

What's

HOT

what's

New

about Glomerulonephritis?

PD Dr. med. Andreas Kistler

Kantonsspital Frauenfeld

www.nephrologie-thurgau.ch

SOCIÉTÉ DE PATHOLOGIE RÉNALE

Une classification, quelle qu'elle soit, comporte toujours une part d'arbitraire, de sorte que ce qui devrait constituer la base incontestée de tout commentaire, n'est souvent que le reflet d'une appréciation personnelle. D'autre part, on peut classer les maladies d'un point de vue clinique, étiologique ou anatomique. Or aussi longtemps qu'une corrélation parfaite entre les lésions histologiques, les facteurs qui les provoquent et les symptômes qu'elles produisent n'apparaît pas clairement, on peut s'attendre à rencontrer une grande variété de classifications, selon qu'elles émanent d'un clinicien, d'un physiopathologiste ou d'un anatomiste.

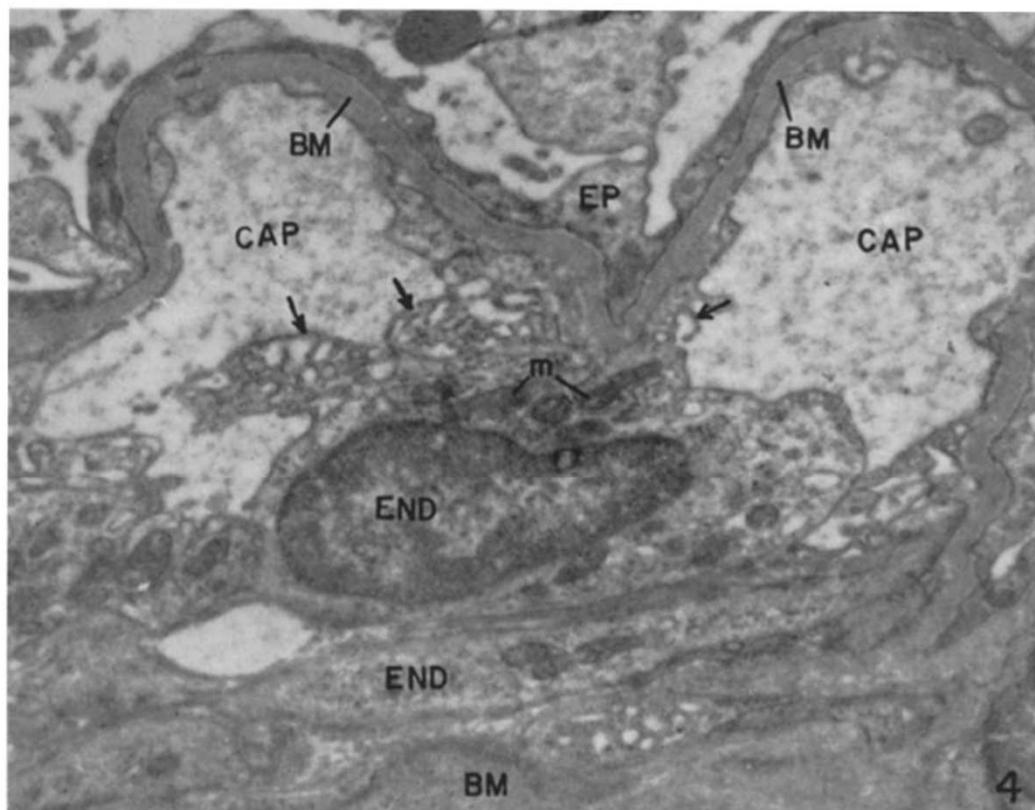
CLASSIFICATION ET NOSOLOGIE DES NÉPHRITES GLOMÉRULAIRES

Par F. REUBI (Berne)

AN ELECTRON MICROSCOPE STUDY OF THE GLOMERULUS IN NEPHROSIS, GLOMERULONEPHRITIS, AND LUPUS ERYTHEMATOSUS

By MARILYN G. FARQUHAR,* Ph.D., ROBERT L. VERNIER,† M.D.,
AND ROBERT A. GOOD,§ M.D.

*(From the Department of Pathology, University of California School of Medicine, San
Francisco, and the Pediatric Research Laboratories of the Variety Club Heart
Institute, Minneapolis, Minnesota)*



(J. Clin. Invest. 36: 26, 1957)

BULLETIN of the JOHNS HOPKINS HOSPITAL

THE PUBLICATION OF THE MEDICAL SCHOOL AND HOSPITAL
SUPPORTED BY THE DE LAMAR FUND OF THE JOHNS HOPKINS UNIVERSITY

First description of FSGS

April, 1957

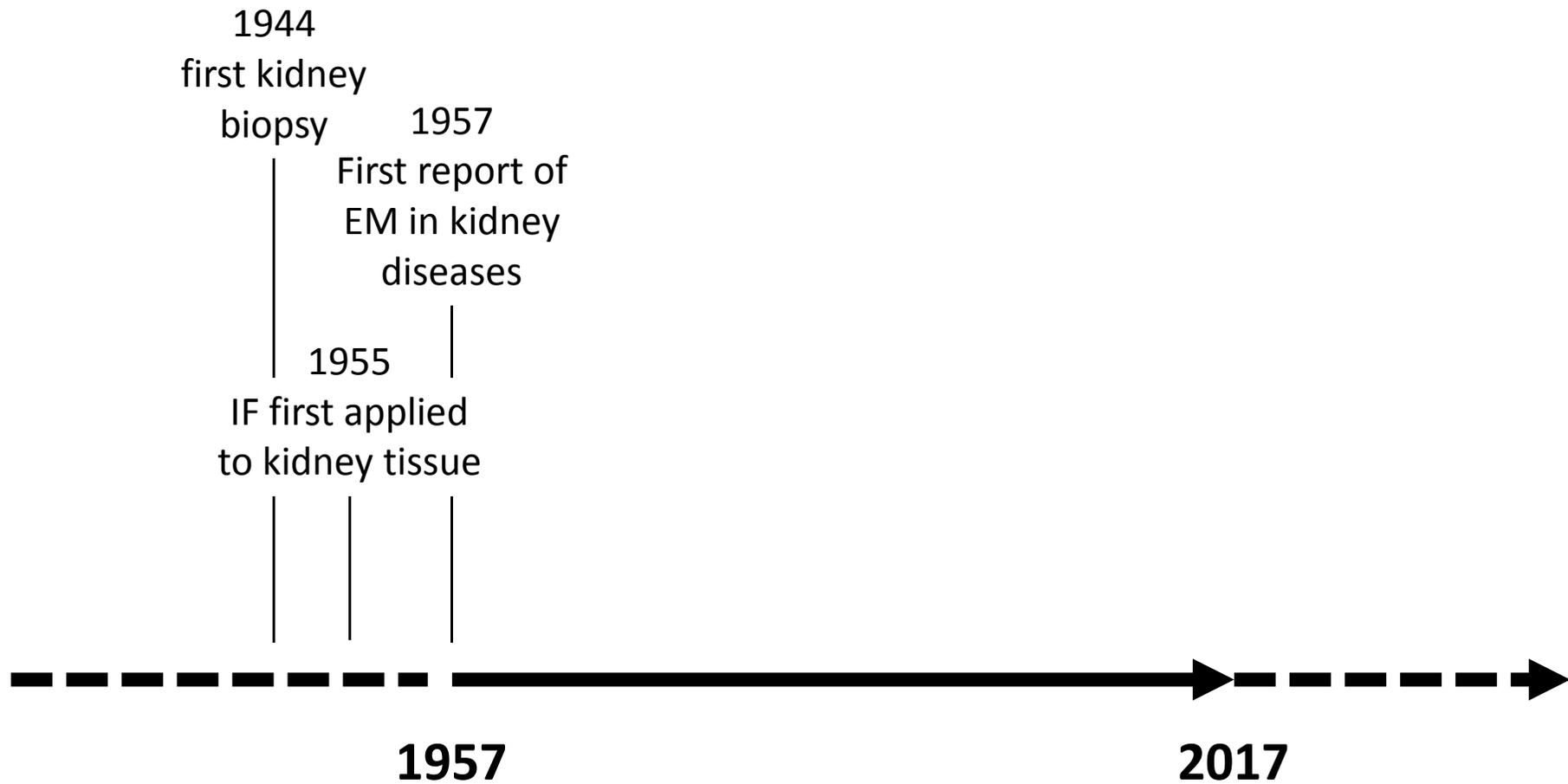
A HITHERTO UNDESCRIBED VULNERABILITY OF THE
JUXTAMEDULLARY GLOMERULI IN
LIPOID NEPHROSIS

ARNOLD R. RICH

The Department of Pathology, The Johns Hopkins University School of Medicine

Received for publication November 14, 1956

„morphologic era“



Membranous Nephropathy
(Membranous Glomerulonephritis)

Article types

- Clinical Trial
- Review
- Customize ...

Text availability

- Abstract
- Free full text
- Full text

PubMed Commons

- Reader comments
- Trending articles

Publication dates

- 5 years
- 10 years
- Custom range...

Species

- Humans
- Other Animals

Search fields

- ✓ Title
- Choose ...

Format: Summary Sort by: Most Recent Per page: 20

Send to

Search results

- [Membranous glomerulonephritis.](#)
2233. PARRISH AE, WATT MF, HOWE JS.
AMA Arch Intern Med. 1957 Oct;100(4):620-9. No abstract available.
PMID: 13457487
[Similar articles](#)
- [Role of gamma globulins in pathogenesis of renal lesions in systemic lupus erythematosus and chronic membranous glomerulonephritis, with an observation on the lupus erythematosus cell reaction.](#)
2234. MELLORS RC, ORTEGA LG, HOLMAN HR.
J Exp Med. 1957 Aug 1;106(2):191-202.
PMID: 13449231 **Free PMC Article**
[Similar articles](#)
- [Healed infectious hepatitis, portal hypertension, membranous glomerulonephritis.](#)
2235. MACMAHON HE, CHILD CG 3rd, PATTERSON JF.
Bull Tufts N Engl Med Cent. 1955 Jul-Sep;1(3):184-92. No abstract available.
PMID: 13284544
[Similar articles](#)

[Serum anti-PI A2R antibody and glomerular PI A2R deposition in Chinese patients with](#)

Article types

- Clinical Trial
- Review
- Customize ...

Text availability

- Abstract
- Free full text
- Full text

PubMed Commons

- Reader comments
- Trending articles

Publication dates

clear

- 5 years
- 10 years

✓ From 2009/01/01

Species

- Humans
- Other Animals

Search fields

clear

✓ Title

Choose ...

Format: Summary Sort by: Most Recent Per page: 20

Send to

Search results

Items: 1 to 20 of 816

<< First < Prev Page 1 of 41 Next > Last >>

Filters activated: Publication date from 2009/01/01, Field: Title. [Clear all](#) to show 17518 items.

[Urinary Volatile Organic Compounds as Potential Biomarkers in Idiopathic Membranous](#)

1. [Nephropathy.](#)

Wang M, Xie R, Jia X, Liu R.

Med Princ Pract. 2017 Jun 19. doi: 10.1159/000478782. [Epub ahead of print]

PMID: 28633145

[Similar articles](#)

[Long-term Low-density Lipoprotein Apheresis in a Patient with Refractory Idiopathic](#)

2. [Membranous Glomerulonephritis.](#)

Yabuuchi J, Suwabe T, Mizuno H, Ueno T, Hoshino J, Sekine A, Kawada M, Yamanouchi M, Hayami N, Hiramatsu R, Hasegawa E, Sawa N, Takaichi K, Fujii T, Ohashi K, Ubara Y.

Intern Med. 2017;56(12):1543-1547. doi: 10.2169/internalmedicine.56.8081. Epub 2017 Jun 15.

PMID: 28626181 **Free Article**

[Similar articles](#)

[Common anti-PLA2G7 antibodies and elevated PLA2G7 detection in Chinese patients with](#)

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

JULY 2, 2009

VOL. 361 NO. 1

M-Type Phospholipase A₂ Receptor as Target Antigen
in Idiopathic Membranous Nephropathy

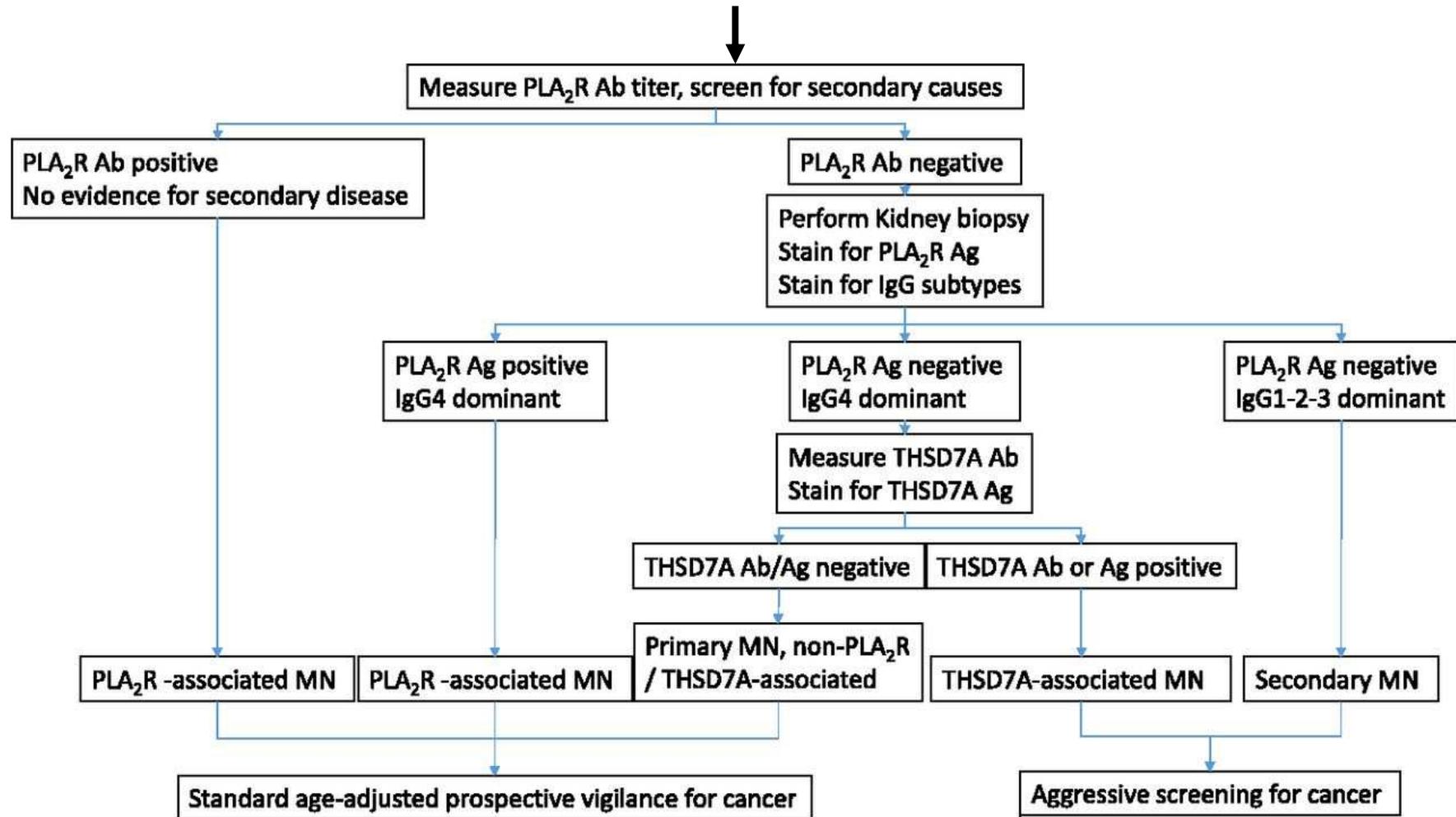
Laurence H. Beck, Jr., M.D., Ph.D., Ramon G.B. Bonegio, M.D., Gérard Lambeau, Ph.D., David M. Beck, B.A.,
David W. Powell, Ph.D., Timothy D. Cummins, M.S., Jon B. Klein, M.D., Ph.D., and David J. Salant, M.D.

