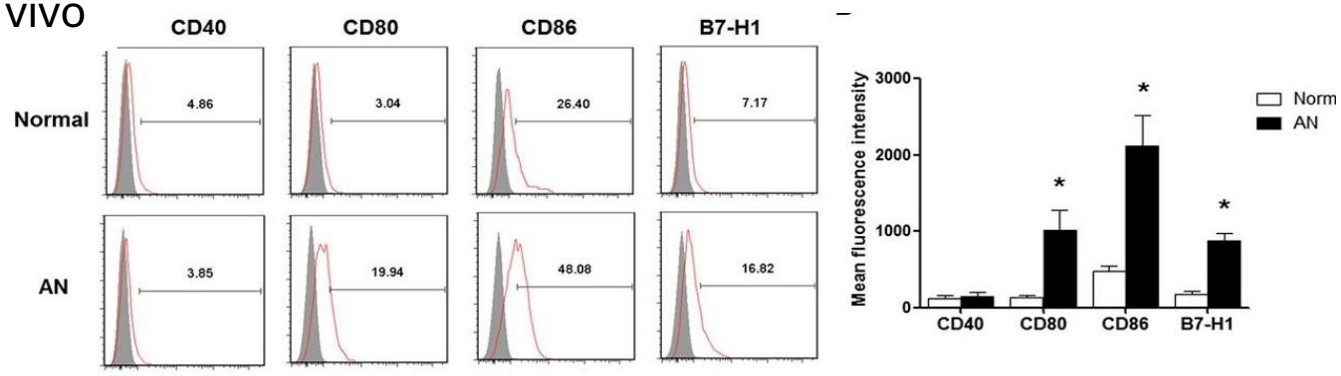


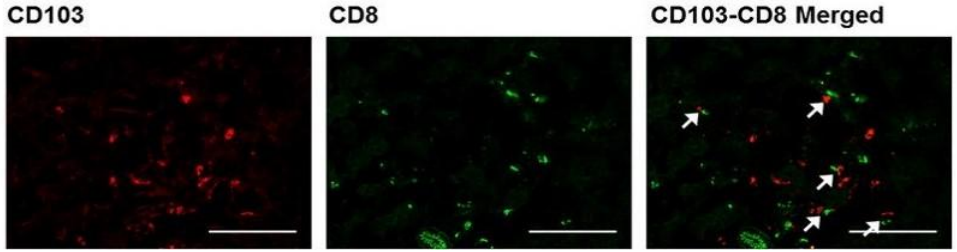
2. cDC1s enhance capacity to activate CD8+ T cells

