

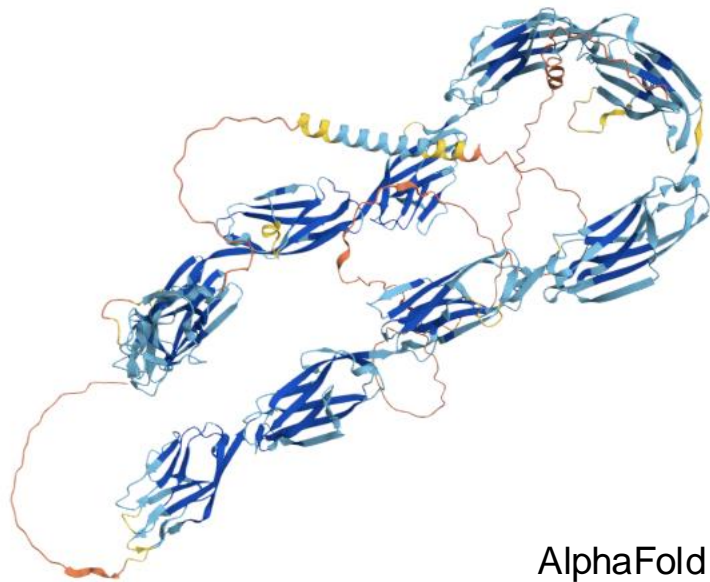
Minimal Change Nephropathie als Autoimmunerkrankung

Nicola M. Tomas
III. Medizinische Klinik und Poliklinik
UKE

Vortragshonorare: CSL Vifor, AstraZeneca, Medfora GmbH, StreamedUp

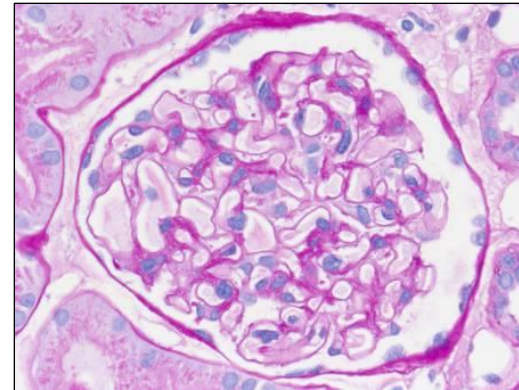
Beratung: Merida Bioscience

- Podozytopathien sind immunvermittelte Erkrankungen der Podozyten (MCD und primäre FSGS)
- Die Pathogenese ist unzureichend verstanden
- Nephrin ist ein integraler Bestandteil der podozytären Schlitzmembran

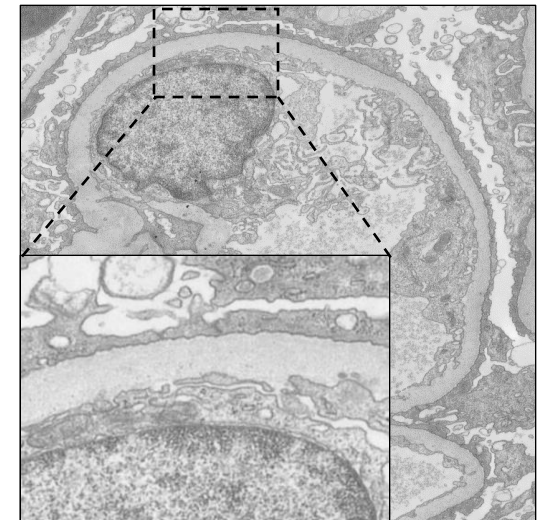
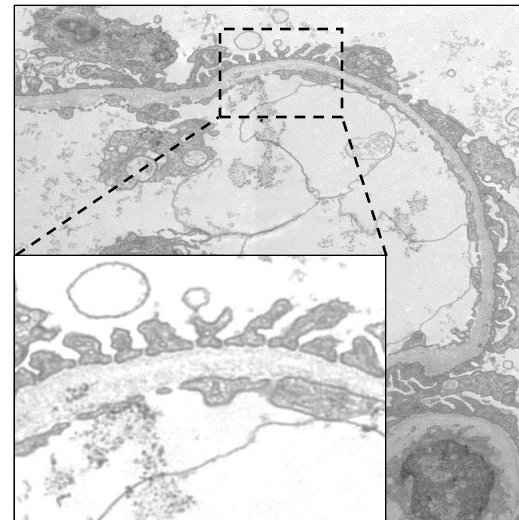
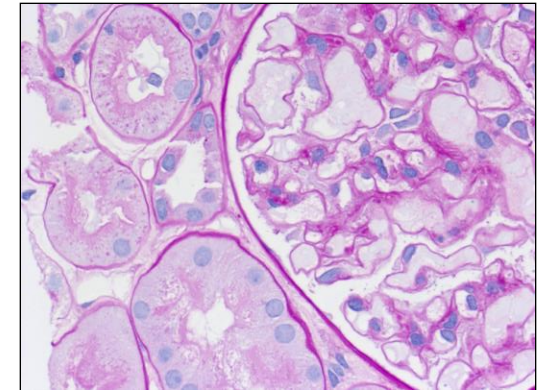


AlphaFold

Normal



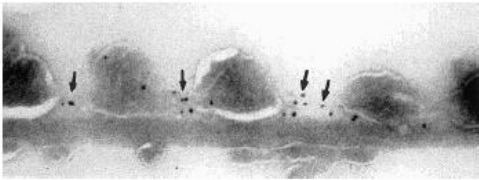
Podocytopathy / MCD



Bilder: Thorsten Wiech, Hamburg

Nephritogenic mAb 5-1-6 is directed at the extracellular domain of rat nephrin

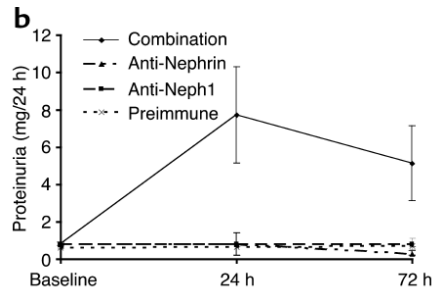
Peter S. Topham,¹ Hiroshi Kawachi,² Samir A. Haydar,¹ Sumant Chugh,¹ Theresa A. Addona,³ Kathryn B. Charron,³ Lawrence B. Holzman,⁴ Michael Shia,¹ Fujio Shimizu,² and David J. Salant¹



