

# **2. DACH ANCA VASKULITIS FORUM 2024**

**22. & 23. NOVEMBER 2024 | MÜNCHEN**

**CSL Vifor**

## **Biomarker in der Therapie der AAV**

**PD Dr. Stefan Schunk**



**Bamberg**





**Sozialstiftung Bamberg**  
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# 2. DACH ANCA-Vaskulitis Forum 2024

## Biomarker in der Therapie der AAV

**PD Dr. med. Stefan J. Schunk**

**Chefarzt – Medizinische Klinik III**

**Nieren- und Hochdruckkrankheiten, Rheumatologie,  
Akutgeriatrie**

# Interessenskonflikte

Datum	Veranstaltung
22.11.2024	Vifor - 2. DACH ANCA-Vaskulitis Forum 2024 – München „Biomarker in der Therapie der AAV“
26.10.2024	Novartis – Öpidmanagement in Klinik und Praxis – Bamberg „Sicherstellungspartner Nephrologie: Ateriosklerose als Systemerkrankung“
29.09.2024	16. Jahrestagung der DGFN – Berlin „Dickkopf 3: Stellenwert für Diagnostik und Prognose“
27.09.2024	16. Jahrestagung der DGFN – Berlin „DKK3 – from patient to lab“
06.06.2024	34. Wissenschaftliches- und Pflegesymposium des Nephrologischen Arbeitskreises Saar-Pfalz-Mosel – Völklingen „Nephrologische Fachpflege – stirbt sie aus?“
06.06.2024	34. Wissenschaftliches- und Pflegesymposium des Nephrologischen Arbeitskreises Saar-Pfalz-Mosel – Völklingen „Update Dialyse im Krankenhaus und Intensivstation“
04.05.2024	21. Erfurter Experten-Meeting „CKD-Progressionshemmung: besser gesteuert mit DKK3?“ online
19.04.2024	Seminar der Jungen Nierenkranken Deutschland e.V. „CKD-Progression und DKK3“ online
21.03.2024	55. Jahrestagung der Gesellschaft für Pädiatrische Nephrologie „DKK3 im Urin zeigt eine kurzfristige Verschlechterung der Nierenfunktion bei Kindern mit CKD an und identifiziert Patienten, die von nephroprotektiven Interventionen profitieren“
07.02.2024	GSK – online „Lupus Nephritis zielgerichtet behandeln“
26.01.2024	Doctorflix – Berlin „Akutes Nierenversagen“ „Progression bei chronischer Nierenerkrankung“
18.11.2023	Jahresgespräch der DN – Köln „Steuerung CKD-Progression mit DKK3 – wo stehen wir?“
07.10.2023	15. Jahrestagung der DGFN – Berlin „DKK3 im Urin zeigt eine kurzfristige Verschlechterung der Nierenfunktion bei Kindern mit CKD an und identifiziert diejenigen, die von nephroprotektiven Interventionen profitieren“
06.10.2023	15. Jahrestagung der DGFN – Berlin „DKK3 – ein Werkzeug zum Progressionsmonitoring“
17.06.2023	ERA – Milan Chair „End Stage Kidney Disease, Haemodialysis, Kidney function replacement Therapies“ und Chair „Dialysis“
16.06.2023	ERA – Milan Chair „AKI and intensive care nephrology“
11.04.2023	GSK Nierenwerkstatt (virtuell) „Diagnostik und Steuerung der CKD-Progression“

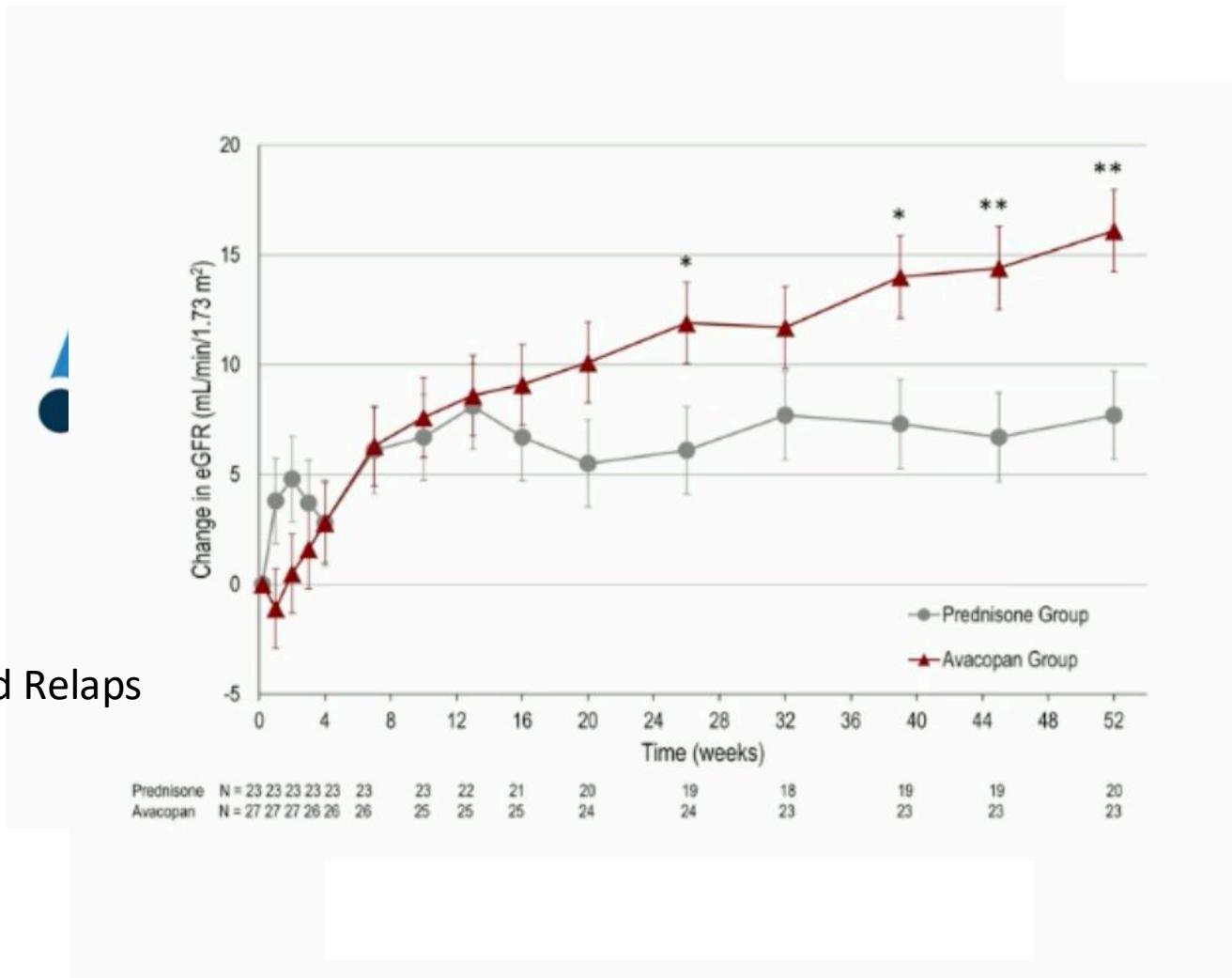
## Prognostische Marker der ANCA-Vaskulitis



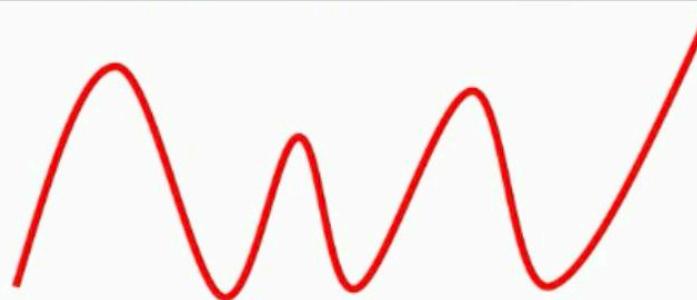
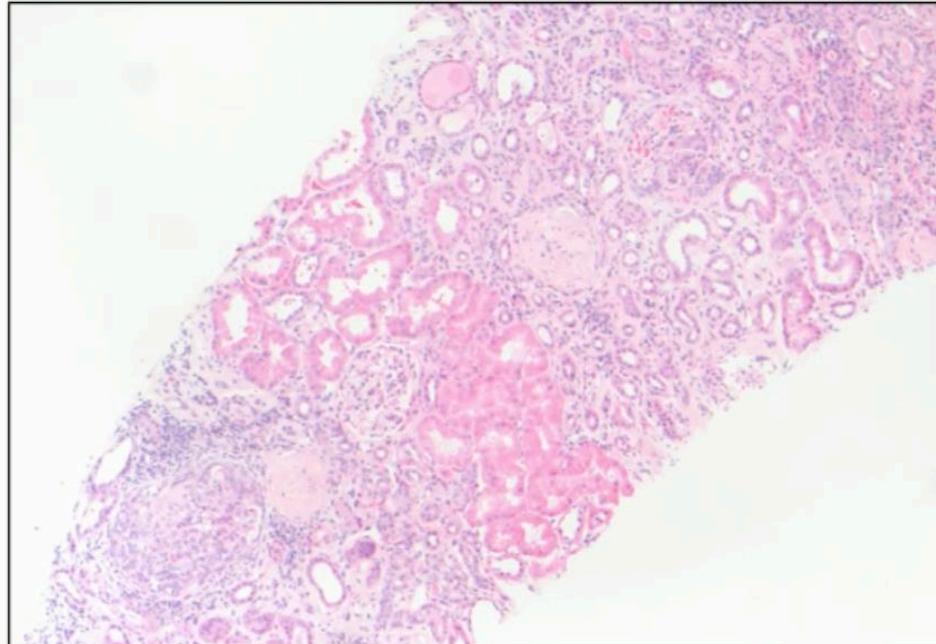
**Dialyse and Tod**