In vitro



In vivo

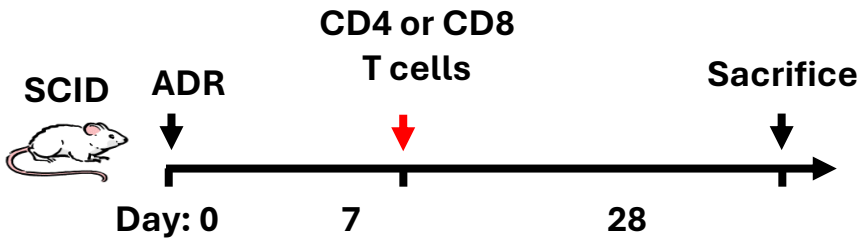




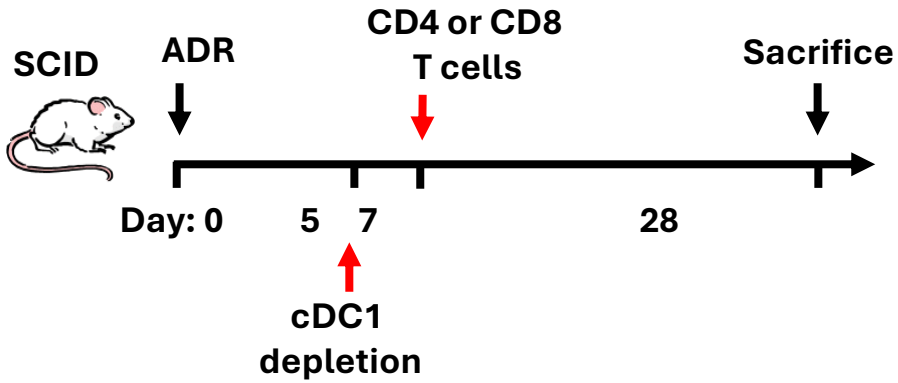
Mechanism: The cDC1 - CD8+ Axis

3. In AN SCID mice, depletion of cDC1 abolishes the pathogenic effect of transfused CD8 T cells

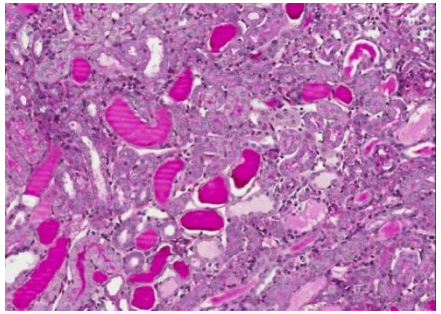
A



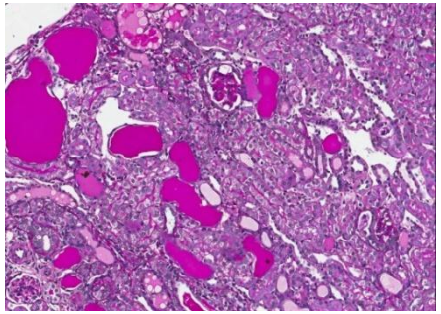
B with cDC1 depletion



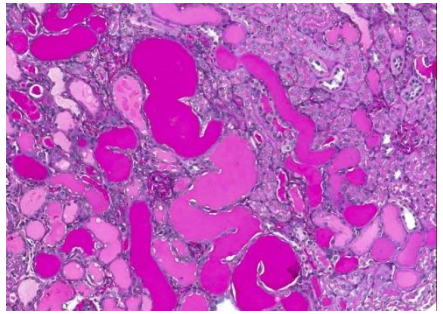
AN + Vehicle



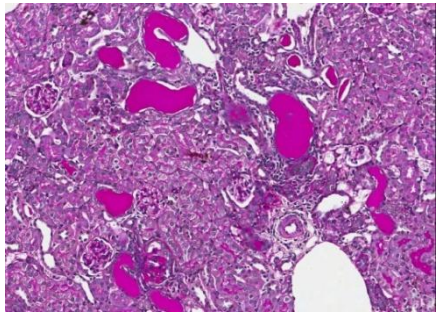
AN + CD4



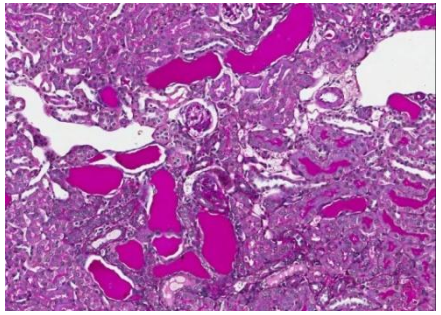
AN + CD8
Exacerbates injury



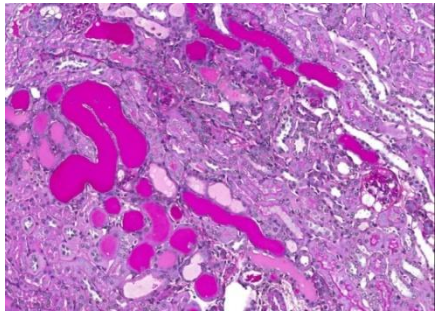
AN
cDC1 depletion



AN+CD4
cDC1 depletion



AN+CD8
cDC1 depletion
Reduces injury



Translation? Drug repurposing

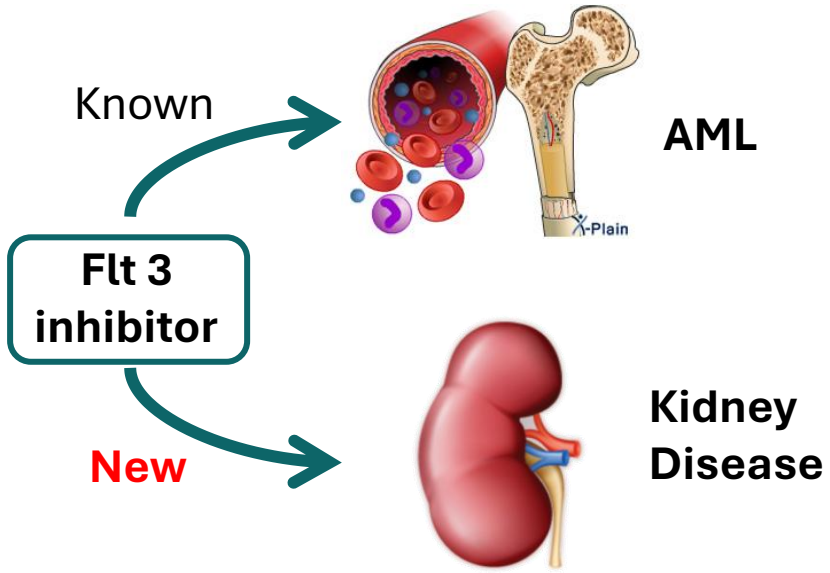
A SHORTER TIMESCALE

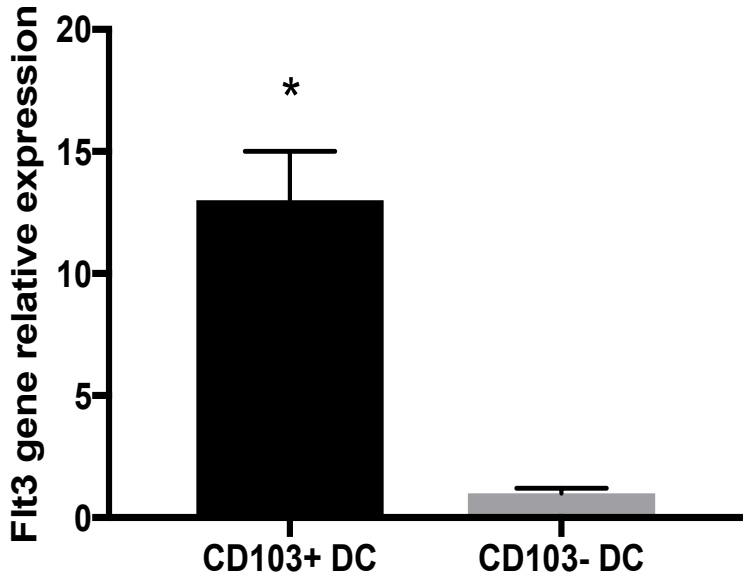
Because most repositioned drugs have already passed the early phases of development and clinical testing, they can potentially win approval in less than half the time and at one-quarter of the cost.