J. Clin. Invest. 104:1559–1566 (1999).

Nephrin and nephrin interaction in the slit diaphragm is an important determinant of glomerular permeability

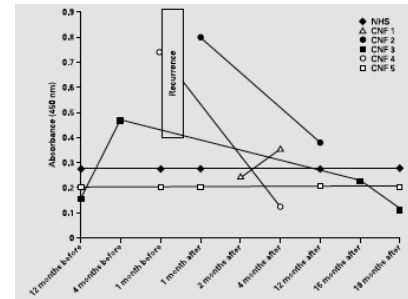
Gang Liu,¹ Beenu Kaw,² Jayson Kurfis,¹ Syed Rahmanuddin,¹ Yashpal S. Kanwar,³ and Sumant S. Chugh¹



J. Clin. Invest. 112:209–221 (2003).

Recurrence of Nephrotic Syndrome after Transplantation in CNF Is due to Autoantibodies to Nephrin

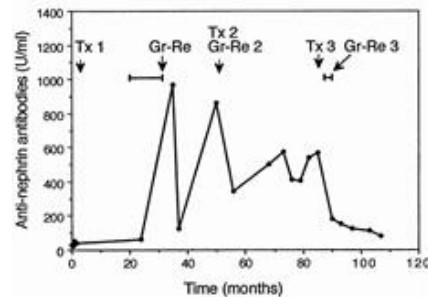
Shi-Xuan Wang Heikki Ahola Tuula Palmén Marja-Liisa Solin Pauliina Luimula Harry Holthöfer



Exp Nephrol 2001;9:327–331

CLINICAL TRANSPLANTATION RECURRENCE OF NEPHROTIC SYNDROME IN KIDNEY GRAFTS OF PATIENTS WITH CONGENITAL NEPHROTIC SYNDROME OF THE FINNISH TYPE

Role of Nephrin¹
Petrakka, Jaakko^{1,2}; Ruotsalainen, Vesa¹; Reponen, Paula¹; Oviit, Erik³; Laine, Jarmo²; Holmberg, Christer²; Tryggvason, Karfi²; Jalanko, Hannu^{2*}



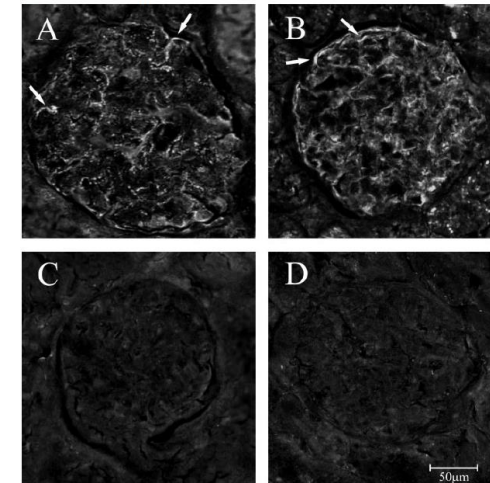
Transplantation 73(3):p 394-403, February 15, 2002.

Circulating antibodies to nephrin in patients with type 1 diabetes

Petri Aaltonen¹, Johanna Rinta-Valkama¹, Anu Päätti¹, Päivi Tossavainen², Tuula Palmén¹, Petri Kulmala², Mikael Knip³ and Harry Holthöfer¹

	Nephrin autoantibodies at diagnosis ^a	
	Positive	Negative
Age (years)	8.4 ± 3.4	8.2 ± 4.0
Male proportion	63%	66%
Systolic blood pressure (mmHg)	110 ± 12	110 ± 14
Diastolic blood pressure (mmHg)	72 ± 11	68 ± 9
Serum creatinine (μmol/l)	67 ± 13	67 ± 20
Blood glucose (mmol/l)	21.2 ± 6.9	21.5 ± 8.4
Glycated haemoglobin (%)	15.9 ± 3.4	14.5 ± 3.3
Blood pH	7.34 ± 0.08	7.35 ± 0.10
Ketosis present at diagnosis	88%	65%
C-peptide (nmol/l)	0.15 ± 0.06	0.18 ± 0.16
Initial insulin dose (U/kg/d)	0.46 ± 0.19	0.39 ± 0.20

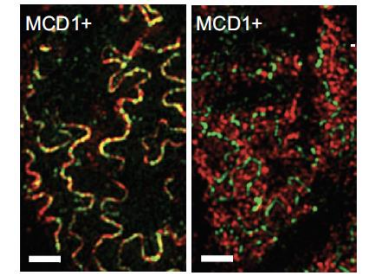
Nephrin antibodies in type 1 diabetes



Nephrol Dial Transplant (2007) 22: 146–153

Discovery of Autoantibodies Targeting Nephrin in Minimal Change Disease Supports a Novel Autoimmune Etiology

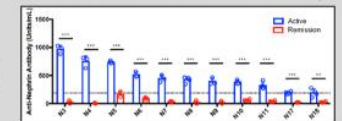
Andrew J.B. Watts^{1,2}, Keith H. Keller¹, Gabriel Lerner^{3,4}, Ivy Rosales⁵, A. Bernard Collins⁶, Miroslav Sekulic^{1,8}, Sushrut S. Waikar^{7,4}, Anil Chandraker², Leonardo V. Riella⁷, Mariam P. Alexander⁹, Jonathan P. Troost⁹, Junbo Chen³, Damian Fermin¹⁰, Jennifer L. Yee¹⁰, Matthew G. Sampson^{11,12}, Laurence H. Beck, Jr.^{1,4}, Joel M. Henderson⁷, Anna Greka^{2,12}, Helmut G. Rennke¹, and Astrid Weins^{1,2}



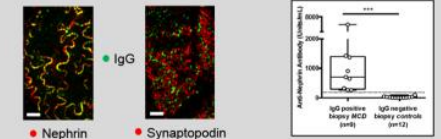
● IgG ● IgG
● Nephrin ● Synaptopodin

Circulating nephrin autoantibodies are present in almost 1/3 of patients with MCD in the NEPTUNE cohort and correlate with disease activity

29%
(18/62)

