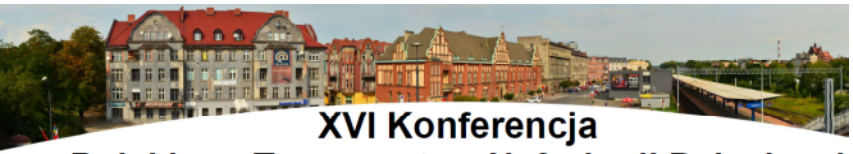
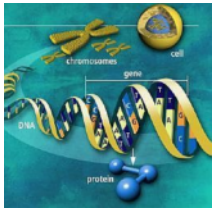


XVI Konferencja
Polskiego Towarzystwa Nefrologii Dziecięcej
11-13 maja 2017r.

# Kwalifikacja biorców i zasady doboru żywych dawców nerek w przypadku schorzeń uwarunkowanych genetycznie




Ryszard Grenda

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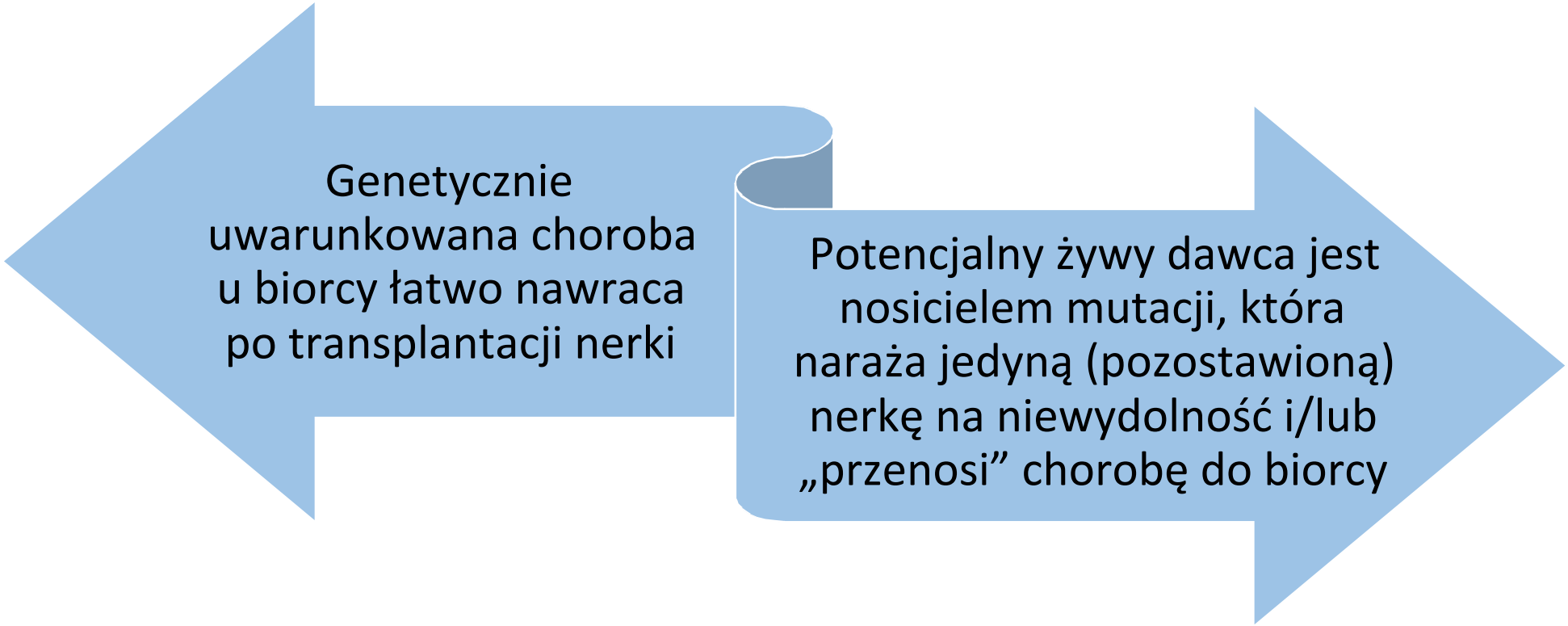
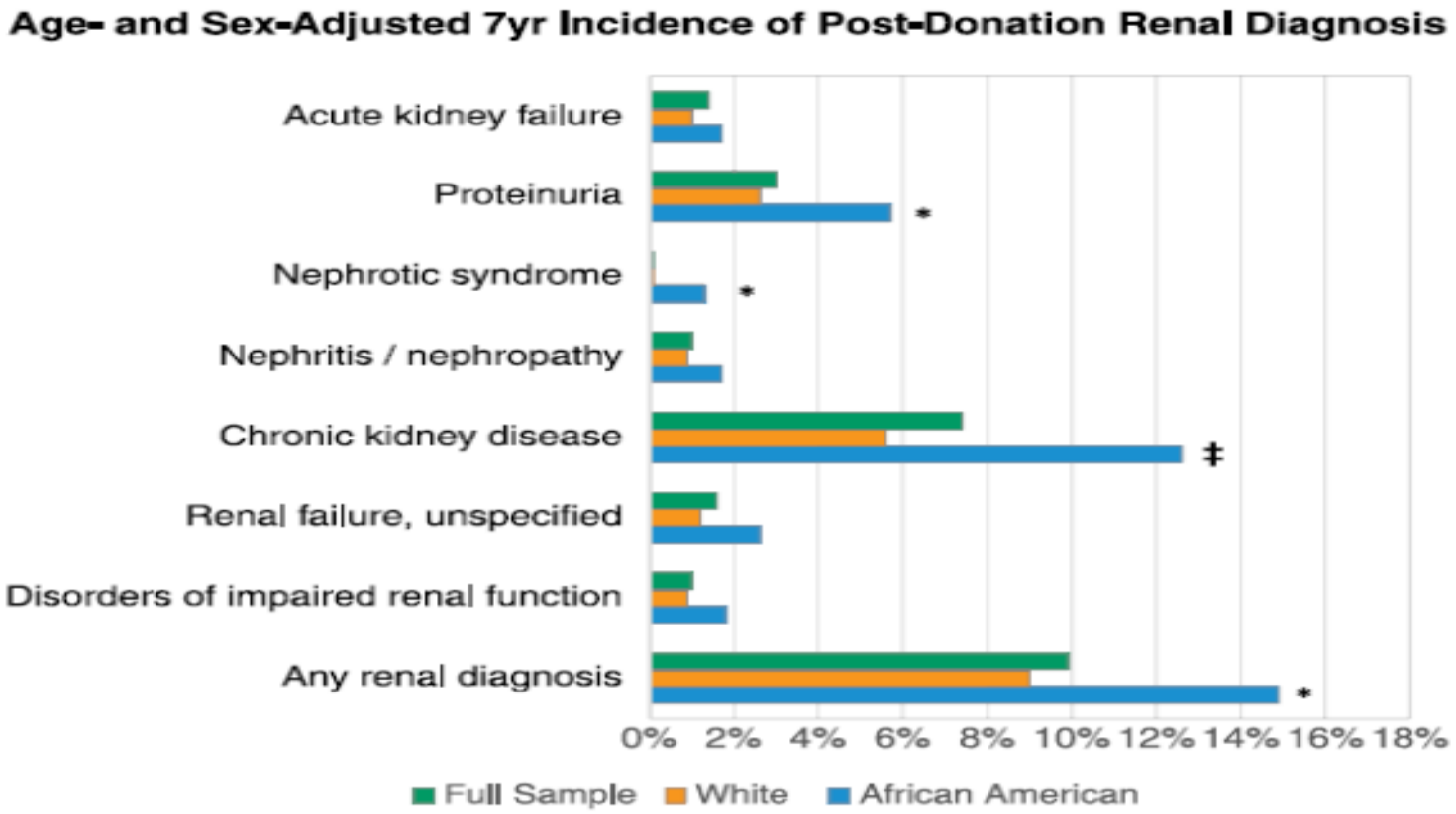
Konflikt interesów – nie występuje