Drug repositioning

—~6 years, **~$300 million** —

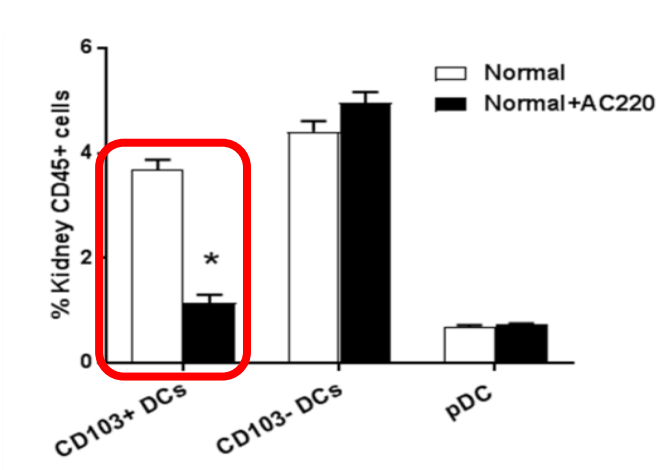
Flt 3 Inhibitor

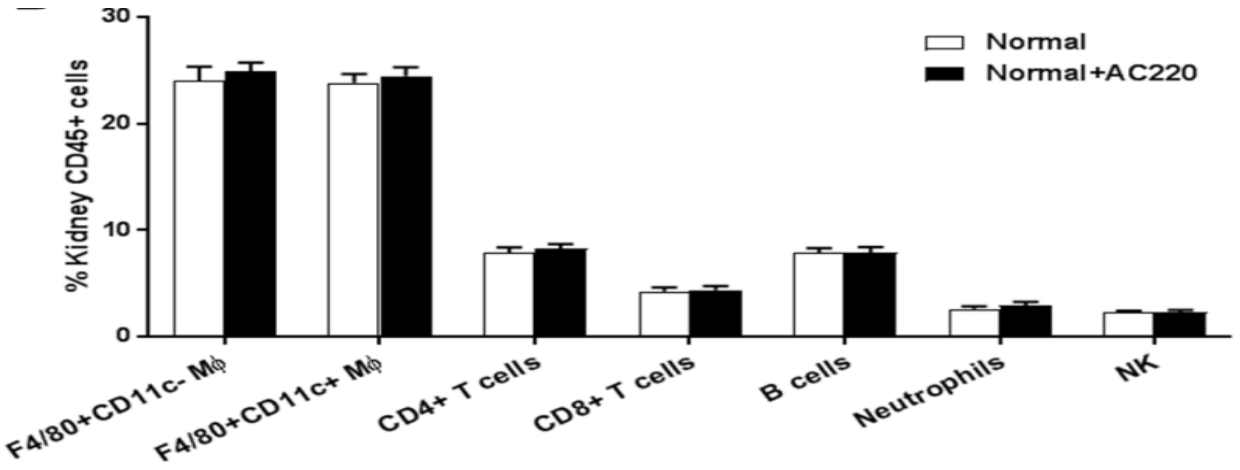