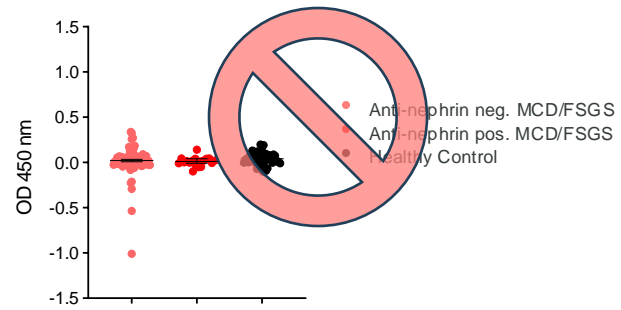


Nephrin autoantibodies are detectable both in serum and renal biopsies of patients with MCD

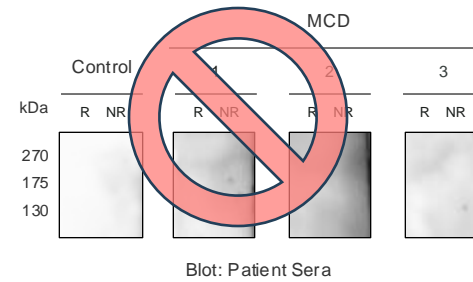


JASN 33: 238–252, 2022.

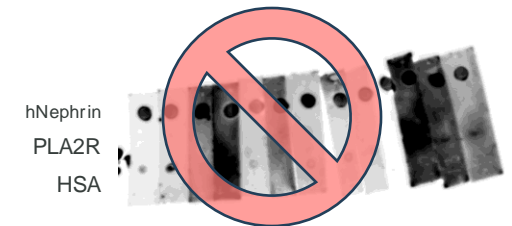
Conventional ELISA



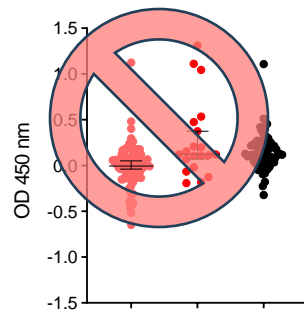
Straight WB



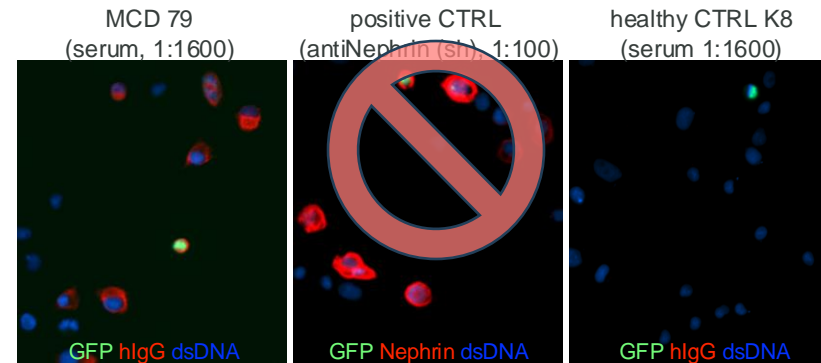
Biotin-Streptavidin-Enhanced Dotblot

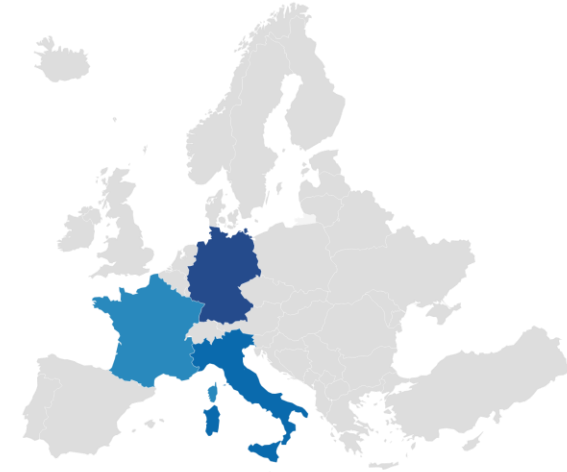
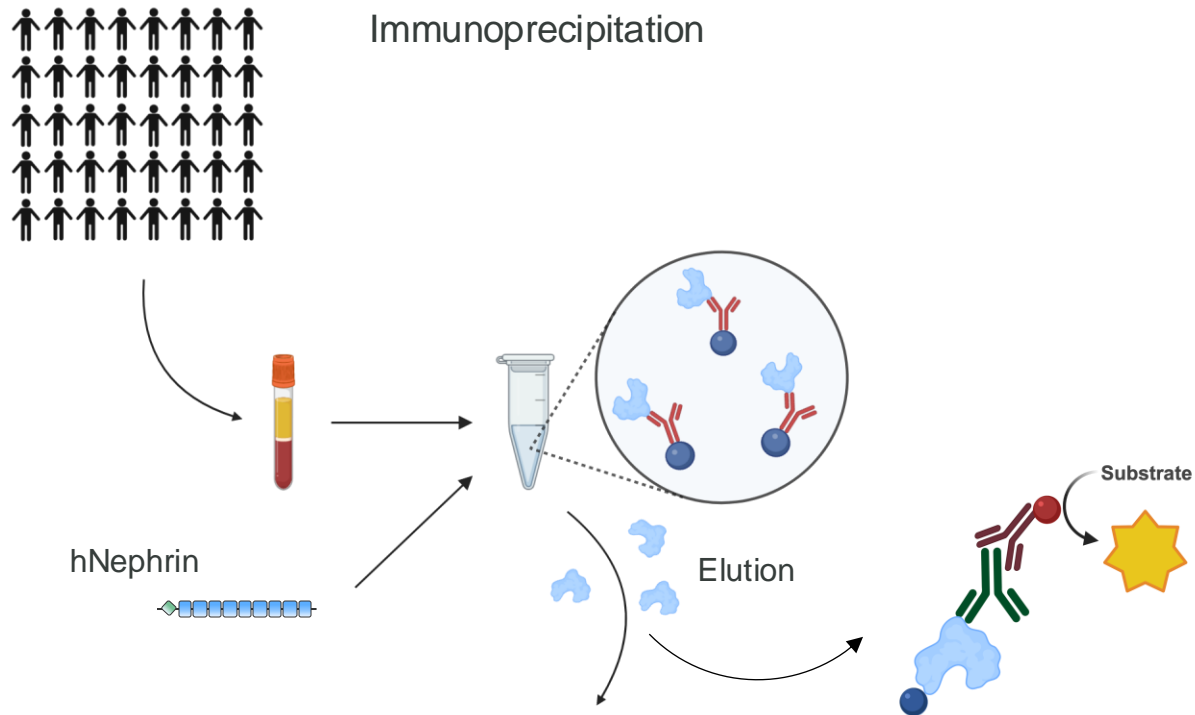