# Prognostische Marker der ANCA-Vaskulitis

Verbesserung und Relaps

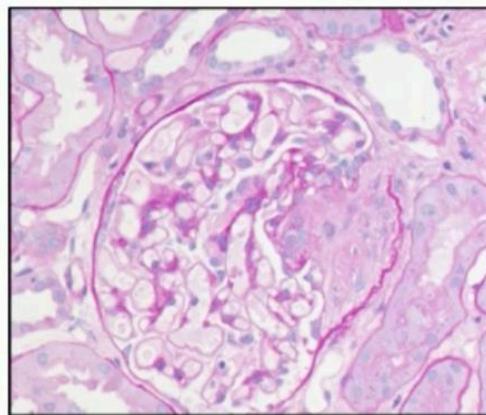


## (Verlaufs-)Formen der Erkrankung



**Chronisch relapsierende,  
sog. chronic relapsing GPA**

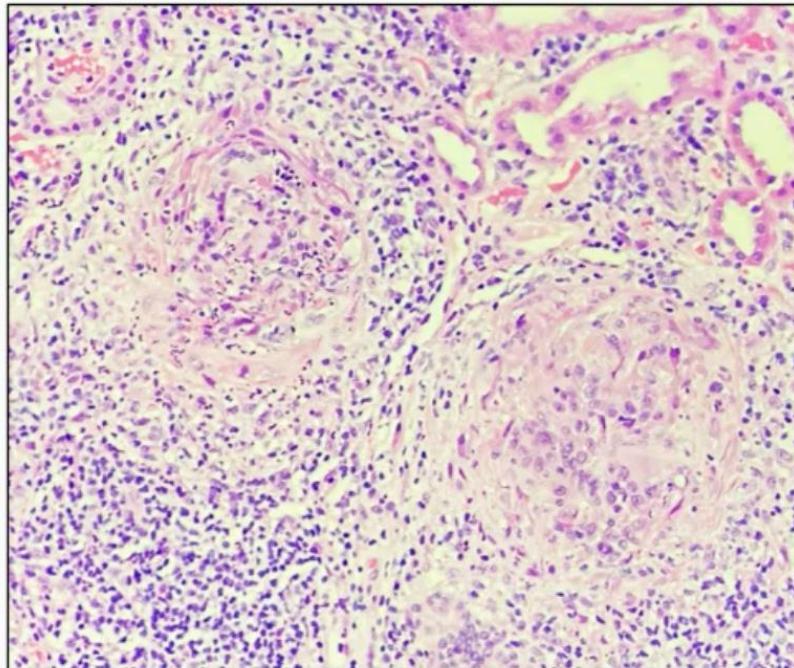
## (Verlaufs-)Formen der Erkrankung



Langsam vernarbende,  
sog. slowly sclerosing MPA

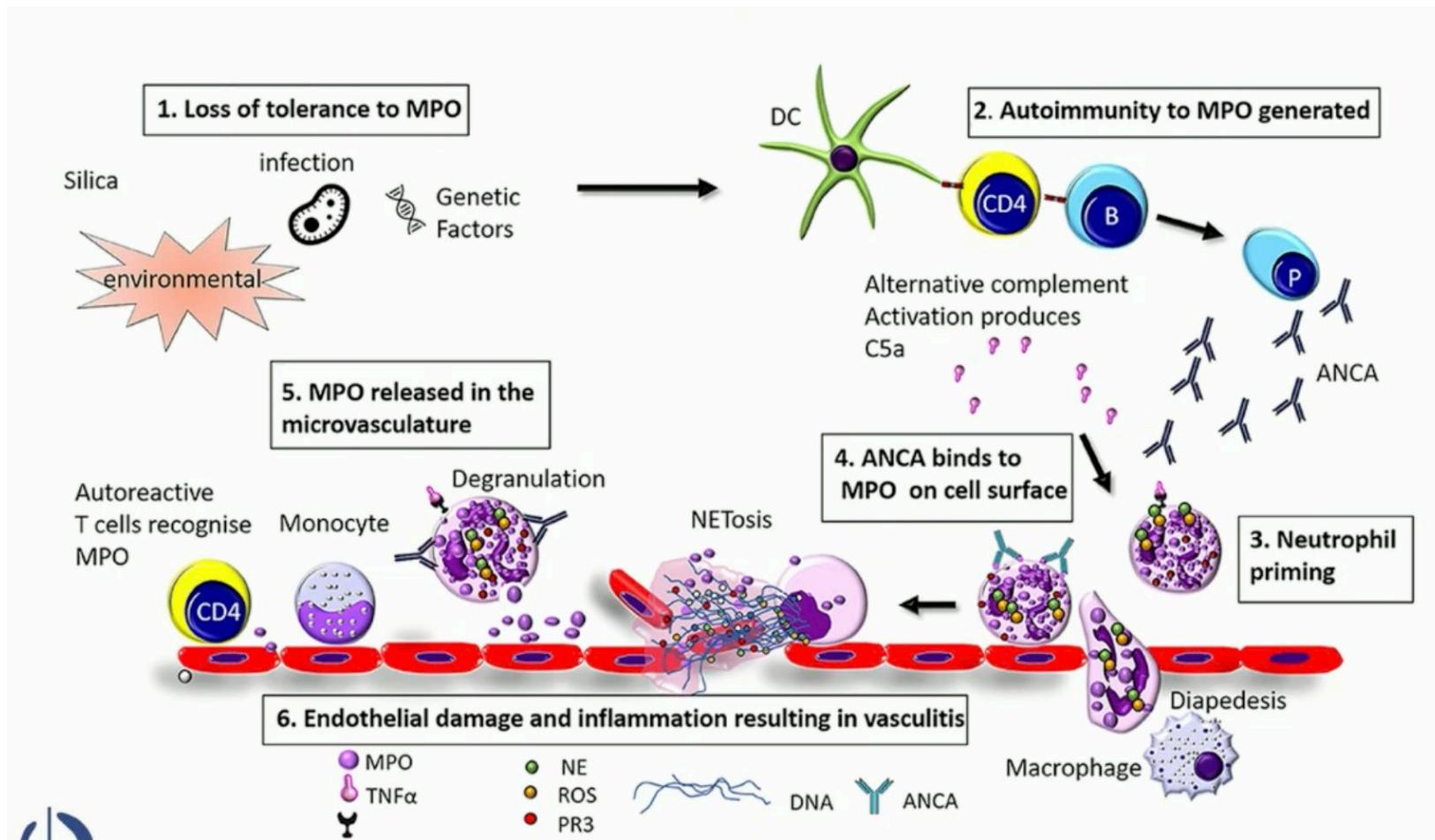


## (Verlaufs-)Formen der Erkrankung

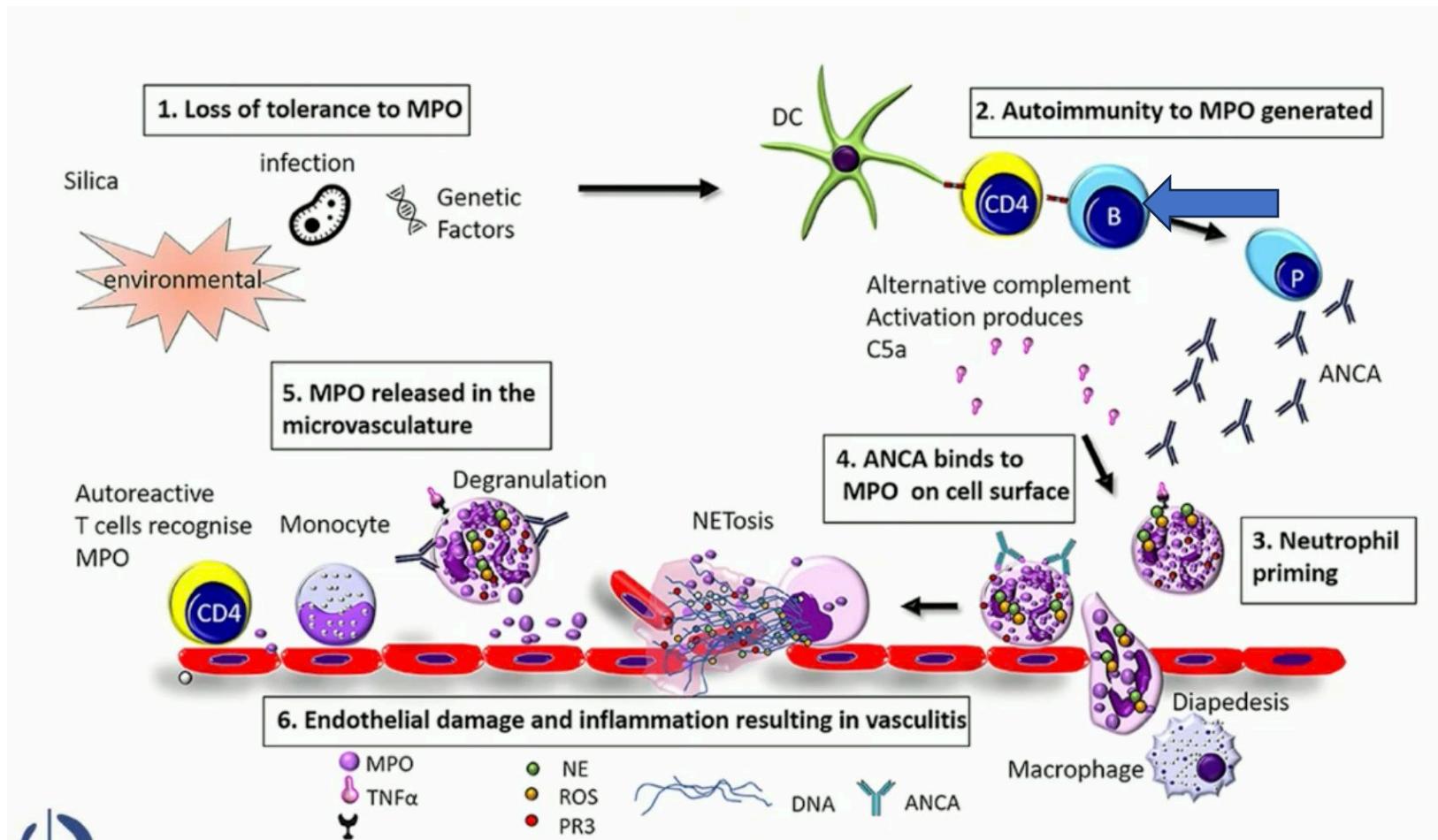


**Rasch Progressive Nekrotisierende  
Halbmond Glomerulonephritis**

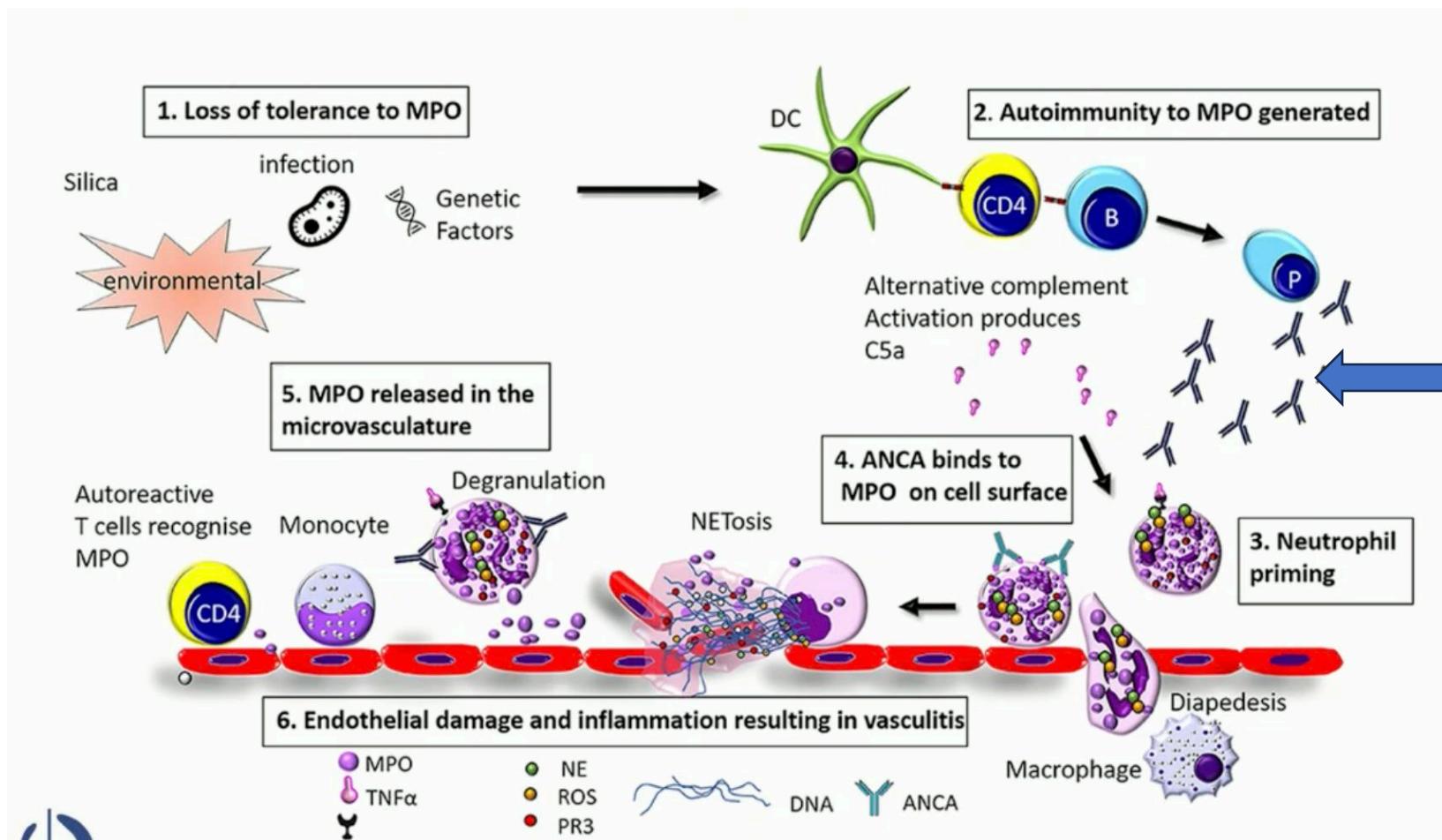
# Potentielle Biomarker der ANCA - Vaskulitis



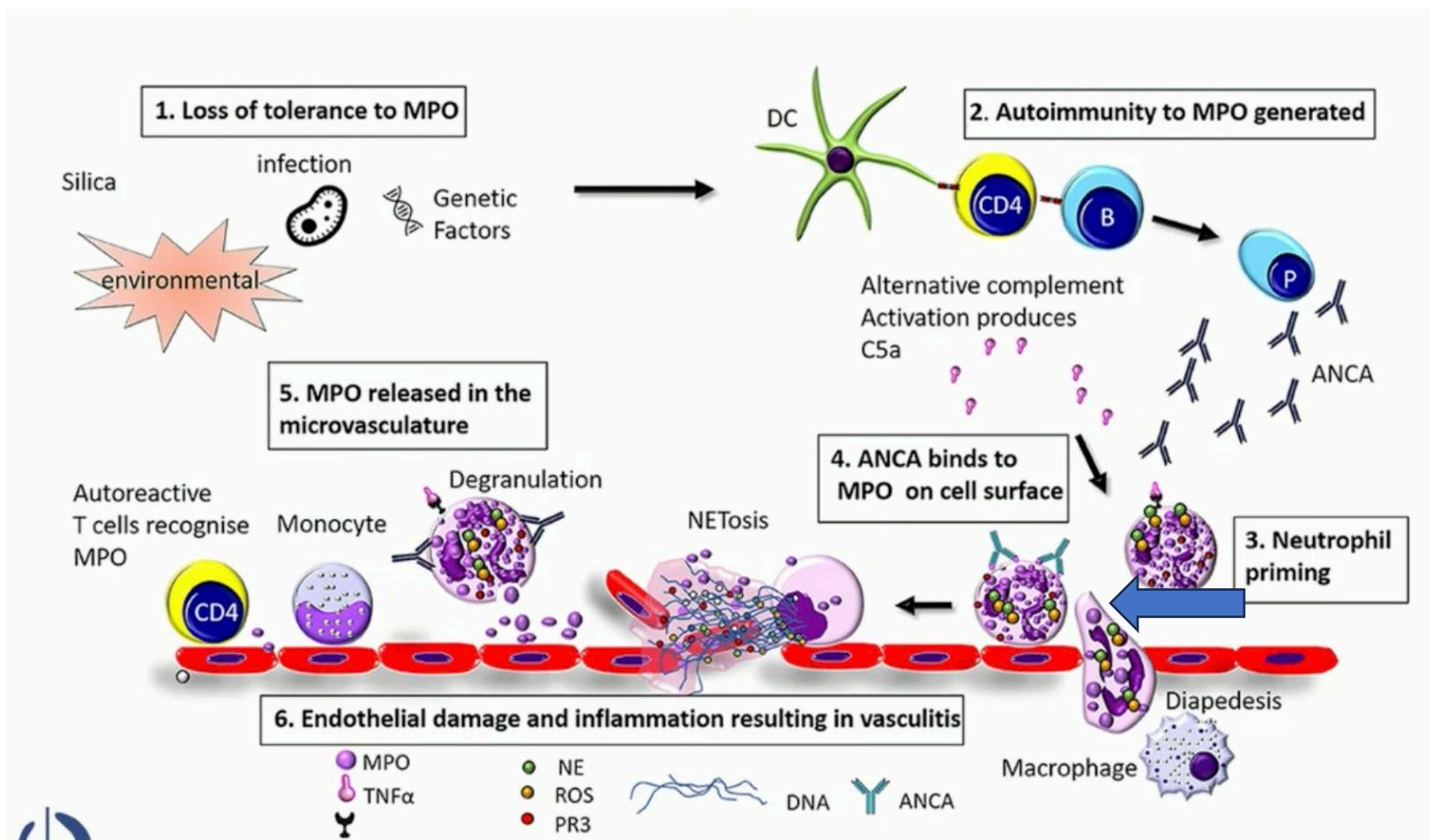
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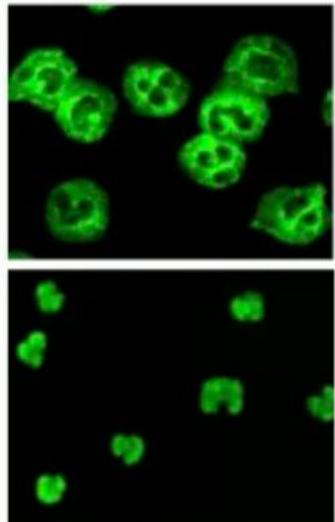
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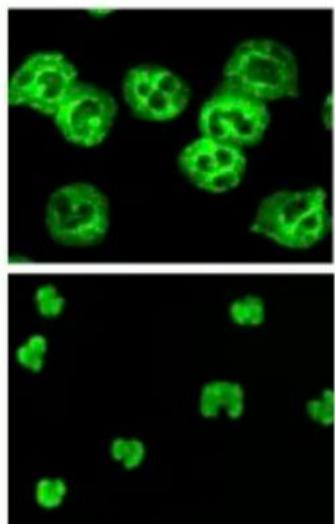
## ANCA