Transplantacja ma przynieść korzyść biorcy,
ale
nie może jednocześnie spowodować
pogorszenia stanu zdrowia lub zwiększenia
ryzyka rozwoju swoistej choroby
u żywego dawcy

# Warianty sytuacji wątpliwych



# Paleta możliwości odległych „nerkowych” skutków donacji nerki




(*Transplantation* 2015;99: 1723–1729)

The AJT Report
News and issues that affect organ and tissue transplantation
American Journal of Transplantation 2012; 12: 2865-2866

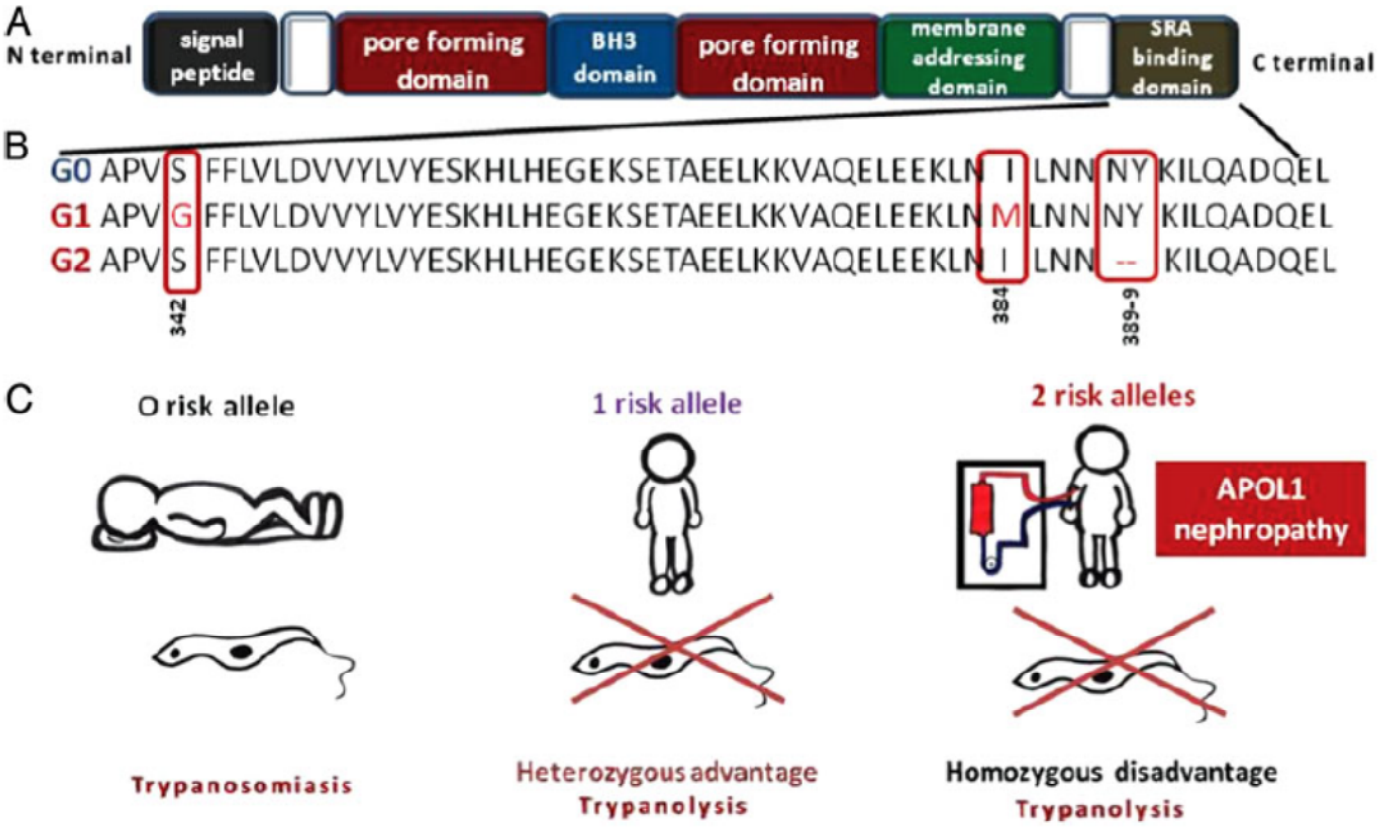
# Genetic Factor May Limit Kidney Donation

## *Should African Americans with two* APOL1 *risk variants be prevented from donating kidneys?*

# *APOL1* nephropathy: from gene to mechanisms of kidney injury

Nephrol Dial Transplant (2016) 31: 349–358

Etty Kruzel-Davila[1,2,*], Walter G. Wasser[2,3,*], Sharon Aviram[1] and Karl Skorecki[1,2]



# Living donor kidney transplantation in patients with hereditary nephropathies

*Patrick Niaudet*

Niaudet, P. *Nat. Rev. Nephrol.* 6, 736–743 (2010)