ABSTRACT

Autoantibodies against the podocyte membrane protein PLA2R are very likely pathogenic in most cases of primary membranous nephropathy...

... clinically, their measurement is useful for diagnostic and prognostic purposes

MN suspected (NS, age)

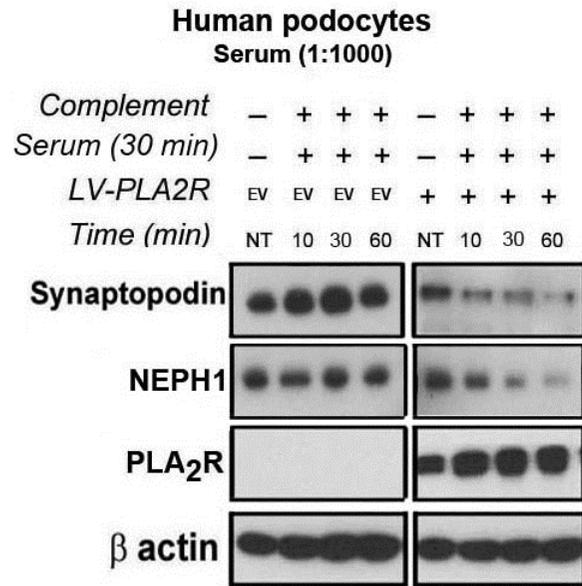


Autoantibodies against the podocyte membrane protein PLA2R are very likely pathogenic in most cases of primary membranous nephropathy...

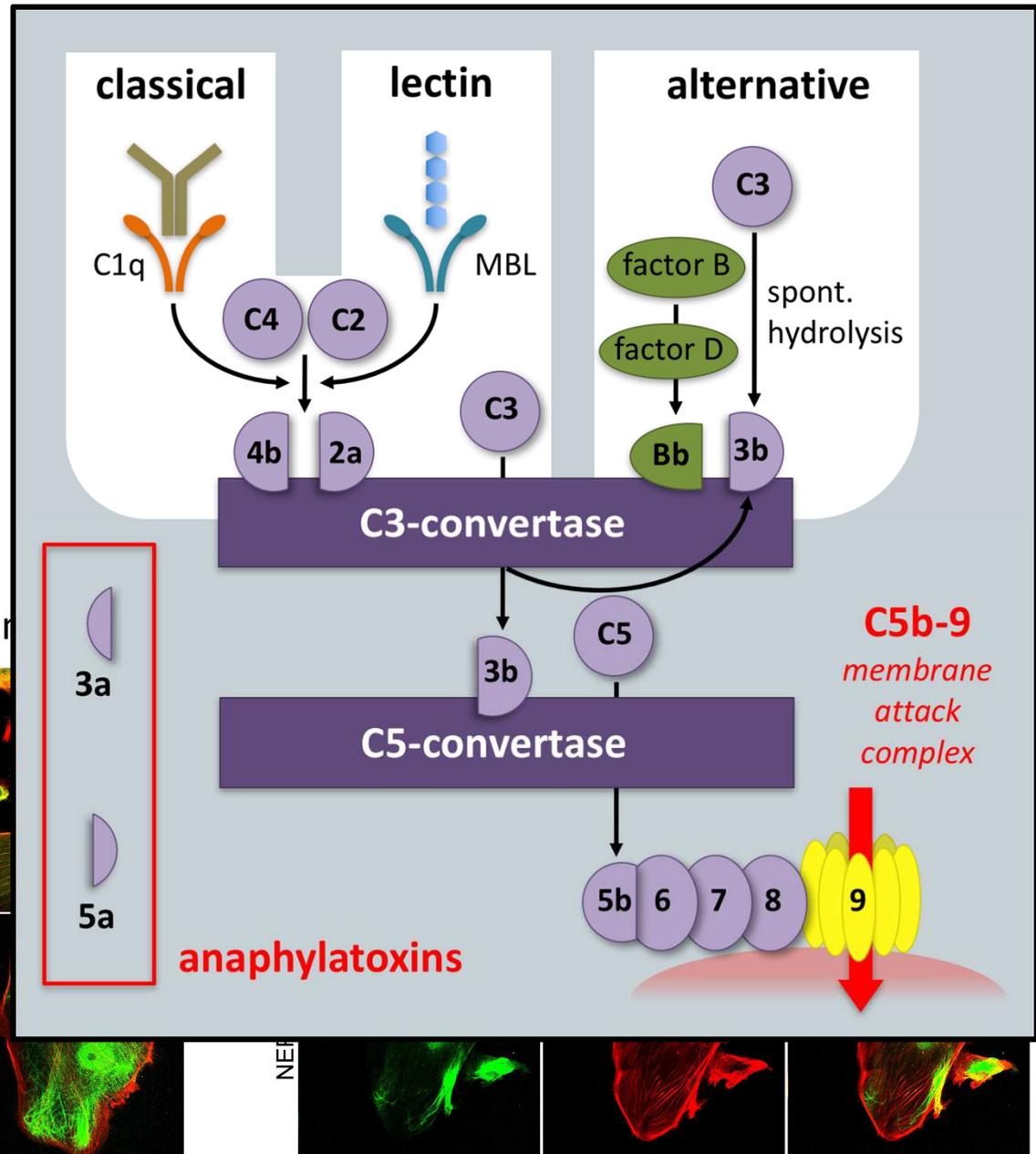
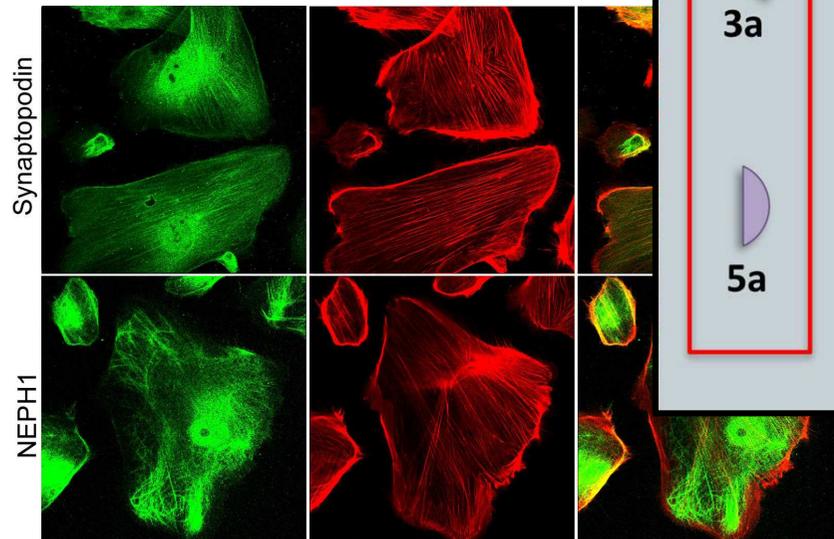
... clinically, their measurement is useful for diagnostic and prognostic purposes

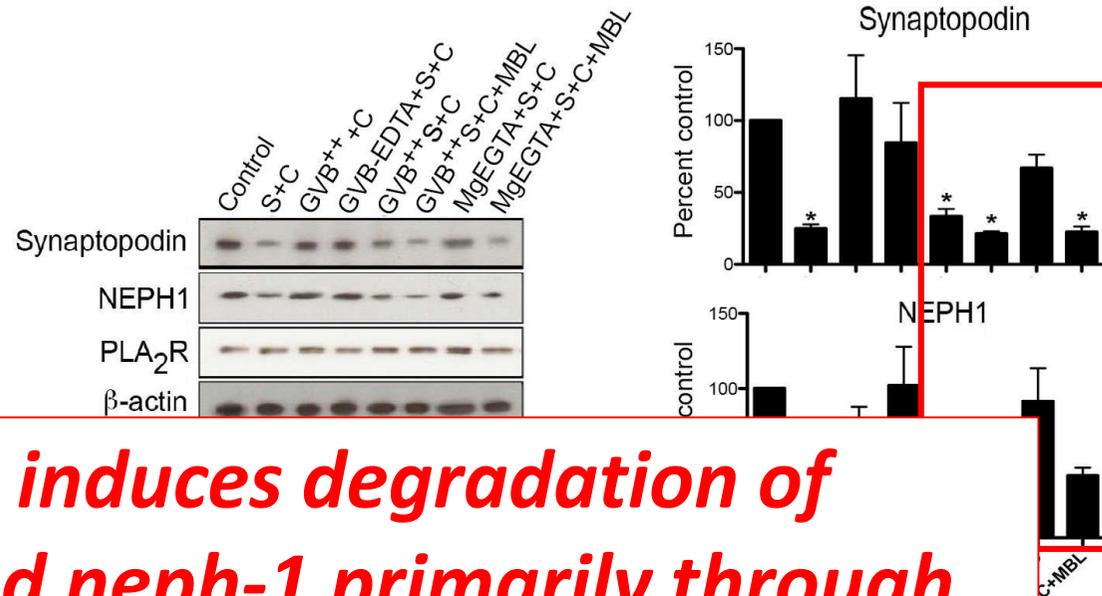
Open questions:

- Why and how do these antibodies arise?***
- How do they damage the podocytes and lead to proteinuria?***

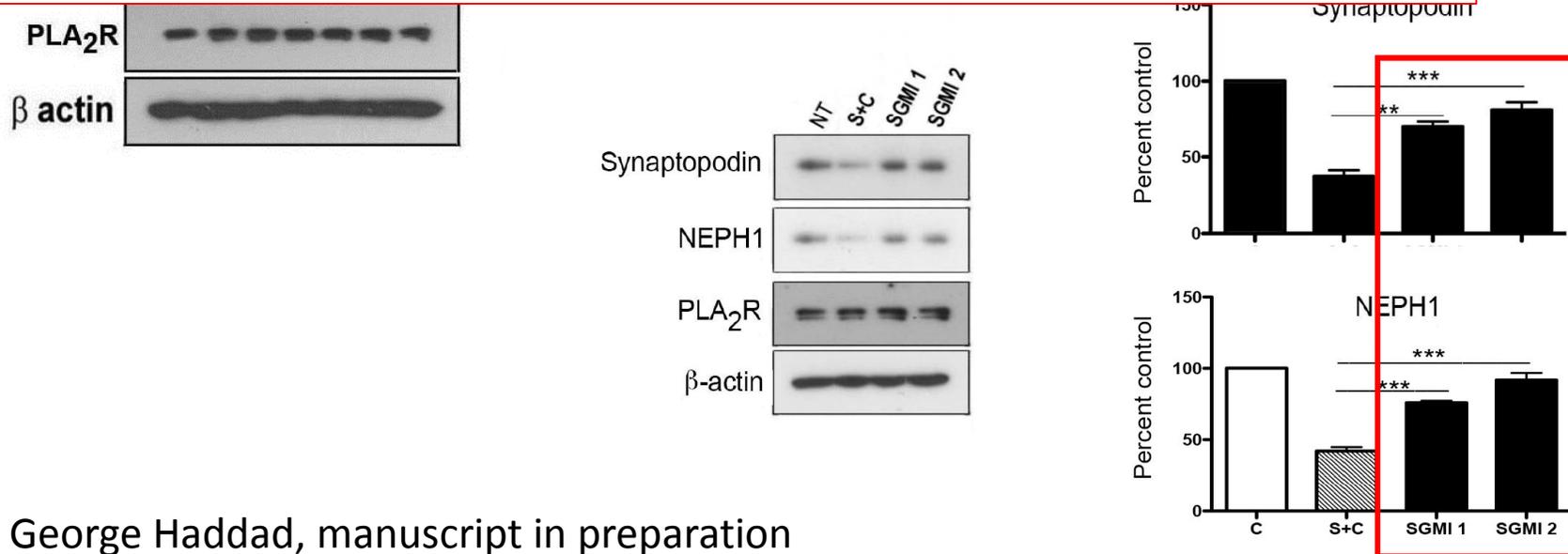


Empty vector + MN serum + com

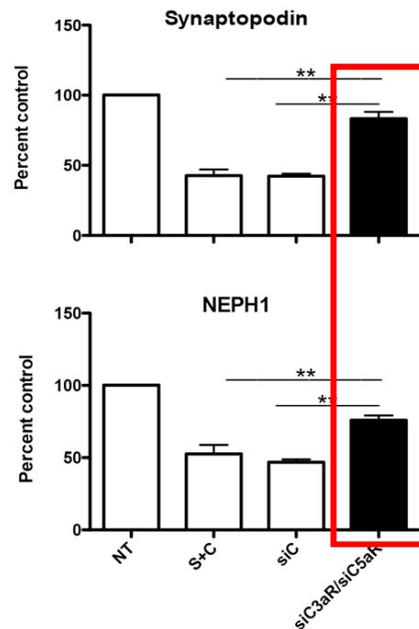
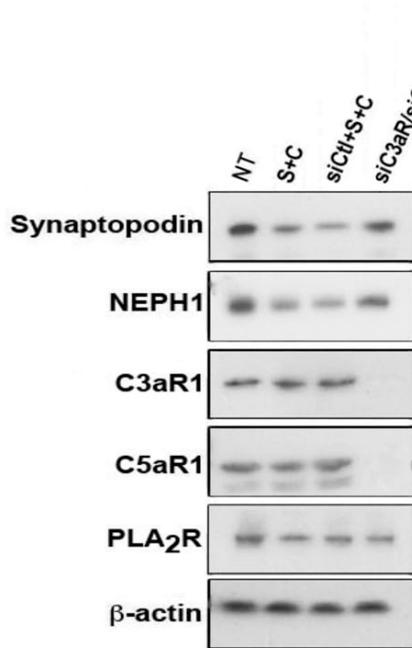
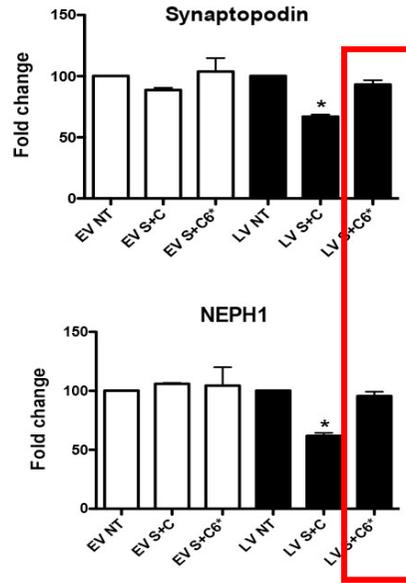
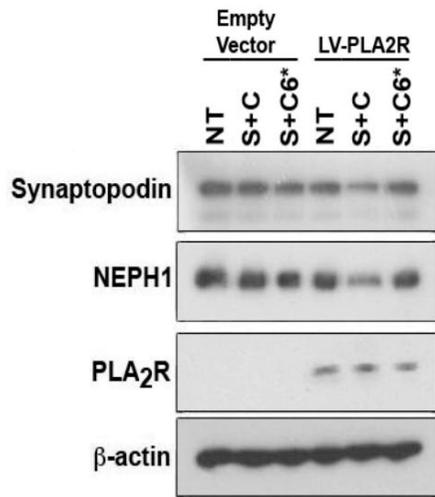