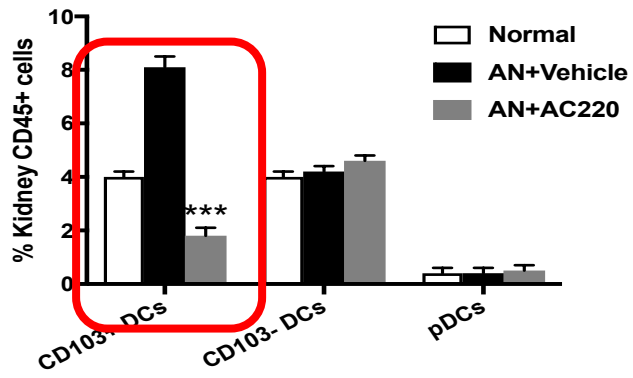
Flt 3 Inhibitor Specificity

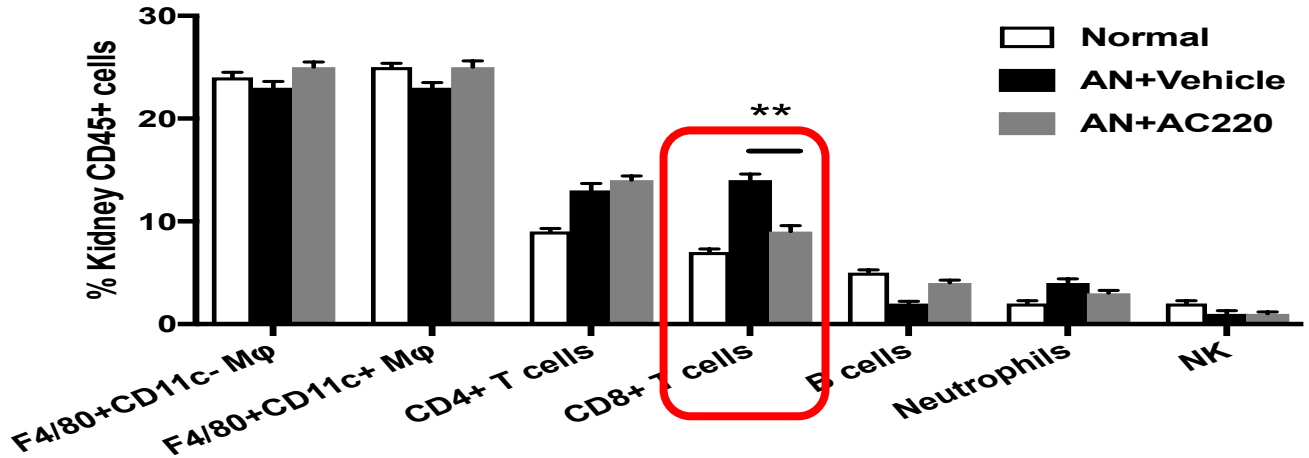
Normal mice kidneys



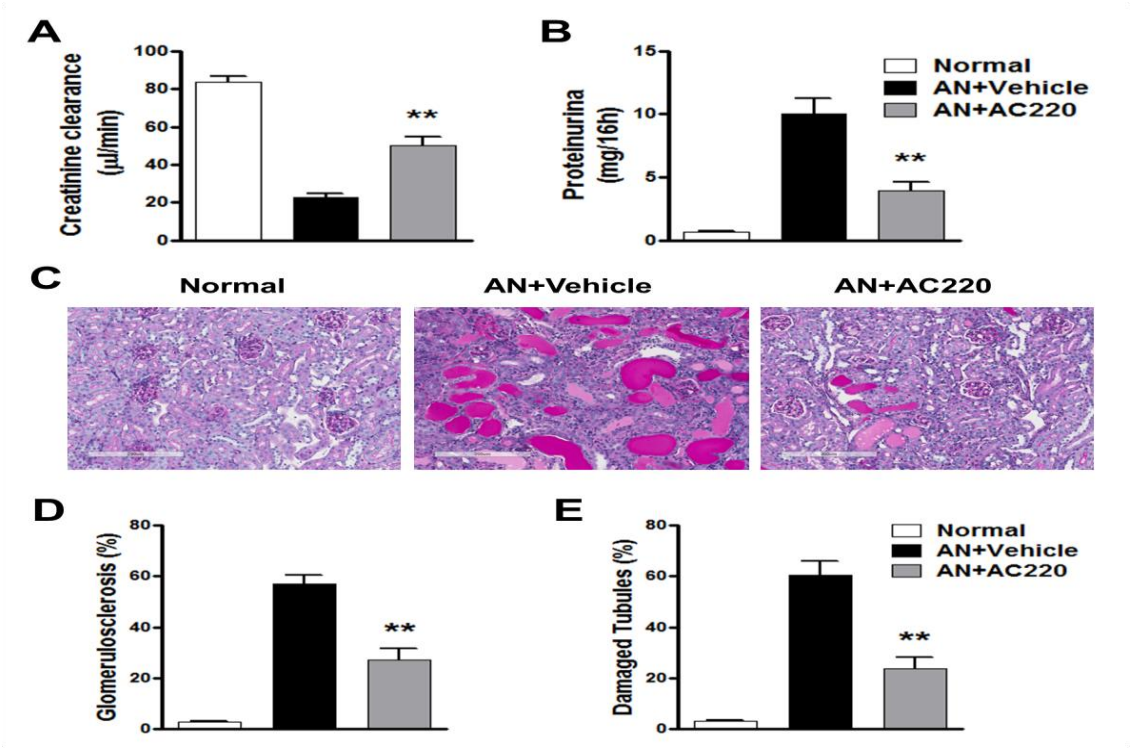


AN mice