## MPO und PR3

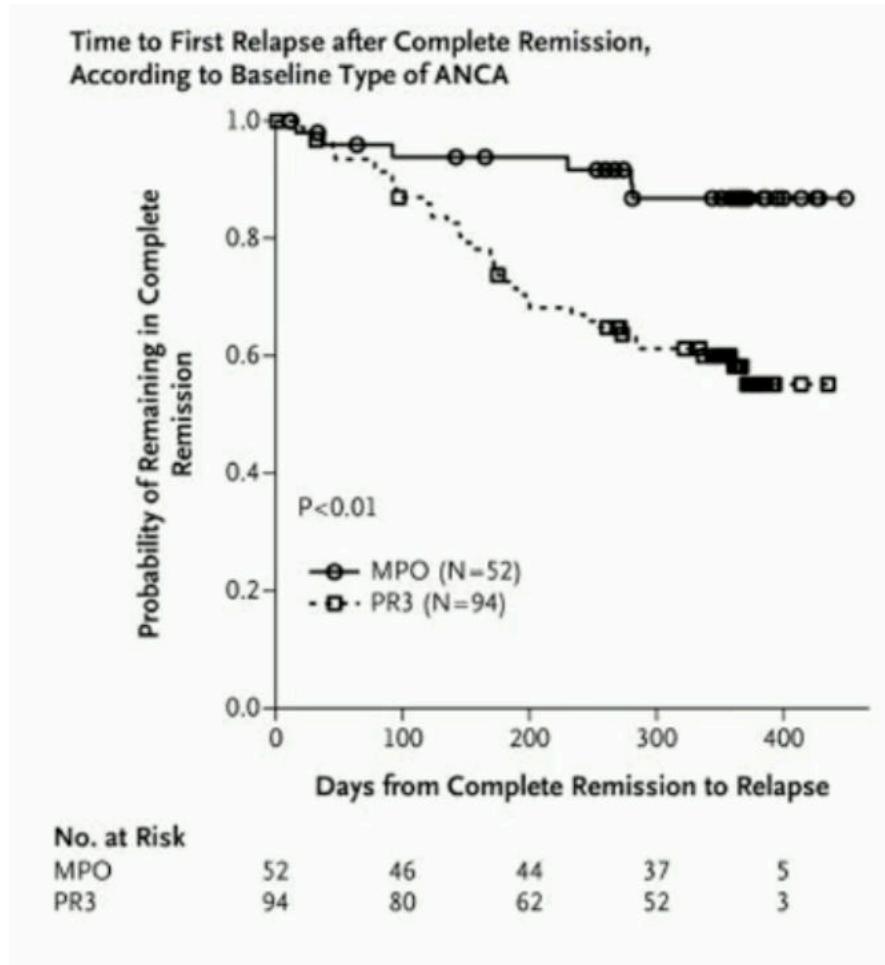
Specks U et al., NEJM 2010

# ANCA



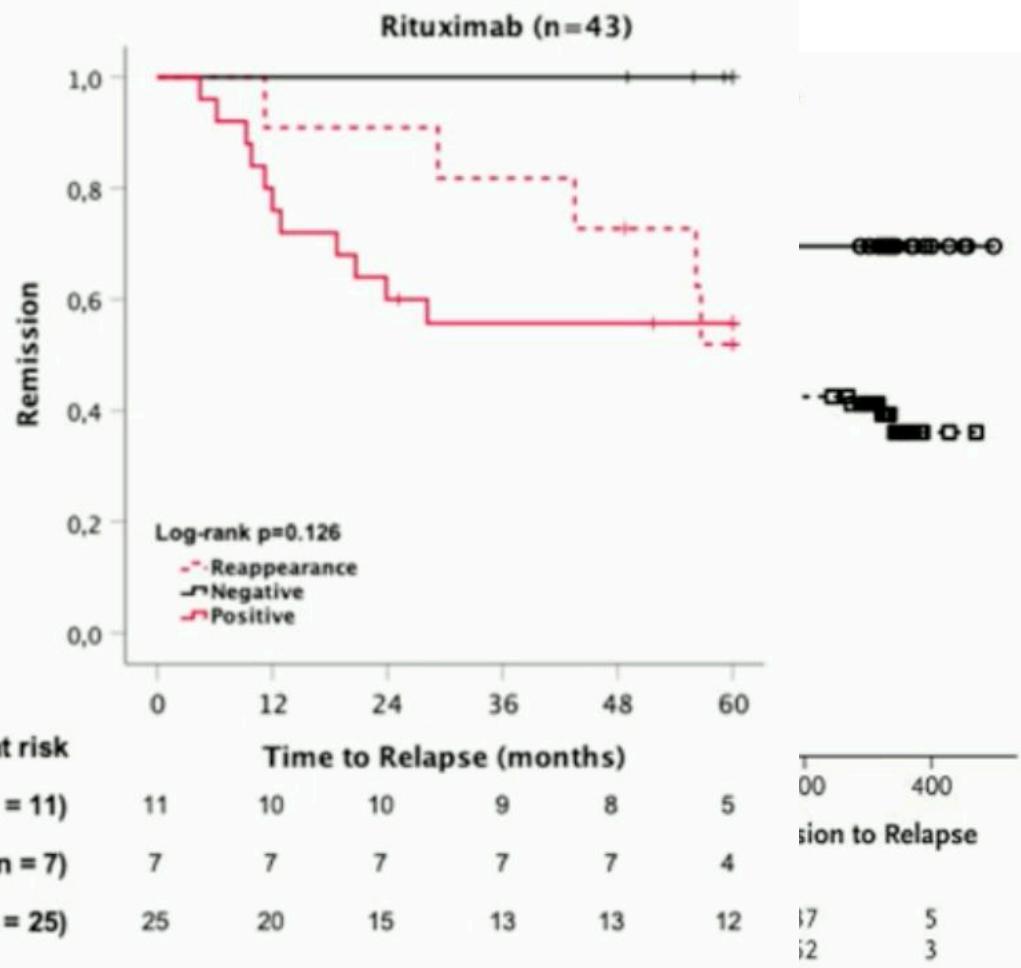
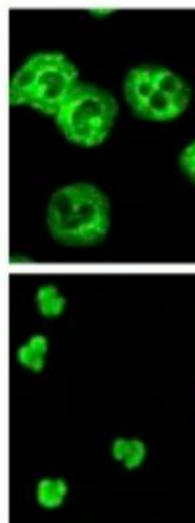
## MPO und PR3

Specks U et al., NEJM 2010



Moura MC et al., CJASN 2023

## ANCA



MPO un

Specks U et al., NEJM 2010

Moura MC et al., CJASN 2023

## BVAS

8. Renal	None <input type="checkbox"/>
Hypertension	
Proteinuria >1+	
● Haematuria $\geq 10$ RBCs/hpf	
Serum creatinine 125-249 $\mu\text{mol/L}$ (1.41-2.82mg/dl)	
Serum creatinine 250-499 $\mu\text{mol/L}$ (2.83-5.64mg/dl)	
● Serum creatinine $\geq 500 \mu\text{mol/L}$ ( $\geq 5.66\text{mg/dl}$ )	
● Rise in serum creatinine $>30\%$ or fall in creatinine clearance $>25\%$	

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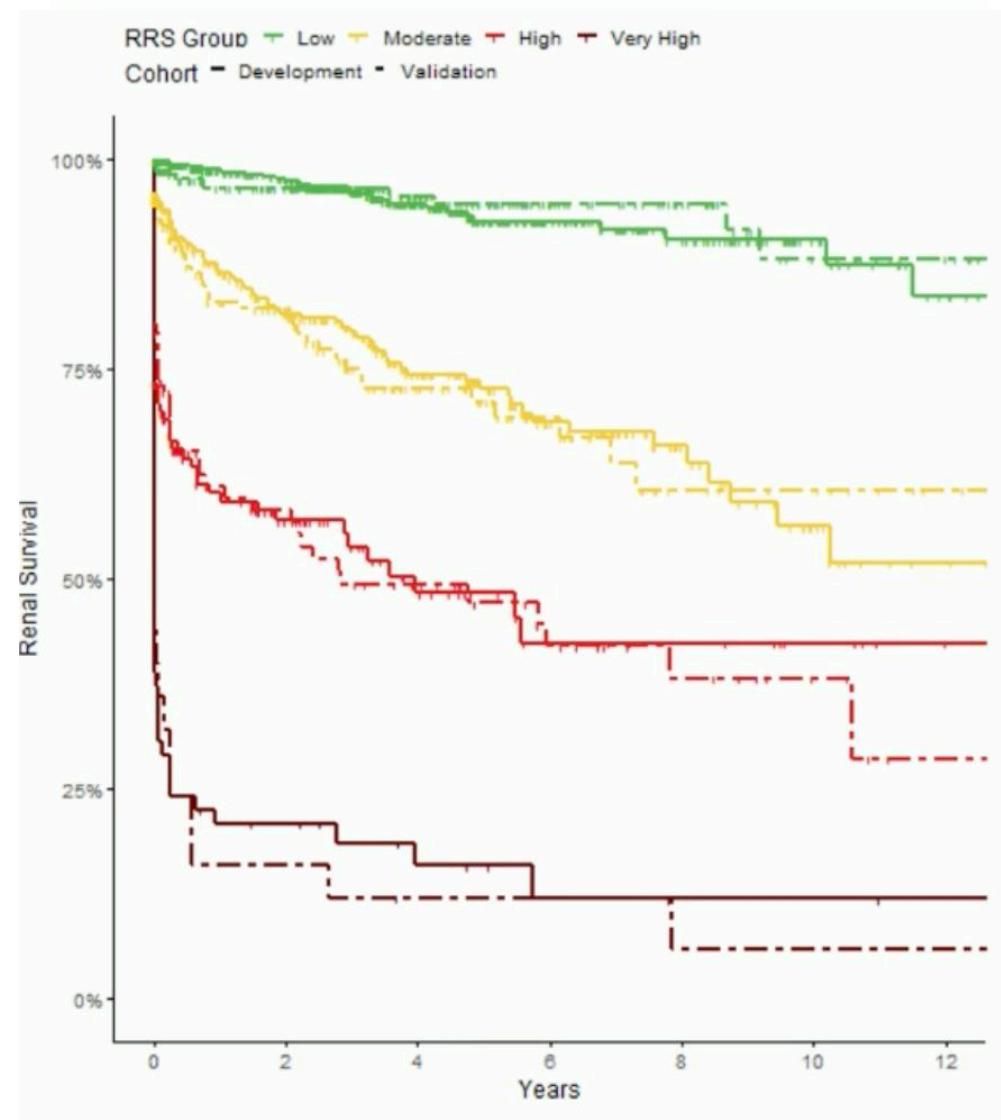
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● Rise in serum creatinine $>30\%$ or fall in creatinine clearance $>25\%$	
<input checked="" type="checkbox"/>	
PERSISTENT DISEASE ONLY: (Tick here if all the abnormalities are due to persistent disease)	

## ANCA kidney risk score (AKRiS)

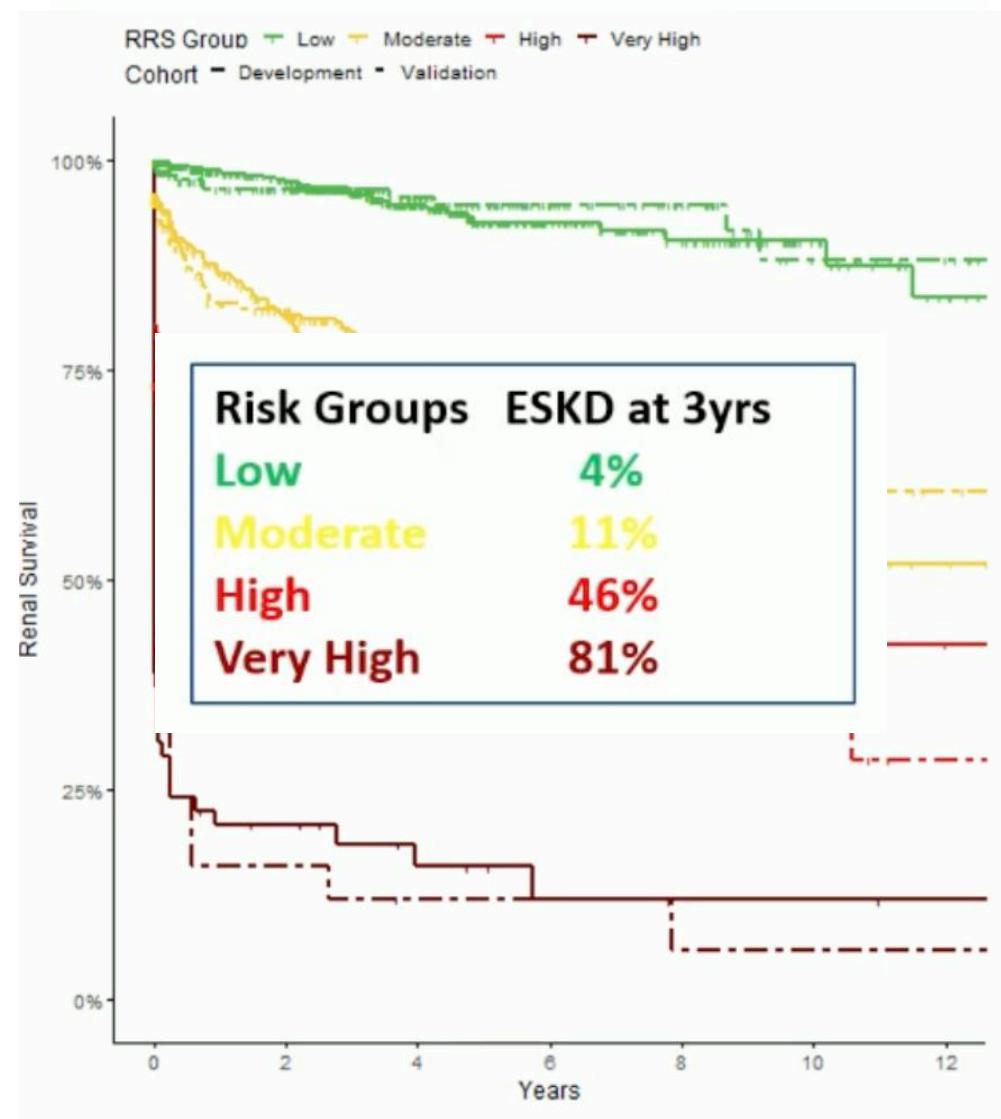
AKRiS	Points
Creatinine ( $\mu\text{mol/l}$ )	
K0: < 250	0
K1: 250 – 450	4
K2: > 450	11
Normal Glomeruli (%)	
N0: > 25	0
N1: 10 – 25	4
N2: < 10	7
IFTA (%)	
T0: none and mild, < 25%	0
T1: $\geq$ mild - moderate, $\geq 25\%$	2

Risk Group	Points
Low	0 – 4
Moderate	5 – 11
High	12 – 18
Very High	21

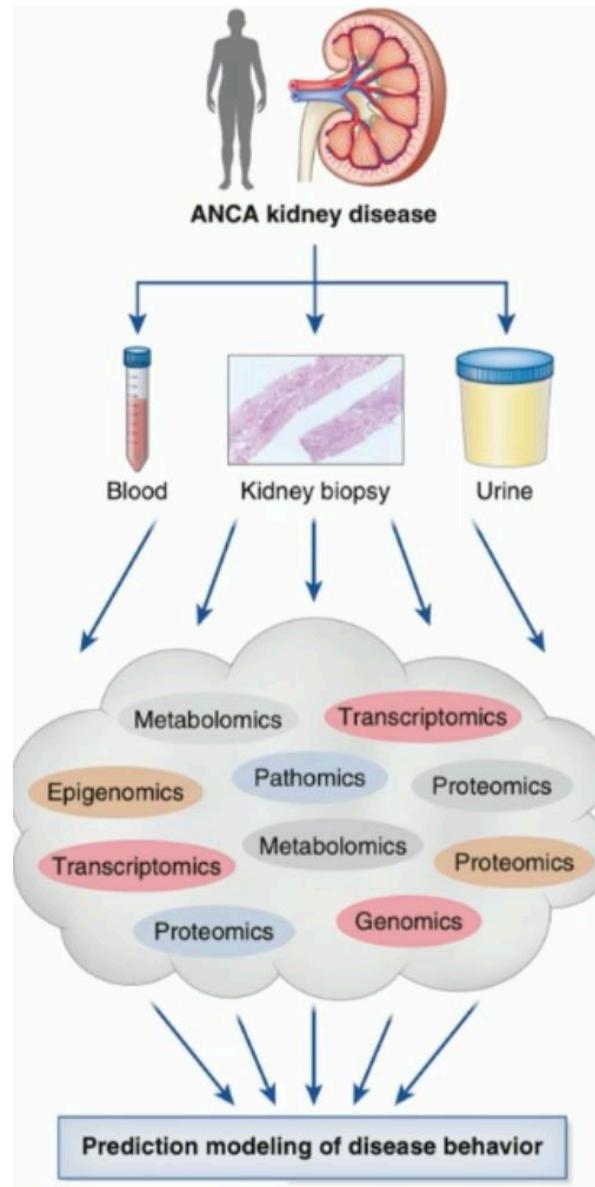
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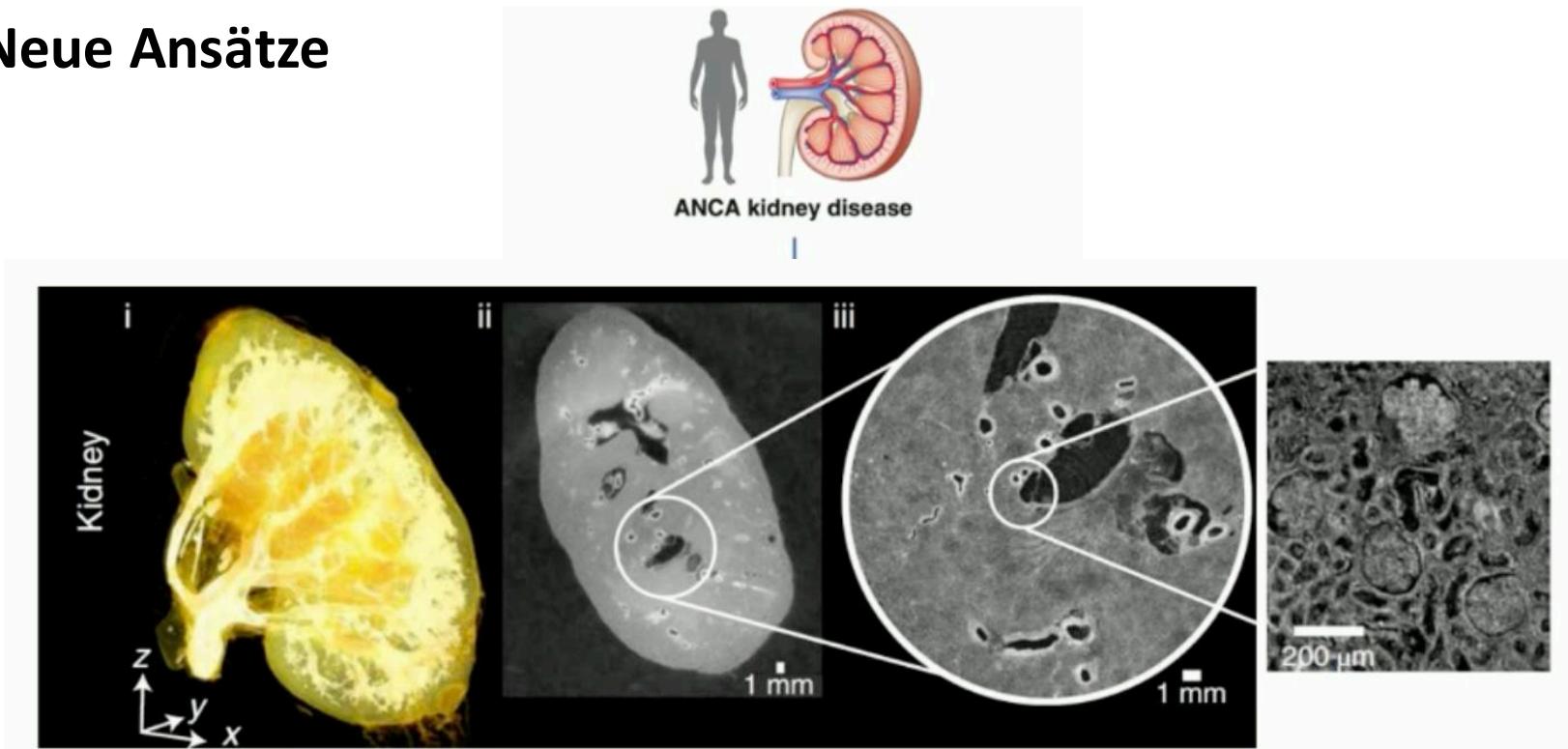