**Table 1** | Autosomal recessive diseases that progress to end-stage renal disease

| Disease | Gene | Gene product | Is living related donor transplantation appropriate? |
|---|---|---|---|
| Congenital nephrotic syndrome (Finnish type) | *NPHS1* | Nephrin | Yes ? |
| Autosomal recessive SRNS | *NPHS2* | Podocin | Yes—after genetic testing to exclude the Arg229Gln (p.R229Q) variant in the donor |
| Autosomal recessive SRNS | *NPHS3* (*PLCE1*) | Phospholipase Cε | Yes |
| Pierson syndrome | *LAMB2* | Laminin β2 | Yes |
| Schimke's immuno-osseous dystrophy | *SMARCAL1* | HepA-related protein | Yes |
| Nephronophthisis | *NPHP1* to *NPHP9* | Nephrocystines 1 to 9 | Yes |
| Cystinosis | *CNTS* | Lysosomal cystine transporter | Yes |
| ARPKD | *PKHD1* | Fibrocystin | Yes |
| Alport syndrome | *COL4A3*, *COL4A4* | α3 and α4 type IV collagen | Yes ? |
| Primary hyperoxaluria | *AGXT* | Alanine glyoxylate aminotransferase | No |
| Atypical HUS | *CFH*, *CFHR1*, *CFHR3*, *CD46* | Complement factor H, complement factor H-related proteins 1 and 3 | No ? |

Abbreviations: ARPKD, autosomal recessive polycystic kidney disease; HUS, hemolytic uremic syndrome; SRNS, steroid-resistant nephrotic syndrome.

**Table 2** | Autosomal dominant diseases that progress to end-stage renal disease

| Disease | Gene | Gene product | Is living related donor transplantation appropriate? |
|---|---|---|---|
| ADPKD type 1 | *PKD1* | Polycystin 1 | Yes—for unaffected relatives |
| ADPKD type 2 | *PKD2* | Polycystin 2 | Yes—for unaffected relatives |

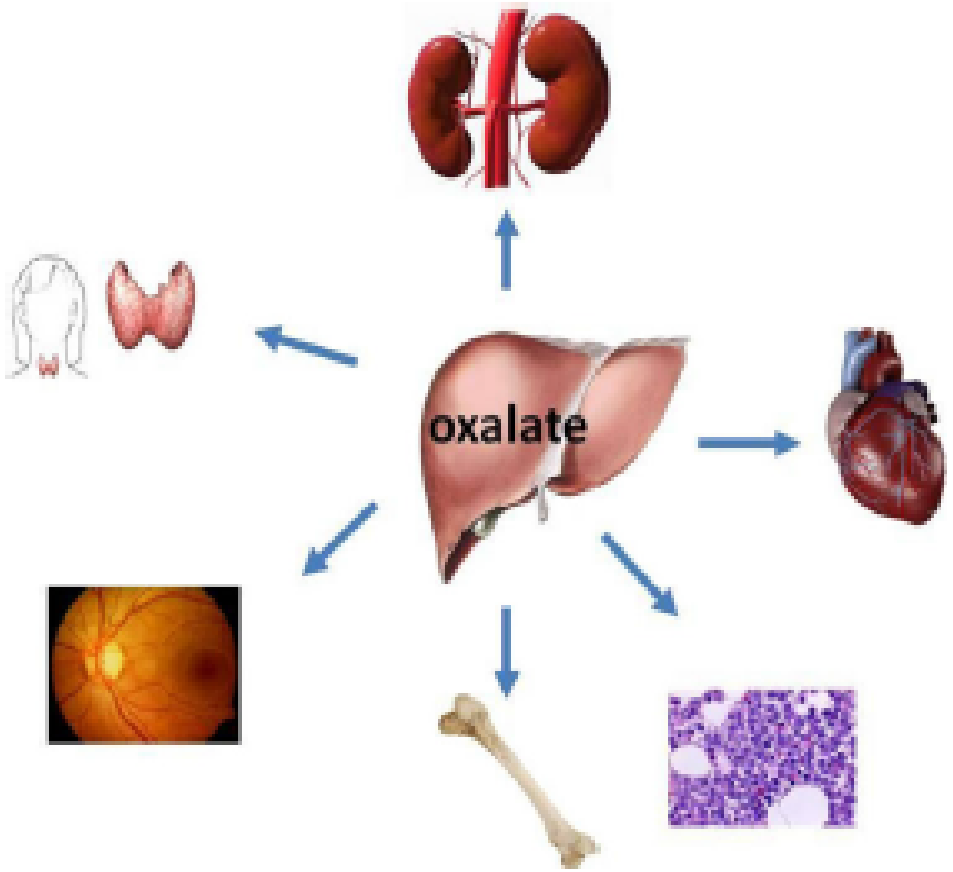
# Kiedy korzystamy/ nie korzystamy z dawstwa rodzinnego?

NIE

# Pierwotna oksaloza - (hiperoksaluria typu I)

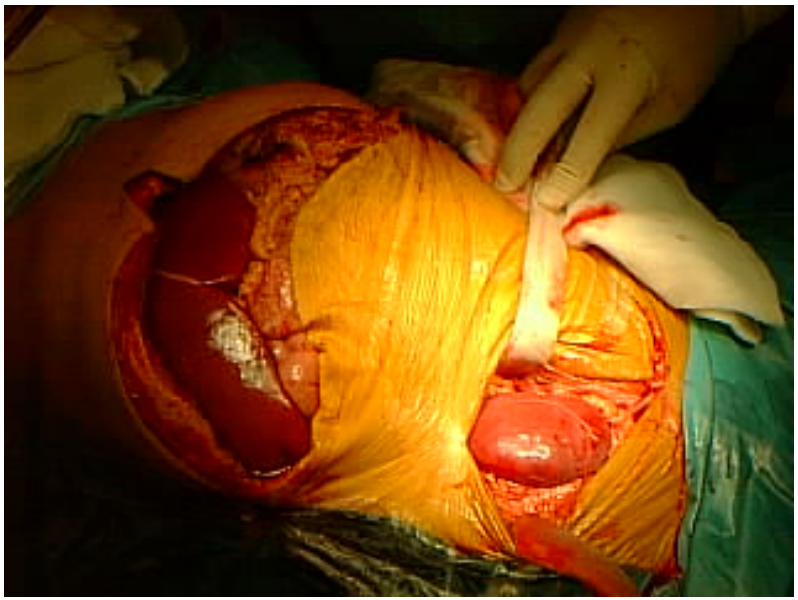
- Przyczyna: dziedziczony w sposób autosomalny recesywny brak aktywności (lub niedocieranie do mitochondriów) wątrobowego (peroksysomalnego) enzymu aminotransferazy alaninowo-glioszczawianowej (AGT)
- Gen: AGXT *locus* 2q37.3, mutacja $G_{630}A$
- Częstość: 1:120 000 urodzeń
- Efekt: odkładanie złogów szczawianów wapnia w nerkach, kośćcu, mięśniu sercowym, siatkówce oka, włóknach nerwowych i innych tkankach - w wyniku tego schyłkowa niewydolność  nerek, ciężkie zmiany kostne i inne patologie

| Disease | Gene | Gene product | Is living related donor transplantation appropriate? |
|---|---|---|---|
| Primary hyperoxaluria | *AGXT* | Alanine glyoxylate aminotransferase | No |