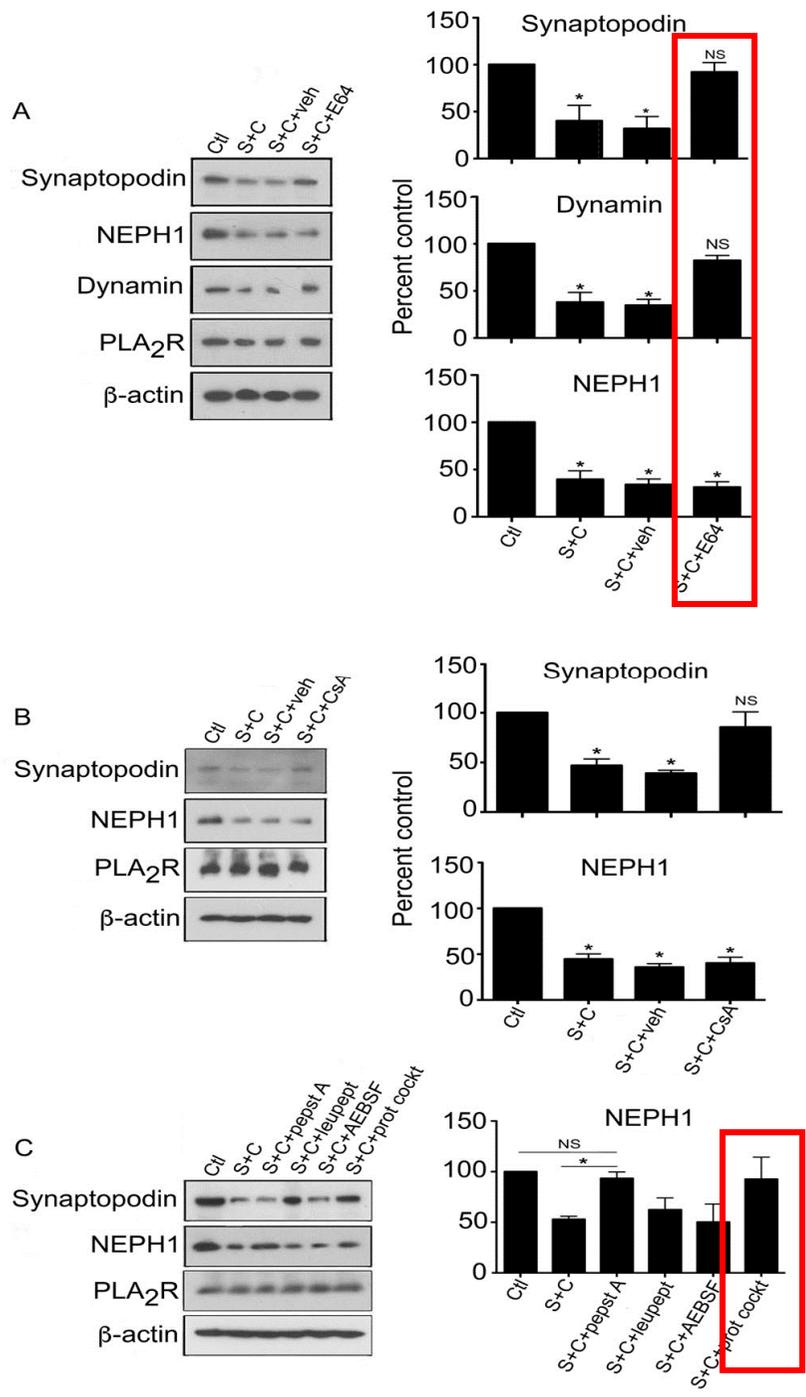
Anti-PLA₂R-IgG4 induces degradation of synaptopodin and neph-1 primarily through the MBL complement pathway



George Haddad, manuscript in preparation



Coincident activation of the complement receptors C3a or C5a and MAC assembly is required for anti-PLA2R-induced sublytic complement injury to podocytes



Synaptopodin and Neph1-degradation are mediated through two different proteolytic pathways (cysteine vs. aspartate proteases, respectively)

How will this translate into treatment of MN?

RESEARCH LETTERS

Research letters

Start IS
Follow PLA2R Ab titer bimonthly

OPEN ACCESS Freely available online

 PLOS ONE

Rituximab

Giuseppe R

Lancet

Rapid
>90%

Design

Alexey V.
Leonid V.
Dmitry S.
Gabibov^{1,2}

1 M.M. Shemyak
of Sciences, Mos
Biology, Moscow
Compiègne, Fran

Targeting downstream pathways?

General mechanisms of foot process effacement?

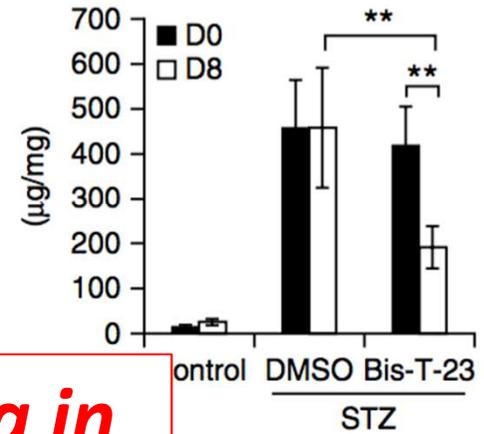
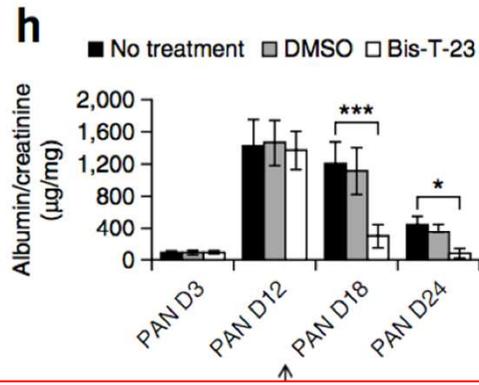
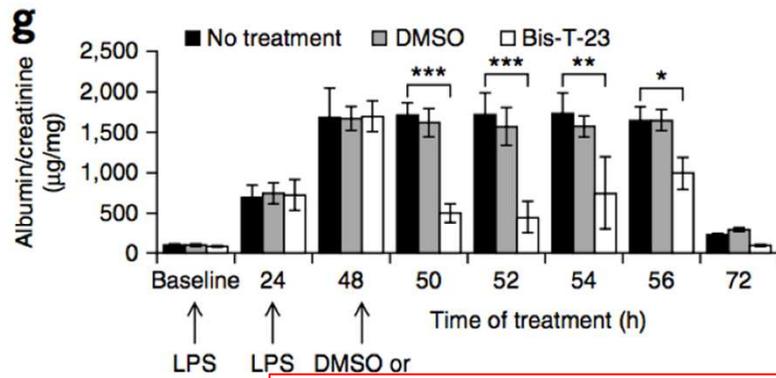
Pharmacologic stabilization of the actin-cytoskeleton rescues proteinuria

ARTICLES

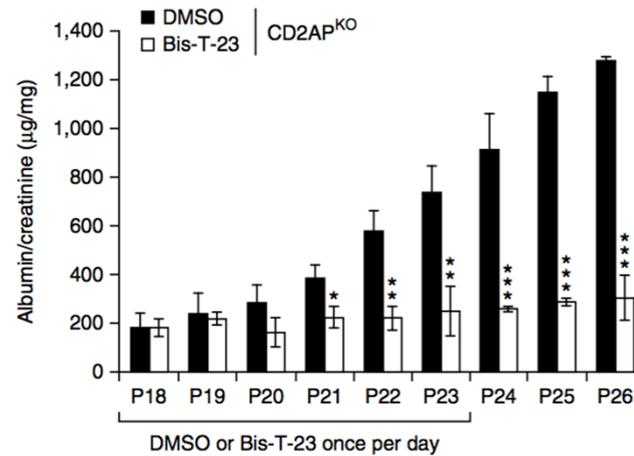
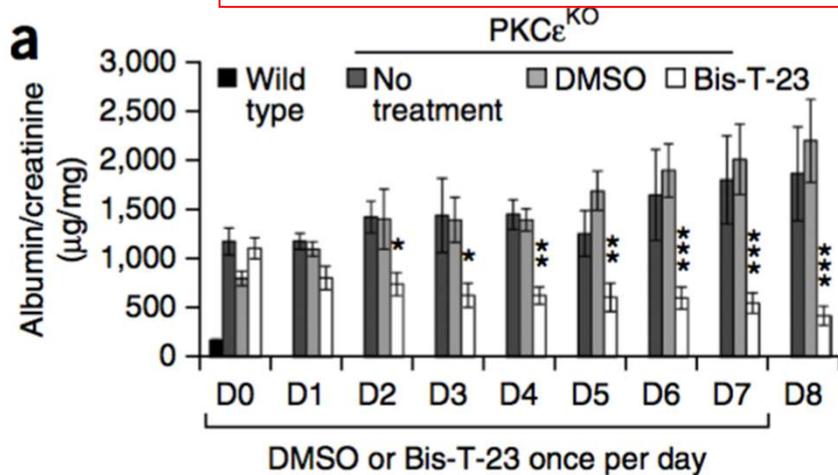
nature
medicine

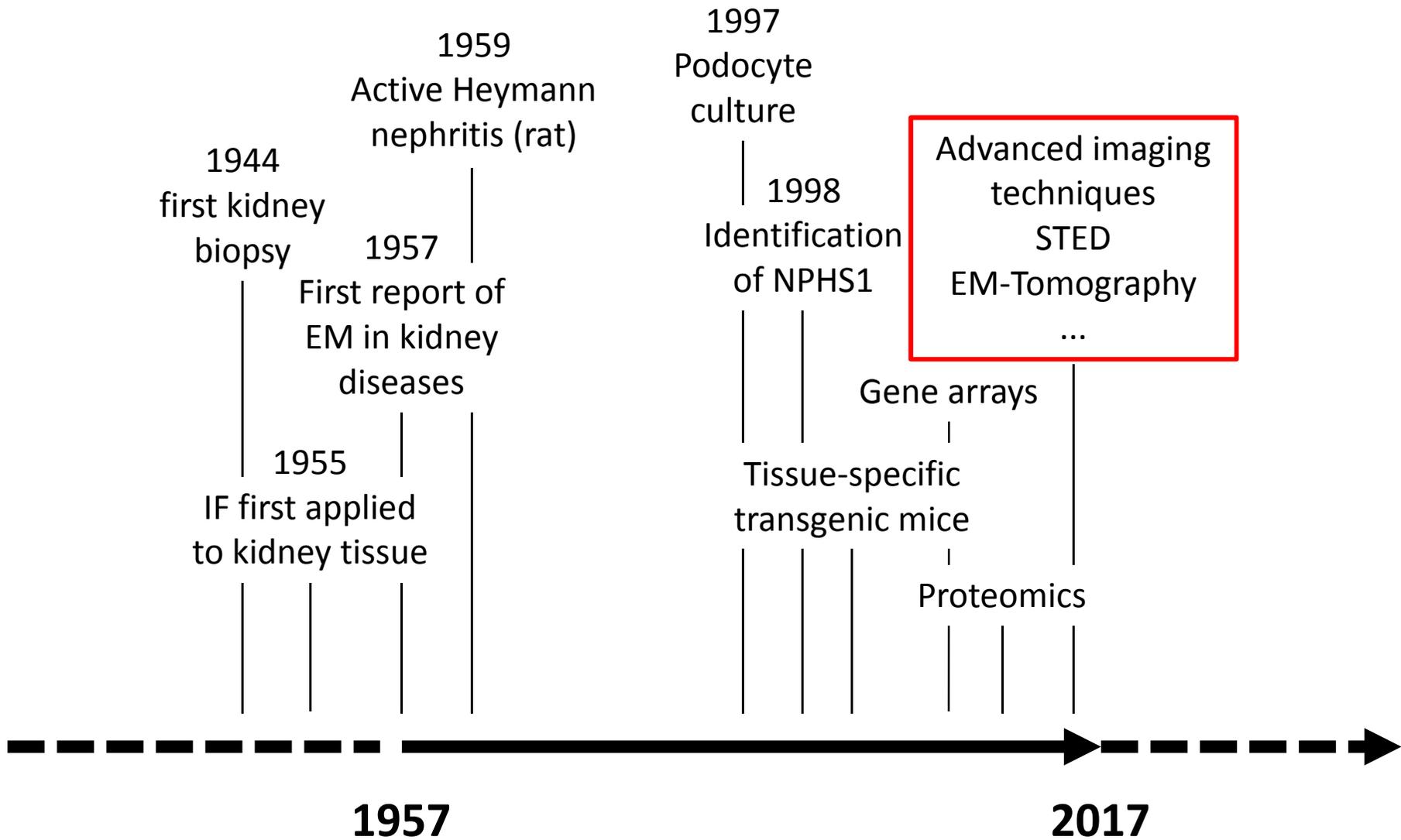
Pharmacological targeting of actin-dependent dynamin oligomerization ameliorates chronic kidney disease in diverse animal models

Mario Schiffer^{1,2,10}, Beina Teng^{1,10}, Changkyu Gu^{3,10}, Valentina A Shchedrina³, Marina Kasaikina³, Vincent A Pham³, Nils Hanke¹, Song Rong¹, Faikah Gueler¹, Patricia Schroder^{1,2}, Irimi Tossidou¹, Joon-Keun Park¹, Lynne Staggs^{1,2}, Hermann Haller^{1,2}, Sergej Erschow⁴, Denise Hilfiker-Kleiner⁴, Changli Wei⁵, Chuang Chen⁵, Nicholas Tardi⁵, Samy Hakrrouch⁶, Martin K Selig⁷, Aleksandr Vasilyev⁸, Sandra Merscher⁹, Jochen Reiser⁵ & Sanja Sever³

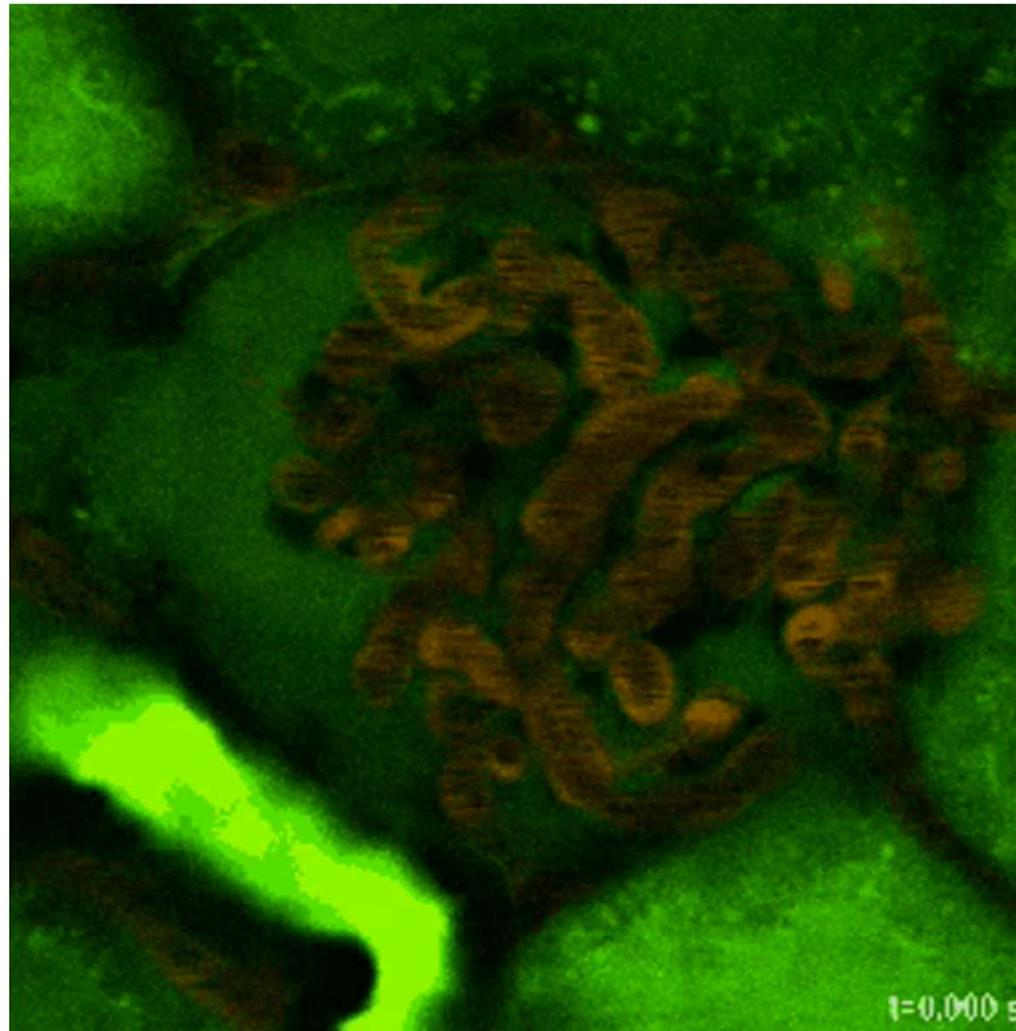


One drug to treat proteinuria in all glomerular diseases?