## Neue Ansätze



Jayne D, JASN 2017  
Walsh CL, Nature 2021  
Brix SR, JASN 2024  
Moran SM et al., JASN 2021

## Neue Ansätze

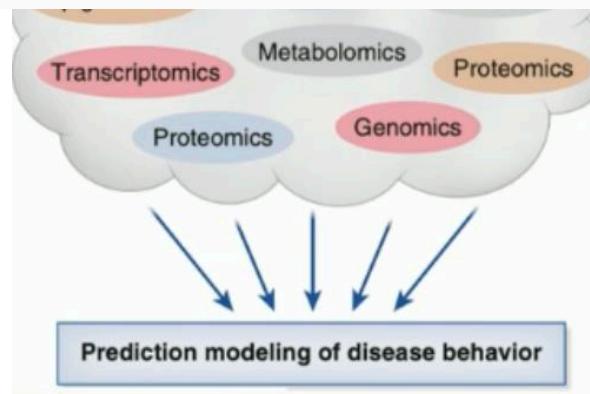


Jayne D, JASN 2017

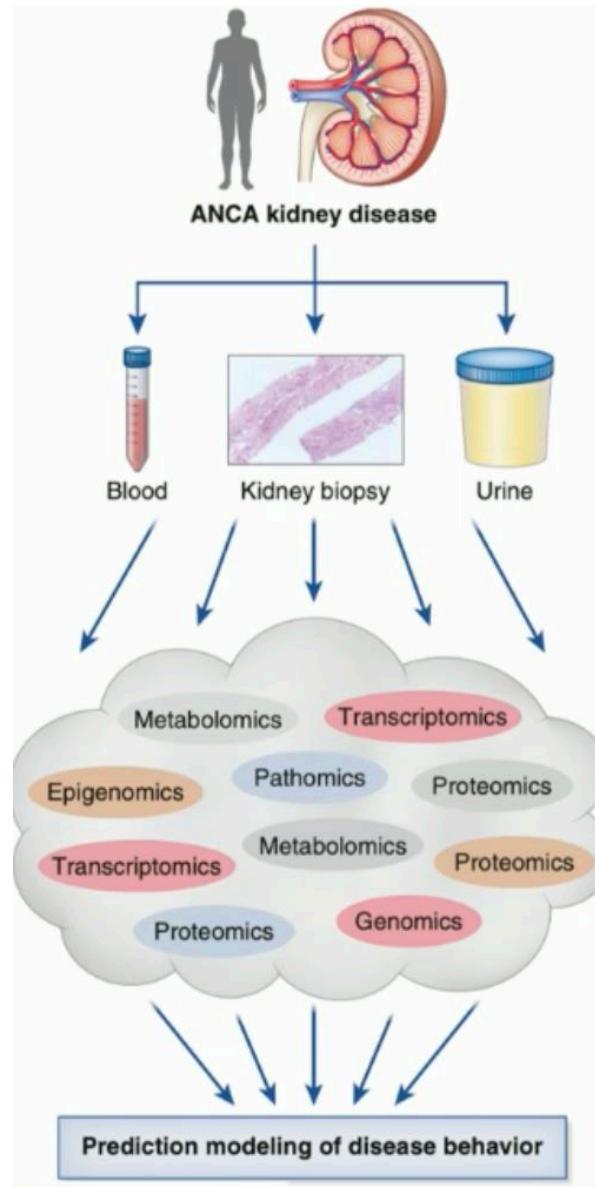
Walsh CL, Nature 2021

Brix SR, JASN 2024

Moran SM et al., JASN 2021



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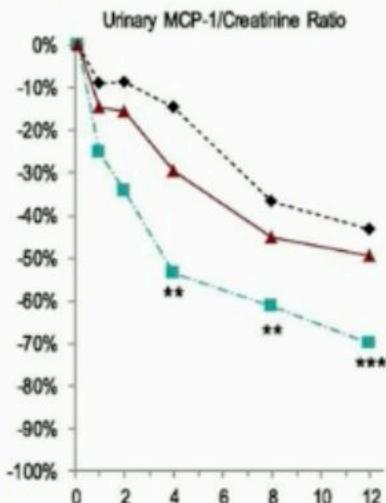


Jayne D, JASN 2017  
Walsh CL, Nature 2021  
Brix SR, JASN 2024  
Moran SM et al., JASN 2021

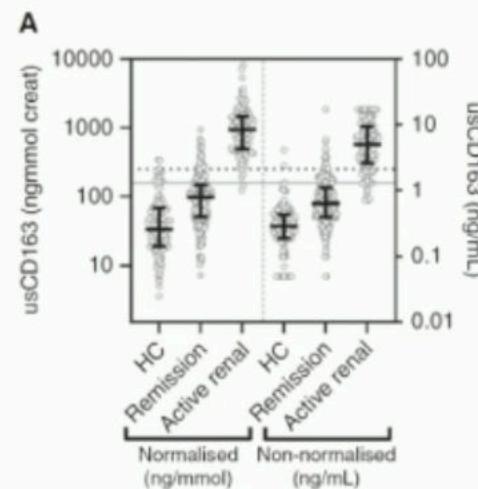
# Neue Ansätze



## MCP1



## uCD163

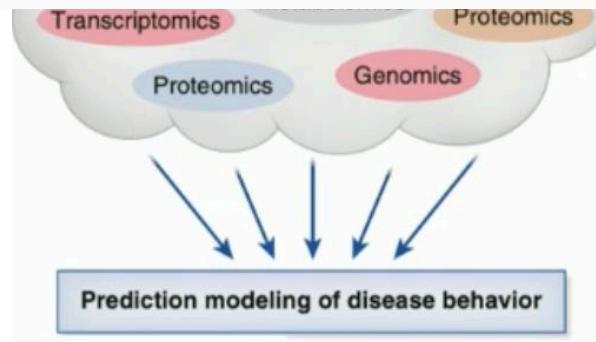


Jayne D, JASN 2017

Walsh CL, Nature 2021

Brix SR, JASN 2024

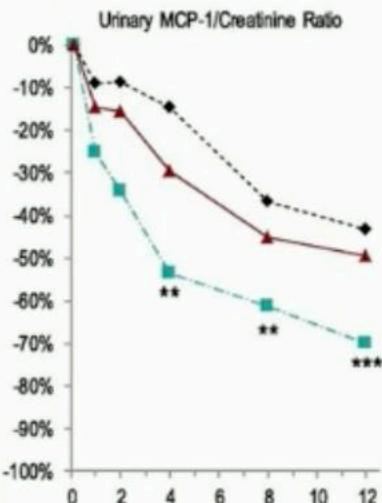
Moran SM et al., JASN 2021



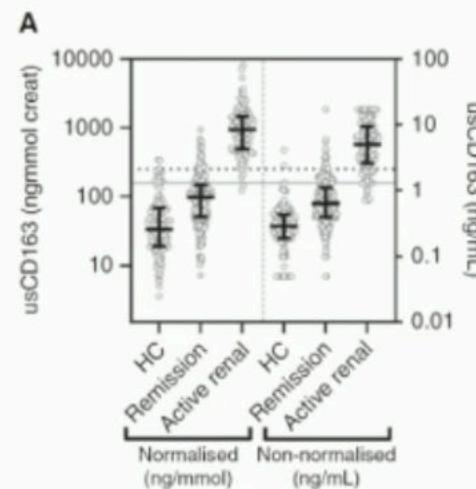
# Neue Ansätze



## MCP1

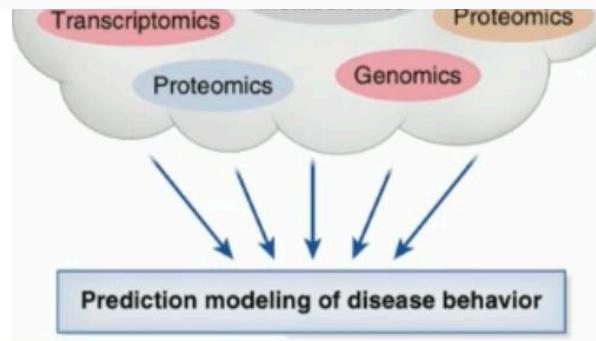


## uCD163



Jayne D, JASN 2017  
Walsh CL, Nature 2021  
Brix SR, JASN 2024  
Moran SM et al., JASN 2021

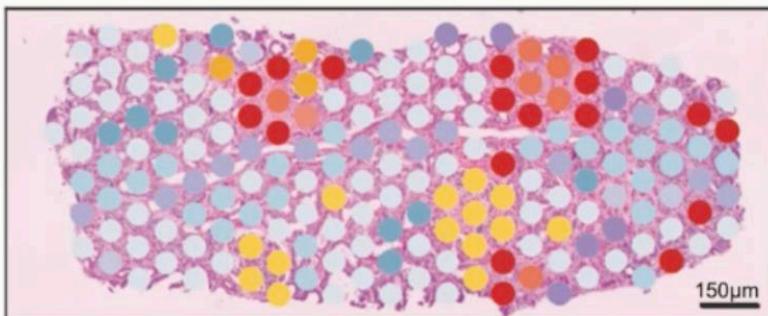
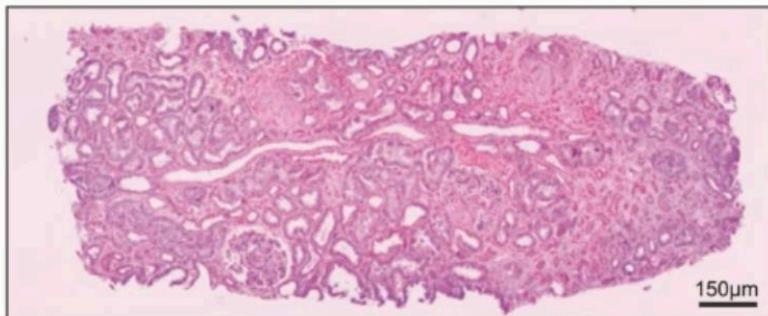
Monozyten/Makrophagen  
basiert  
(störanfällig?; spät?)



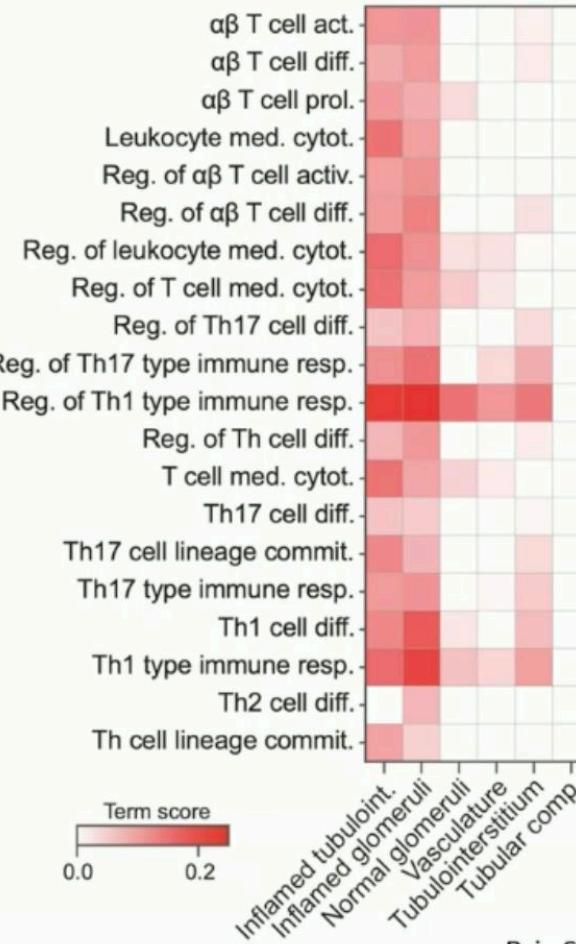
# Neue Ansätze



## Spatial transcriptomics



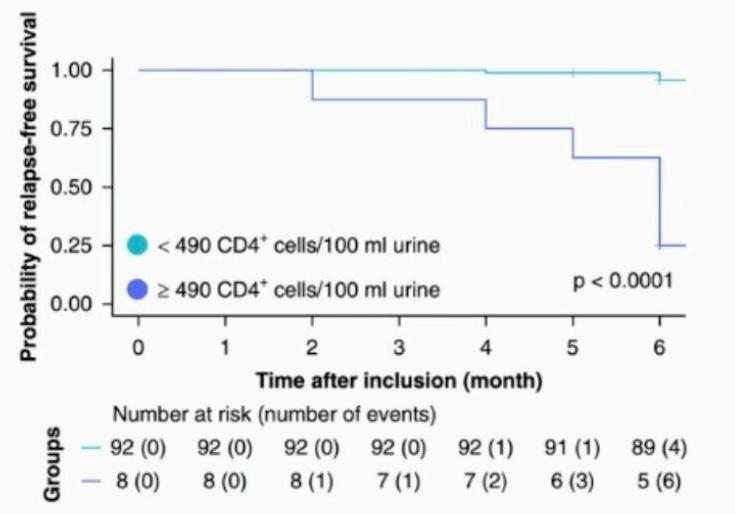
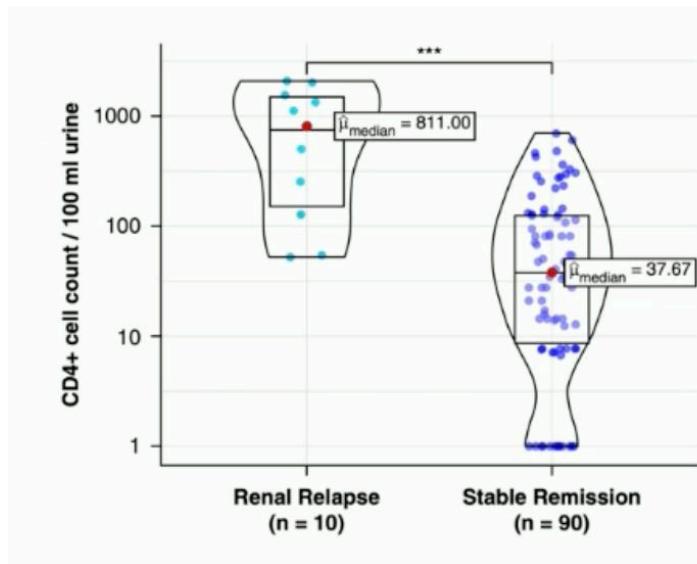
## T cell related pathways



