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LINS 05.03.2026
Fallvorstellung

M. Heller

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Patientin E.T. *1965

- Vorstellung via ZNA bei Dyspnoe und Verdacht auf symptomatische renale Anämie

- *Eigenanamnese*:
  - CKD G3bAx unklarer Genese, seit mind. 10/2023 bestehend
  - Vitamin-D-Mangel
  - nicht-klassifizierbare Kolitis, ED 2015
- *Familienanamnese*:
  - Vater: Dialysepflicht (anamnest. nach Aneurysmaruptur)
  - 1 gesunde Tochter
- *Medikation*: Dekristol, Mesalazin
- *Körperlicher Status*: o.B., RR 131/78 mmHg, keine Ödeme, keine Blutungsstigmata

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Laborbefunde

Blut

		Blutbild (Automat) (
WBC	Gpt/l	11.07
RBC	Tpt/l	2.48 -
HGB	mmol/l	4.60 -
HCT	l/l	0.21 -
MCV	fl	84.3
MCH	fmol	1.86
MCHC	mmol/l	22.0
Thrombo	Gpt/l	415 +
MPV	fl	10.4
HBA1C (IFCC)	mmol/molHb	35.0
HBA1C	%Hb	5.4

Creatinin	µmol/l	409 +
GFR (CKD-EPI)	ml/min/1.73m²	10 -
GFR berechnet nach MDRD	ml/min/1.73m²	10 -
Cystatin C	mg/l	3.12 +
GFR (aus Cystatin C)	ml/min/1.73m²	13 -

		Autoantikörper (Serum)
Zellkerne (ANA-Screening)	Titer	1:160 +
Fluoreszenz-Muster Zellkerne		Midbody (AC-27)
Proteinase 3 (Zielantigen f. c-ANCA im IFT)	IU/ml	<0.2
Myeloperoxid. (Zielantigen f. p-ANCA im IFT)	IU/ml	<0.2
glomeruläre Basalmembran	U/ml	<0.8

Urin

		Urinstatus (Teststr
Spezif.Gewicht		1.009
Urin pH-Wert		6.0
Leukozyten i.U.	Leuko/µl	neg
nitritbildende Keime		neg
Gesamteiweiß	g/l	0.12-0.5 +
Glucose i.U.	mmol/l	norm
Ketonkörper	mmol/l	positiv, 1.5 +
Urobilinogen	µmol/l	norm
Bilirubin	µmol/l	neg
Erythrozyten i.U.	Ery/µl	20-40 +

		Klinische Chemie (S
Calcium i.U.	mmol/l	0.63
Chlorid i.U.	mmol/l	87
Kalium i.U.	mmol/l	16.6
Natrium i.U.	mmol/l	106.6
Albumin i.U.	mg/l	17.4
Albumin/Creatinin-Quotient i.U.	mg/g Crea	53.7 +
Creatinin i.U.	µmol/l	2865
Harnstoff i.U.	mmol/l	81.2
Protein i.U.	mg/l	162 +
Protein/Creatinin-Quotient i.U.	mg/g Crea	500.4 +

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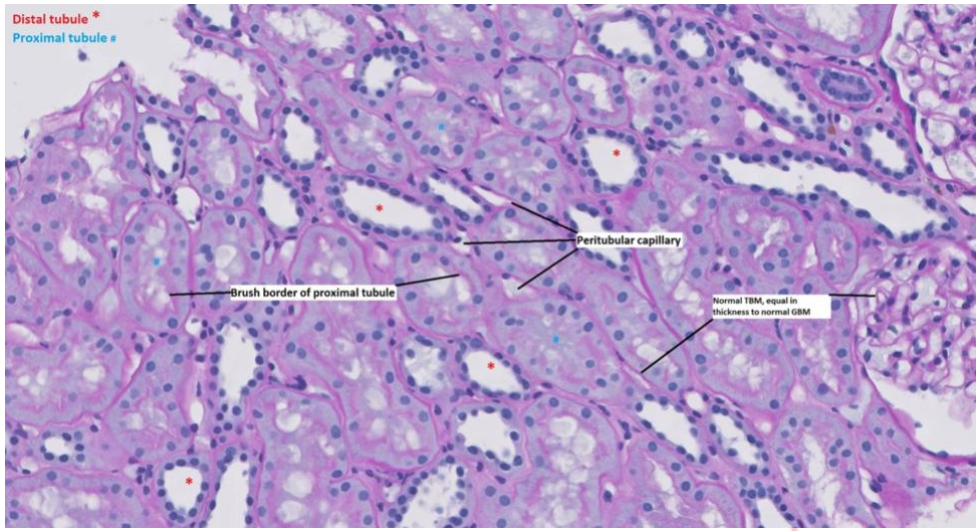
Nierenpunktion am 31.01.25