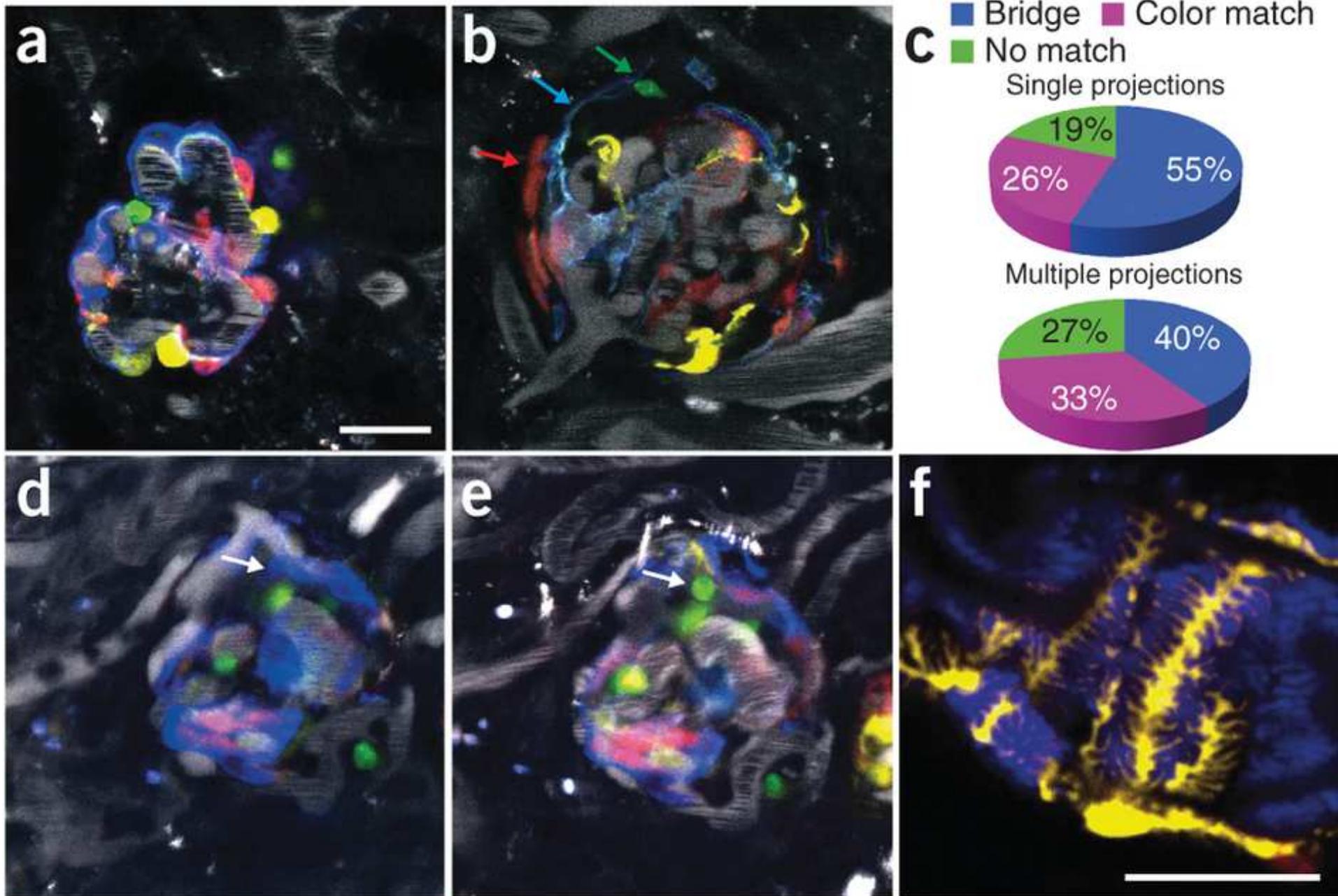


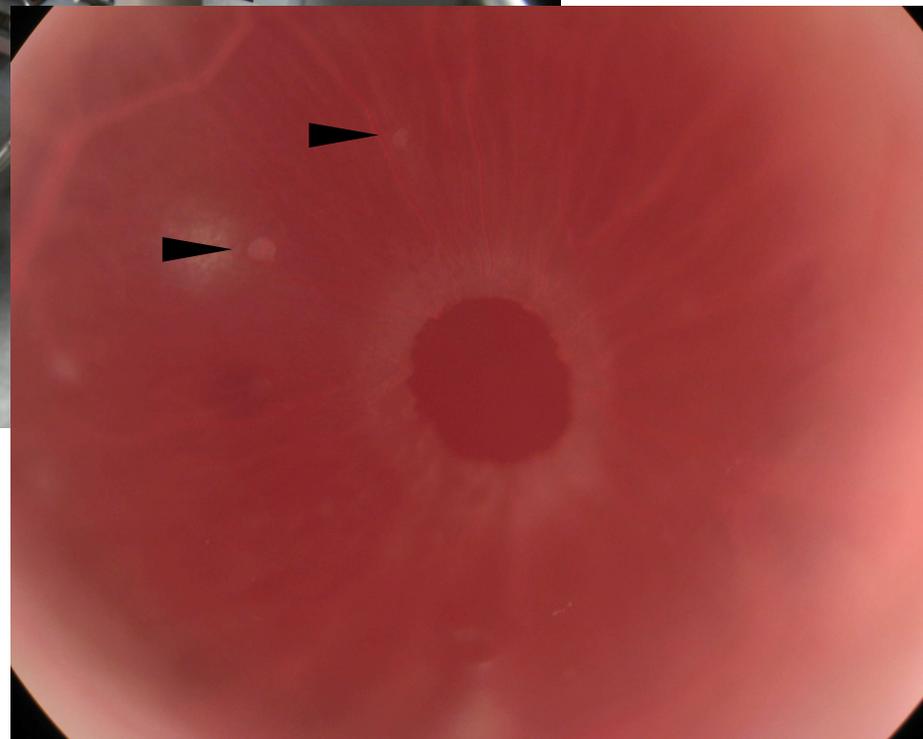
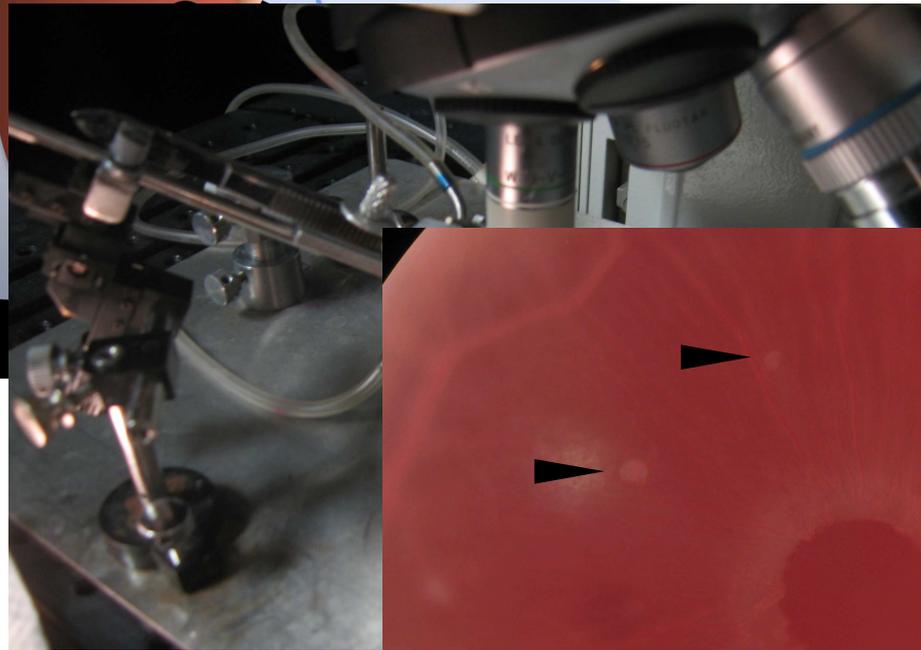
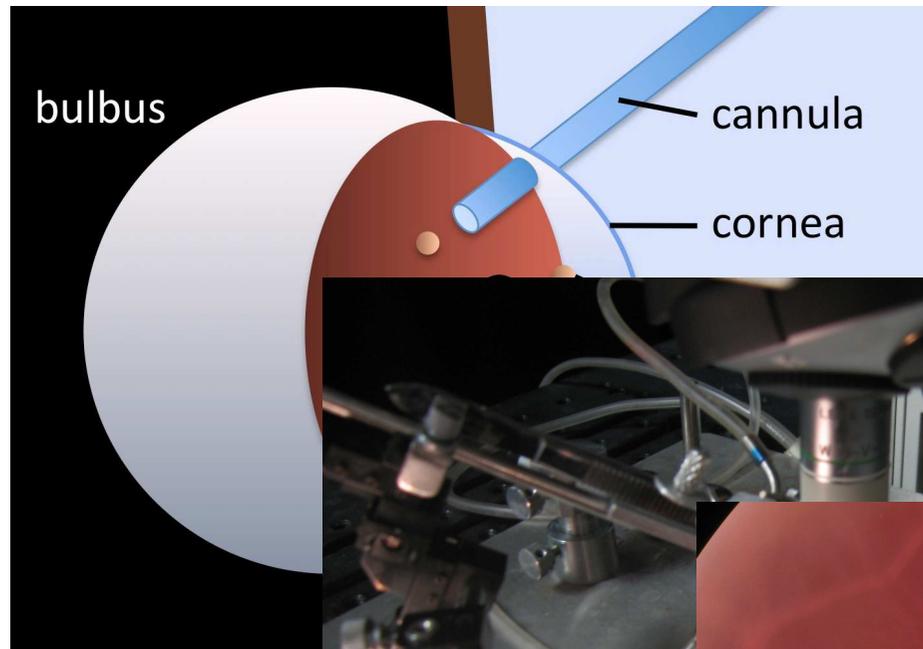