Biotin-Streptavidin-Enhanced ELISA



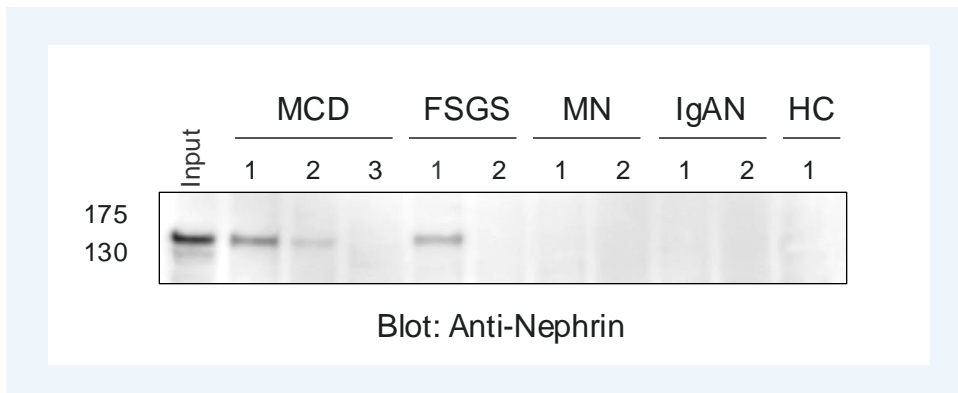
Immunofluorescence test



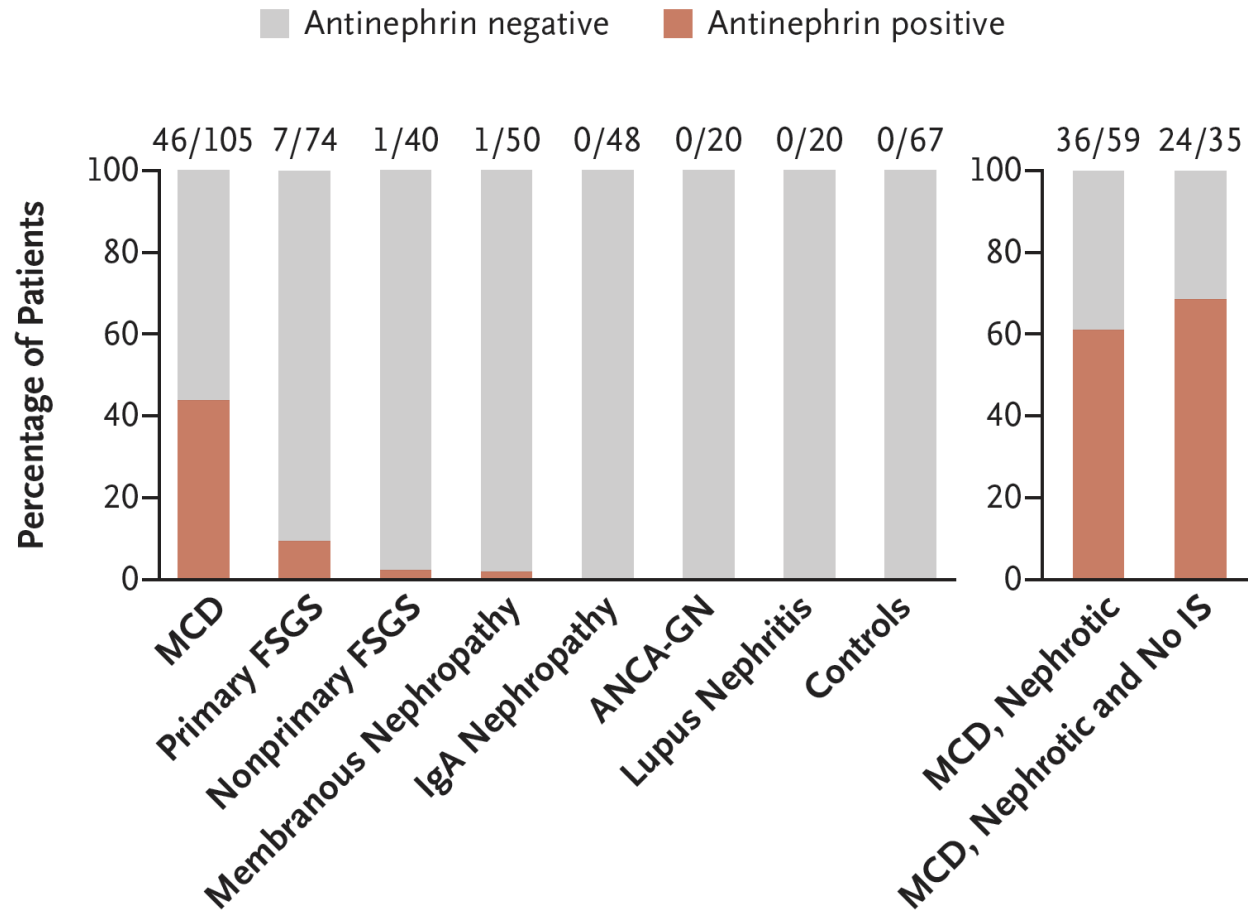


539 patients (357 adults and 182 children)
117 controls

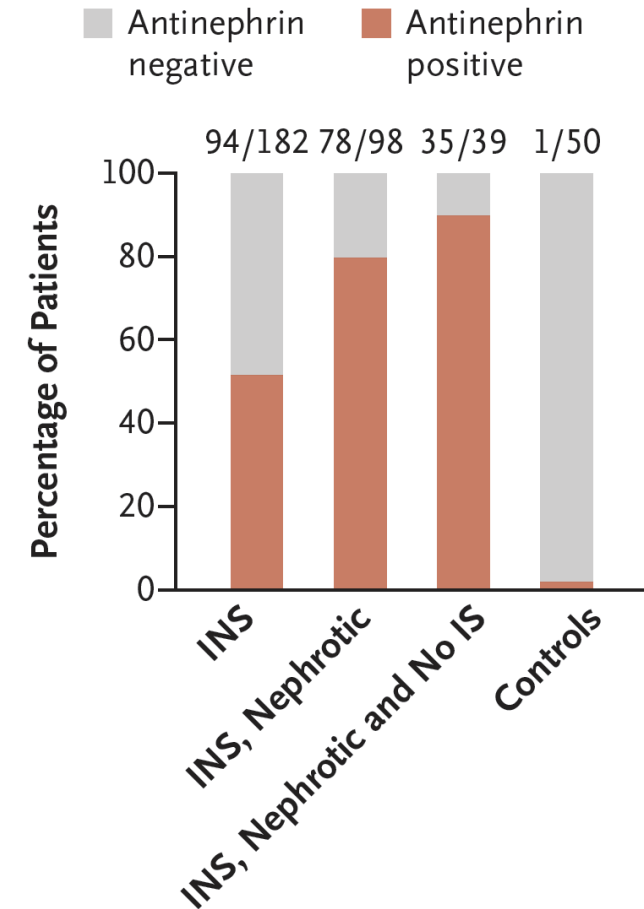
Minimal Change Disease	105
FSGS	114