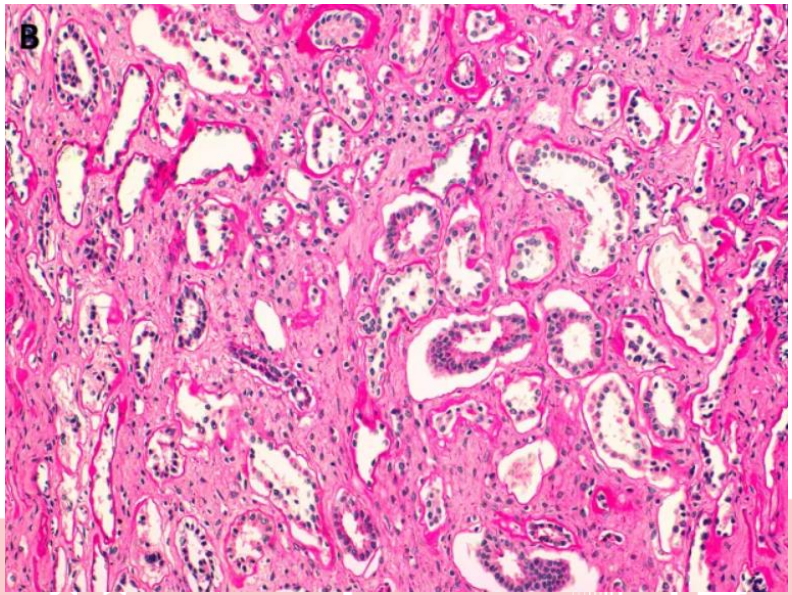
Diagnose

Mittelschwere Intimafibrose intrarenaler Arterien. Geringgradige Arteriolohyalinose. Mäßiggradige herdförmige Tubulusatrophie und interstitielle Fibrose der Rinde mit Hypertrophie der Restnephrone. Diskrete IgA-Nephropathie (M0, E0, S0, T1, C0). IFTA 30%

Normales Tubulointerstitium



Interstitielle Fibrose und Tubulusatrophie



CKDx?

SPECIAL REPORT

OXFORD ERA ndt

Nephrol Dial Transplant, 2025, **40**, 2390–2400
https://doi.org/10.1093/ndt/gfaf092
Advance access publication date: 3 June 2025

Chronic Kidney Disease of unexplained cause (CKDx): a consensus statement by the Genes & Kidney Working Group of the ERA

Jan Halbritter[1,*], Lucile Figueres[2,3,*], Albertien M. Van Eerde[4,*], Giovambattista Capasso[5,6], Ewout J. Hoorn[7], Tom Nijenhuis[8], Maria Vanessa Perez-Gomez[9,10,11], John A. Sayer[12,13,14], Matias Simons[15], Stephen Walsh[16,†], Nikola Zagorec[17,18], Roman-Ulrich Müller[19,20,21,‡] and Emilie Cornec-Le Gall[17,22,‡]; on behalf of the Genes & Kidney Working Group of the ERA

Practice point 1.1:
CKDx is a diagnosis of exclusion. We suggest classifying the cause of CKD as CKDx in all cases in which a specific cause cannot be defined in a given healthcare system after reasonable diagnostic workup; taking into account potential limitations in access to and availability of modern diagnostic technologies.

Statement 4.1:
Genetic testing should be considered in all cases of CKDx. The expected diagnostic rate of genetic testing depends on the presence of several factors in the patient history. In individuals under 60 years of age, it is increasingly regarded as a standard diagnostic approach; omission of testing in this population should be supported by a clear clinical rationale.