Brix SR, JASN 2024

Engesser J et al., NatCom 2024

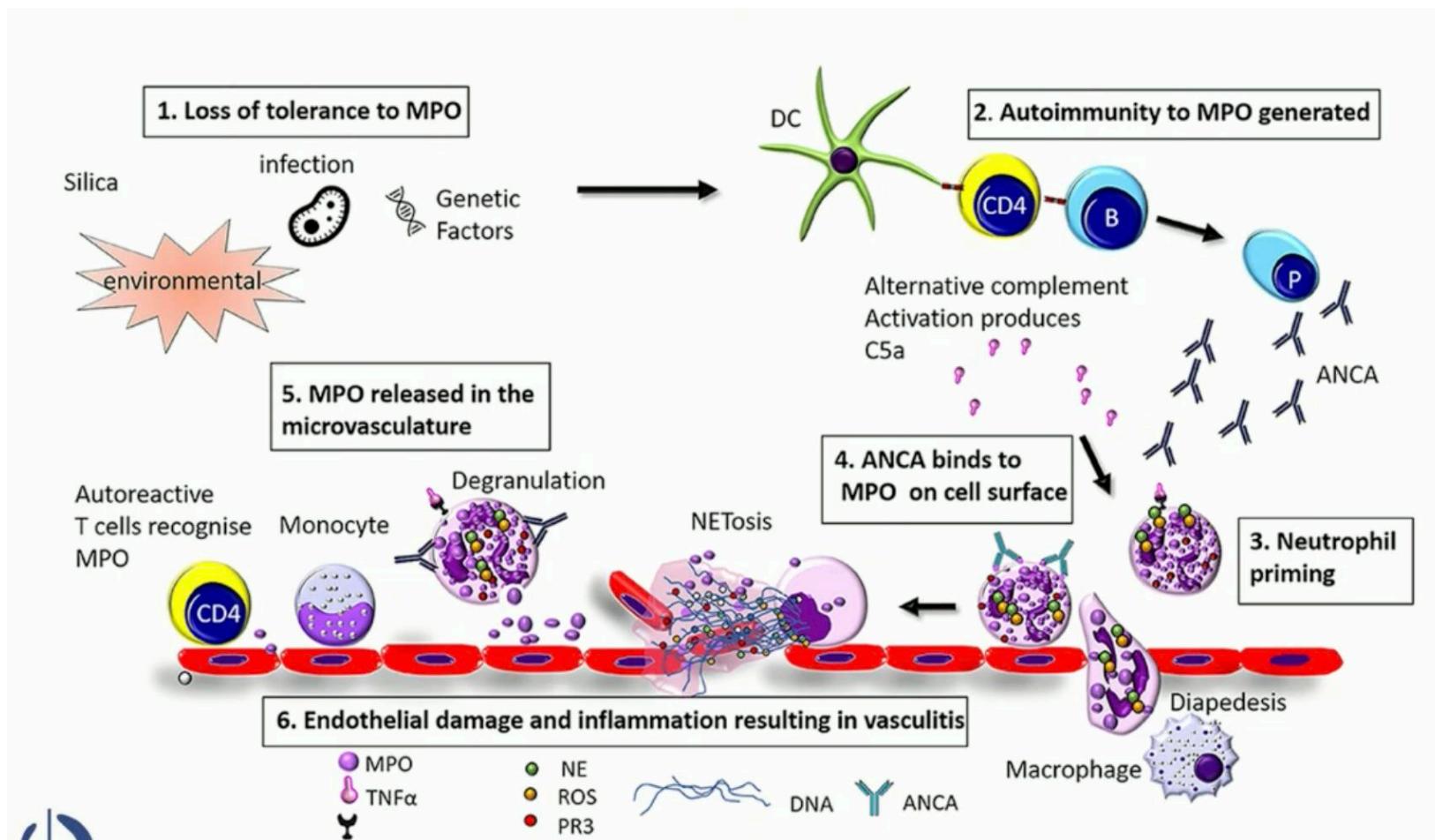
# Neue Ansätze



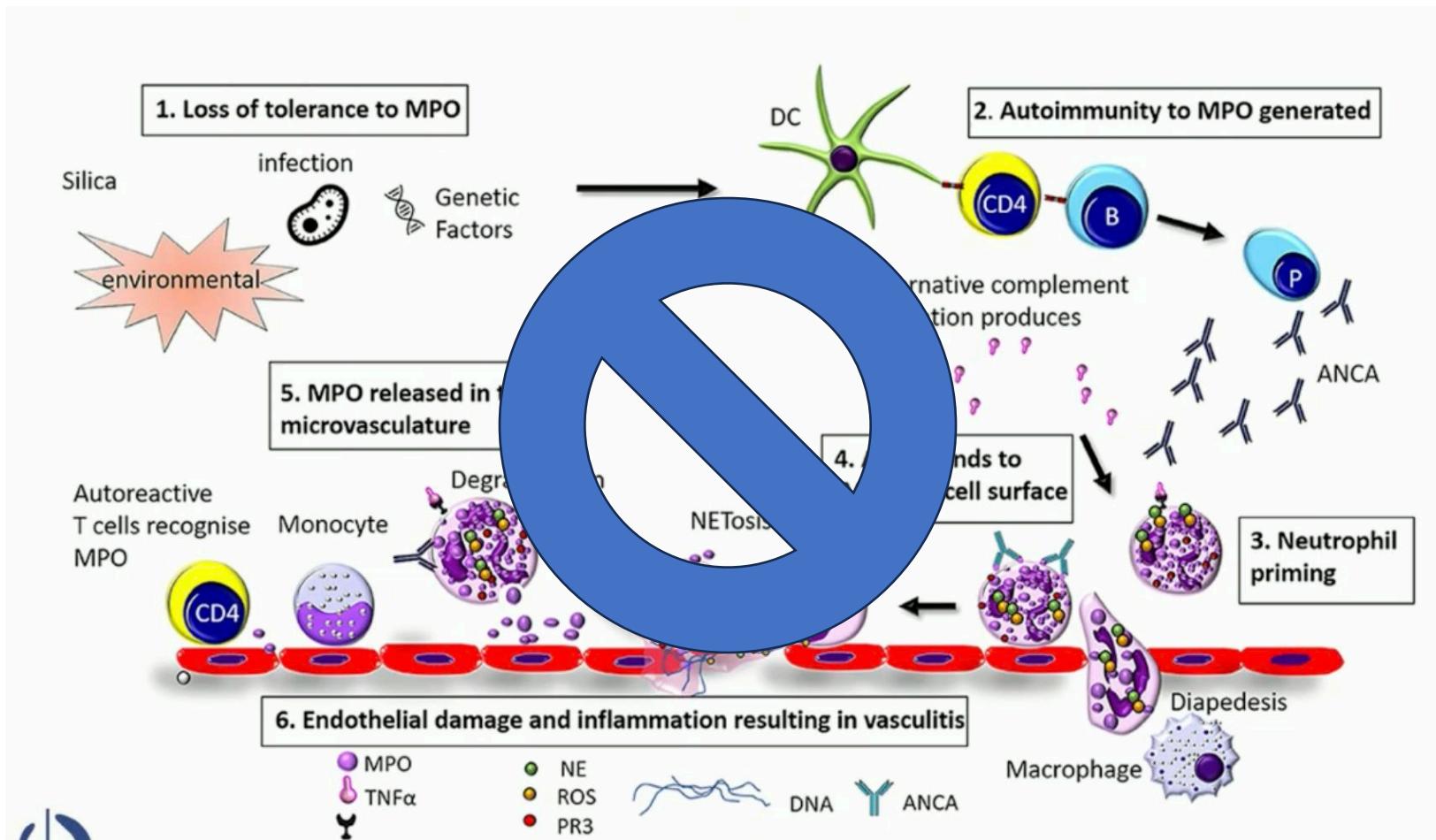
Prskalo et al., JASN 2024

Sonnemann et al., KIRep 2023

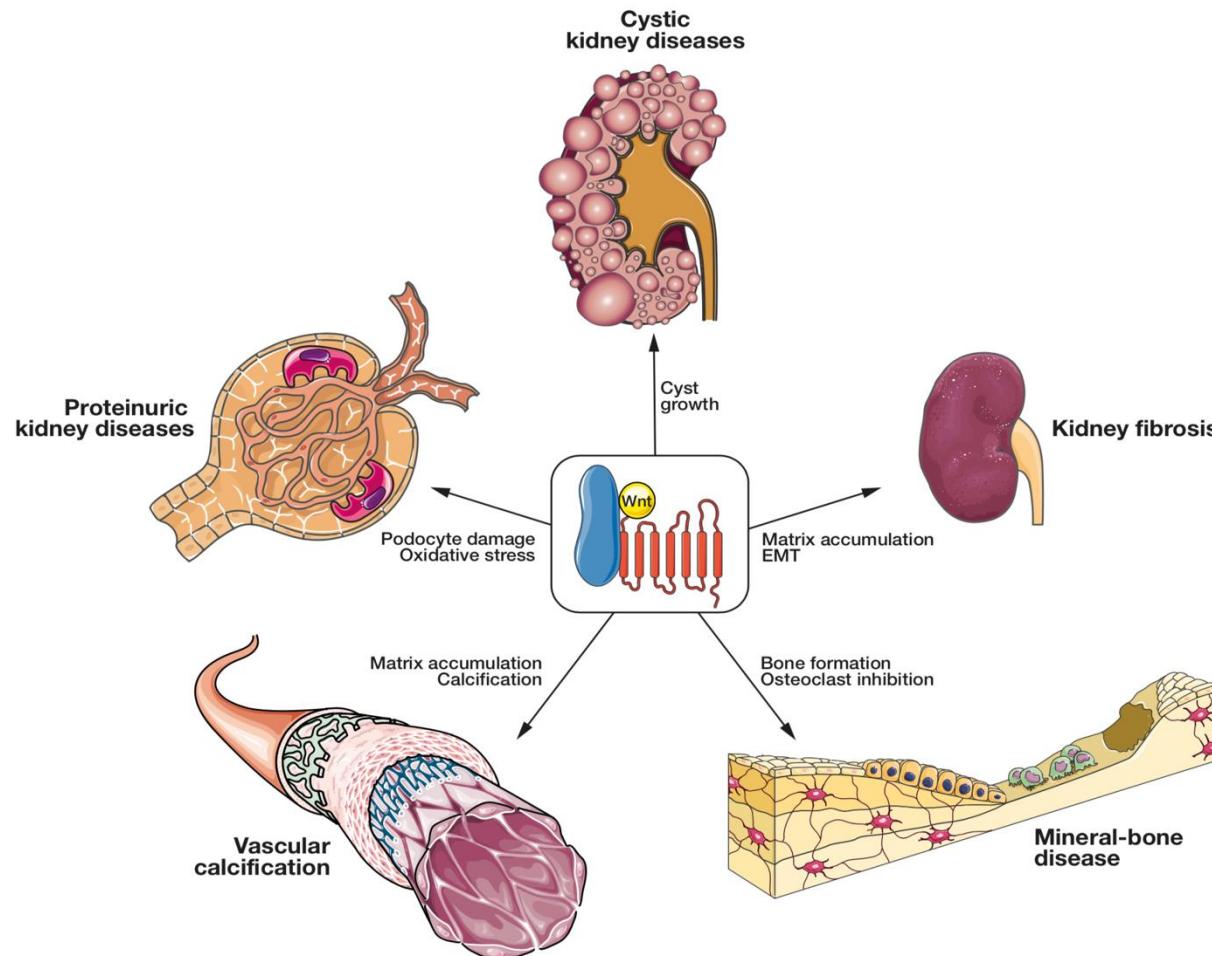
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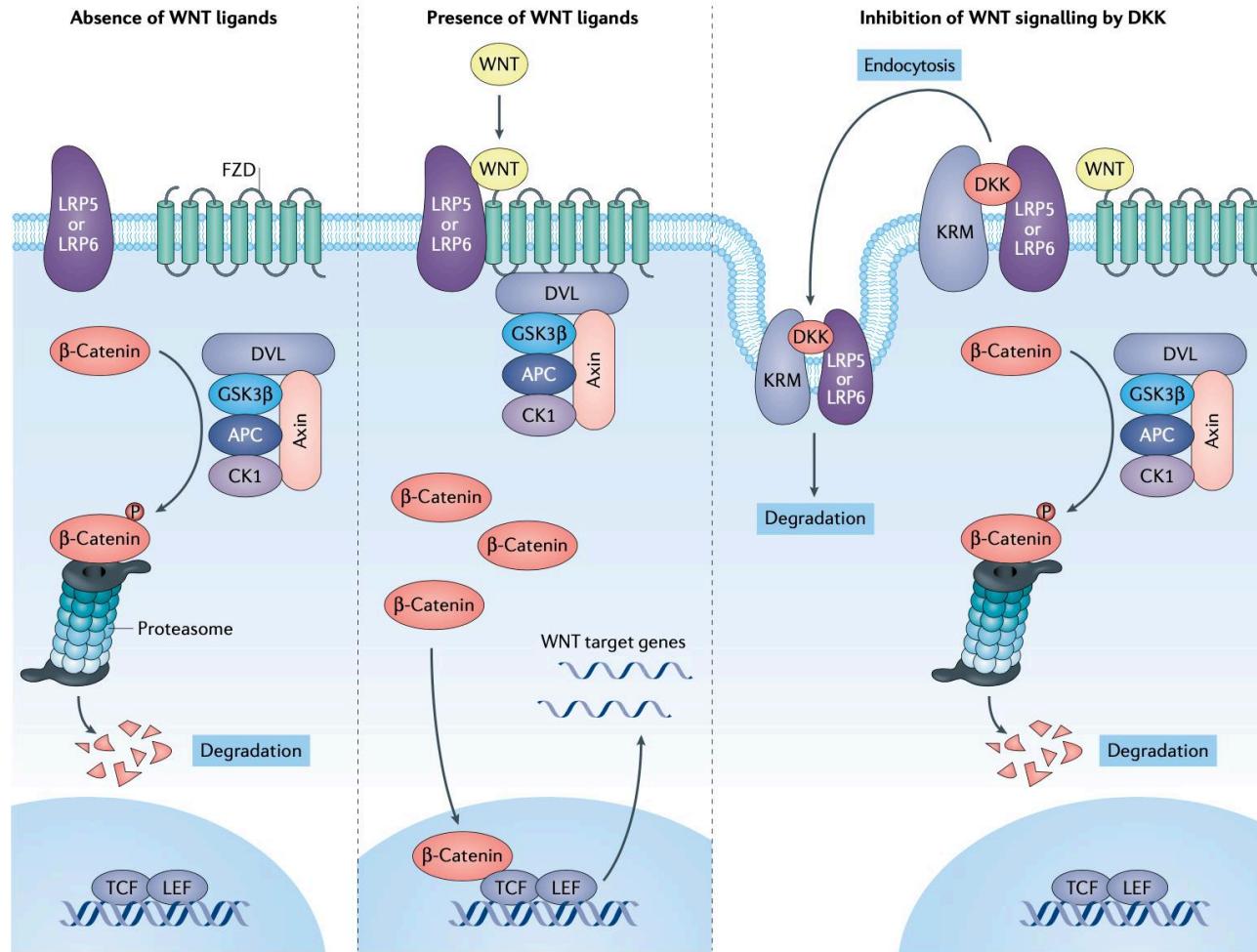
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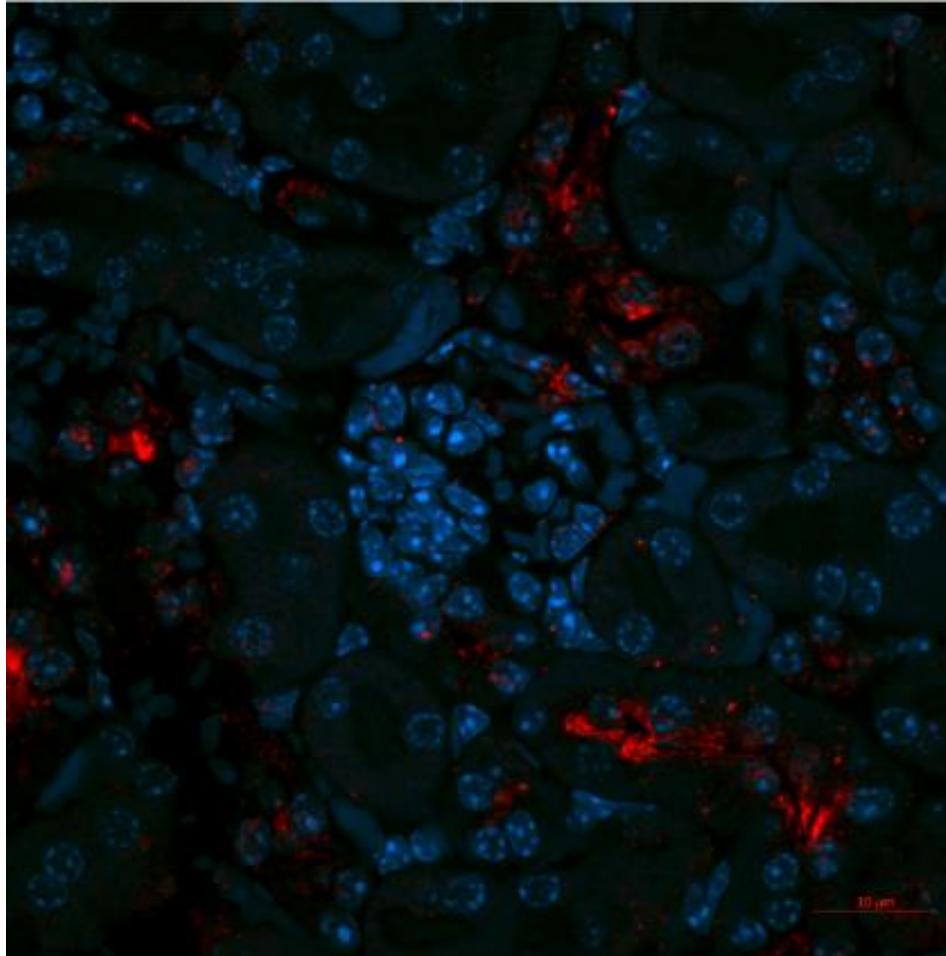
# Rolle des Wnt-Pathways bei Nierenerkrankungen