Multiphoton in vivo fluorescent imaging



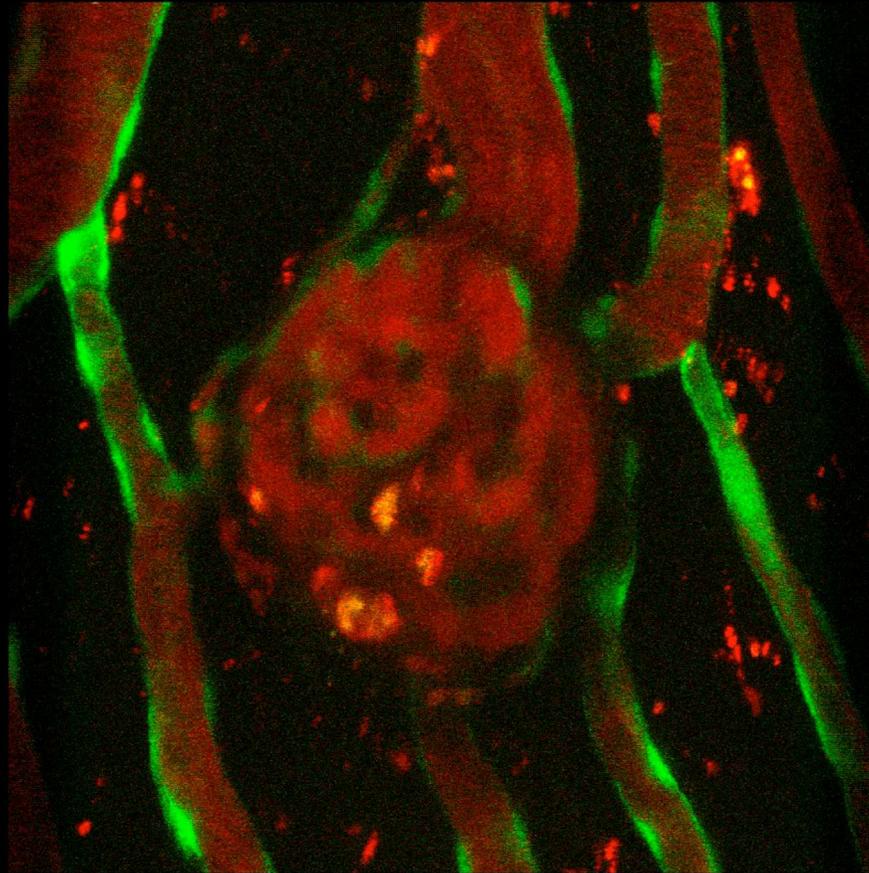
Peti-Peterdi, JASN 2010





Results: reperfusion of transplanted glomeruli

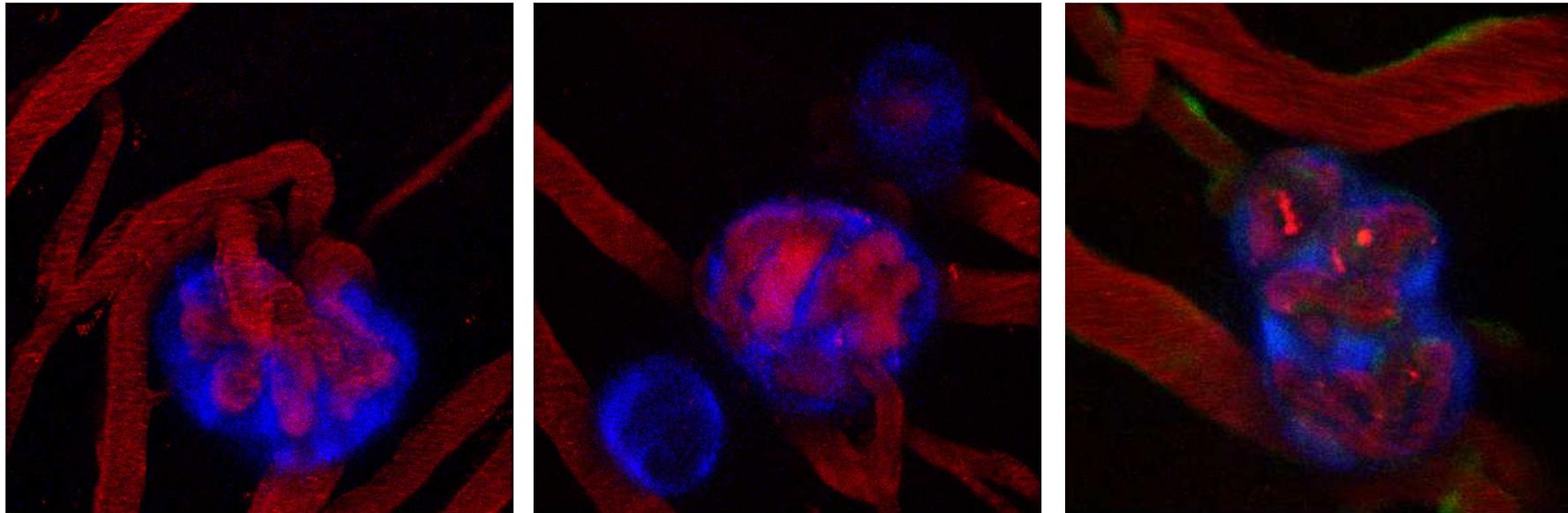
Z-stack, maximum projection



2.000 kDa dextran red

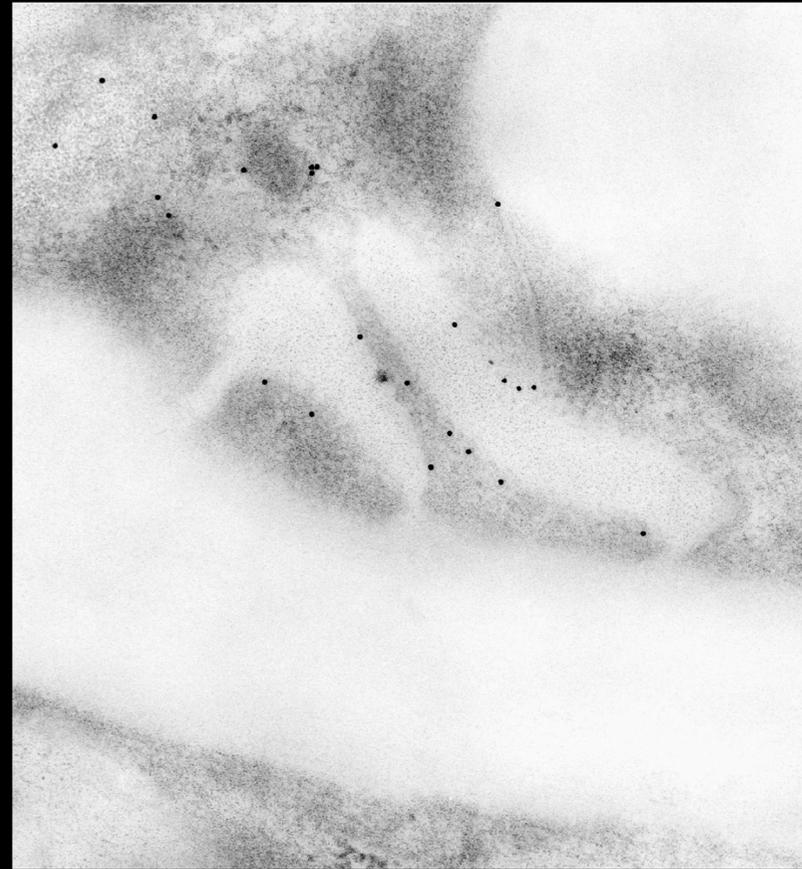
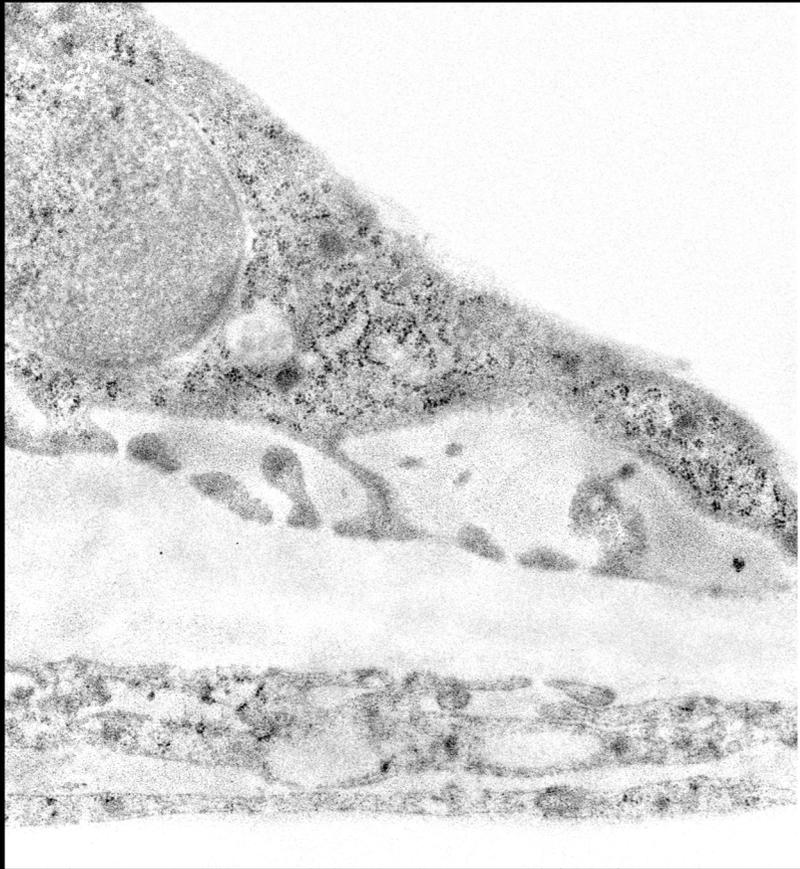
Tie-2 GFP recipient

Results: survival of podocytes



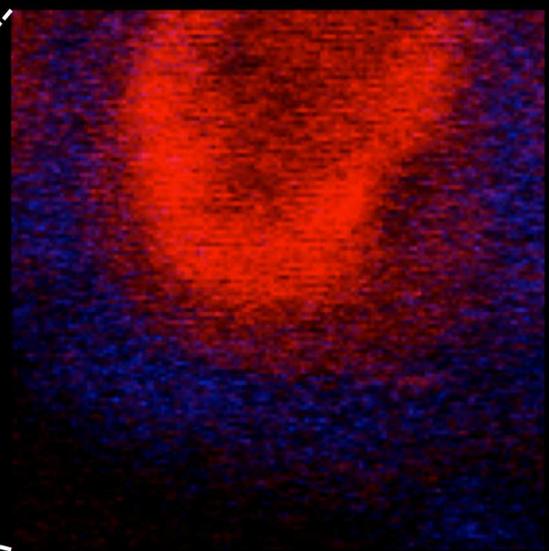
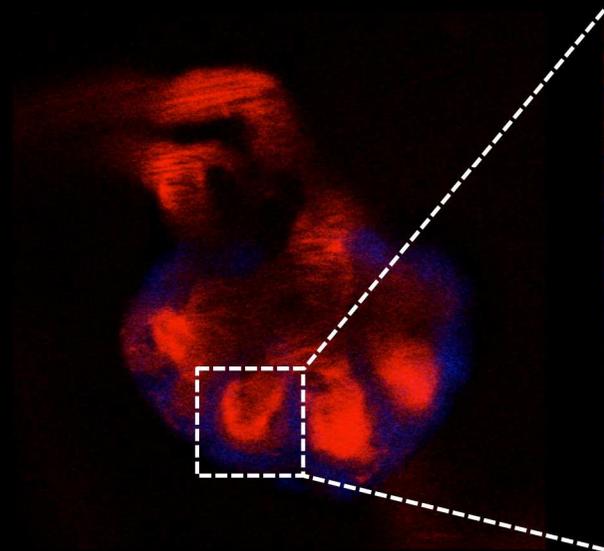
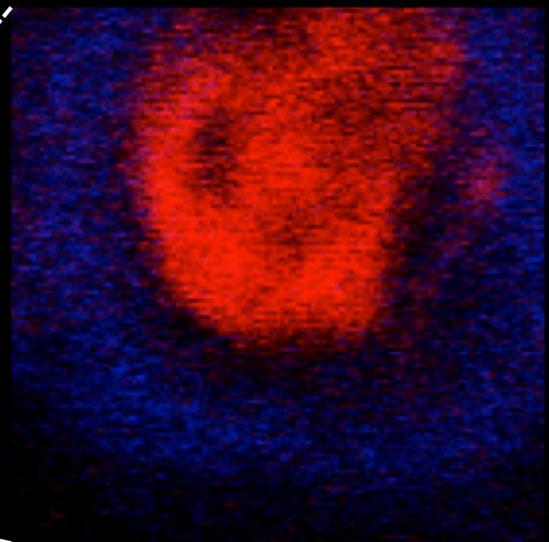
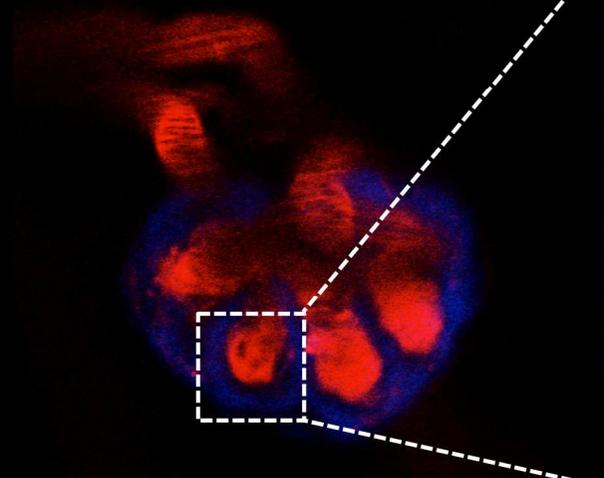
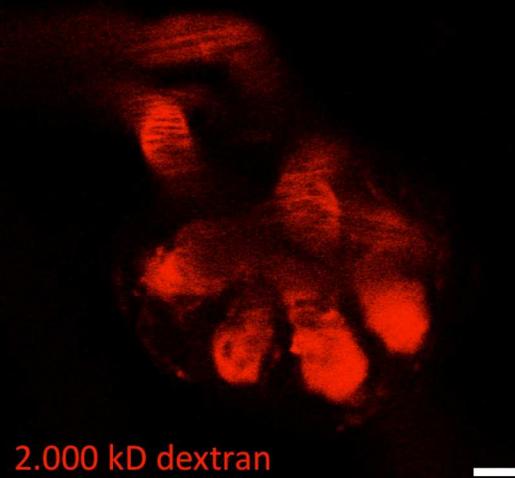
NPHS1-CFP donor Tie-2 GFP recipient 70 kD dextran

Results: preservation of differentiated interdigitating foot processes

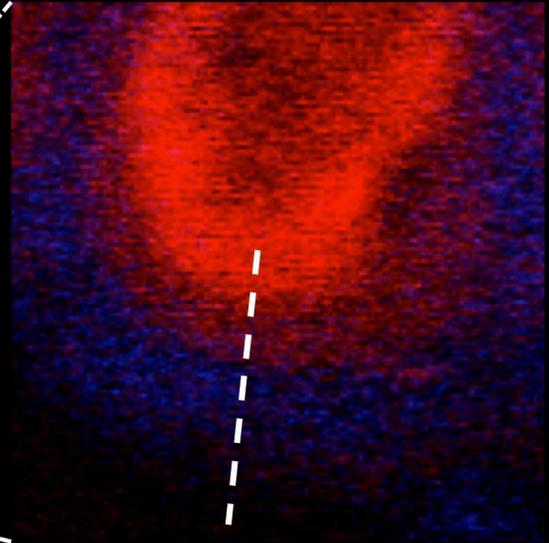
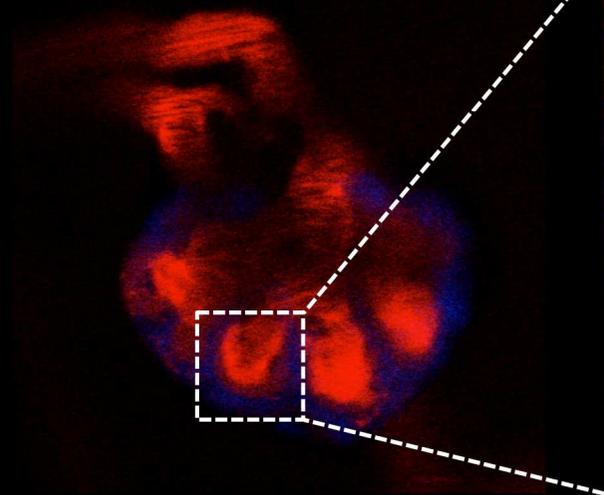
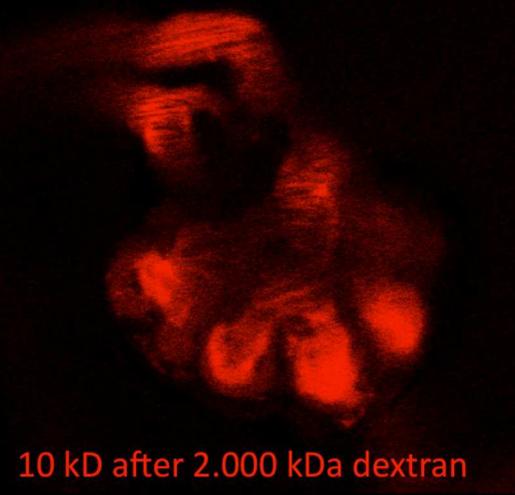
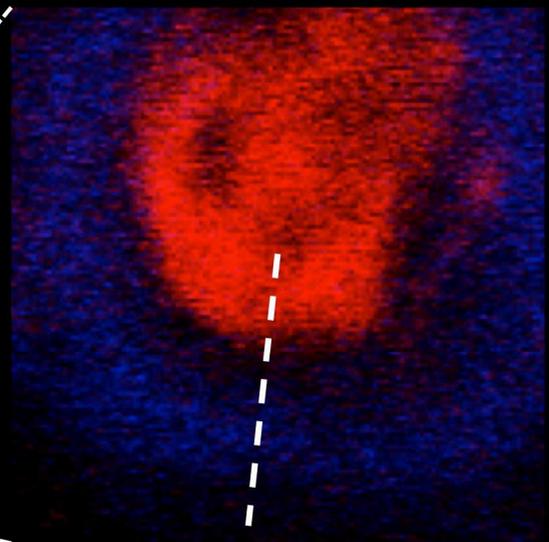
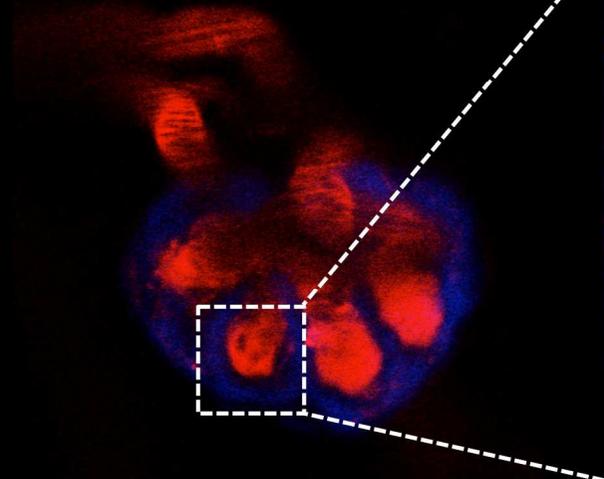
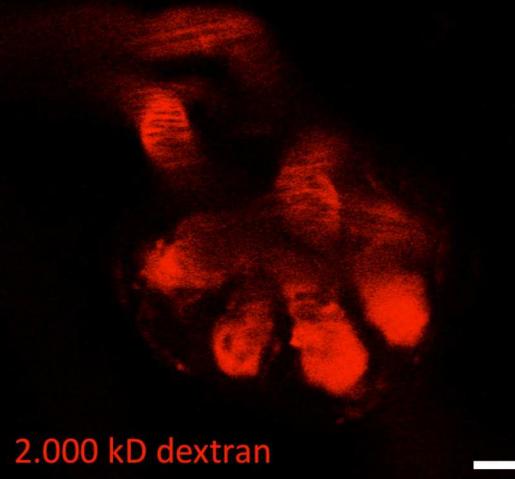


immunogold: podocalyxin

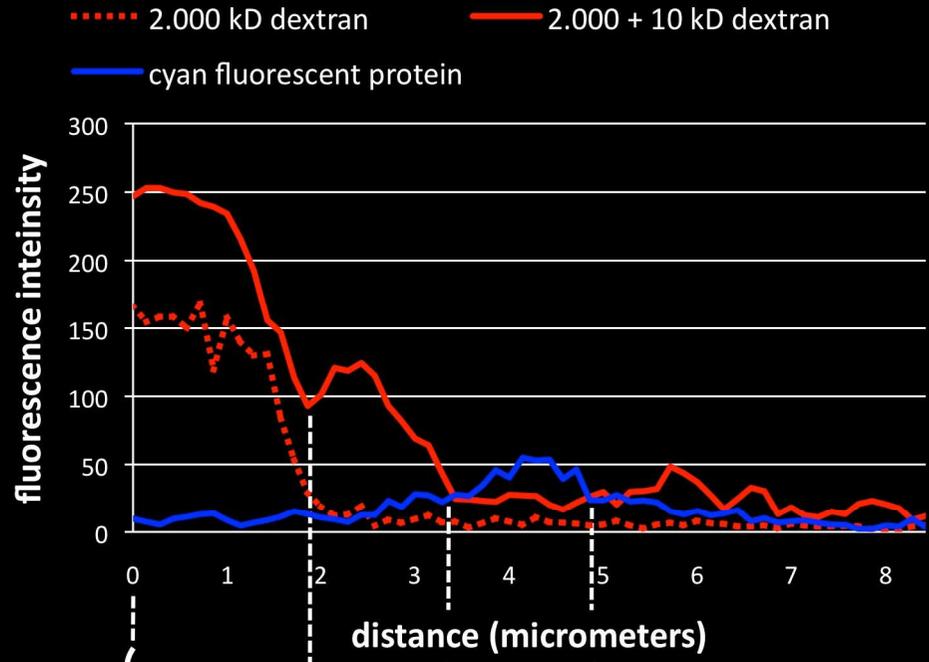
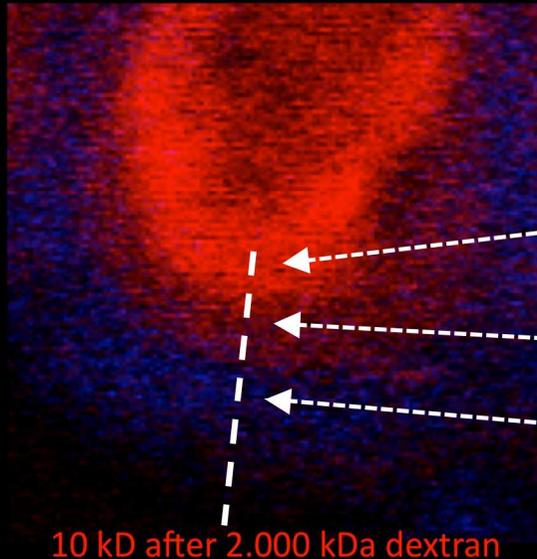
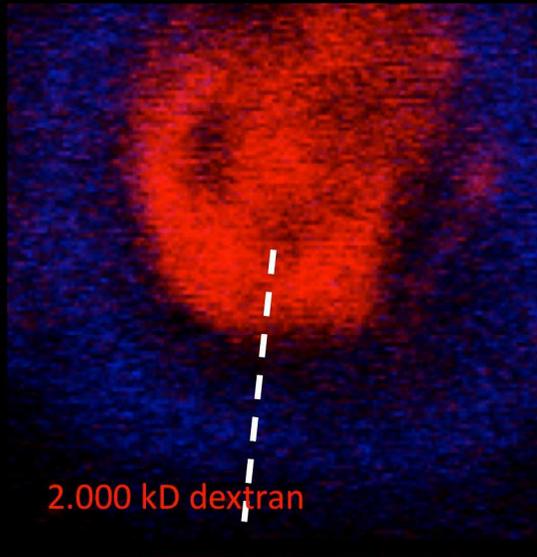
Results: filtration of LMW dextran