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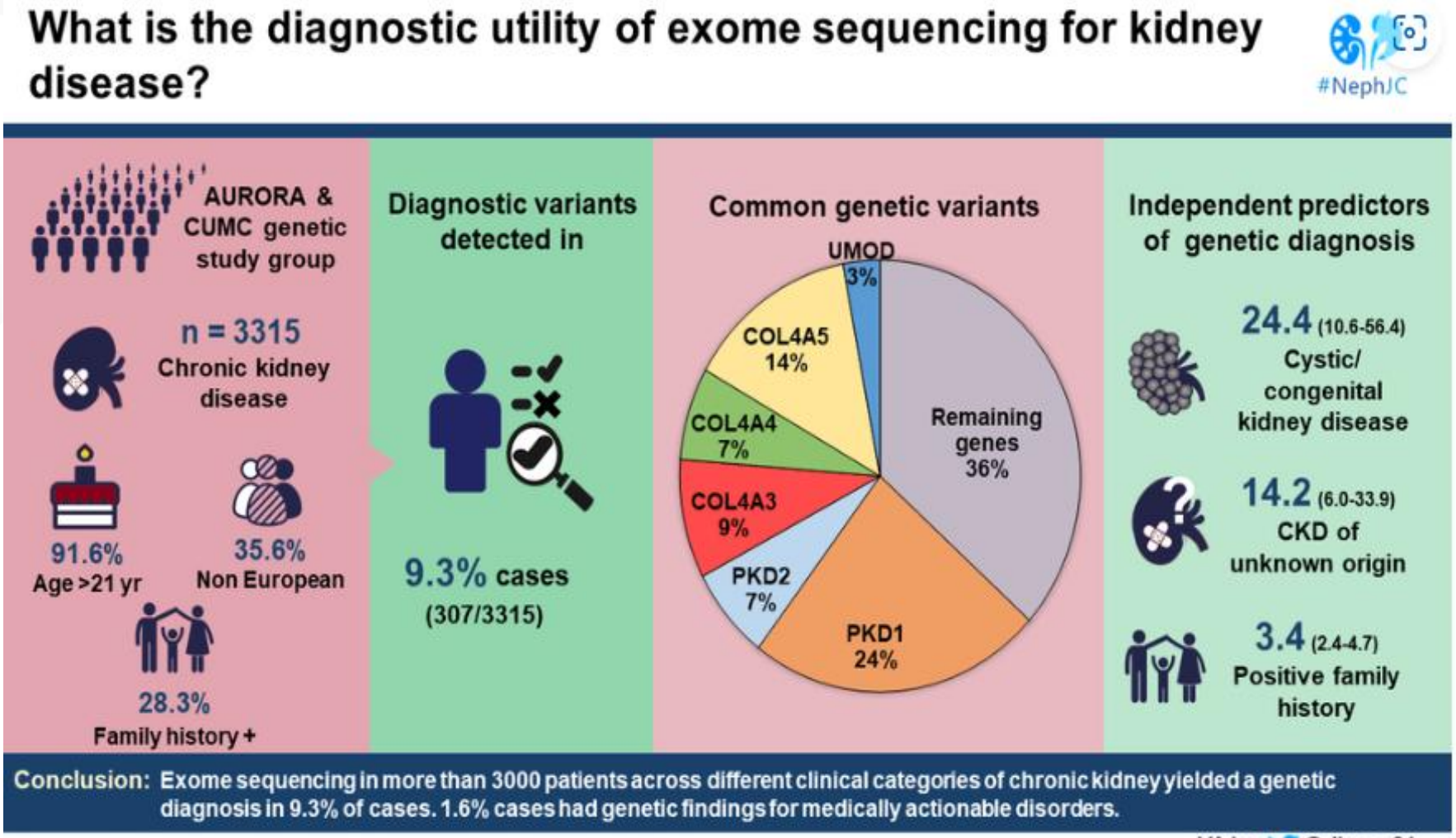
Genetic kidney disease – the elephant in the room