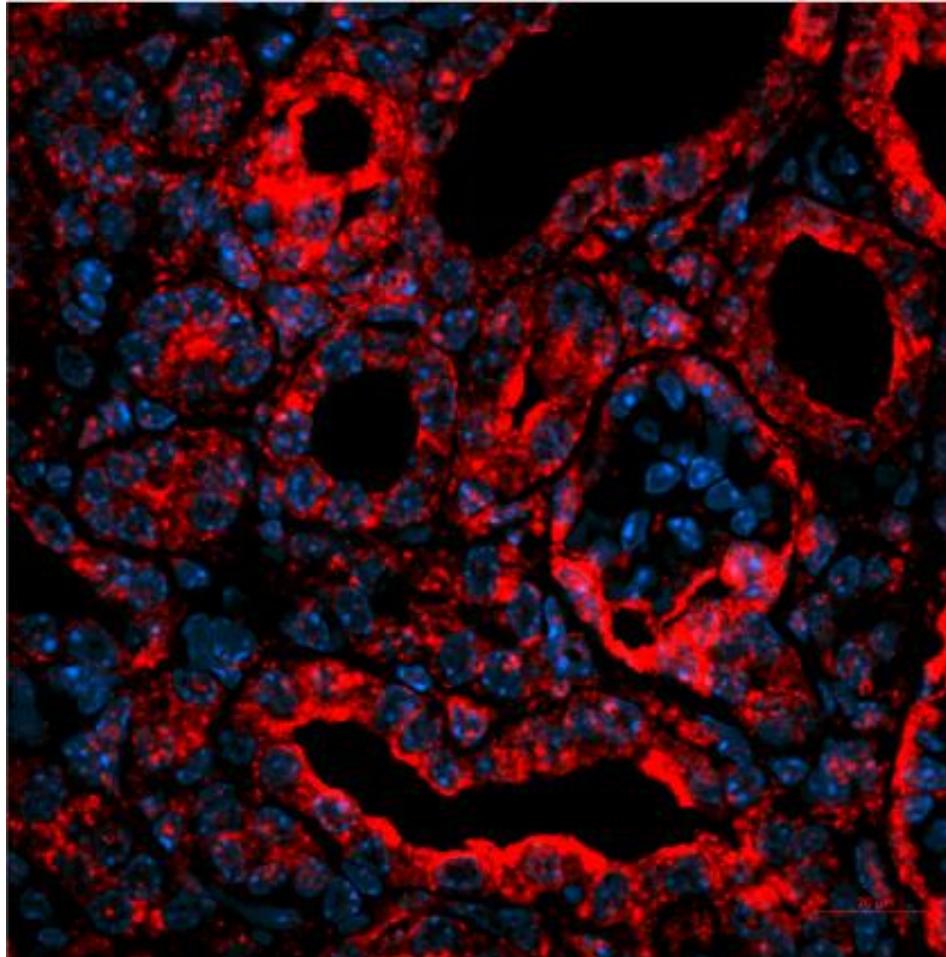
# Rolle der DKK-Proteine im Wnt-Pathway



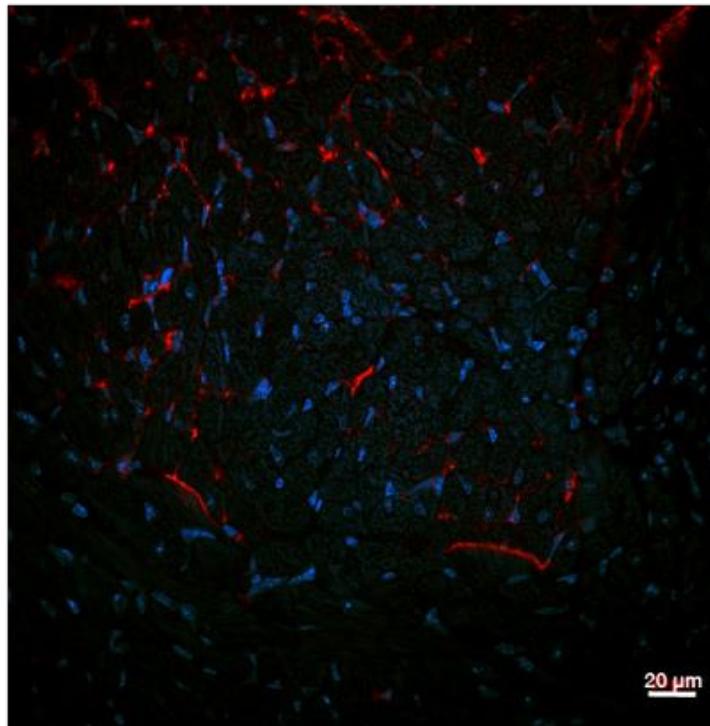
## Dickkopf-3 (DKK3) ist ein tubulärer Stress-Marker



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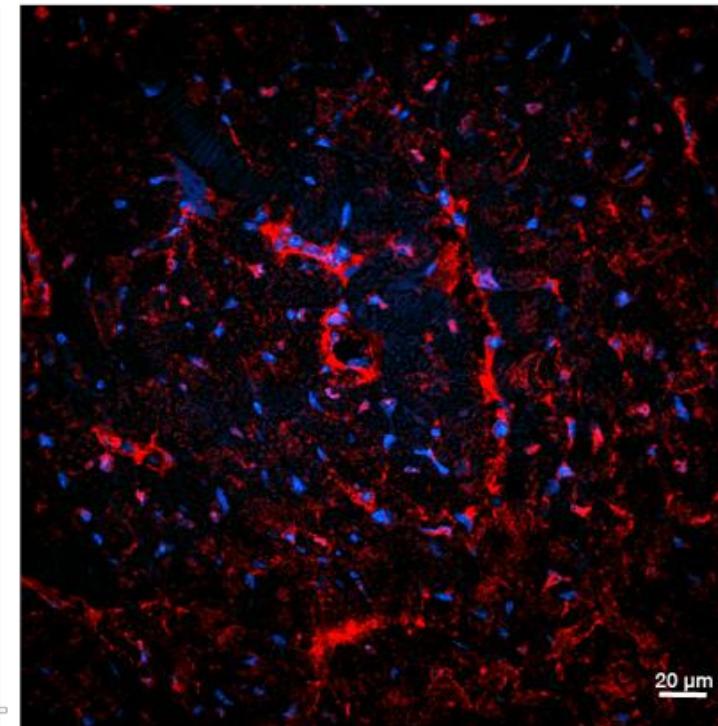


## Dickkopf-3 (DKK3) ist ein genereller Organschädigungsmarker



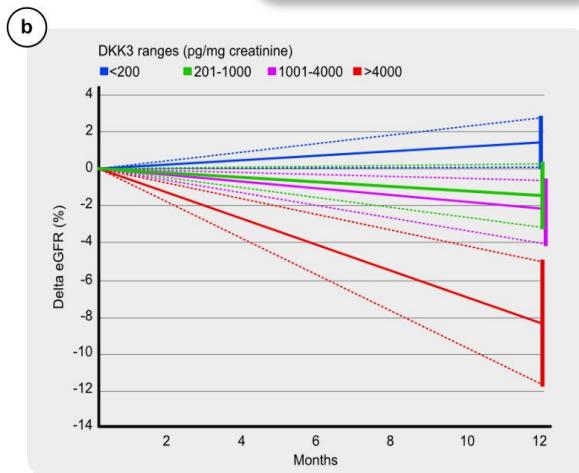
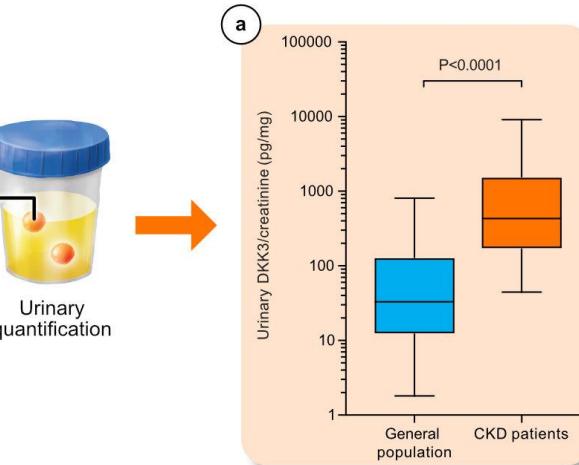
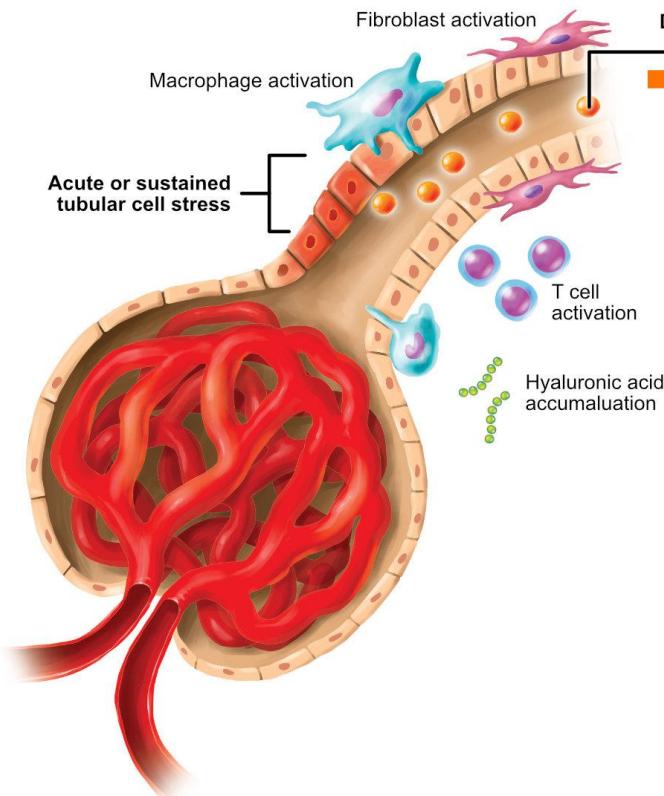
TAC 1 Woche