Results: filtration of LMW dextran



Results: the subpodocyte space restricts passage of the filtered dye



Intravascular space

subpodocyte space

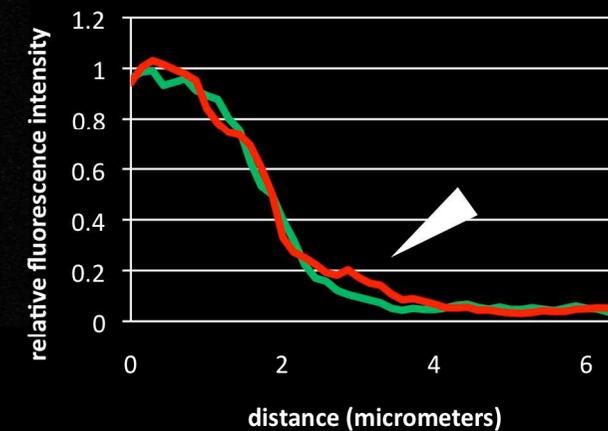
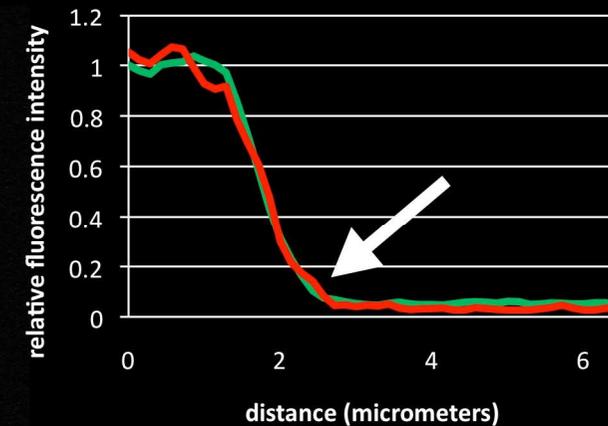
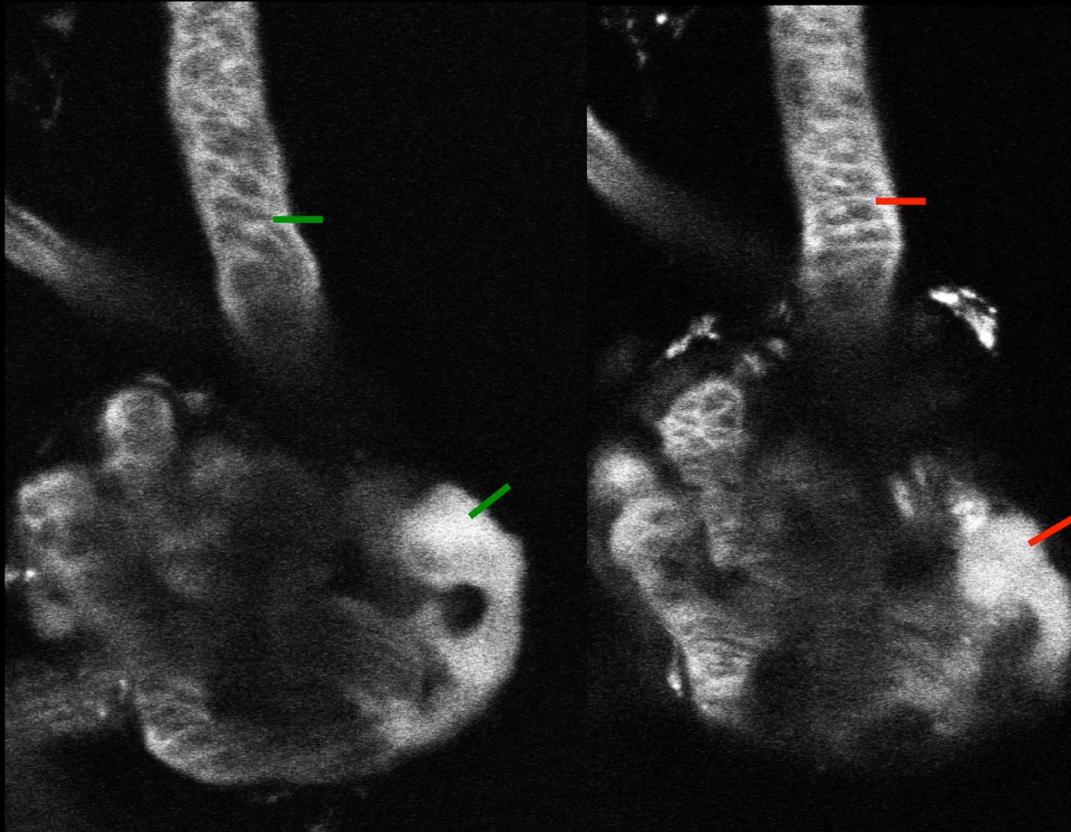
podocyte cell body

White dashed arrows point from these labels to the corresponding regions in the microscopy images. Brackets on the graph indicate the distance ranges for each region: Intravascular space (0-2 micrometers), subpodocyte space (2-4 micrometers), and podocyte cell body (4-5 micrometers).

Results: leakage of 70 kD dextran in an inducible genetic model of proteinuria

baseline

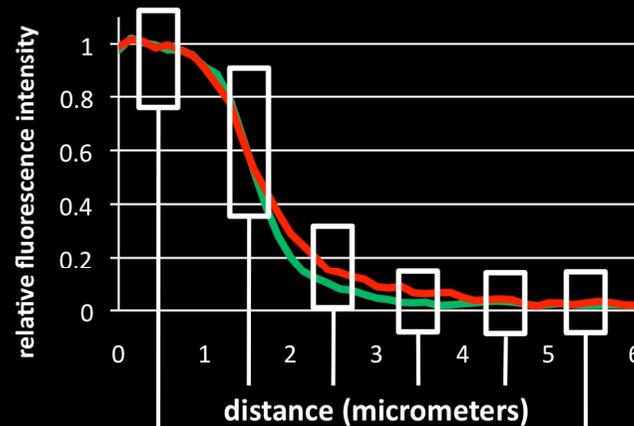
9 days doxy



donor: podocin-rtTA / TetO-HA-NFATc1^{nuc}

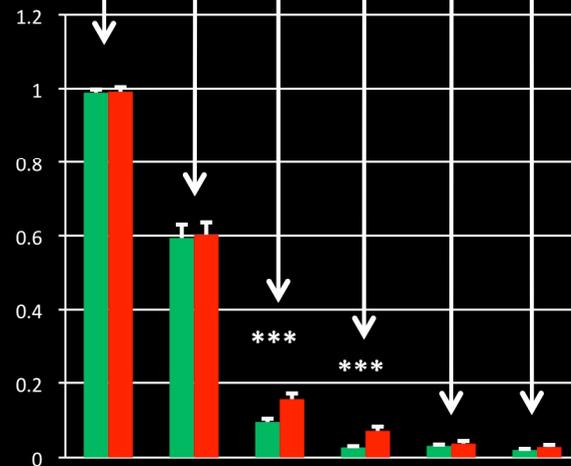
*dox inducible podocyte-specific expression of constitutive active NFAT
-> heavy proteinuria within 5-7 days of induction*

Results: leakage of 70 kD dextran in an inducible genetic model of proteinuria

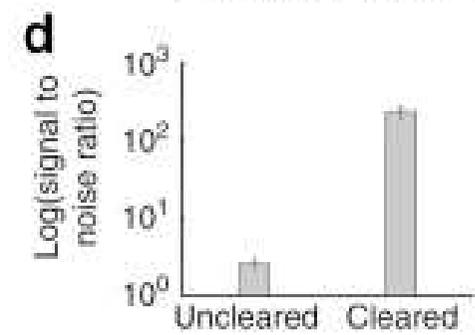
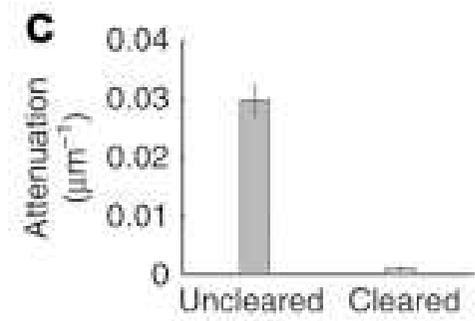
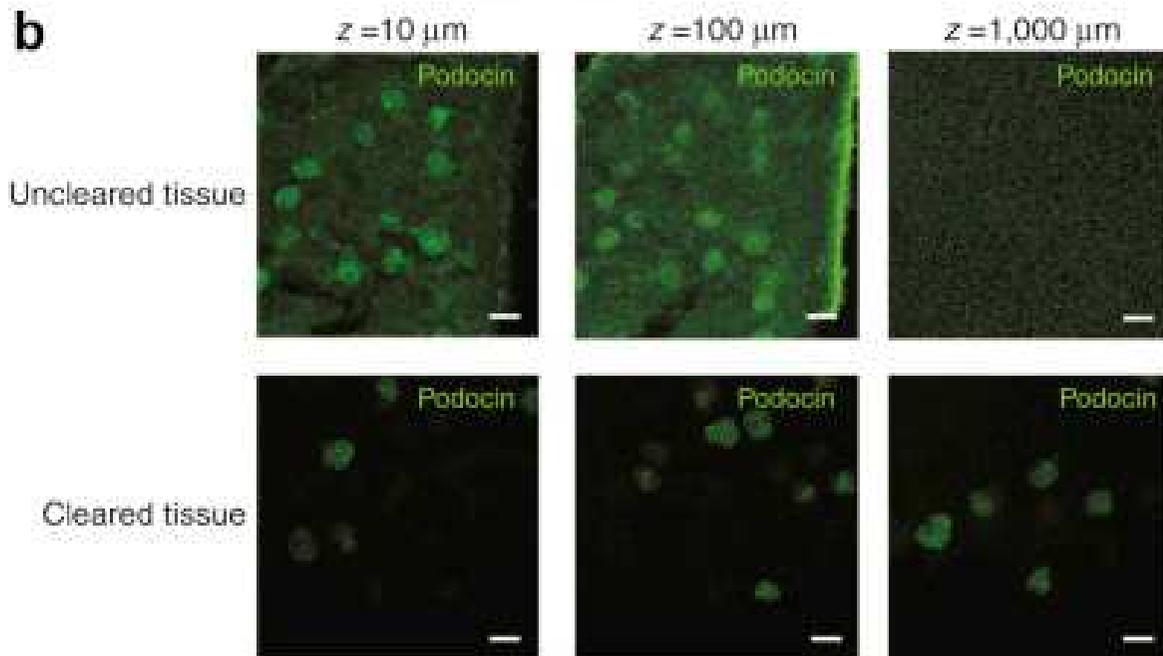


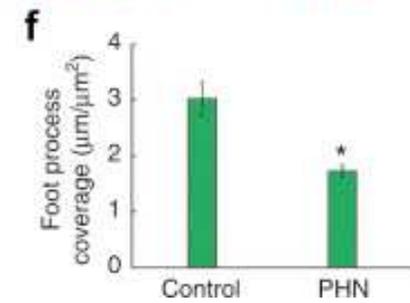
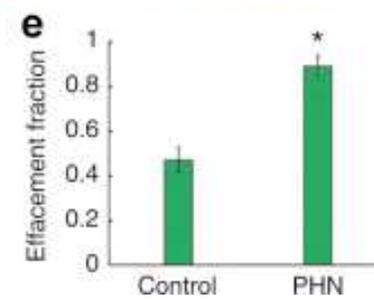
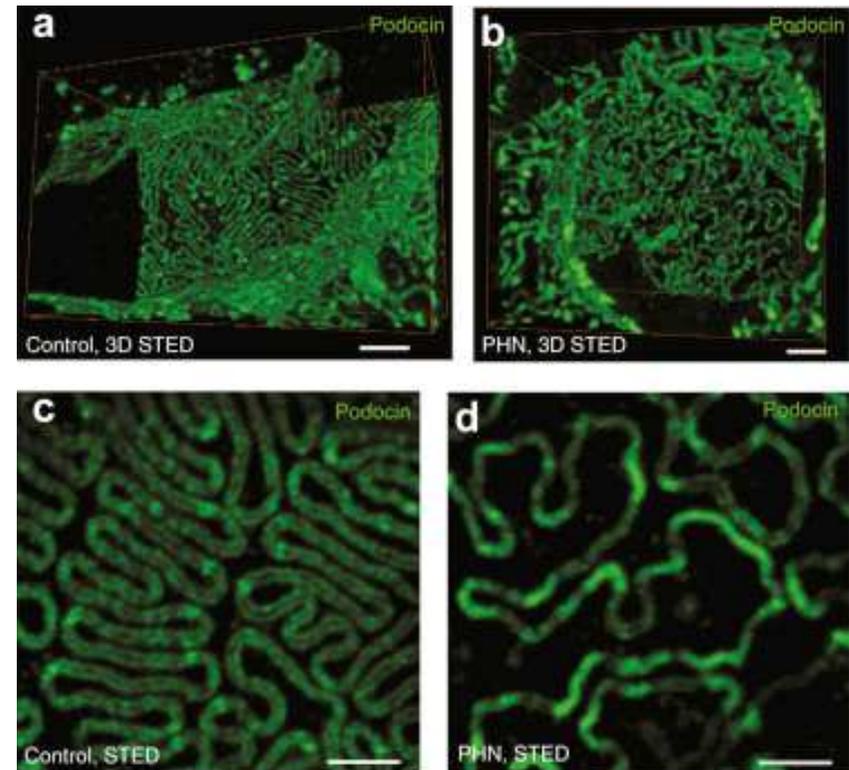
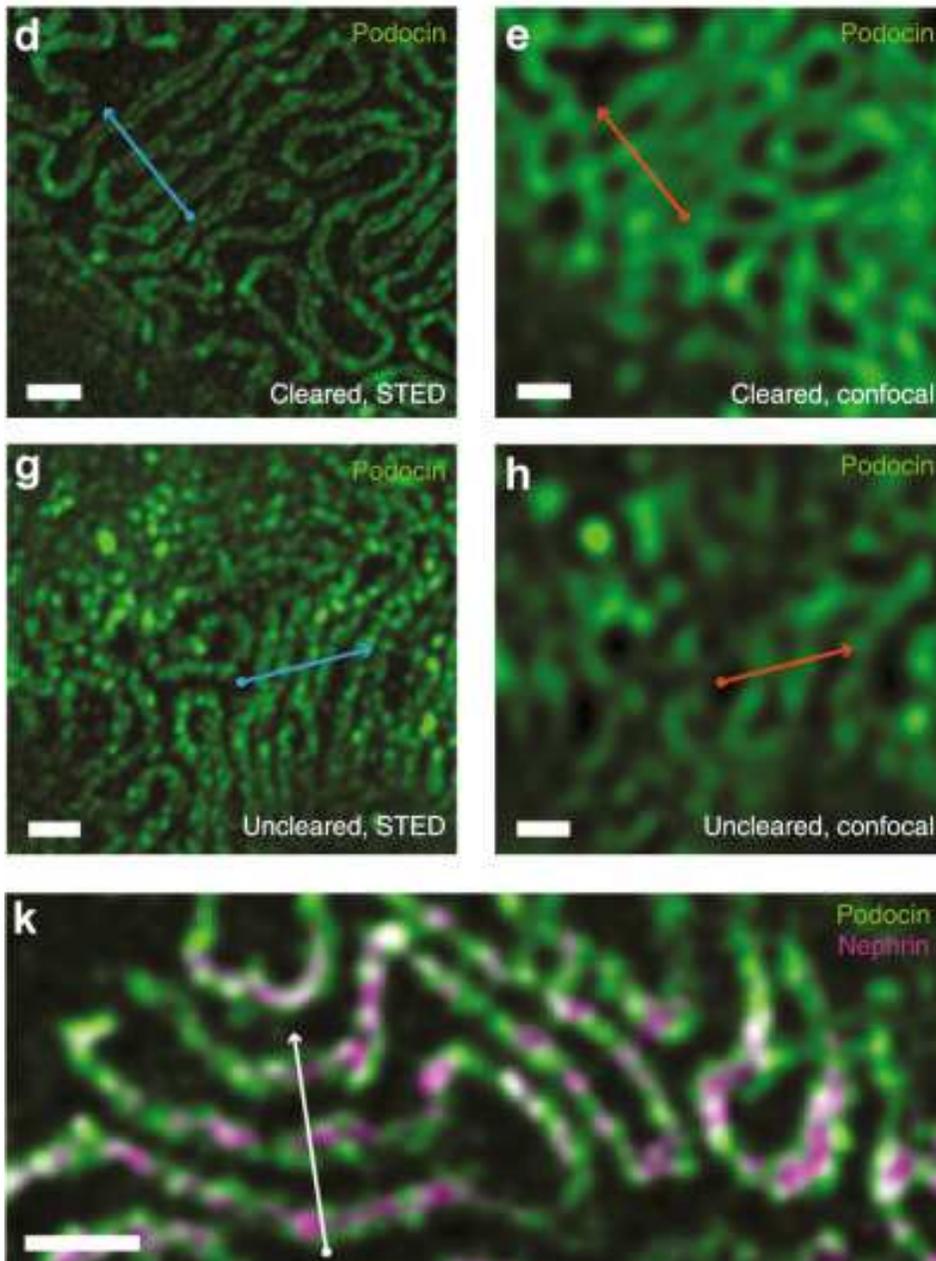
average values of