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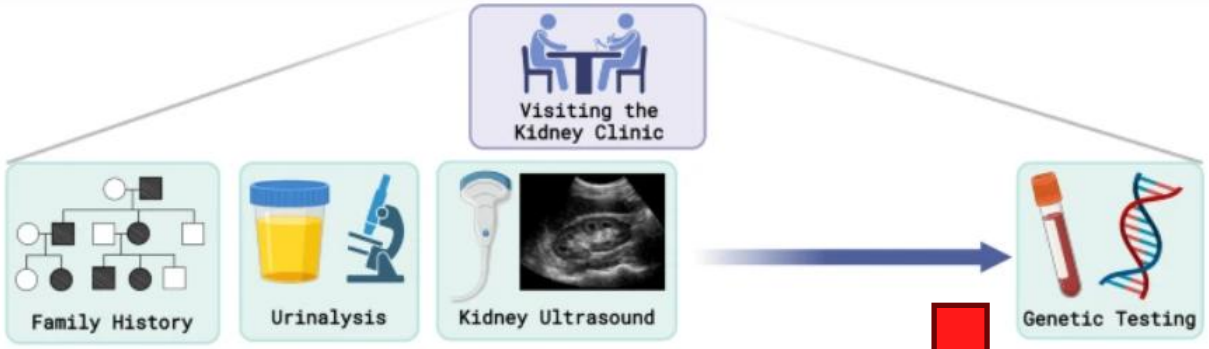
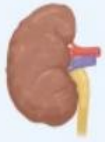
Genetic kidney diseases



Top 3 Most Likely Diagnoses

	Autosomal Dominant Polycystic Kidney Disease (ADPKD)	Alport Syndrome	Autosomal Dominant Tubulointerstitial Kidney Disease (ADTKD)
			
Kidney Size:	Large with multiple cysts	Small	Normal/small
Urine Sediment:	Often blood/protein	Blood	No blood/protein
Inheritance Pattern:	Autosomal dominant	X-linked recessive Autosomal recessive Autosomal dominant	Autosomal dominant
Percentage of end stage kidney failure cohort in the UK:	10%	3-5%	3%

Mabillard, H., Olinger, E. & Sayer, J.A. UMOD and you! Explaining a rare disease diagnosis. J Rare Dis 1, 4 (2022)

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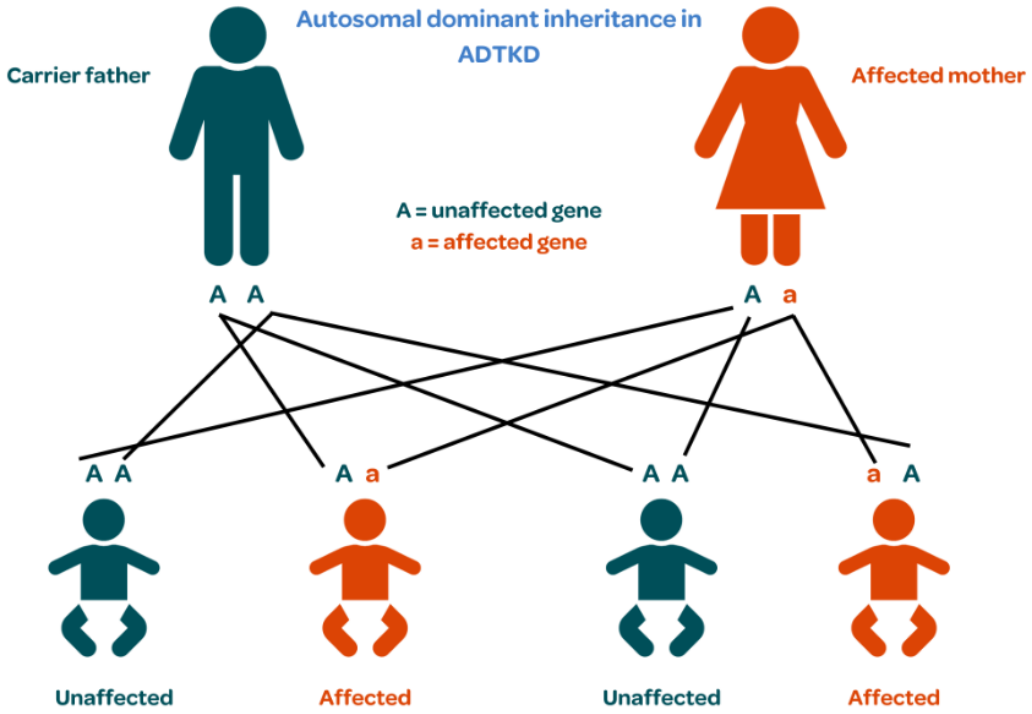
ADTKD