## Pierwotna oksaloza (PH1)

SKOJARZONE
PRZESZCZEPIENIE
WĄTROBY I NERKI
WCZEŚNIE (GFR < 20),
ZANIM DOJDZIE DO
CIĘŻKICH USZKODZEŃ
WIELONARZĄDOWYCH
(*pre-emptive*
*transplantation)*



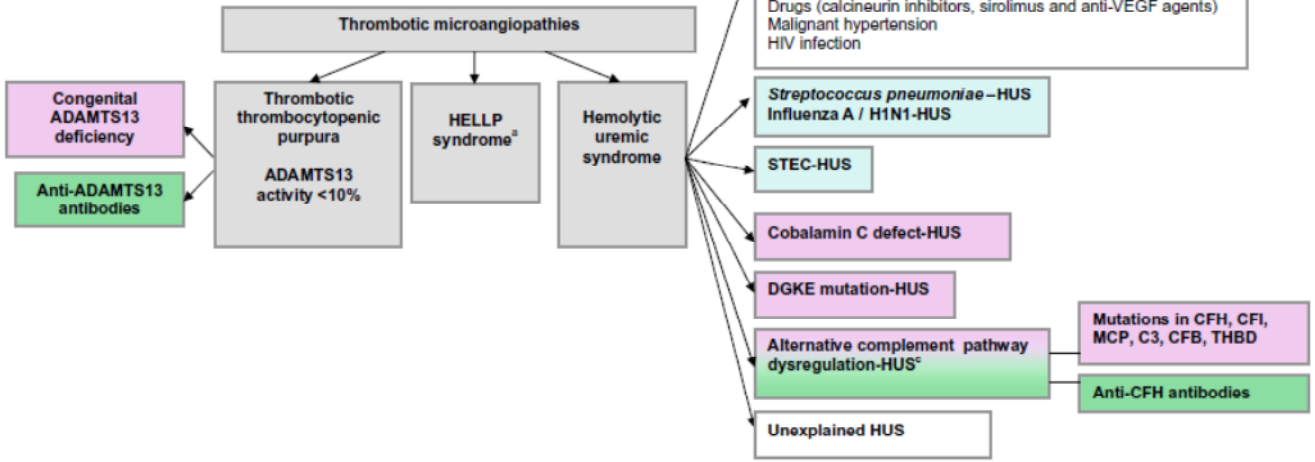
Dawca żywy ? – wykluczone !

**An international consensus approach to the management of atypical hemolytic uremic syndrome in children**

Cl Pediatr Nephrol khouri · Gema Ariceta · Nesrin Besbas · Martin Bitzan · Anna Bjerre · Rosanna Coppo · Francesco Emma · Sally Johnson · Diana Karpman · Daniel Landau · Craig B Langman · Anne-Laure Lapeyraque · Christoph Licht · Carla Nester · Carmine Pecoraro · Magdalena Riedl · Nicole C. A. J. van de Kar · Johan Van de Walle · Marina Vivarelli · Véronique Frémeaux-Bacchi · for HUS International

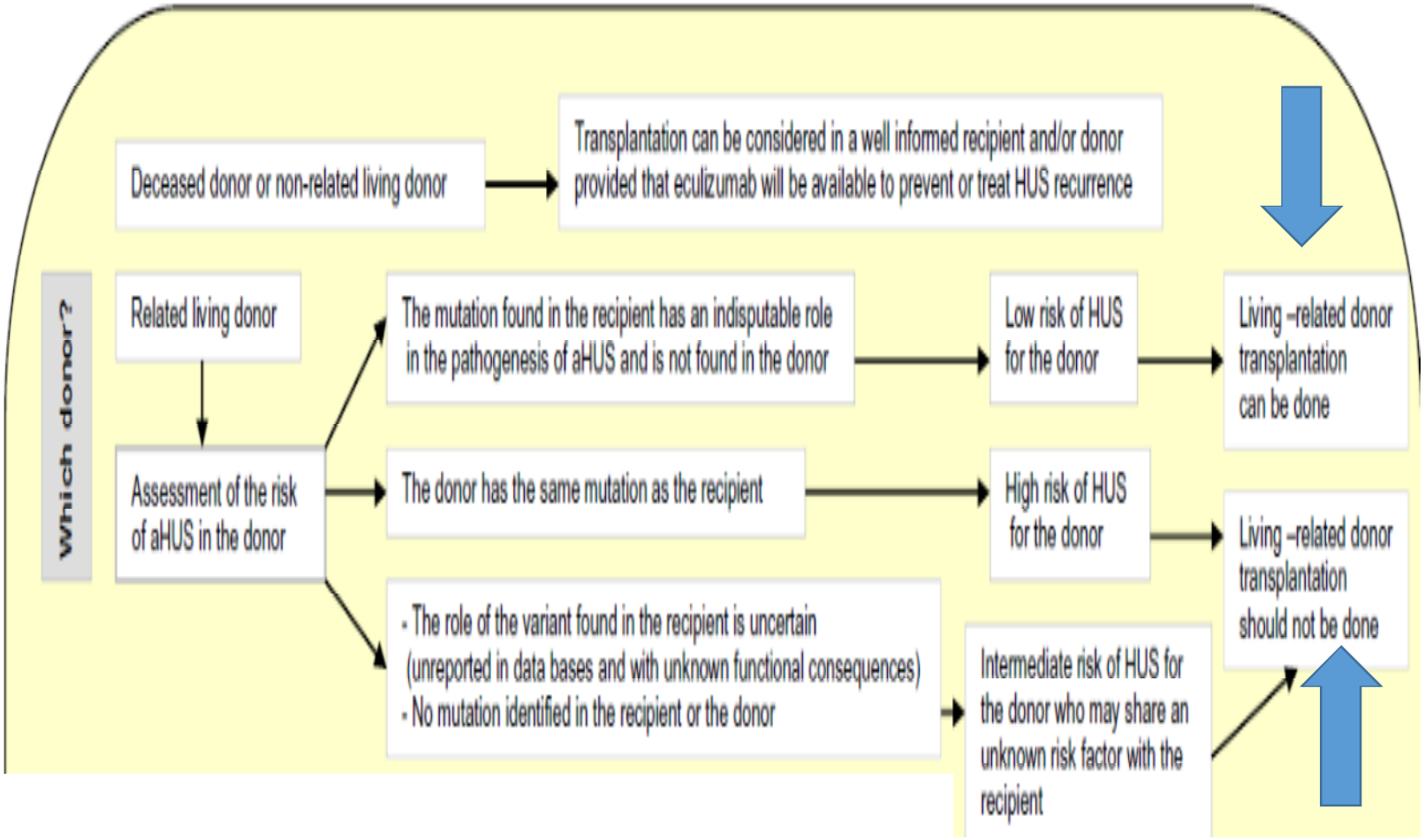
| Disease | Gene | Gene product | Is living related donor transplantation appropriate? |
|---|---|---|---|
| Atypical HUS | *CFH, CFHR1, CFHR3, CFB, CFI, C3* | Complement proteins | No |