DKK3 DAPI

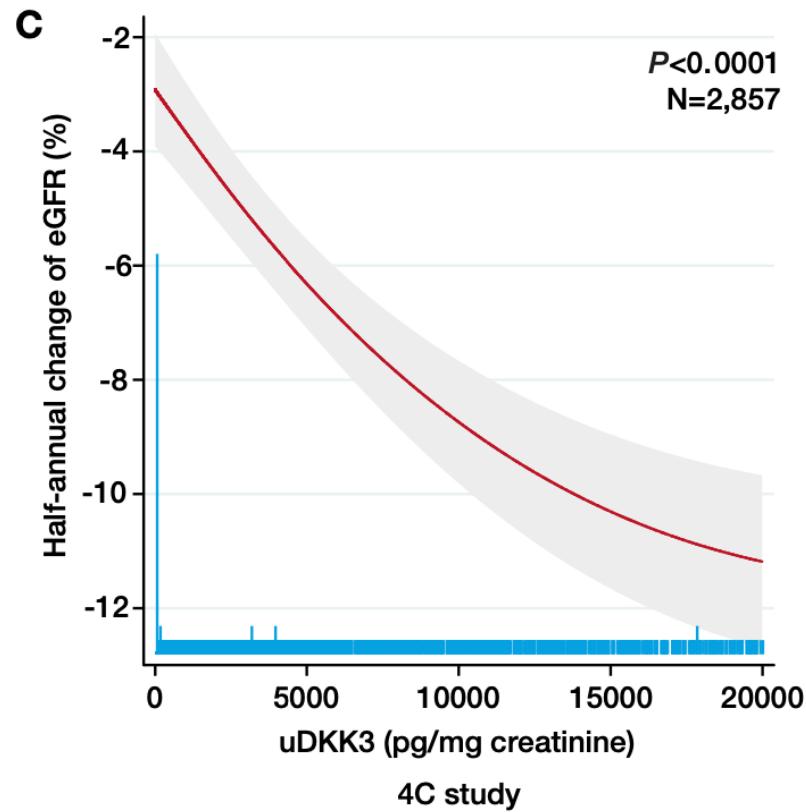
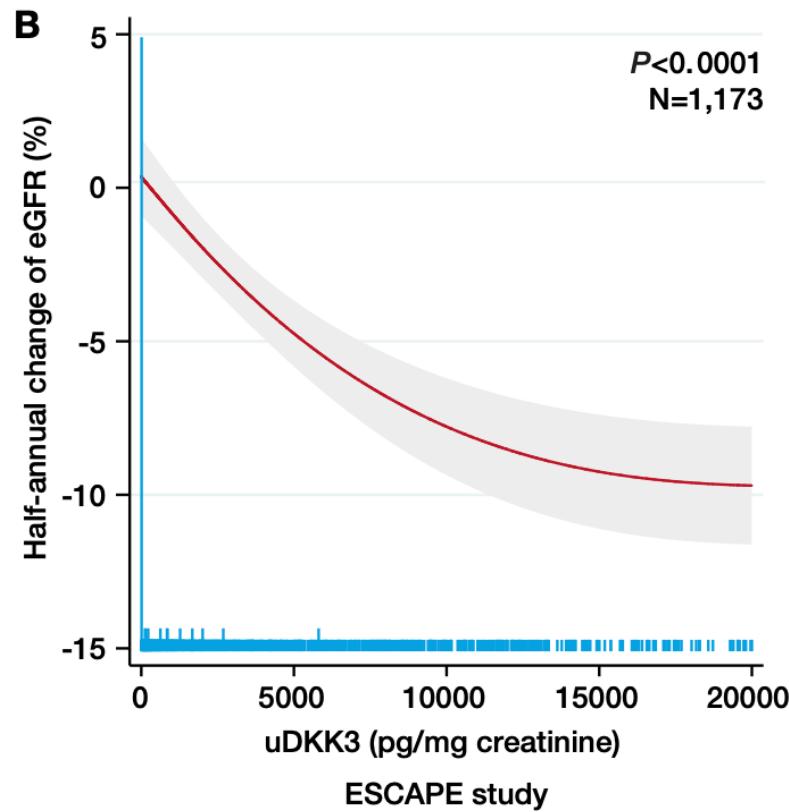


TAC 4 Wochen

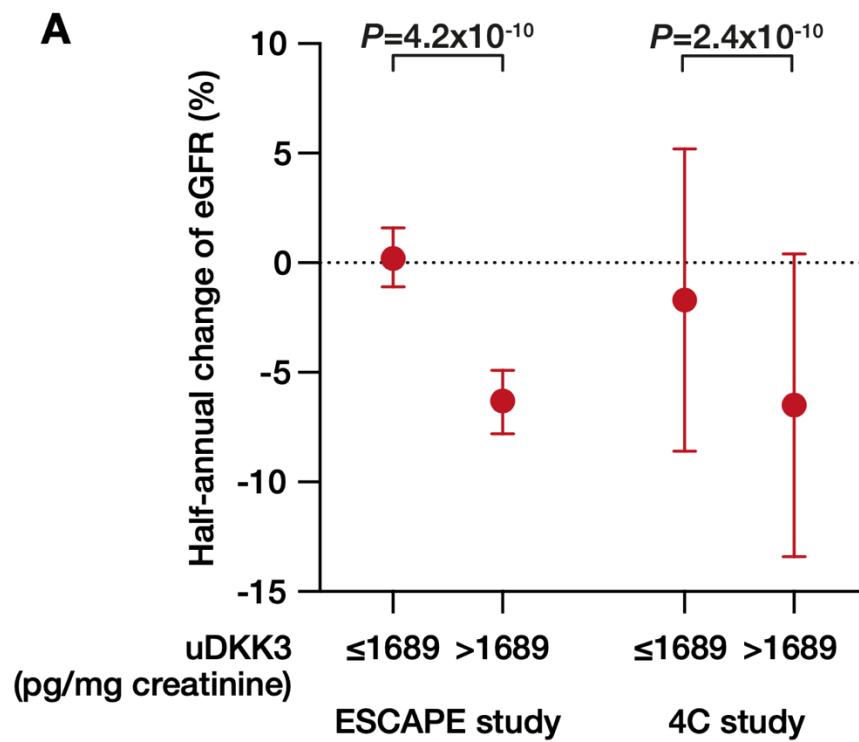
# Dickkopf-3 (DKK3) ist ein tubulärer Stresssensor



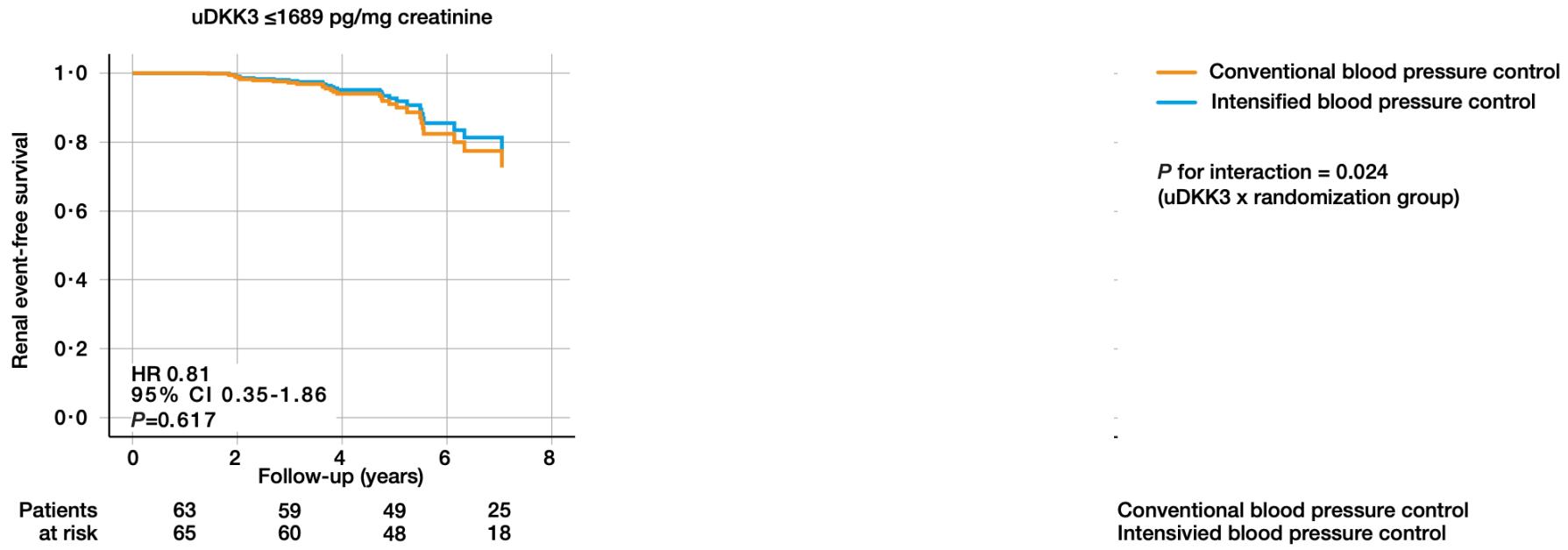
## DKK3 und CKD-Progression bei Kindern



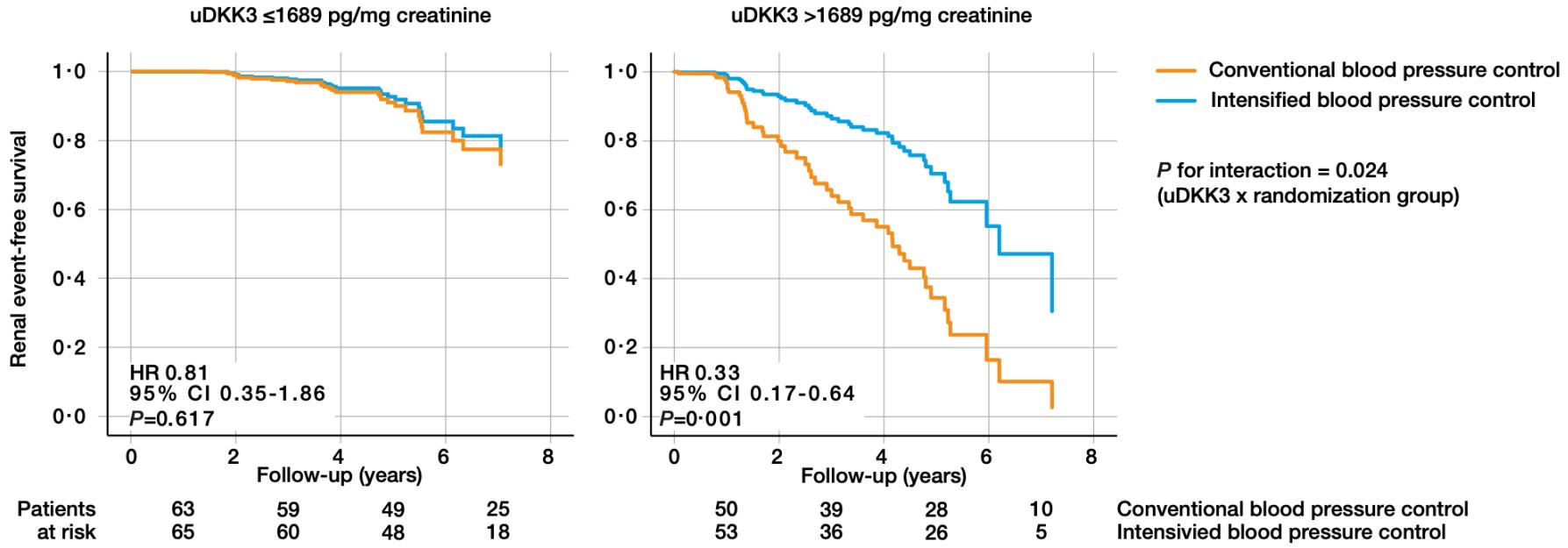
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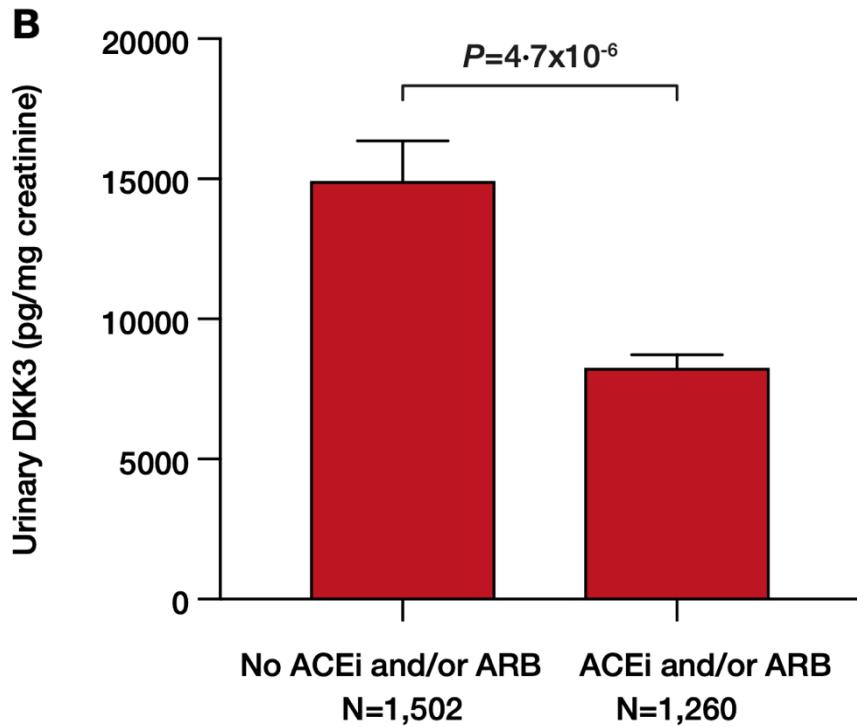
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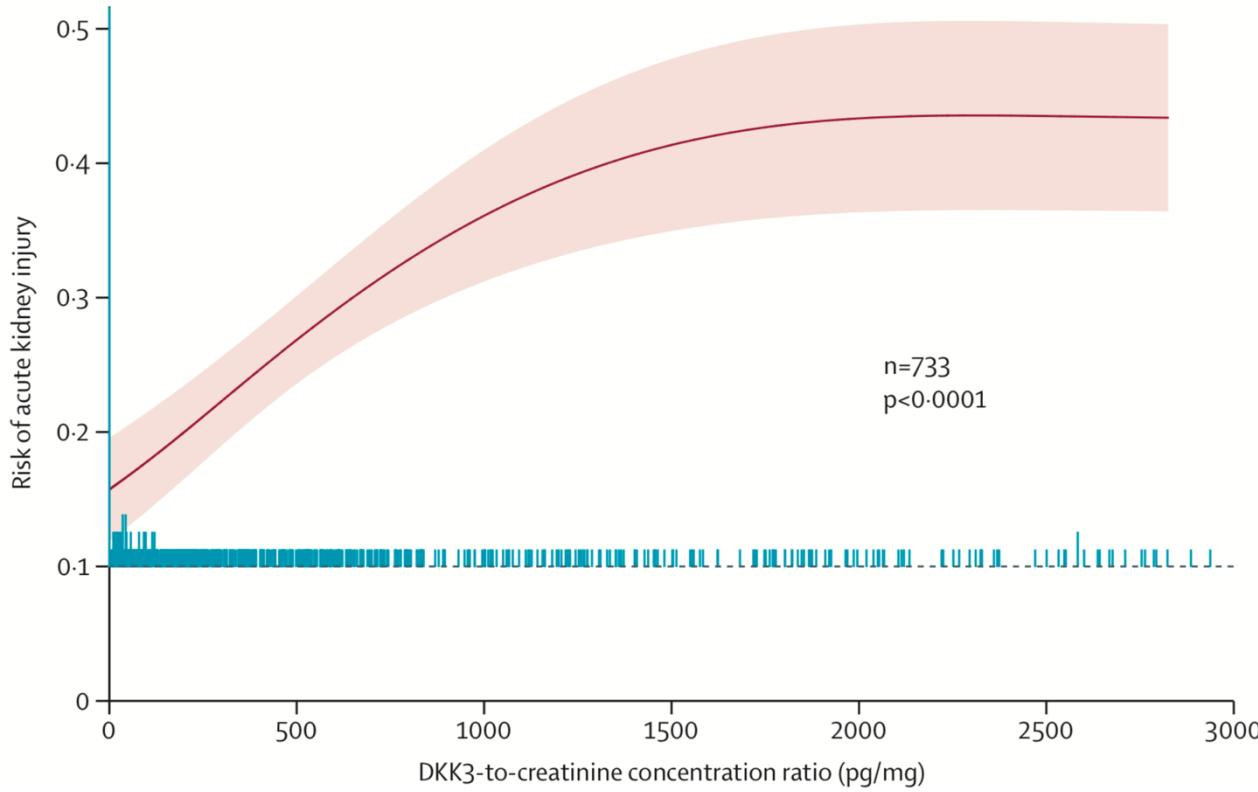