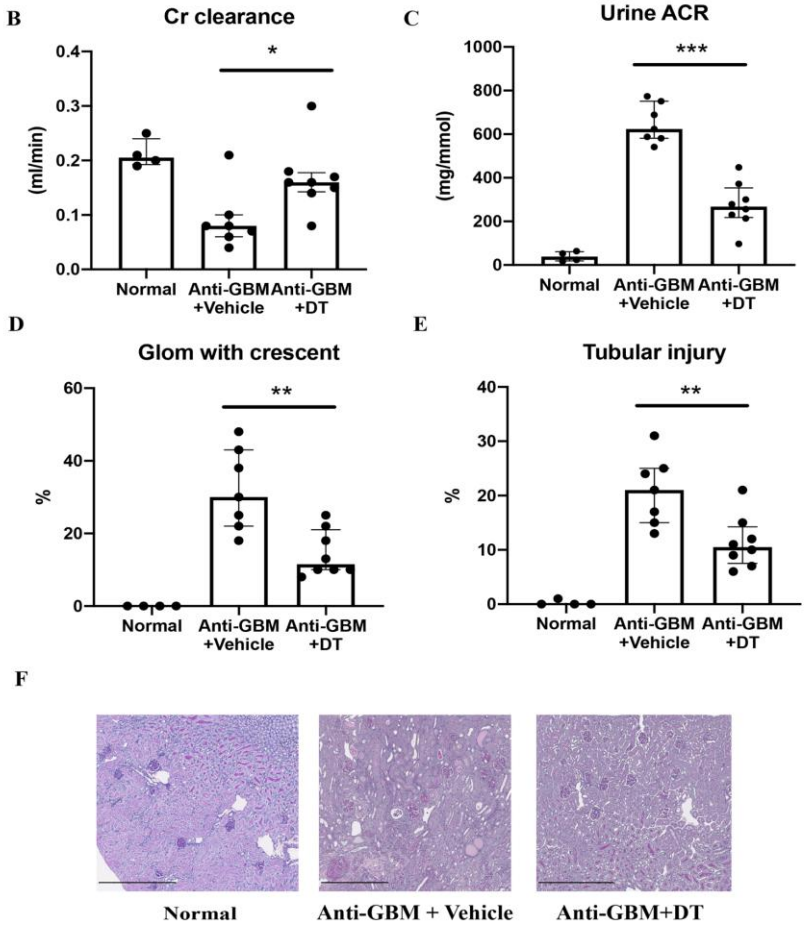


Flt 3 Inhibitor in Adriamycin Nephropathy



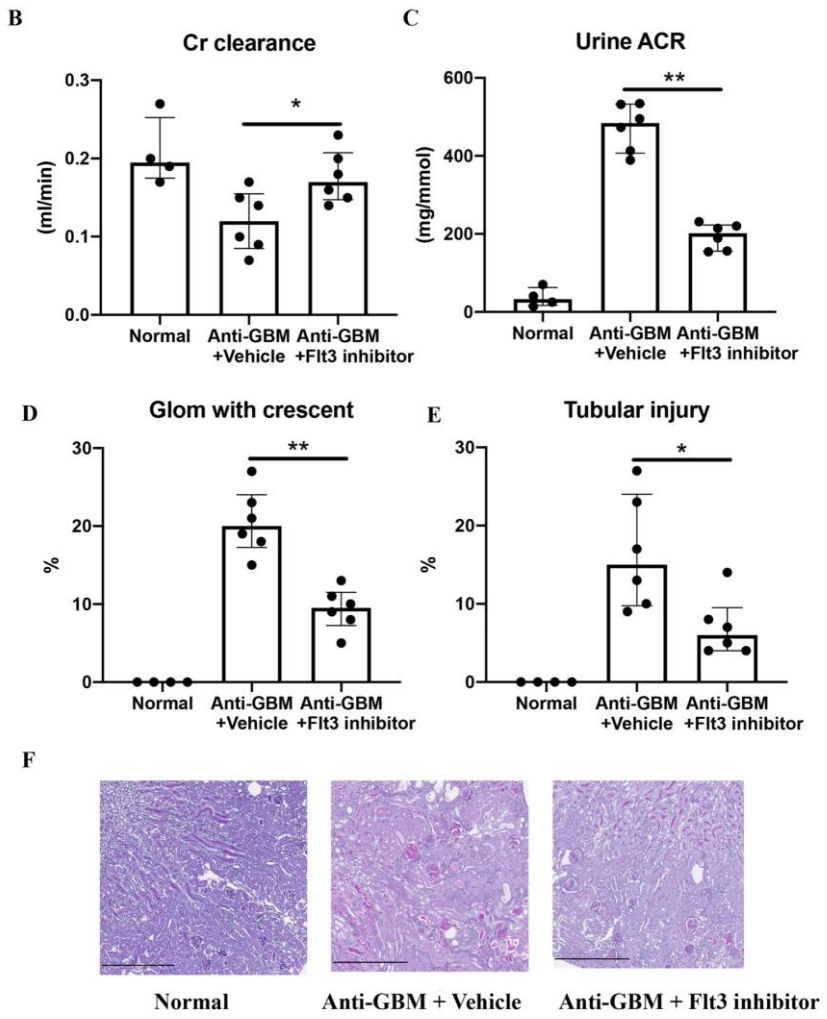
Flt 3 inhibitor protects against renal injury