**When**




**Why**

Genetic characterization necessary for
- Confirmation that the disease is complement-dependent or not
- Establishing prognosis, risk of relapses and of progression to ESRD
- Genetic counselling to parents and family
- Decisions for kidney transplantation: choice of the donor, treatment schedule to prevent or treat post-transplant recurrence, decision of combined kidney-liver transplantation
- Further prospective studies are required to establish the safety of complement blockade treatment discontinuation, according to the genetic background

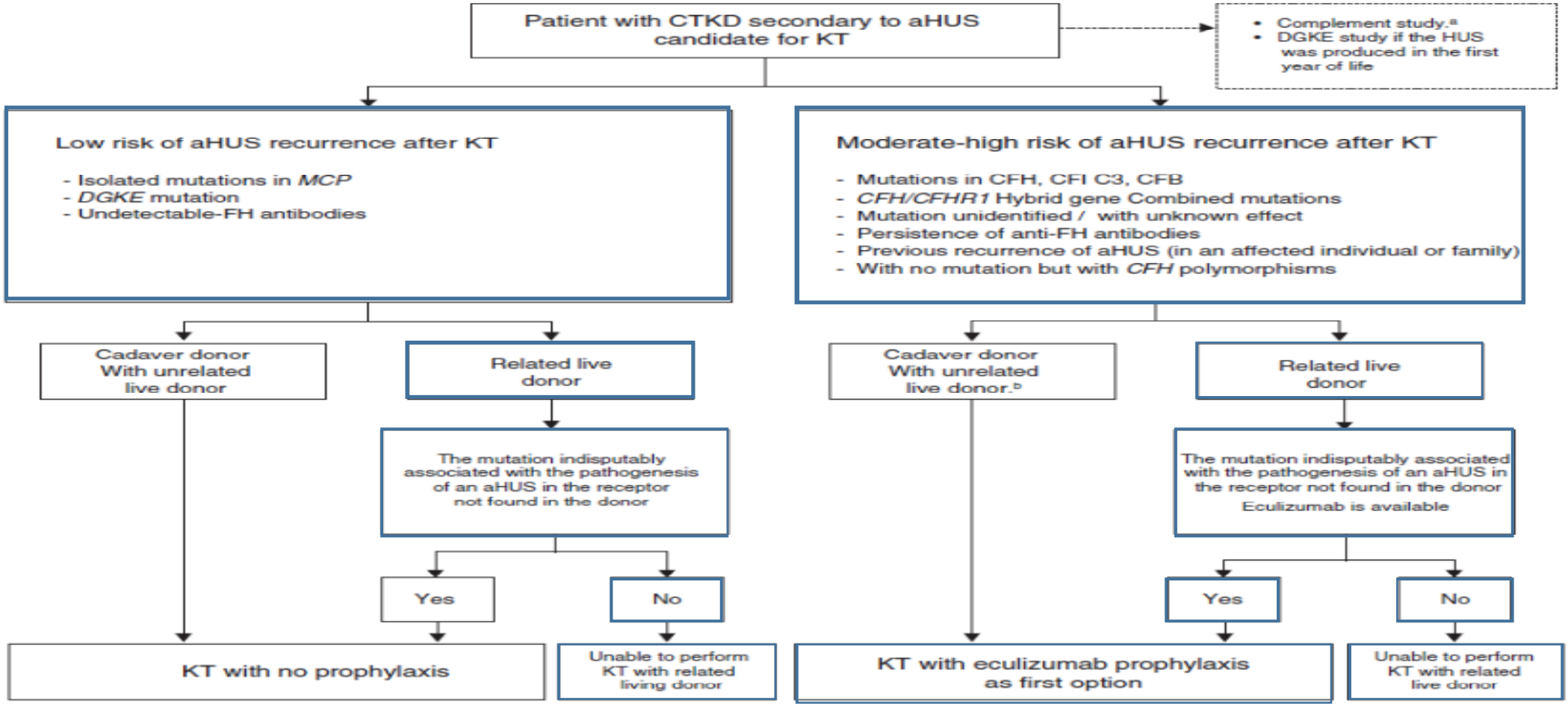

Which donor?
Deceased donor or non-related living donor
Transplantation can be considered in a well informed recipient and/or donor provided that eculizumab will be available to prevent or treat HUS recurrence
Related living donor
Assessment of the risk of aHUS in the donor
The mutation found in the recipient has an indisputable role in the pathogenesis of aHUS and is not found in the donor
Low risk of HUS for the donor
Living –related donor transplantation can be done
The donor has the same mutation as the recipient
High risk of HUS for the donor
Living –related donor transplantation should not be done
- The role of the variant found in the recipient is uncertain (unreported in data bases and with unknown functional consequences)
- No mutation identified in the recipient or the donor
Intermediate risk of HUS for the donor who may share an unknown risk factor with the recipient

# An update for atypical haemolytic uraemic syndrome: Diagnosis and treatment. A consensus document☆

*Josep M. Campistol[a,*], Manuel Arias[b], Gema Ariceta[c], Miguel Blasco[a], Laura Espinosa[d], Mario Espinosa[e], Josep M. Grinyó[f], Manuel Macía[g], Santiago Mendizábal[h], Manuel Praga[i], Elena Román[h], Roser Torra[j], Francisco Valdés[k], Ramón Vilalta[c], Santiago Rodríguez de Córdoba[l]*