Membranous Nephropathy	50
IgA Nephropathy	48
ANCA-GN	20
Lupus nephritis	20
Idiopathic Nephrotic Syndrome	182
Healthy Controls Adults	67
Control Children	50

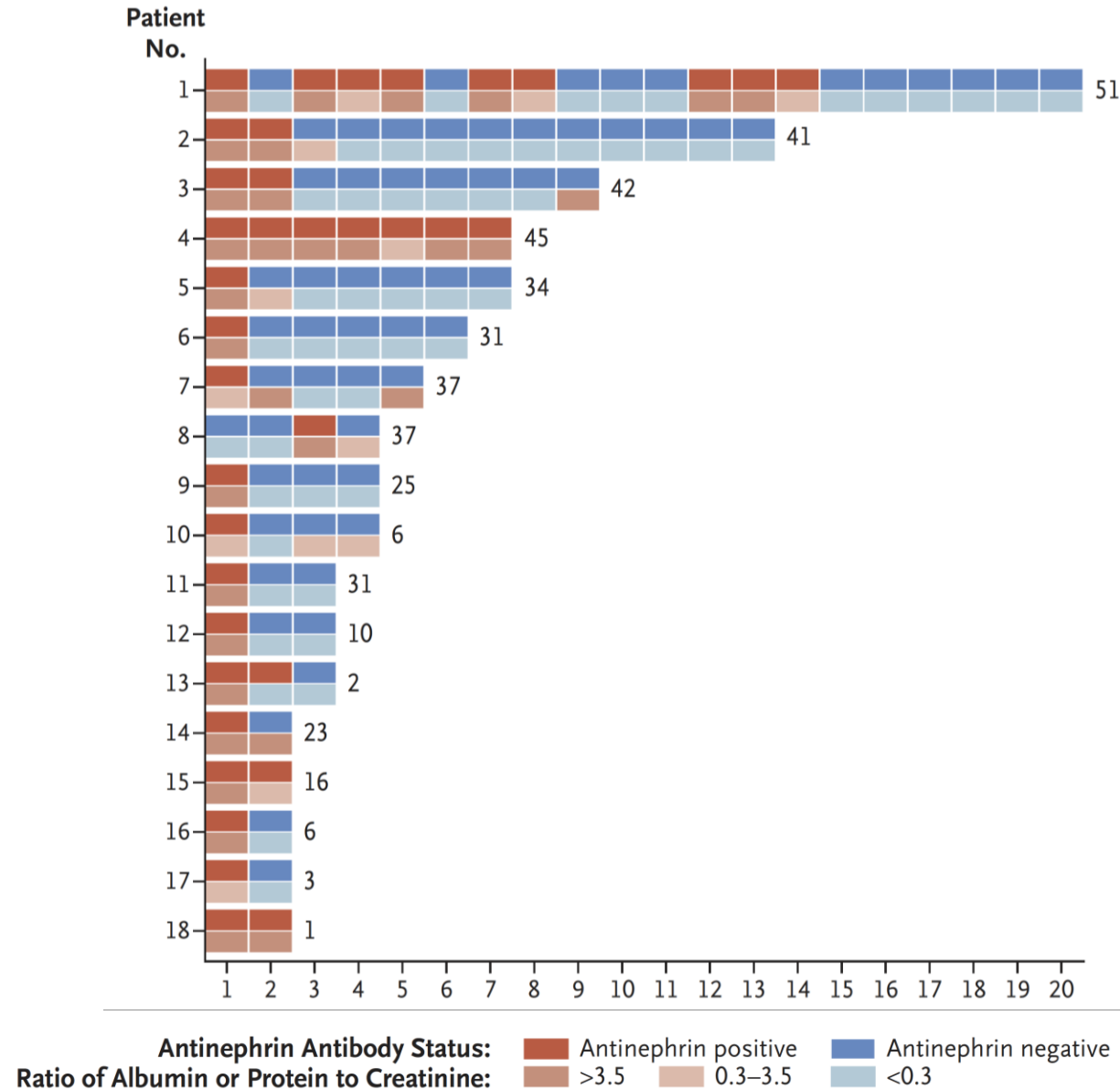


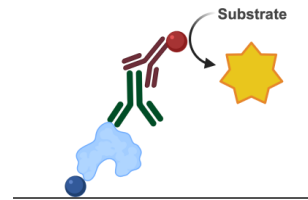
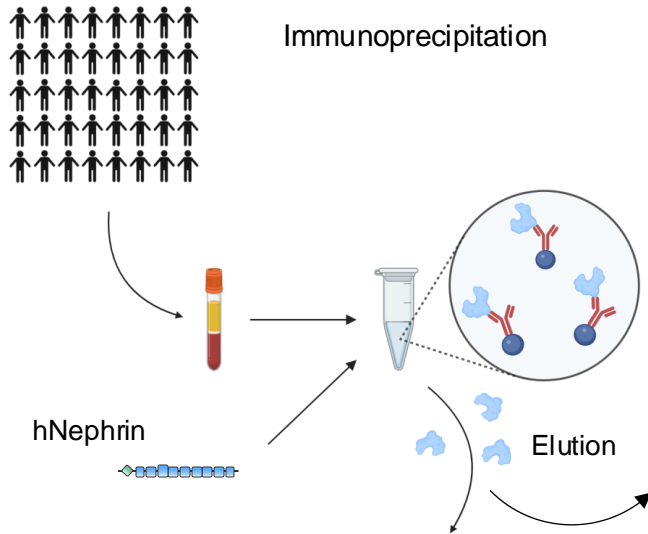
Erwachsene