= autosomal dominante tubulointerstitielle Nierenerkrankung

- 3.häufigste Ursache genetischer Nierenerkrankungen
- 2-5% aller monogenetischen Nierenerkrankungen



kidneycareuk.org

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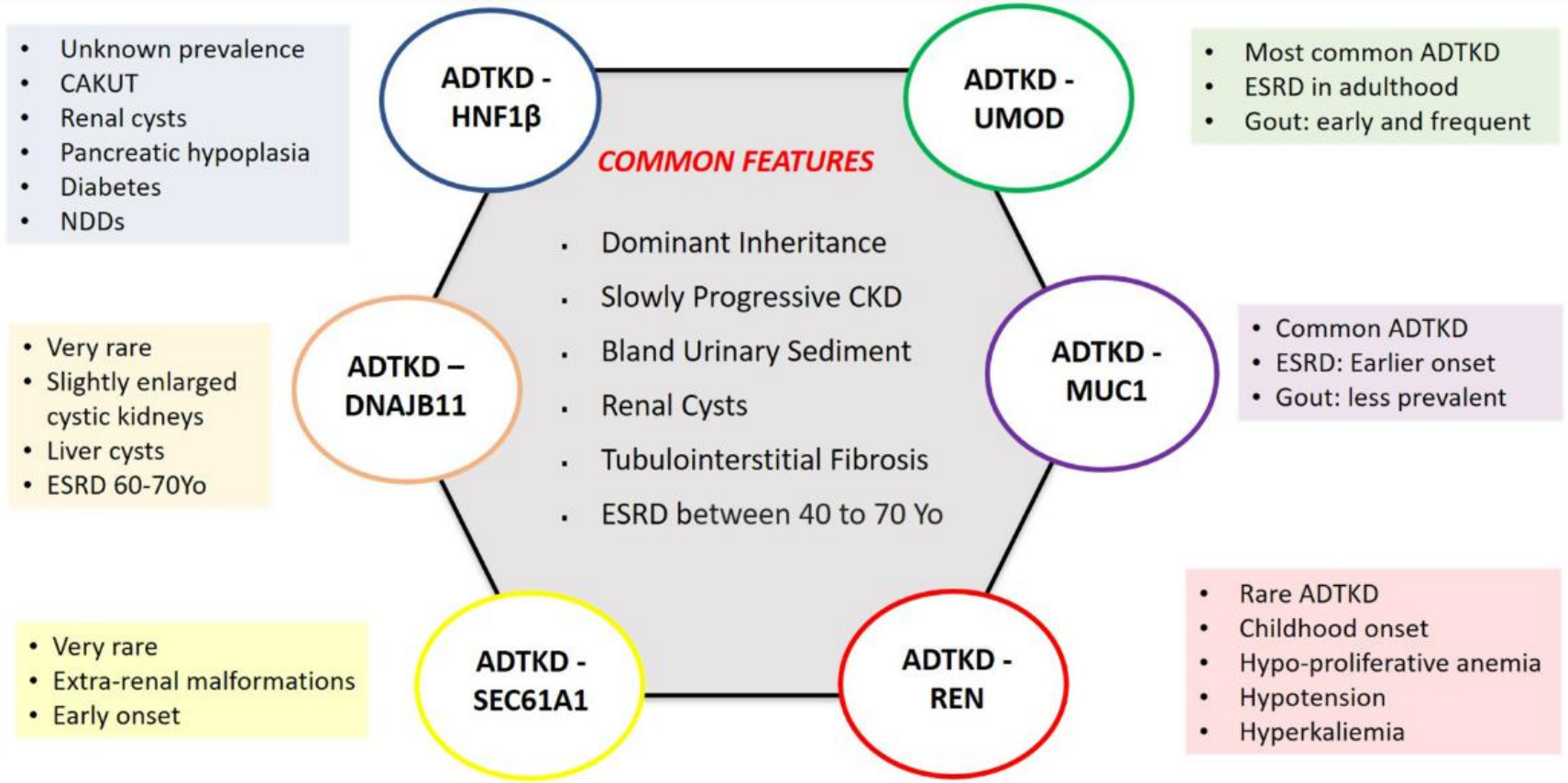
ATDKD - Subtypen