NEFROLOGIA. 2015;

nefrología
Revista de la Sociedad Española de Nefrología



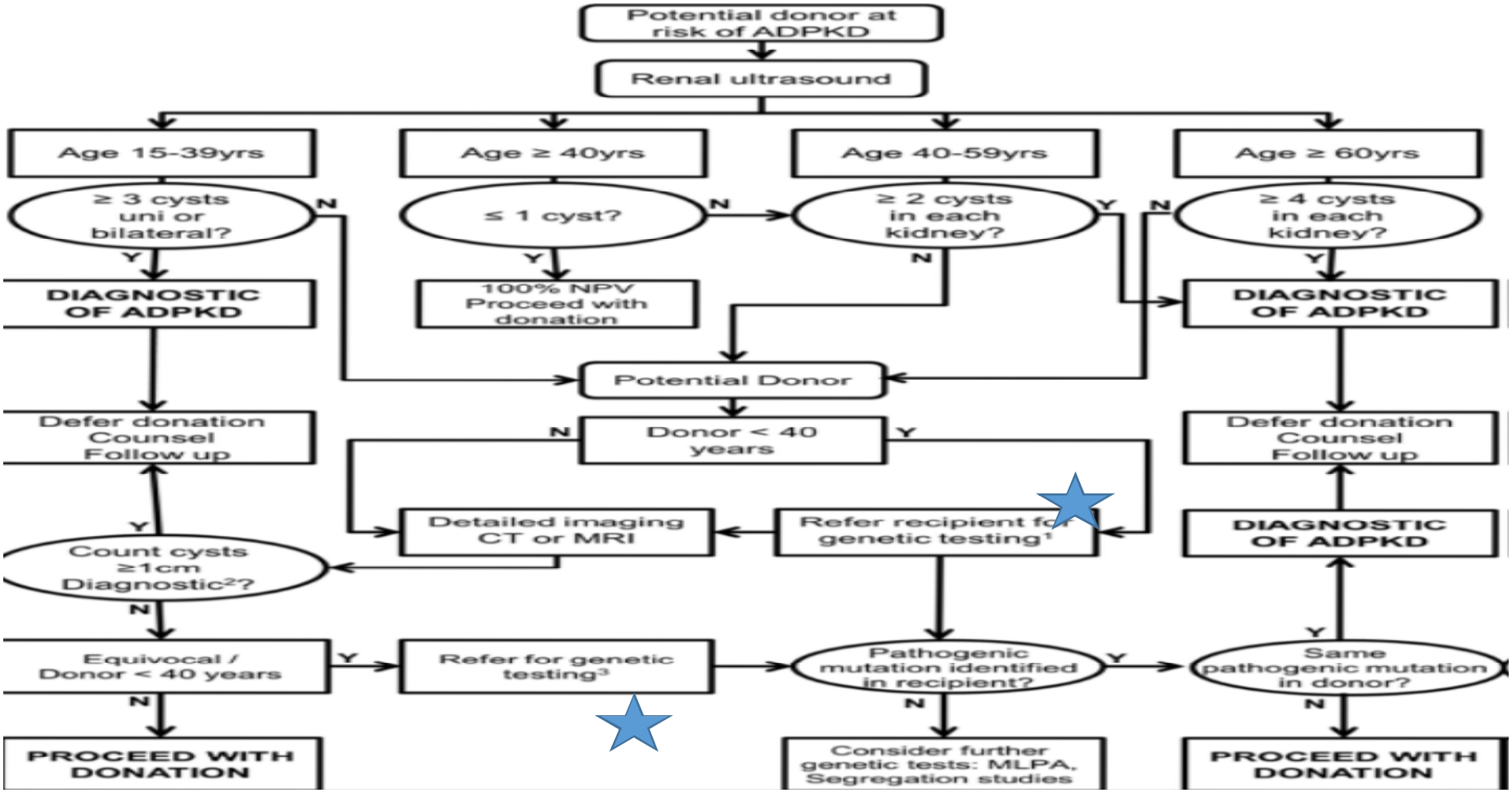
# Tak lub nie

| Disease | Gene | Gene product | Is living related donor transplantation appropriate? |
|---|---|---|---|
| ADPKD type 1 | *PKD1* | Polycystin 1 | Yes—for unaffected relatives |
| ADPKD type 2 | *PKD2* | Polycystin 2 | Yes—for unaffected relatives |

# Genetic Testing in the Assessment of Living Related Kidney Donors at Risk of Autosomal Dominant Polycystic Kidney Disease

(*Transplantation* 2015;99: 1023–1029)

Roslyn J. Simms,[1,2,3] Debbie L. Travis,[4] Miranda Durkie,[4] Gill Wilson,[4] Ann Dalton,[4] and Albert C.M. Ong[2,3]



# Autosomal dominant polycystic kidney disease: Emerging concepts of pathogenesis and new treatments

WILLIAM E. BRAUN, MD
Glickman Urological and Kidney Institute, Cleveland Clinic

CLEVELAND CLINIC JOURNAL OF MEDICINE VOLUME 76 • NUMBER 2 FEBRUARY 2009

## Ravine ultrasonographic criteria for diagnosing autosomal dominant polycystic kidney disease

| AGE | POSITIVE FAMILY HISTORY | NEGATIVE FAMILY HISTORY |
|---|---|---|
| < 30 years | 2 cysts bilaterally (or unilaterally) | 5 cysts bilaterally |
| 30–60 years | 4 cysts bilaterally | 5 cysts bilaterally |
| > 60 years | 8 cysts bilaterally | 8 cysts bilaterally |

# Inadvertent Transmission of Polycystic Kidney Disease in Kidney Transplantation

Amit Langote*
Andrea Mazarova*
John Mahoney
Brian Blew
Greg A. Knoll

© Am J Case Rep, 2015; 16: 115-118

American Journal of Case Reports

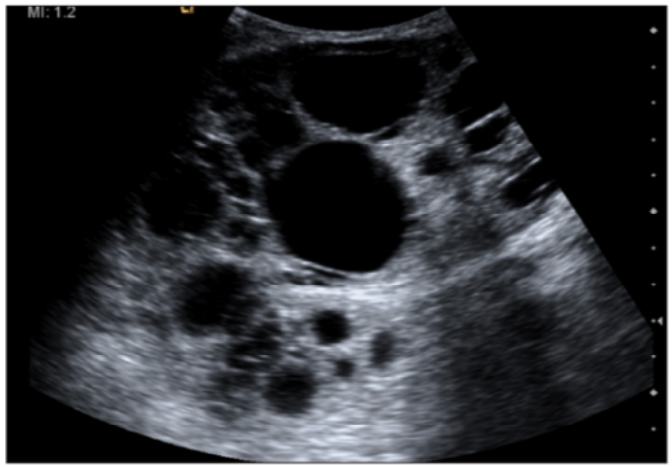



**Figure 1.** Ultrasound image from Case 1 showing multiple cortical cysts replacing the entire renal parenchyma of the transplant kidney.