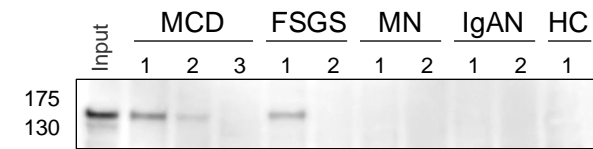
Kinder



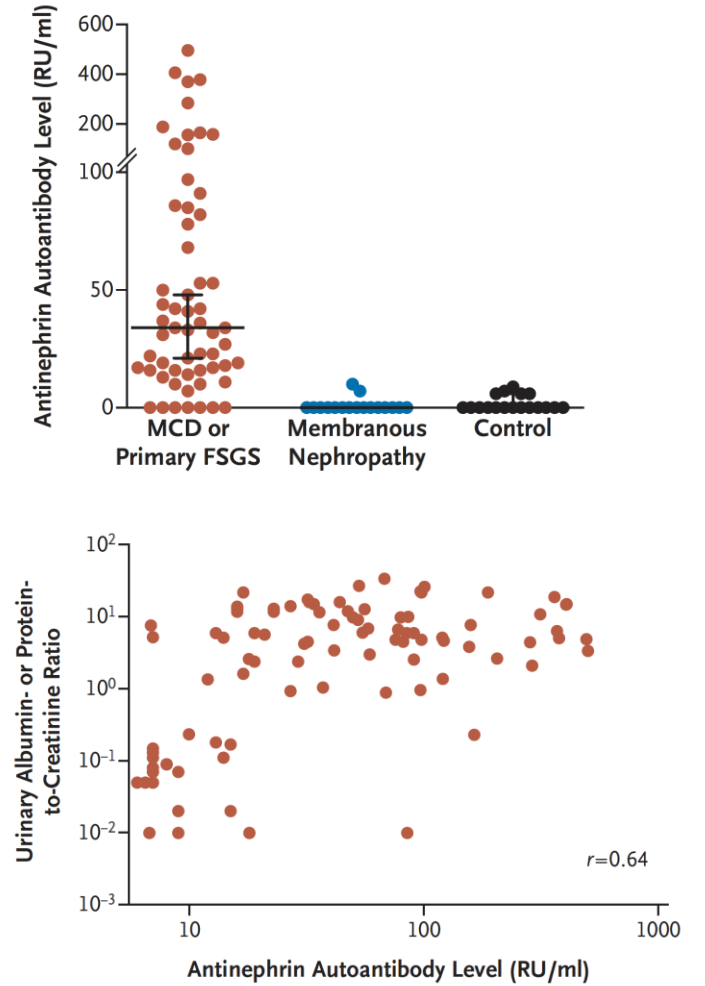


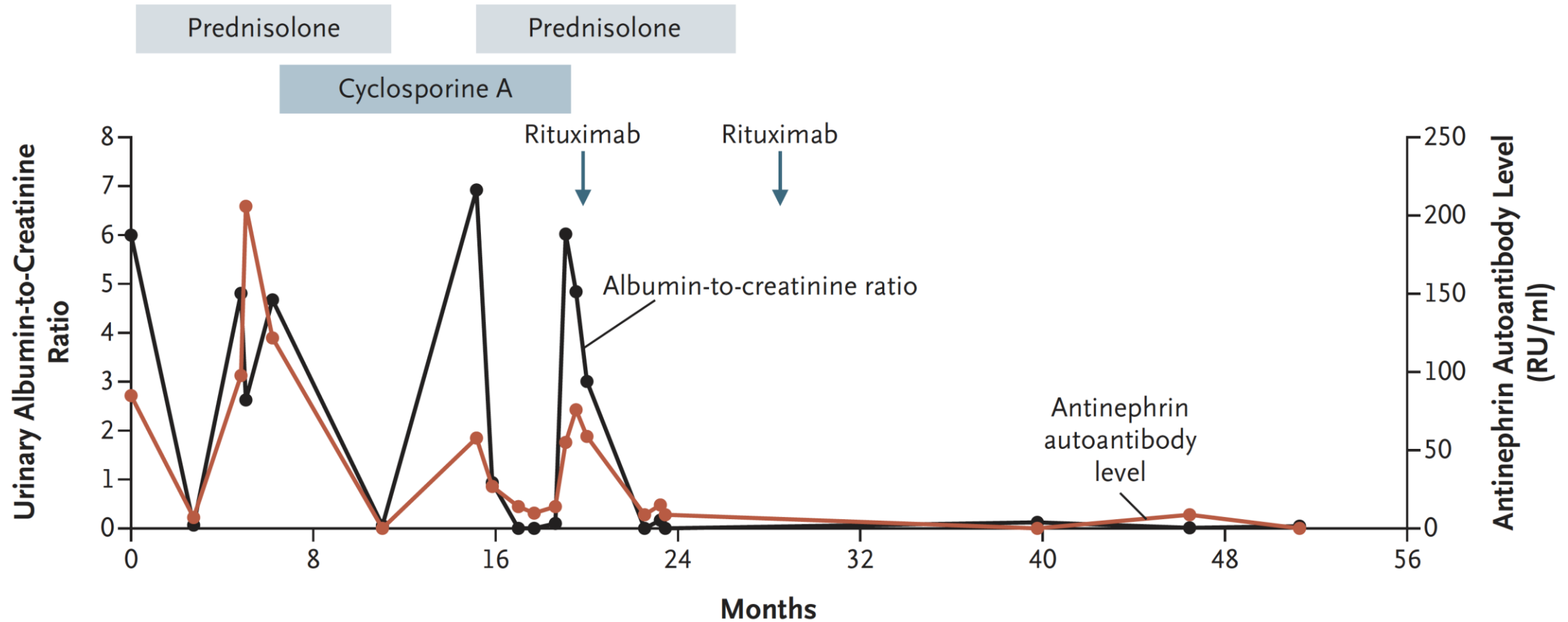