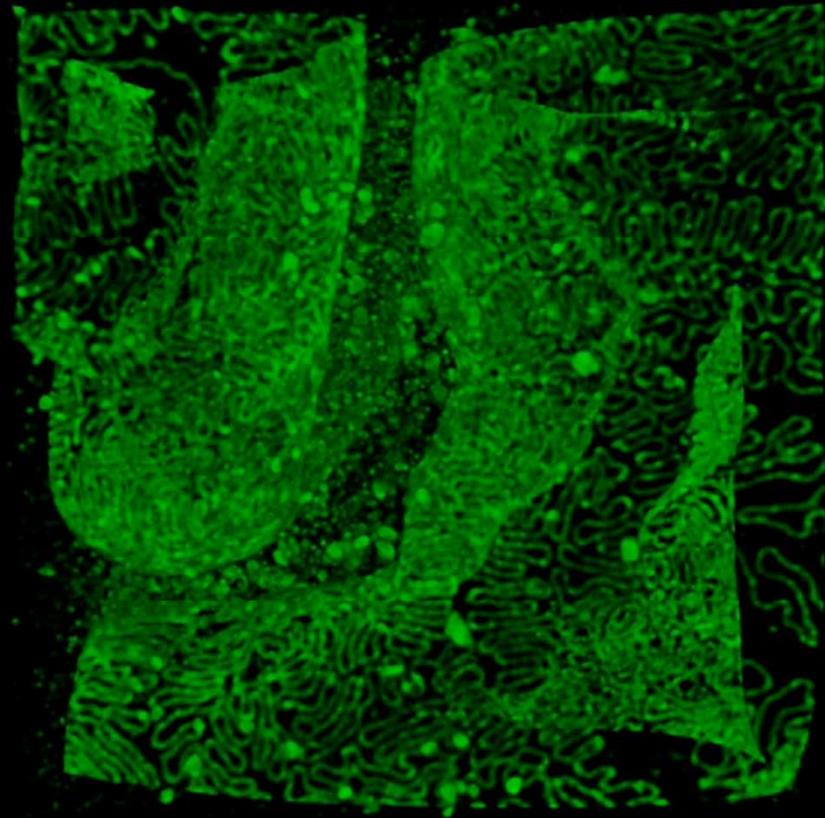
- 6 crosssections per capillary
- 2 capillary loops per glomerulus
- 2 glomeruli per animal
- 2 animals

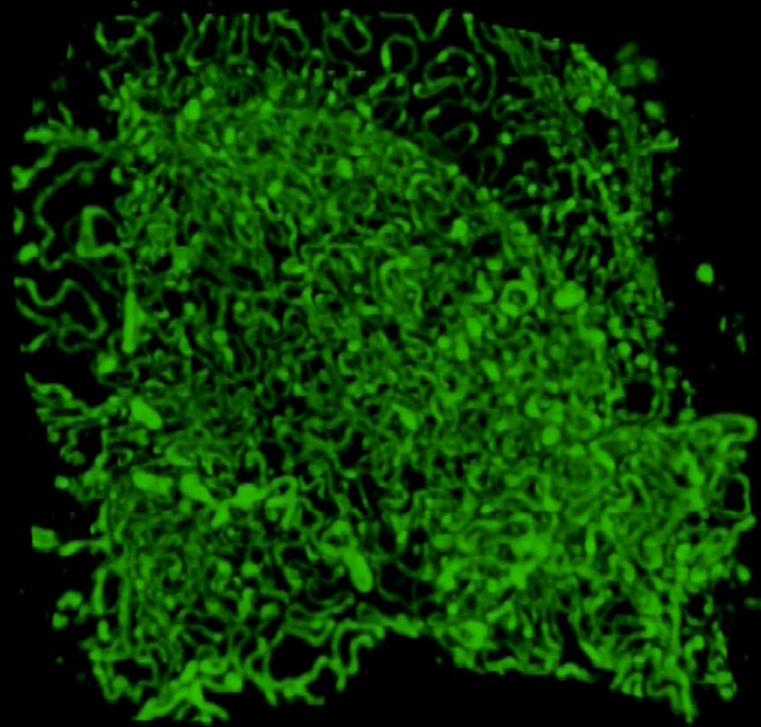


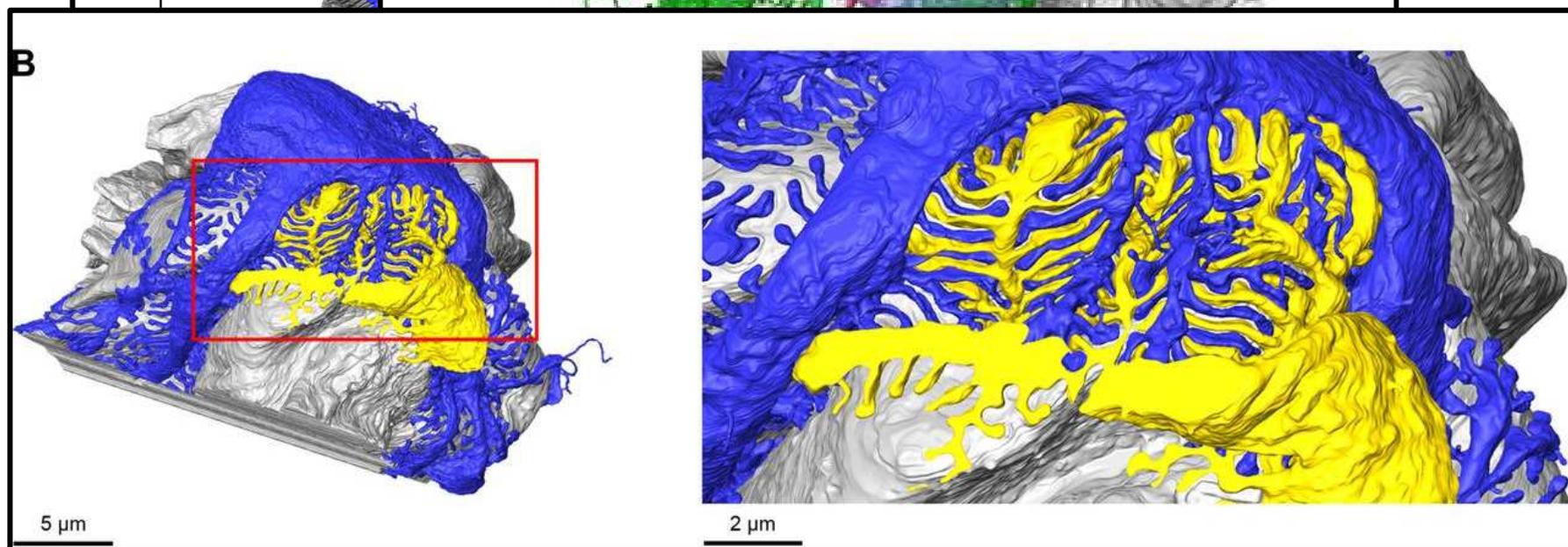
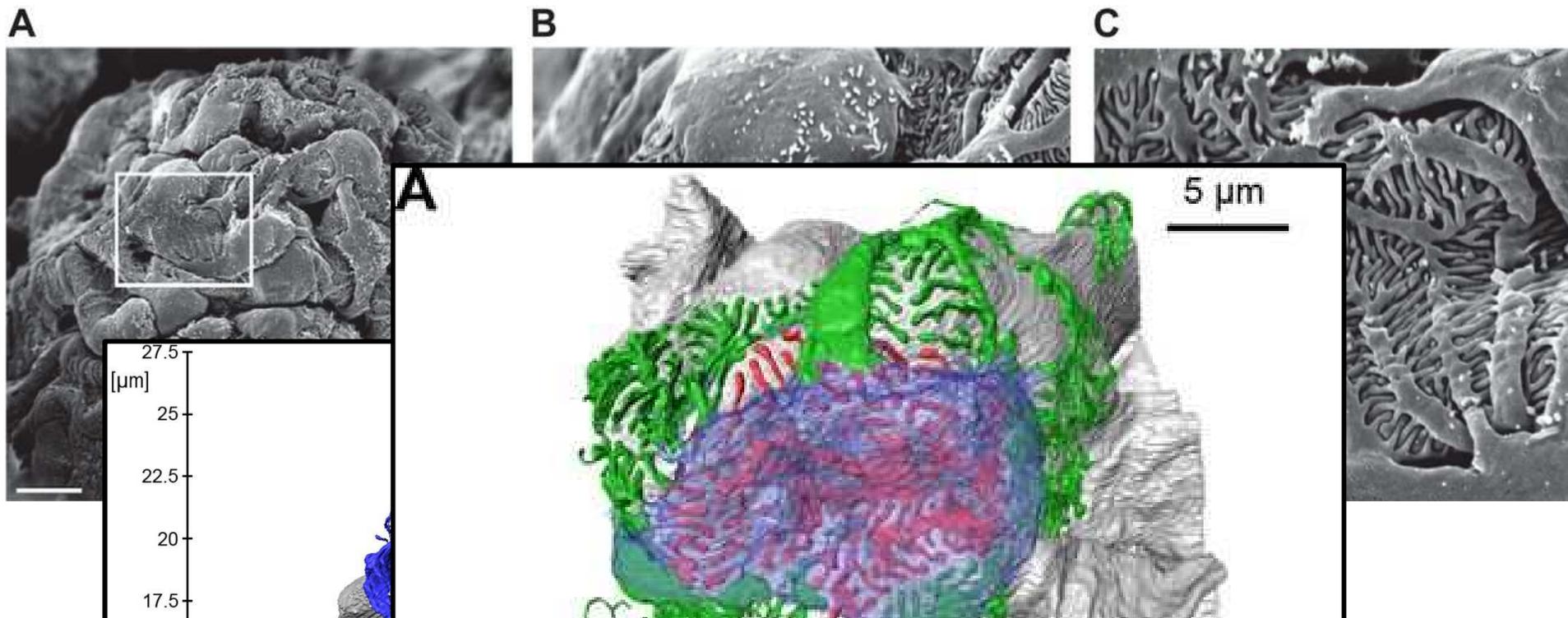
Super-resolution fluorescence microscopy

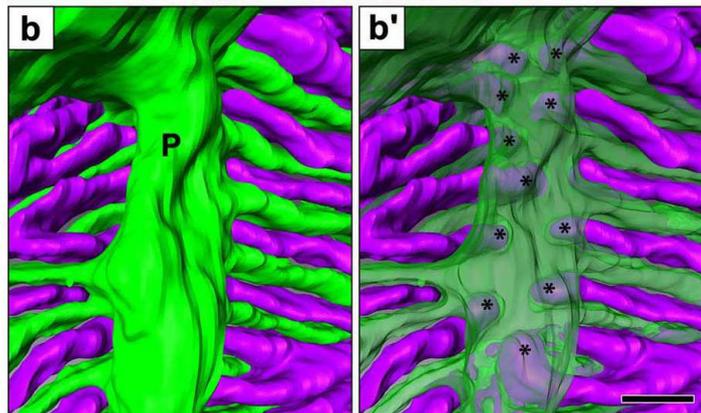
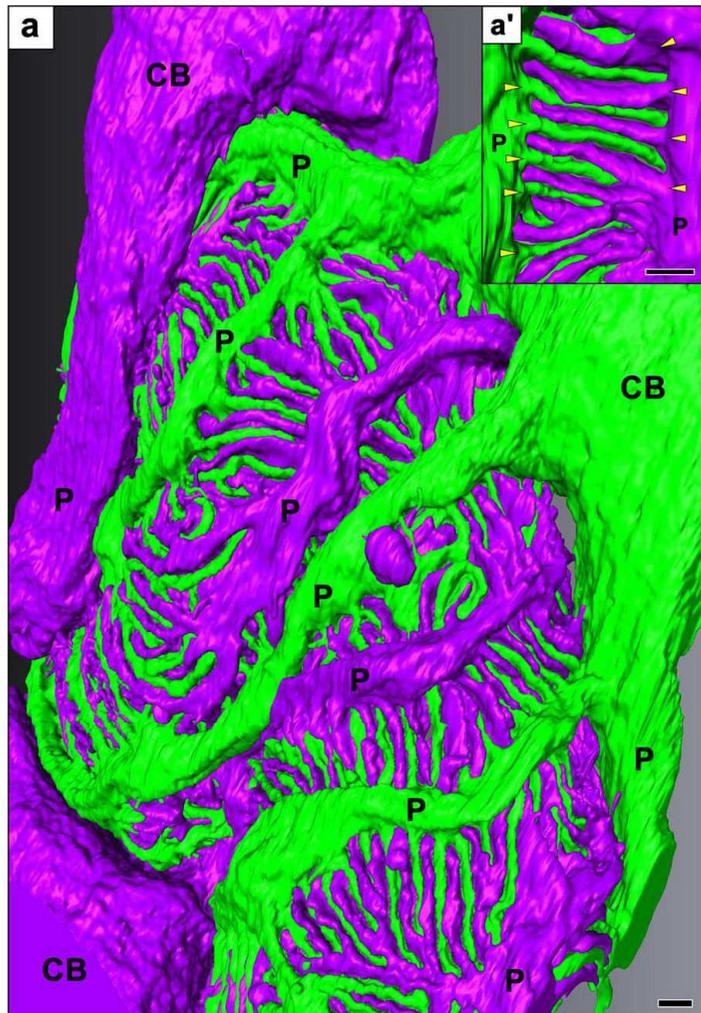