Izzi et al; Kidney International Reports, Nov. 2022, Vol.7, Issue 11, 2332-2344

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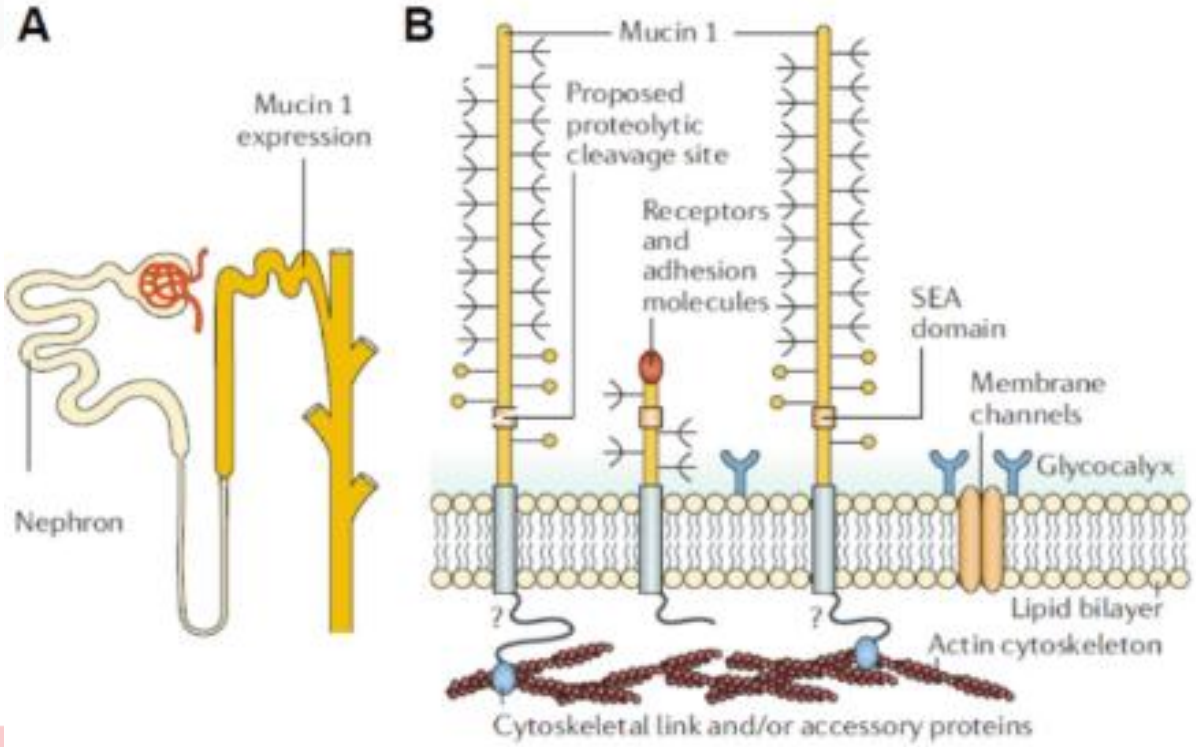
Mucin-1

- membrangebundenes Glykoprotein auf Epithel vieler Gewebe (u.a. Verdauungstrakt, Gebärmutter, Prostata, Lunge,…)
- in der Niere hauptsächlich in Henle-Schleife und früh-distalem Tubulus exprimiert
- Funktion: Signaltransduktion sowie Epithelschutz