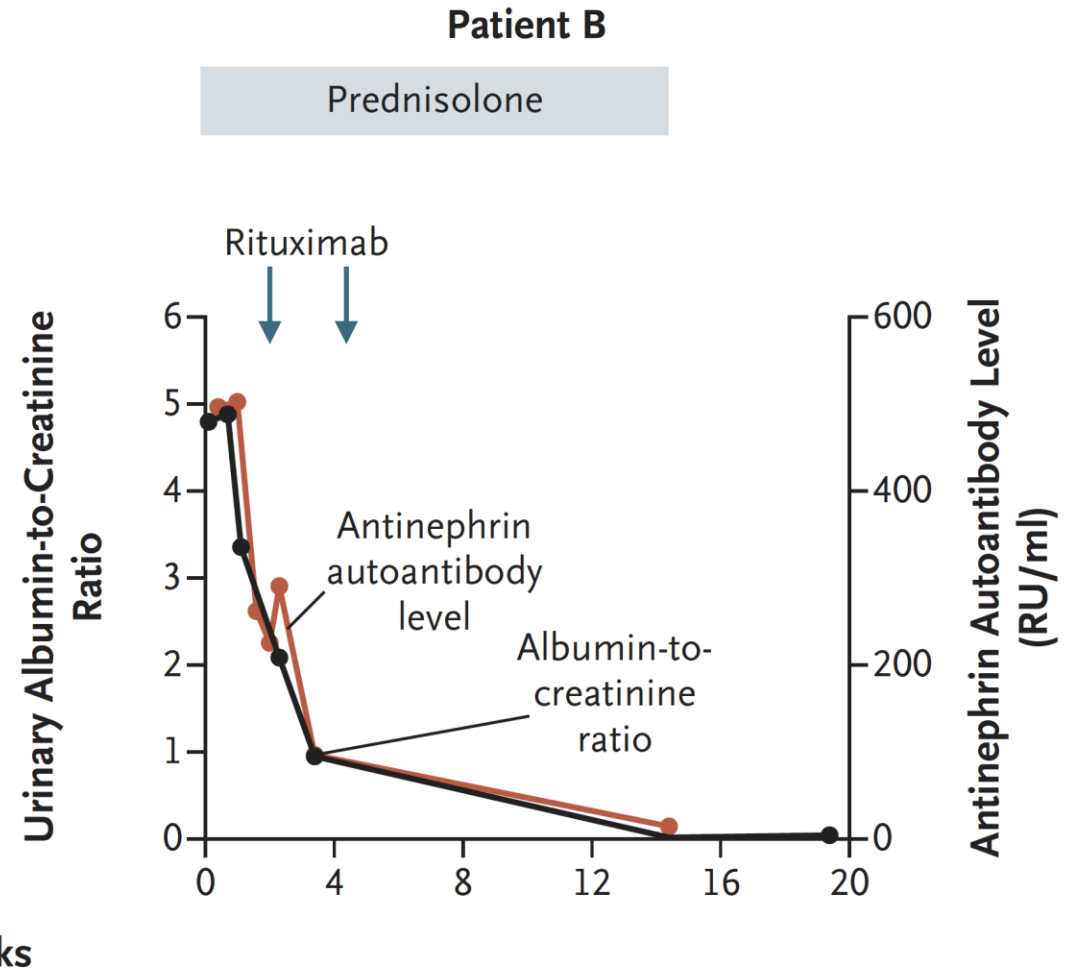
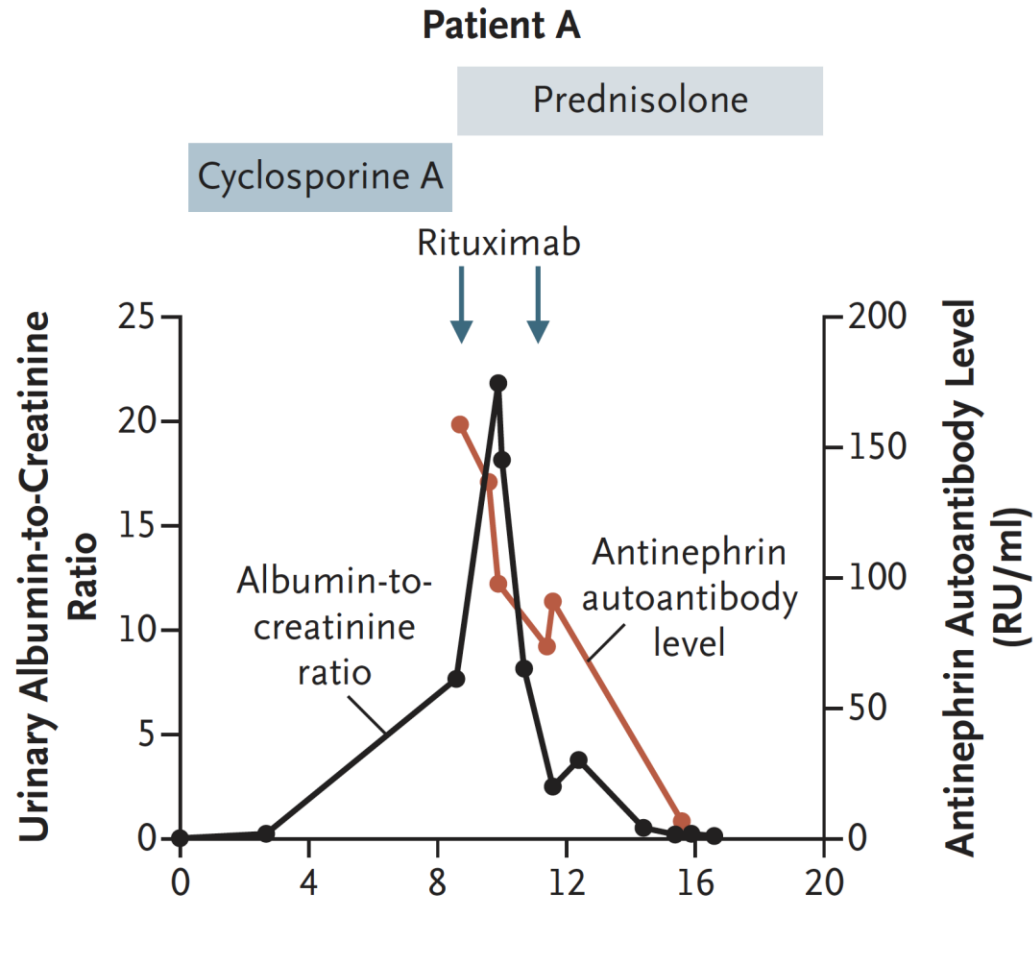
Nephrin
quantification