Anti-GBM Disease Mice



cDC1 is pathogenic in anti-GBM

Flt 3 Inhibitor in Anti-GBM Disease



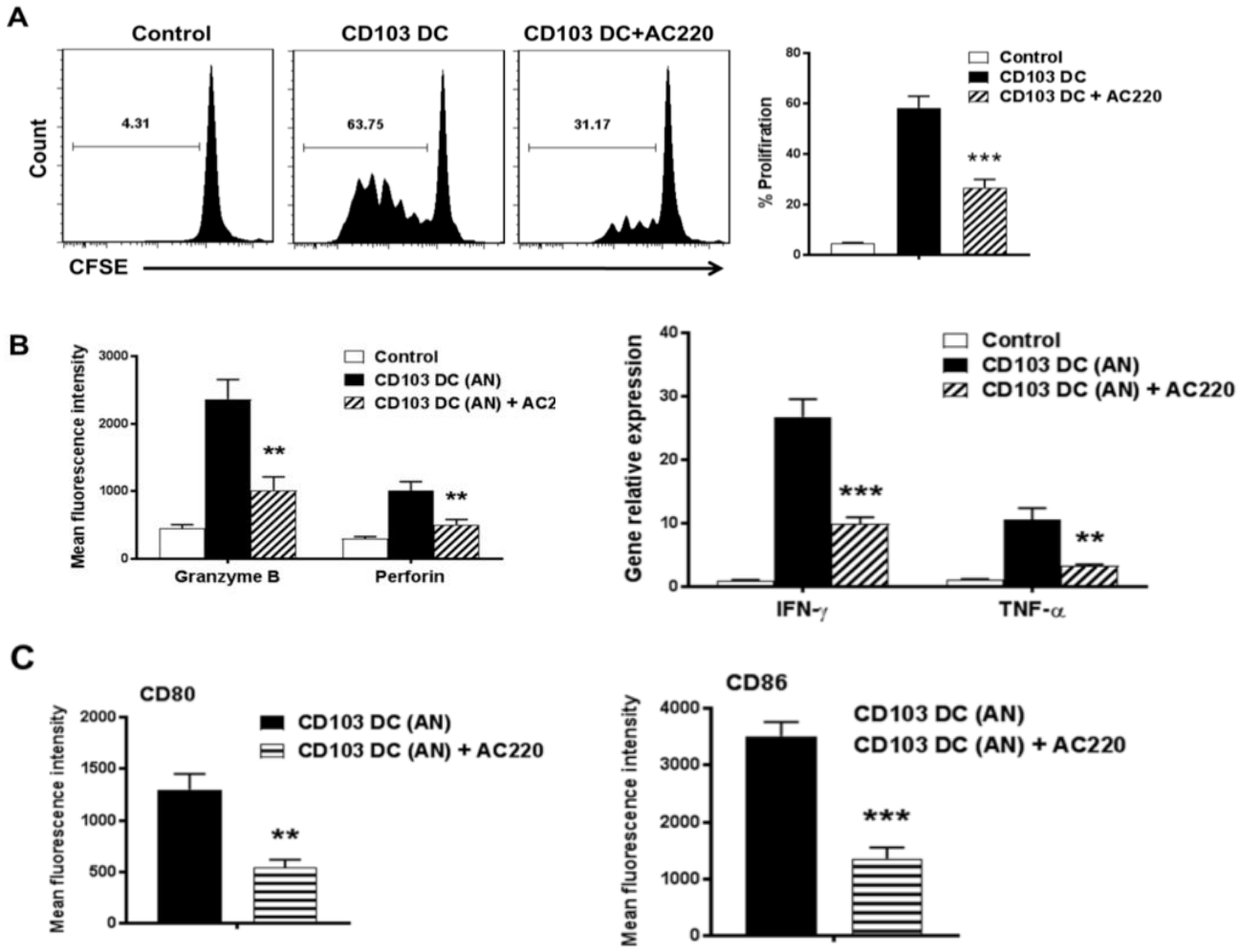
Flt3 inhibitor is protective in anti-GBM