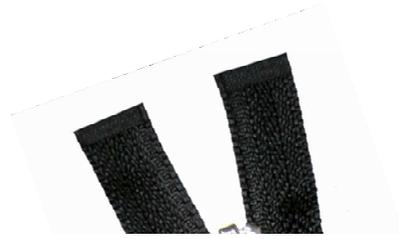
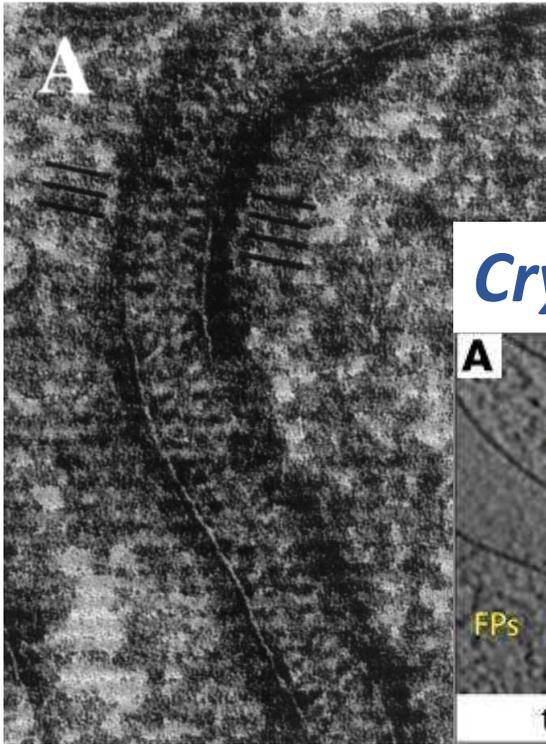




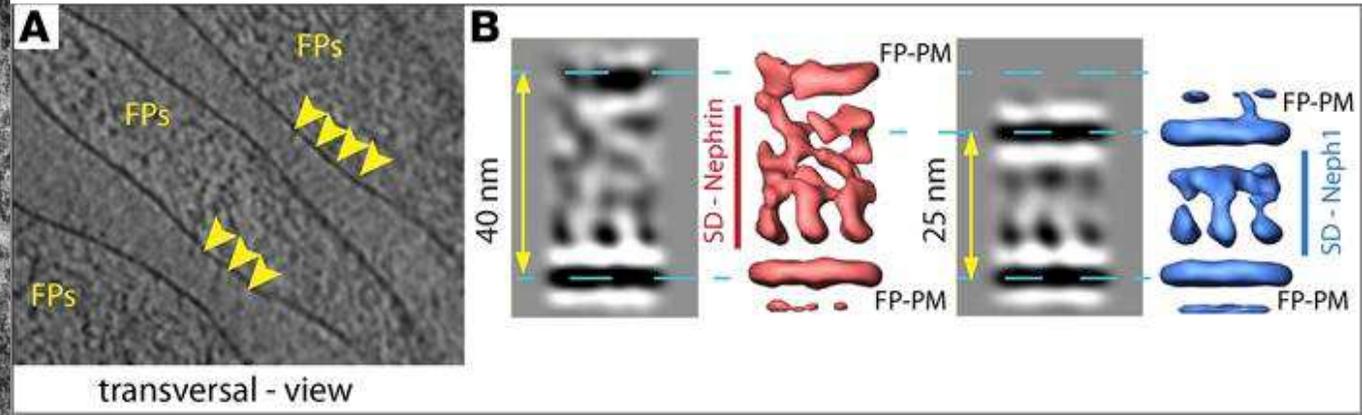




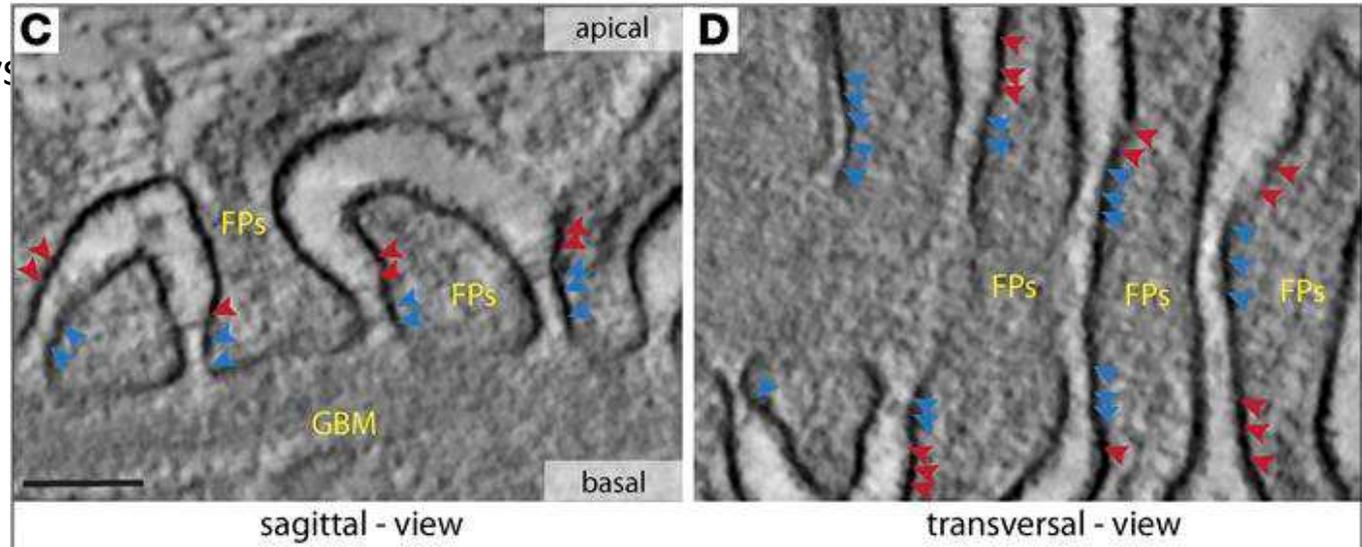




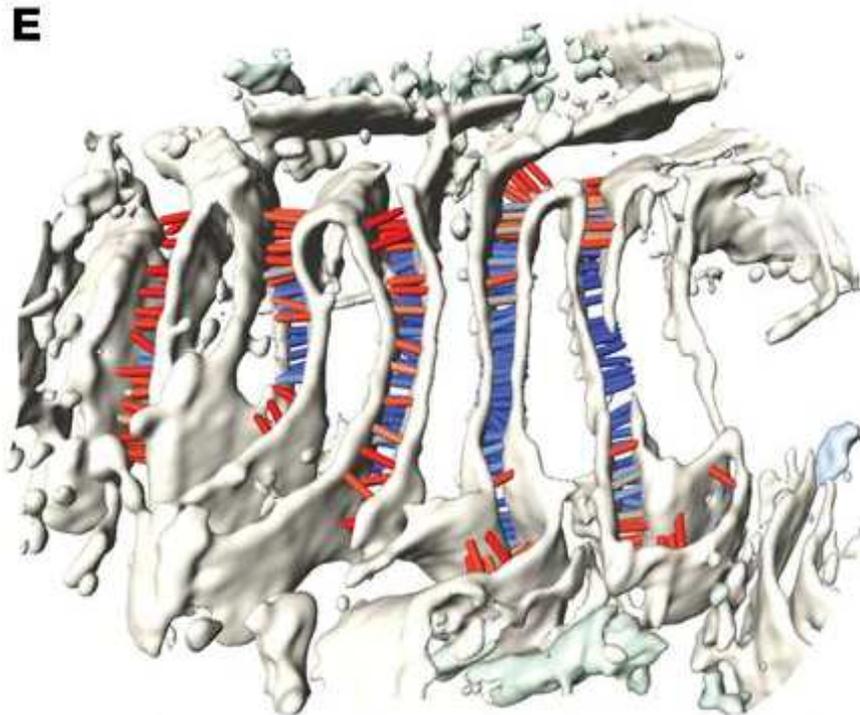
Cryo-electron tomography (CET)



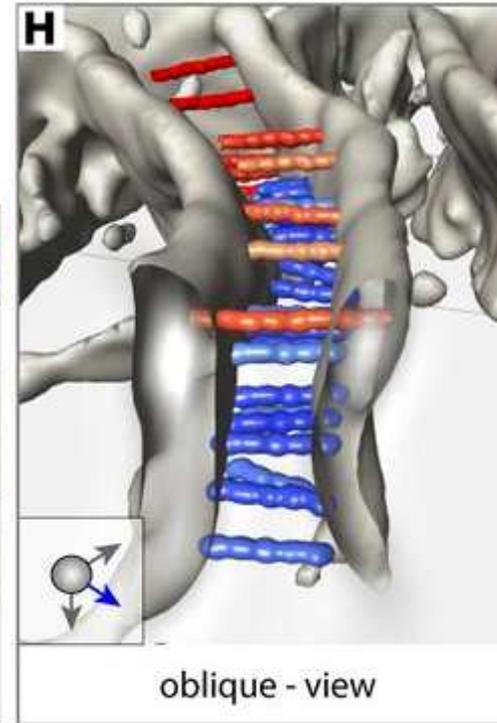
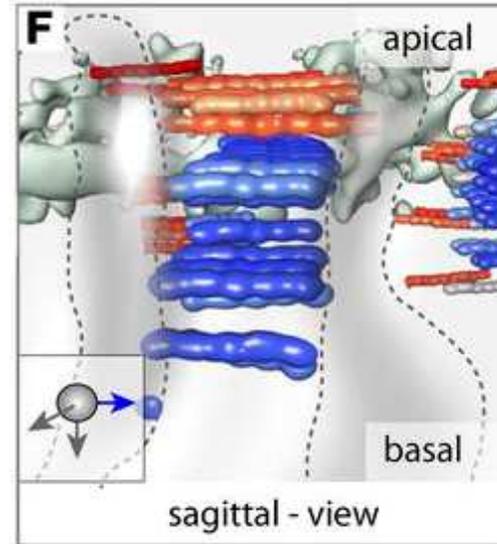
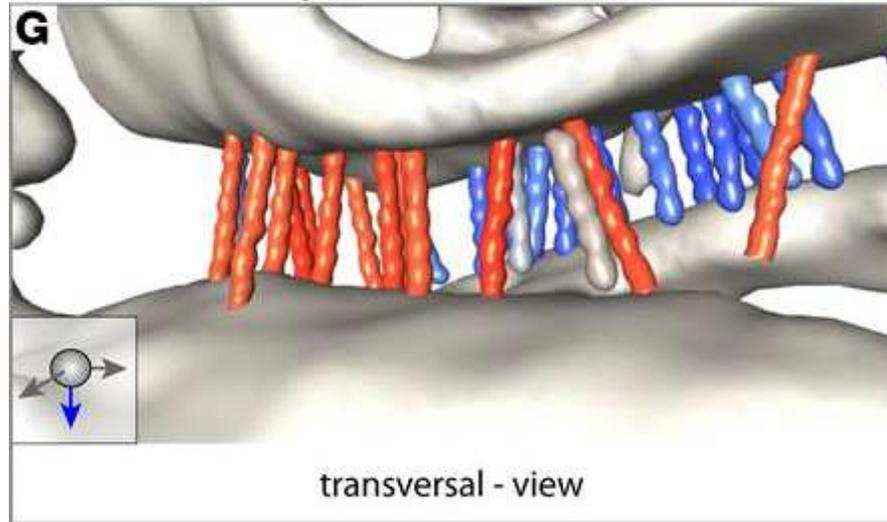
Rodewald and Karnovs



Grahammer, JCI insight 2016



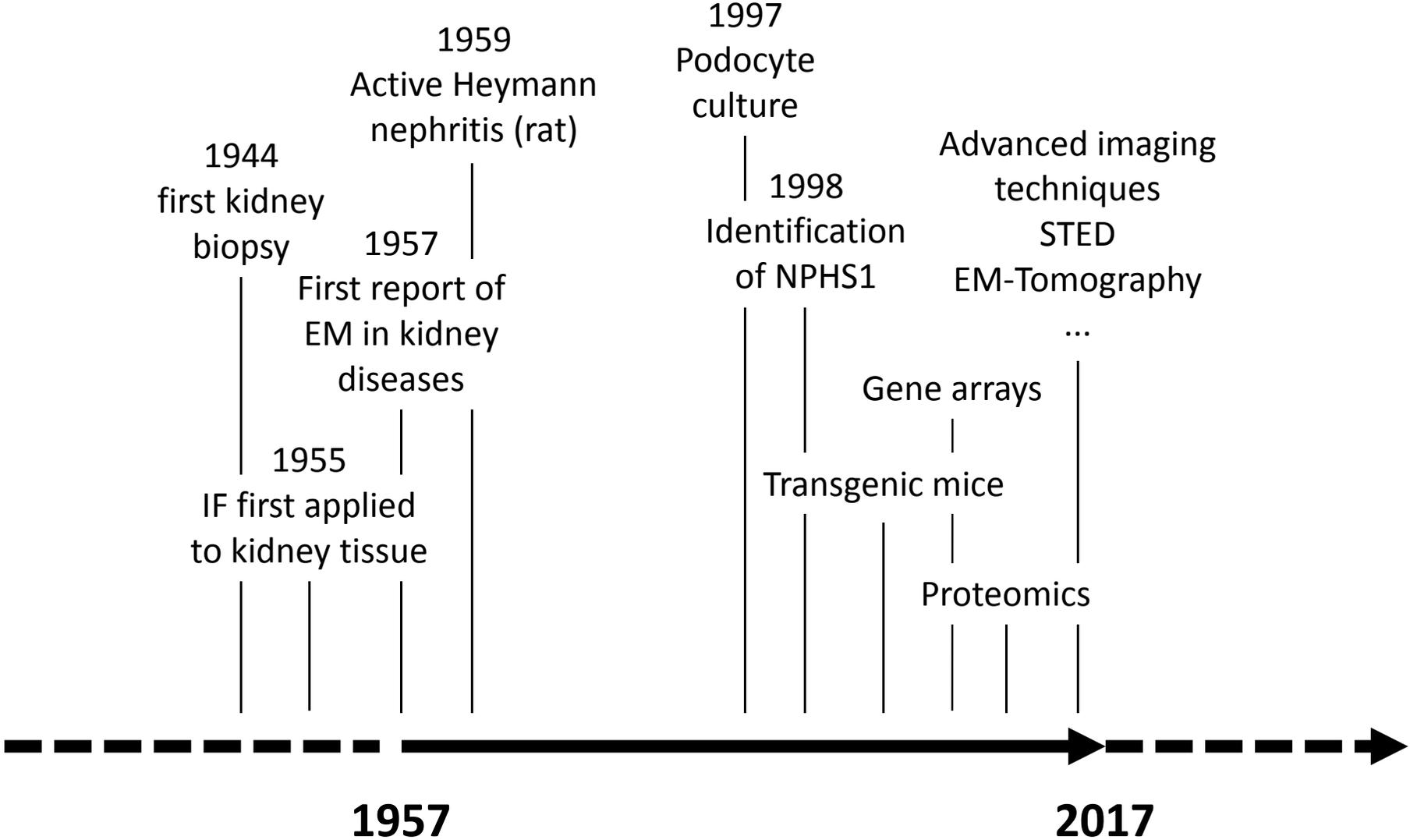
Rendered SD junctions with distance color code



functional genomics etc.

„morphologic era“

new morphologic era?



So ...

***... do we have to redefine
nephrology?***

... do we have to redefine nephrology?

- *Many publications about molecular mechanisms of glomerular injury in the last 2 decades*
- *But not much transfer into clinics yet...*

Stay cool!



Stay cool!

- *Be critical before translating basic science into clinical practice*
- *But stay tuned for novel developments!*

Thank you!

andreas.kistler@stgag.ch
www.nephrologie-thurgau.ch