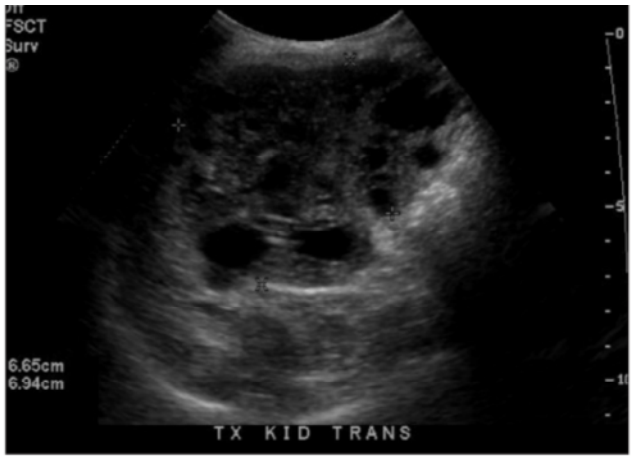



**Figure 2.** Ultrasound image from Case 2 showing multiple cysts throughout the kidney transplant replacing the normal

donor was a 30-year-old man who died due to rupture of an intracranial aneurysm. There was no clinical evidence of kidney disease in either the donor or his family. However, both recipients gradually developed PKD phenotype in their renal grafts. Subsequently, the donor's genetic testing results confirmed a novel PKD1 mutation.

*Kidney Int*. 2015 April ; 87(4): 671–673. doi:10.1038/ki.2015.16.

# Should kidney donors be genotyped for *APOL1* risk alleles?

**Barry I. Freedman, MD**[1] and **Bruce A. Julian, MD**[2]

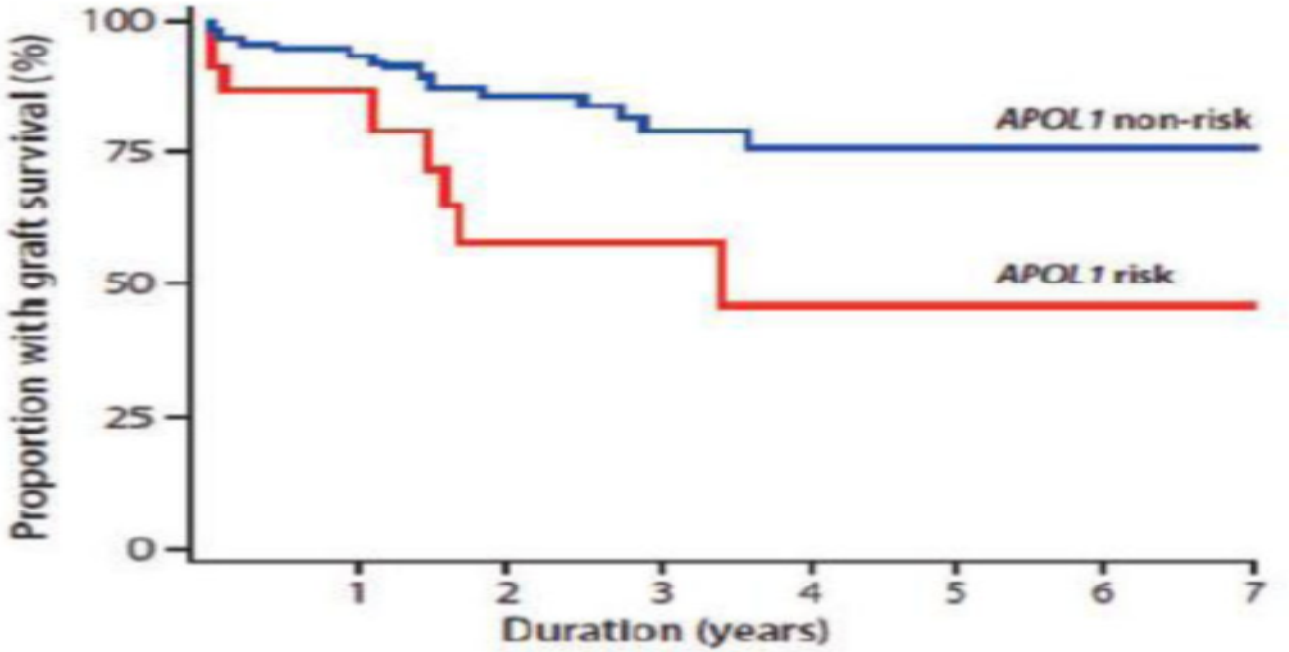



**Figure 1. Renal allograft survival according to *APOL1* genotype**

Kaplan-Meier renal allograft survival curve for recipients of donor kidneys with (red line) and without (blue line) two *APOL1* risk variant alleles.

Nephrol Dial Transplant (2009) 24: 1626–1630
doi: 10.1093/ndt/gfn635
Advance Access publication 21 November 2008

NDT
Nephrology Dialysis Transplantation

# Living donor kidney transplantation from relatives with mild urinary abnormalities in Alport syndrome: long-term risk, benefit and outcome

Oliver Gross[1], Manfred Weber[2], Jochen W. U. Fries[3] and Gerhard-Anton Müller[1]