Flt3 Inhibitor Suppresses cDC1 Mediated CD8+ T cell Activation (in vitro)

1. CD8+ T cell priming capacity ⬇

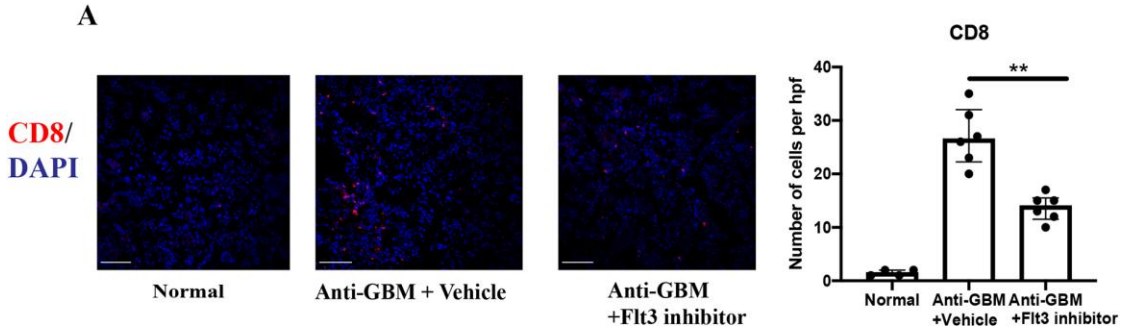
2. Cytotoxic molecules & inflammatory cytokines ⬇

3. Costimulatory molecules ⬇

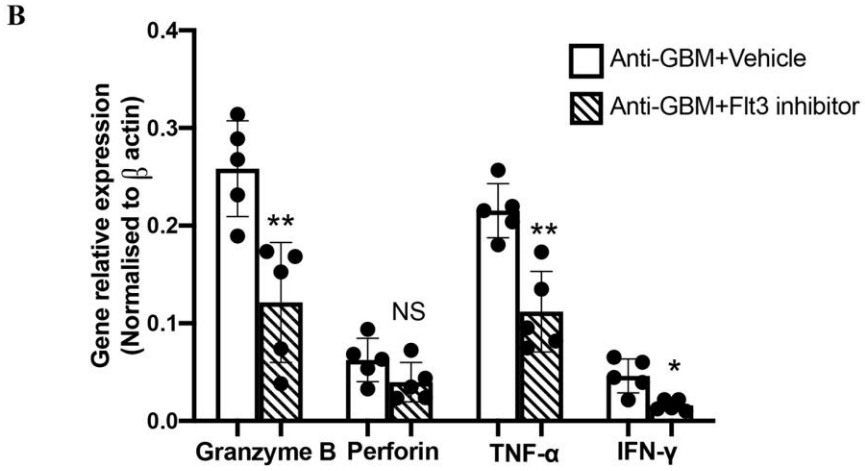


Flt3 Inhibitor Suppresses cDC1 Mediated CD8+ T Cell Activation (in vivo)