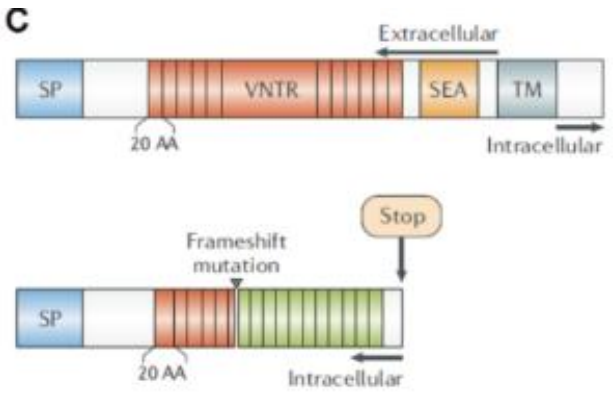


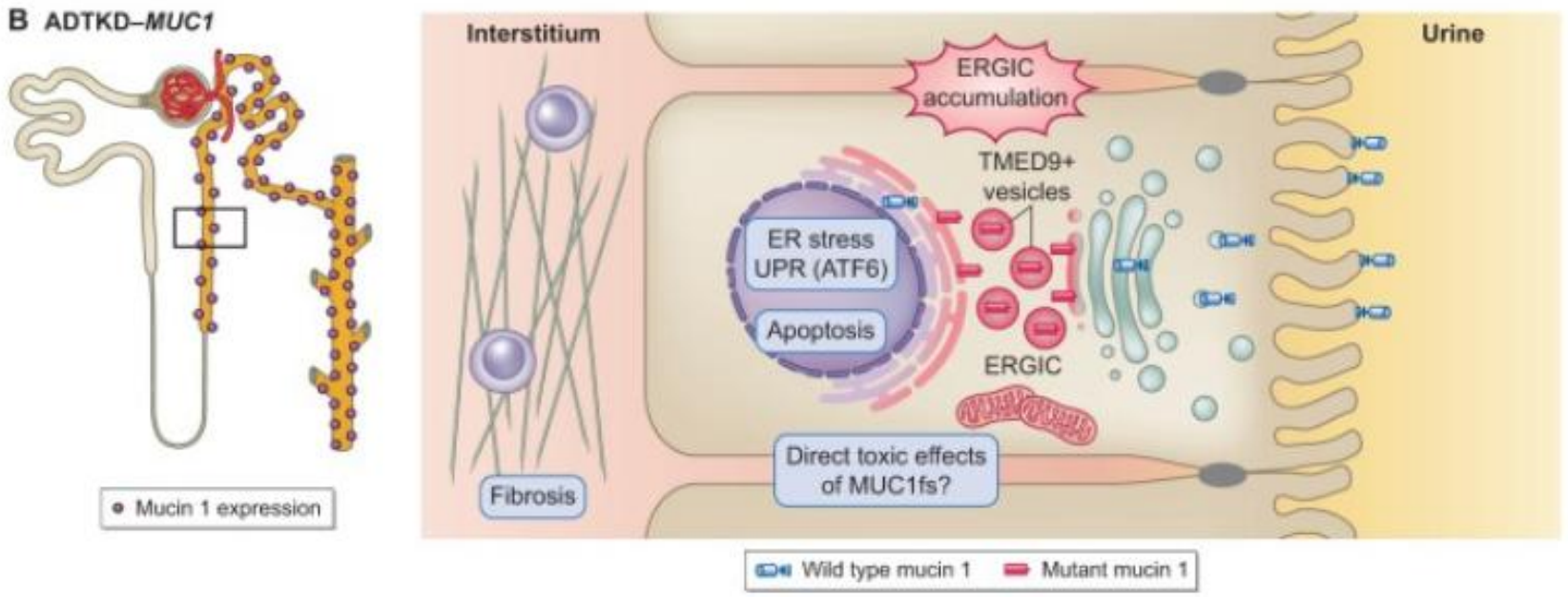
Devuyst, O. et al. Autosomal dominant tubulointerstitial kidney disease. Nat Rev Dis Primers 5, 60 (2019)