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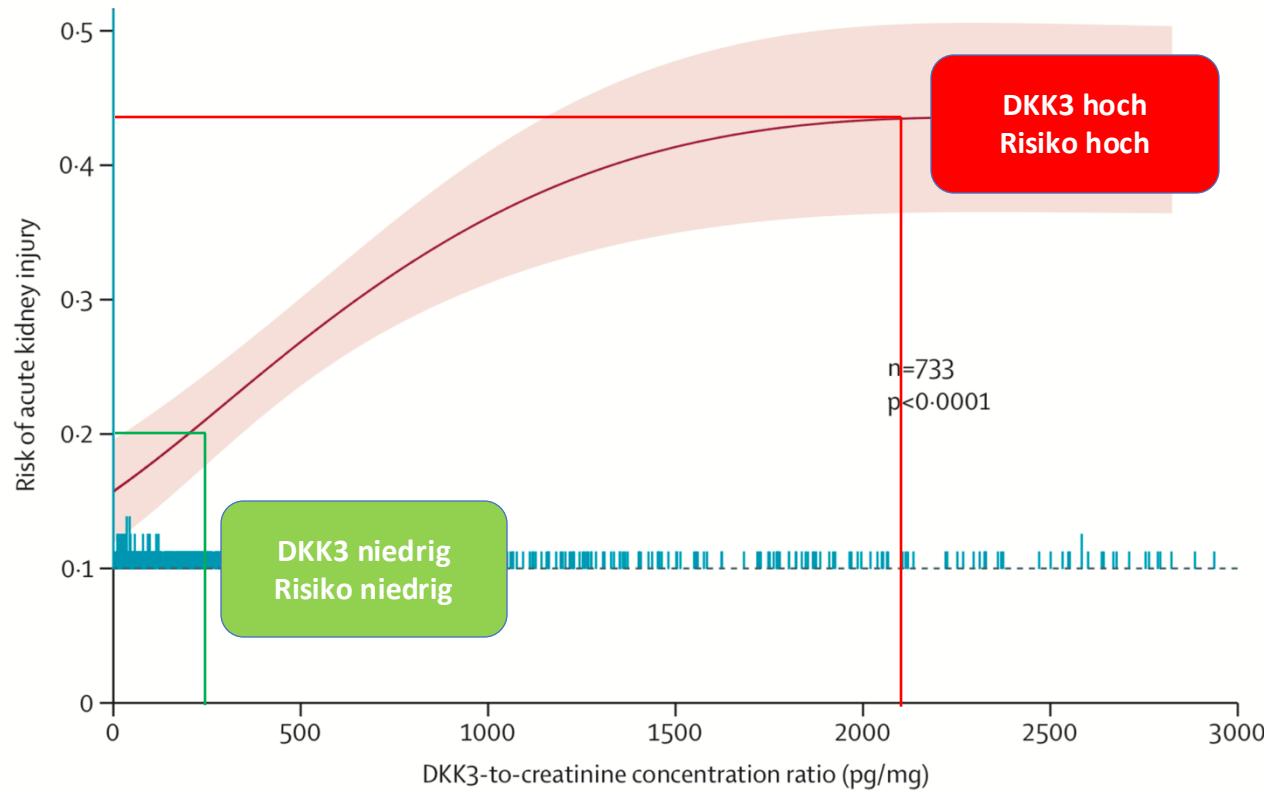


6 Monate nach Beginn einer  
Therapie mit ACEi/ARB  
Ist uDKK3 halbiert

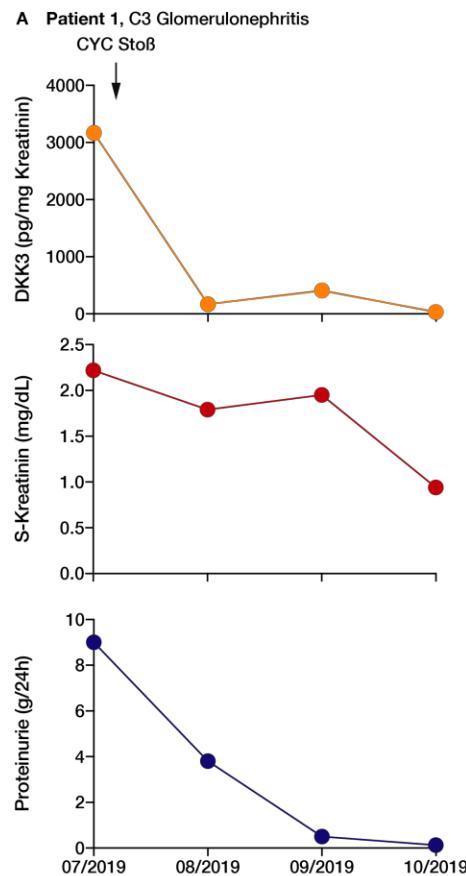
## DKK3 vor OP und postoperatives akutes Nierenversagen

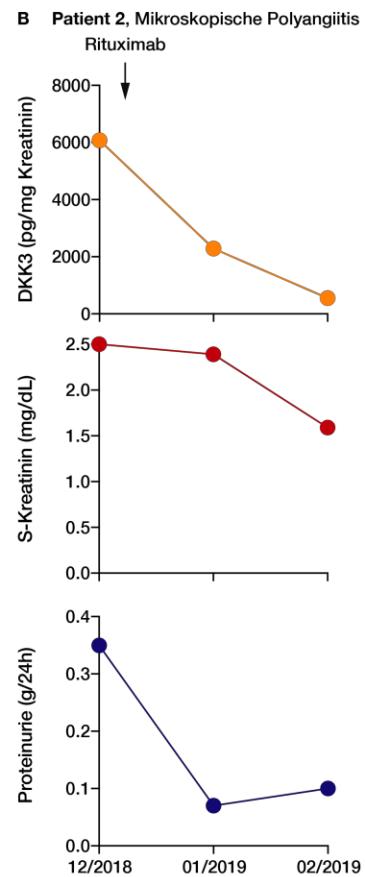
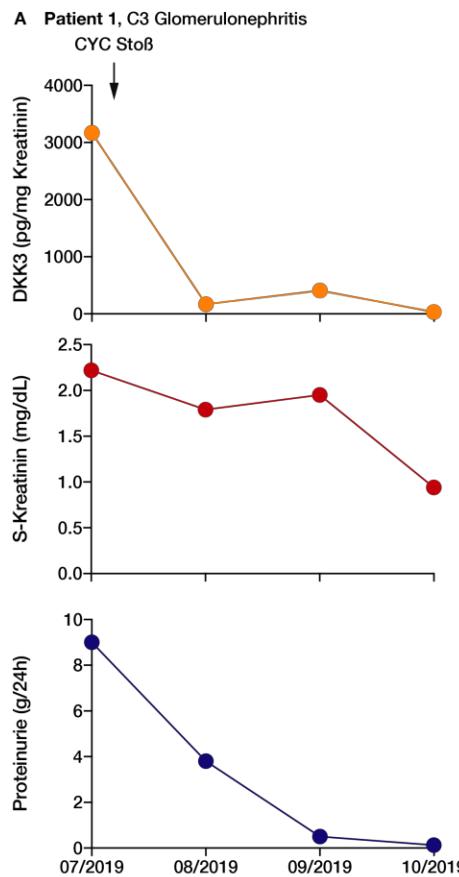


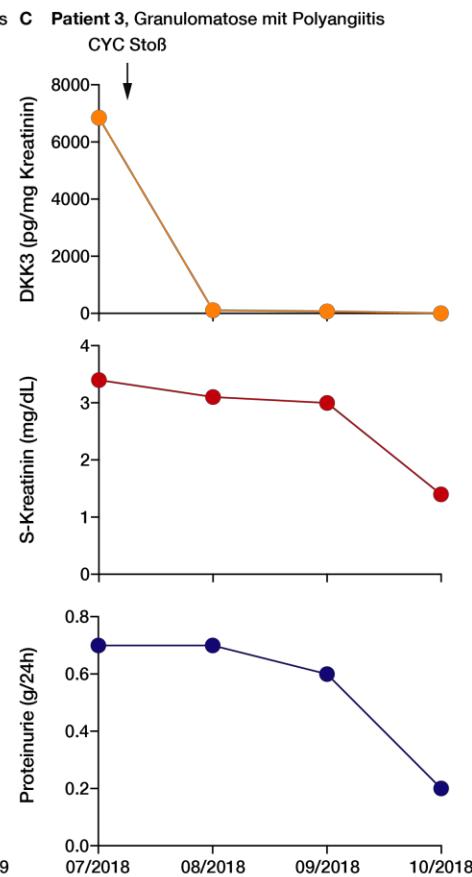
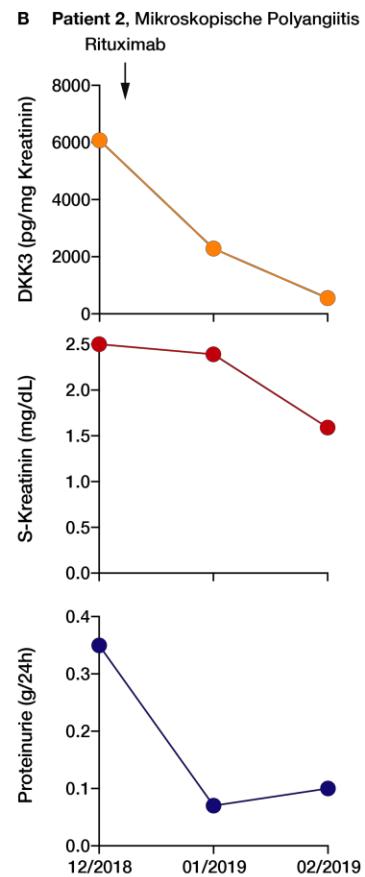
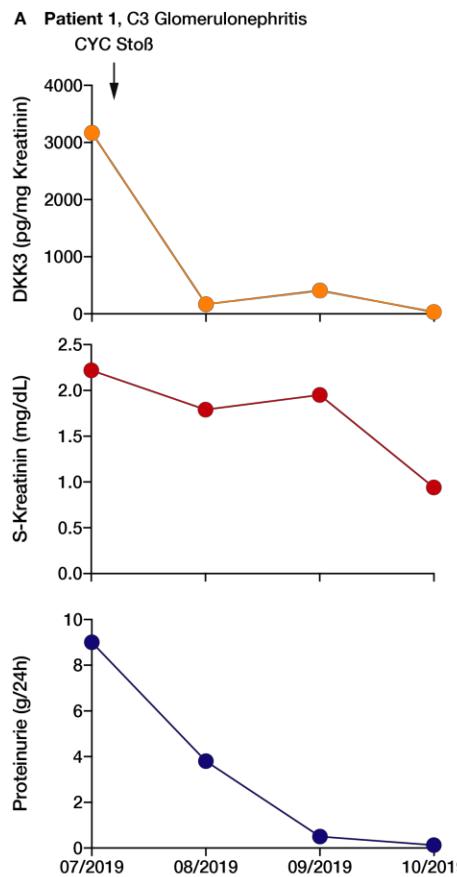
## DKK3 vor OP und postoperatives akutes Nierenversagen











## Zusammenfassung

- **Nierenbeteiligung bei ANCA – Vaskulitis ist sehr variabel**
  - Erschwert für Einsatz von Biomarkern und für Therapieziele
- **Endpunkte** reevaluieren (mit den Biomarkern)
- Bekannte Marker gut zur **Risikostratifizierung**, nicht zur **Therapiesteuerung**
- **AKRiS – Score** hohe prognostische Vorhersagekraft
- **Neue Technologien**
- **DKK3** als potentieller **therapeutischer Marker** bei immunologischen Nierenerkrankungen



**Sozialstiftung Bamberg**

Wenn Sie uns brauchen.

**DFG**  
SFB/TRR 219



**Vielen Dank für die  
Aufmerksamkeit**

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# Gekürzte Verschreibungsinformationen

## Schweiz:

**Tavneos®.** **Z:** Avacopan. **I:** Tavneos, als ergänzende Therapie zu einer immunsuppressiven Standardbehandlung auf Basis von Rituximab oder Cyclophosphamid mit Glukokortikoiden, ist für die Behandlung erwachsener Patienten mit schwerer aktiver ANCA-Vaskulitis (GPA/MPA) indiziert. **D:** Orale Einnahme morgens und abends 2x täglich 30 mg (3 Kapseln zu je 10 mg) mit Nahrung. **KI:** Überempfindlichkeit gegen den Wirkstoff oder einen der Hilfsstoffe. **VM:** Hepatotoxizität; Angioödem; Überwachung des Blutbildes (weiße Blutkörperchen); Schweren Infektionen; Reaktivierung des Hepatitis-B-Virus; Herzbeschwerden; Bösartige Tumore; Macroglycerinhydroxystearat. **S/S:** Eine Anwendung während der Schwangerschaft und bei Frauen im gebärfähigen Alter, die keine Verhütungsmethode anwenden, ist nicht empfohlen. Es ist nicht bekannt, ob Avacopan in die Muttermilch ausgeschieden wird. Der Nutzen des Stillens für das Kind sollte gegen den Nutzen der Behandlung für die Patientin abgewogen werden. **UW:** Sehr häufig: Infektion der oberen Atemwege, Nasopharyngitis; Kopfschmerzen; Erbrechen, Durchfall, Übelkeit; erhöhter Lebertest; verminderte Anzahl weißer Blutkörperchen. Häufig: Lungenentzündung, Infektion der unteren Atemwege, Influenza, Bronchitis, Zellulitis, Infektion der Harnwege, Herpes zoster, Sinusitis, orale Candidose, Herpes im Mundbereich, Otitis media, Rhinitis, Gastroenteritis; Neutropenie; Oberbauchschmerzen; Anstieg der Kreatinphosphokinase im Blut. Gelegentlich: Angioödeme. **IA:** Avacopan ist ein Substrat von CYP3A4. Die gleichzeitige Verabreichung von Induktoren oder Inhibitoren dieses Enzyms kann die Pharmakokinetik von Avacopan beeinflussen. Siehe Fachinformation. **P:** Tavneos 10 mg: 30 und 180 Hartkapseln. **Liste B:** Detaillierte Informationen: [www.swissmedicinfo.ch](http://www.swissmedicinfo.ch). Stand der Information: Januar 2024. **Zulassungsinhaberin:** Vifor Fresenius Medical Care Renal Pharma Ltd., St. Gallen. **Vertrieb:** Vifor Pharma Switzerland AG, CH-1752 Villars-sur-Glâne |

▼ Dieses Arzneimittel unterliegt einer zusätzlichen Überwachung. Für weitere Informationen, siehe Fachinformation TAVNEOS® auf [www.swissmedicinfo.ch](http://www.swissmedicinfo.ch).

# Gekürzte Verschreibungsinformationen

## Österreich:

### Tavneos® Fachkurzinformation

#### Tavneos®10mg Hartkapsel

**Zusammensetzung:** Jede Hartkapsel enthält 10 mg Avacopan. Sonstige Bestandteile mit bekannter Wirkung: 245 mg Macrogolglycerolhydroxystearat(Ph.Eur). **Anwendungsgebiete:** Tavneos® ist in Kombination mit einem Rituximab- oder Cyclophosphamid-Dosierungsschema indiziert zur Behandlung erwachsener Patienten mit schwerer aktiver Granulomatose mit Polyangiitis (GPA) oder mikroskopischer Polyangiitis (MPA). **Gegenanzeigen:** Überempfindlichkeit gegen den Wirkstoff oder einen der sonstigen Bestandteile. **Pharmakotherapeutische Gruppe:** Komplement-Inhibitoren **ATC-Code:** L04AJ05 **Inhaber der Zulassung:** Vifor France, 100-101 Terrasse Boieldieu Tour Franklin La Defense 8 92042 Paris La Defense Cedex, Frankreich. Rezept- und apotheekenpflichtig. Weitere Angaben zu Warnhinweisen und Vorsichtsmaßnahmen für die Anwendung, Wechselwirkungen mit anderen Arzneimitteln oder sonstigen Wechselwirkungen, Schwangerschaft und Stillzeit und Nebenwirkungen sowie Gewöhnungseffekten sind der veröffentlichten Fachinformation zu entnehmen. Stand der Information: Mai 2023

▼ Dieses Arzneimittel unterliegt einer zusätzlichen Überwachung. Dies ermöglicht eine schnelle Identifizierung neuer Sicherheitsdaten. Angehörige der Gesundheitsberufe werden gebeten, alle Verdachtsfälle von unerwünschten Wirkungen zu melden.