1. CD8+ T cell infiltration ⬇

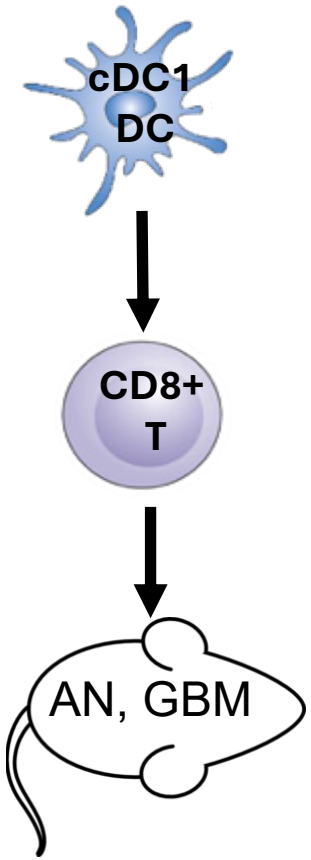


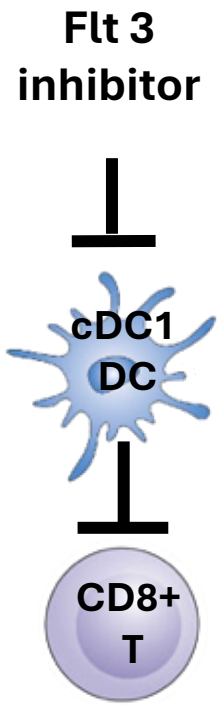
2. CD8+ T cytotoxic molecules & inflammatory cytokines ⬇

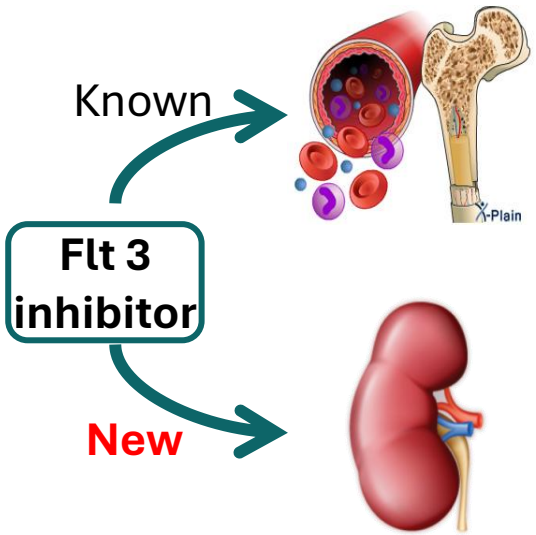


Summary

Pathogenic role of cDC1s	cDC1–CD8 axis as a driver of injury	Therapeutic effect of Flt3 inhibition	Translational strategy for DC targeting







Future Direction

1. **Precision Medicine:**
    i. Single-cell/spatial transcriptomics to define DC states
2. **Diagnostics**
    i. Biomarkers
    ii. The evolving role of renal biopsy : AI driven biopsy qualification
3. **Therapeutic**
    i. Phase I/II clinical trials of Flt3 inhibitors in treatment-resistant GN
    ii. Synergistic effects with existing immunosuppressants
4. **Learning from other fields: Cancer and IBD**

Acknowledgements

- Professor David Harris and his team
- Funding providers
  - NHMRC postgraduate scholarship
  - RACP Jaquote
  - Travel scholarships: ANZSN, APSN
  - ICPMR Jerry Koutts scholarship
  - Rotary club scholarship
  - John and Anne Leece Family Top-up Grant
  - University of Sydney PRS
  - NHMRC project grant
- Monash University, Melb
  - Prof David Nikolic-Paterson
- Wakayama Medical University, Japan
  - Prof Tsuneyasu Kaisho
- The Peter Doherty Institute, Melb
  - Prof William Heath
- Westmead Institute for Medical Research
  - Dr Qi Cao, Dr Yiping Wang, Dr Ruifeng Wang, Dr Guoping Zheng, Dr Padma Rao, Prof Wayne Hawthorne, Dr Karen Keung, Dr Elvira Jimenez-Vera, Dr Min Hu, Dr Ross Matthews, Dr Maggie Wang, Dr Hong Yu
- Westmead Children's Hospital, Prof Stephen Alexander
- Department of Renal Medicine
  - Prof David Harris, Dr Natasha Rogers, Dr Brian Nankiville, Mr Paul Robertson, Mr Chris Zhang, Mr Renan Gaspi
- Department of Urology, Prof Manish Patel
- Department of Immunology
  - Prof David Brown, Dr Jocelyn Jiang, Mr David Campbell, Ms Sue Culican
- Department of Anatomical Pathology, Dr Heok Ping

Titi.Chen@sydney.edu.au