Blot: Anti-Nephrin

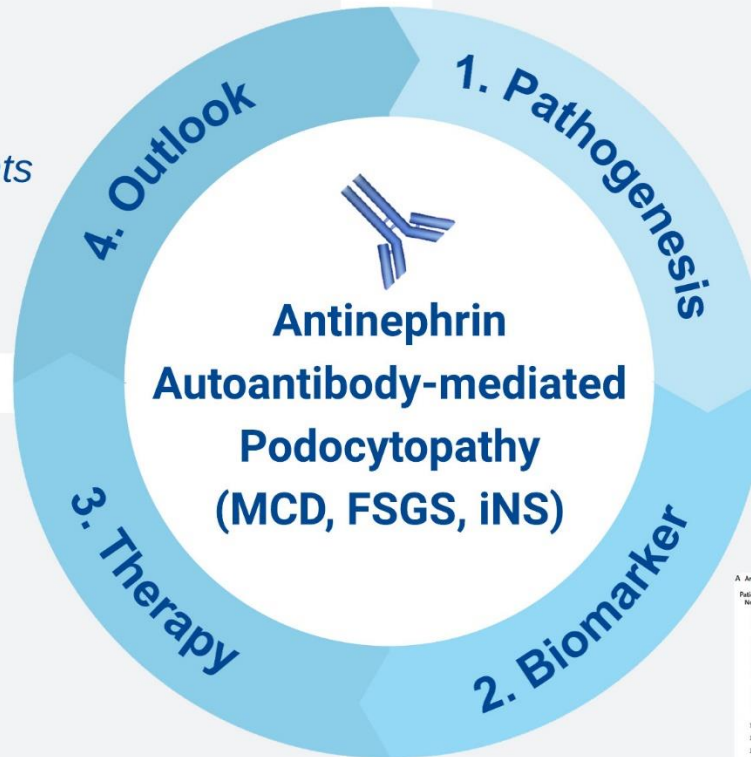
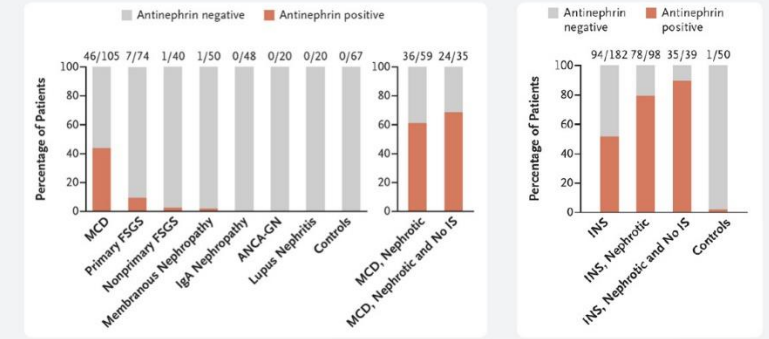




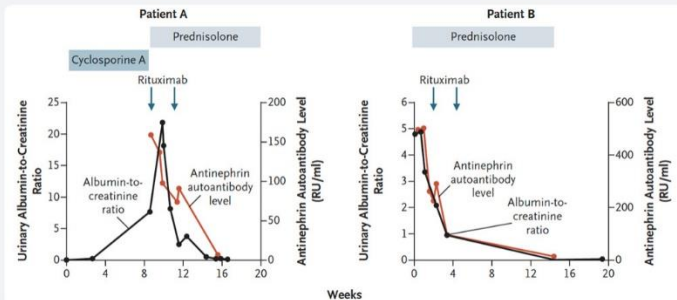


- **Diagnosis**
- **Monitoring** of disease course
- **Outcome prediction**
- **Therapy guidance**, e.g. *rNS* in *TX* Patients driven by Antinephrin Autoantibodies

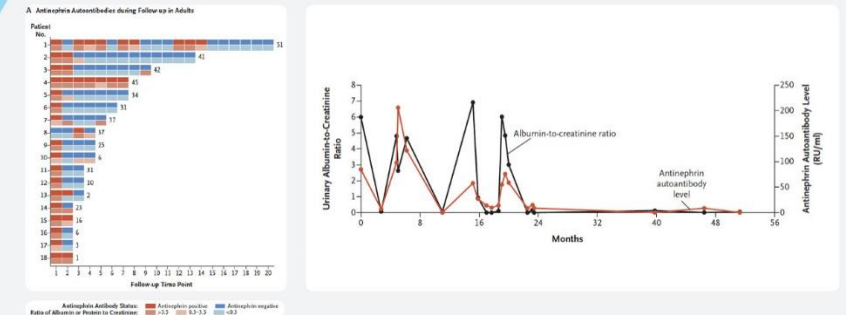
Antinephrin Autoantibodies are associated with Disease



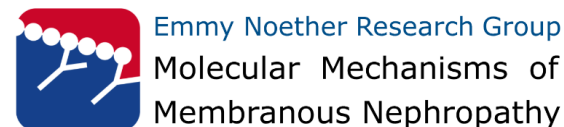
Antinephrin Autoantibody titers can be used for Therapy Guidance



Antinephrin Autoantibodies correlate with Disease Activity



- Anti-Nephrin Autoantikörper finden sich bei einem substantiellen Teil der Patientinnen und Patienten mit der histologischen Diagnose einer MCD
- Die Autoantikörper sind an der Pathogenese beteiligt
- Die Autoantikörper sind mit einem guten Therapieansprechen assoziiert



UKE

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Anke Diemert
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Ming Huang
Sybille Köhler
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