ATDKD-MUC1

Frameshift-Mutation

führt zur Akkumulation fehlgefalteter Proteine, intrazellulärem Stress, Apoptose





Devuyst, O., Olinger, E., Weber, S. et al. Autosomal dominant tubulointerstitial kidney disease. Nat Rev Dis Primers 5, 60 (2019)

ADTKD(-MUC1): Klinische Manifestation

- langsam fortschreitende CKD
- durchschnittlicher eGFR-Verlust: 2-3 ml/min/Jahr
- Durchschnittsalter bei Erreichen ESKD 46 Jahre
- i.d. Regel wenig bis keine Proteinurie
- keine Biomarker
- sonografisch keine festen Diagnosekriterien

Findings	*UMOD* Patients	*MUC1* Patients	Total
Normal kidney size without cysts	5 (31%)	17 (32%)	22
Normal kidney size with cysts	2 (13%)	14 (26%)	16
Small hyperechogenic kidneys	8 (50%)	16 (30%)	24
Hyperechogenic kidneys with cortical cysts	—	6 (11%)	6
Other findings	1 (6%)	—	1

Ayasreh, Nadia et al., AJKD, Volume 72, Issue 3, 411 - 418

ADTKD(-MUC1): Therapie

Keine kausale Therapiemöglichkeit, maximale Renoprotektion

- RASi in maximal tolerierter Dosierung
- RR-Einstellung, Zielblutdruck < 120 mmHg systolisch, sofern toleriert
- SGLT-2-Hemmertherapie (?)
- Absolute Nikotinkarenz
- Anstreben von Normalgewicht

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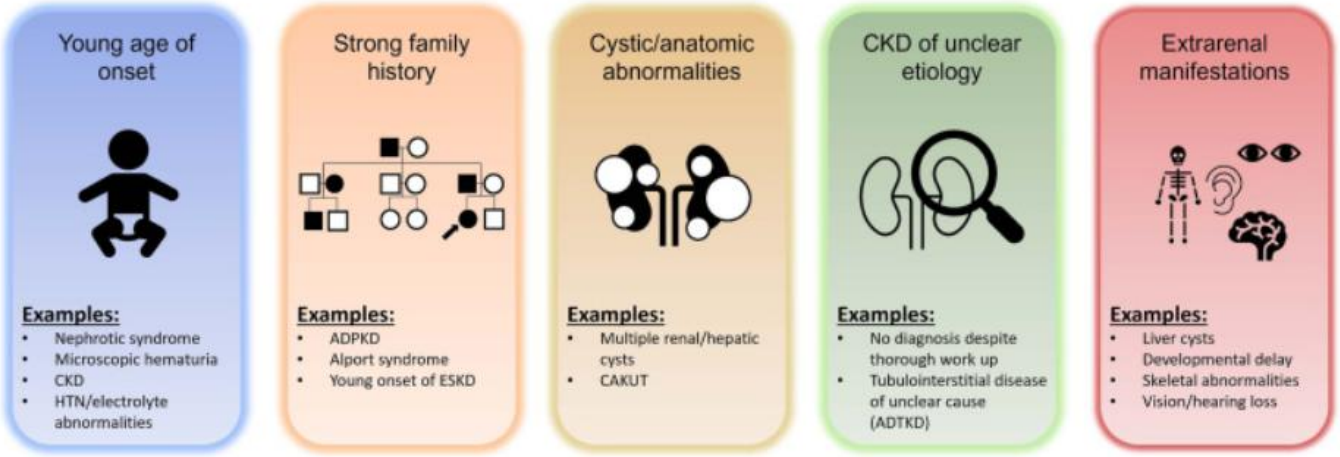
Zusammenfassung

- Mögliche Kriterien für Indikation zur genetischen Diagnostik:
  - CKD-Beginn im jungen Patientenalter
  - Positive Familienanamnese
  - Syndromale Erkrankungen mit extrarenalen phänotypischen Auffälligkeiten
  - Unklares Nierenbiopsie-Ergebnis bei Hämaturie und/oder Proteinurie



Aron, Abraham W. et al., American Journal of Kidney Diseases, Volume 84, Issue 5, 632 - 645

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Vielen Dank
für Ihre Aufmerksamkeit