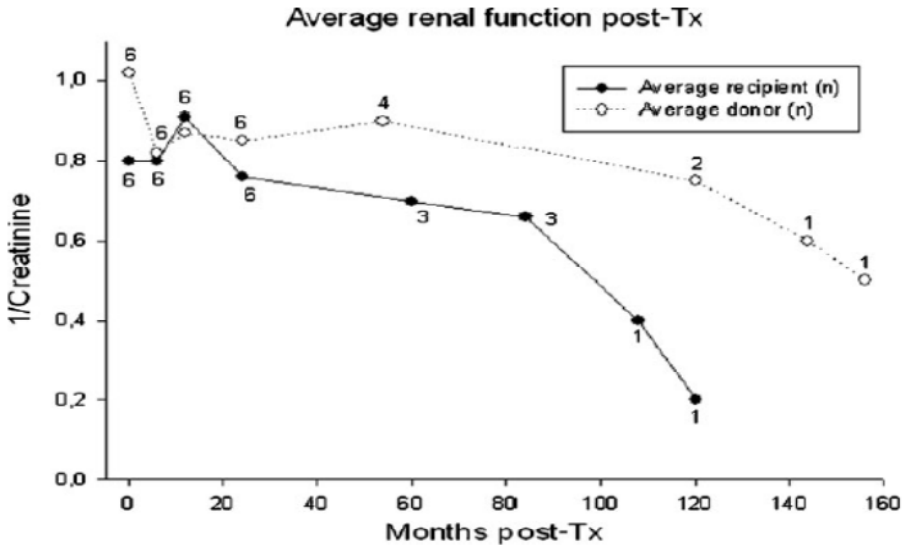



**Fig. 4.** Average decrease of renal function (1/creatinine) in recipients and donors.

**Conclusion.** Living donor Tx from relatives in Alport families is an ambivalent option. Proteinuria should be an exclusion criterion. Yet, even in donors with isolated microhaematuria, families and their physicians should be aware of an increased risk of renal failure in donor and recipient. This risk might be minimized by careful donor evaluation including biopsy and nephroprotective strategies after Tx in both donor and recipient.

| Disease | Gene | Gene product | Is living related donor transplantation appropriate? |
|---|---|---|---|
| Alport syndrome | COL4A3, COL4A4 | α3 and α4 type IV collagen | Yes |

?

Renal transplantation in patients with Alport syndrome

**Clifford E. Kashtan**

*Pediatr Transplantation 2006: 10: 651–657*

Table 2. Relative risk of kidney donation among relatives of patients with X-linked Alport syndrome, based on gender and results of urinalysis

| Gender of potential donor | Hematuria | Is there increased risk of progressive disease in donor? |
|---|---|---|
| Male | Yes | Yes (absolute contraindication to donation) |
| Male | No | No (no contraindication to donation) |
| Female | Yes | Yes (relative contraindication to donation) |
| Female | No* | No (no contraindication to donation) |

*5–7% of female heterozygotes are asymptomatic.

Table 3. Post-transplant anti-GBM nephritis: two susceptibility models

| | Broad | Restricted |
|---|---|---|
| Susceptibility | Most | Some (conferred by mutation type) |
| Allogeneic response (anti-GBM antibody production) | Common | Infrequent |
| Anti-GBM nephritis | Rare | Rare |

Table 4. Factors that should raise suspicion of post-transplant anti-GBM nephritis in a patient with Alport syndrome

| |
|---|
| Delayed graft function |
| Elevated serum creatinine |
| Hematuria |
| Proteinuria |
| Positive anti-GBM ELISA |

Fabry disease is a rare, X-linked, lysosomal storage disease (OMIM #301500) caused by mutations in the gene encoding the acid hydrolase enzyme alpha-galactosidase A (EC 3.2.1.22), which catalyses removal of a galactose moiety from neutral sphyngolipids, predominantly globotriaosylceramide ($Gb_3$). Deficiency in this enzyme causes intracellular accumulation of $Gb_3$ and related glycosphingolipids in a wide range of cell types throughout the body [1]. The major clinical manifestations include pain in the hands and feet (acroparaesthesia), angiokeratoma, as well as renal, cardiac, and cerebrovascular disease [2].

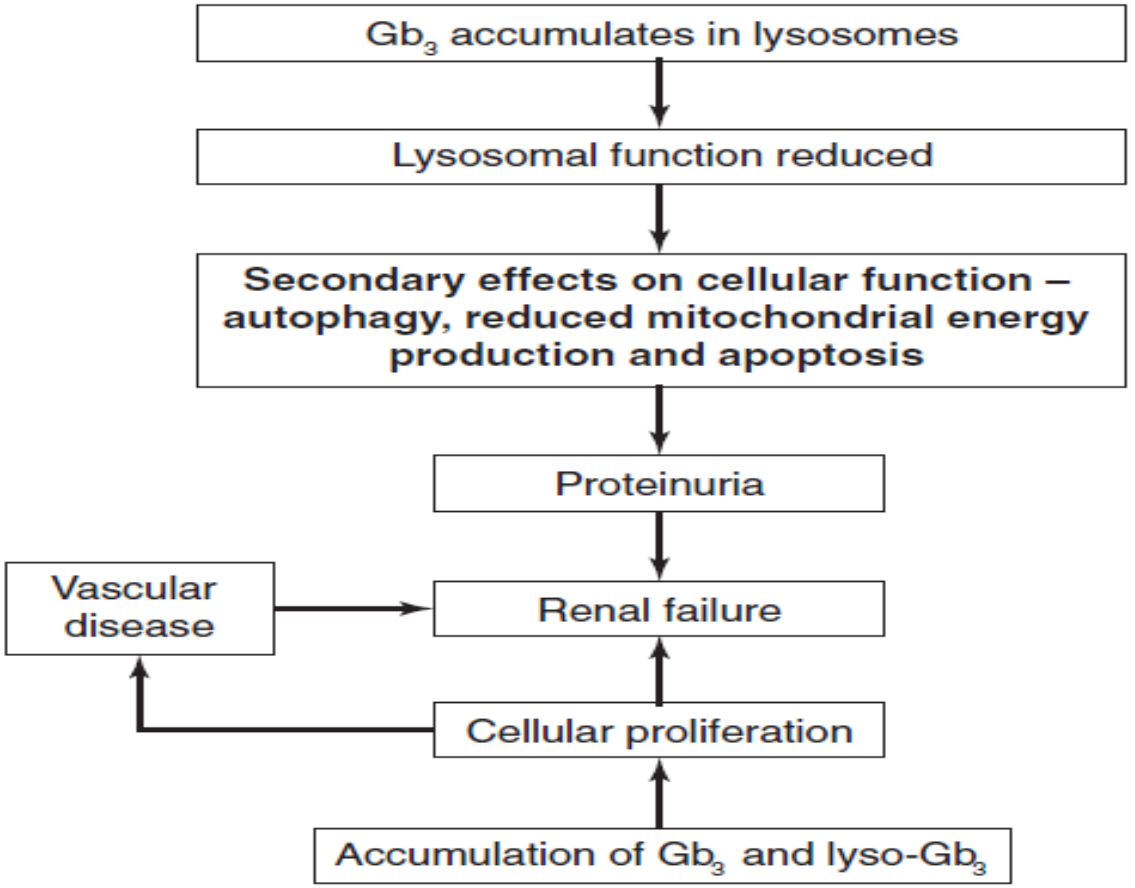



**Figure 1 Pathogenesis of Fabry nephropathy.** $Gb_3$, globotriaosylceramide; lyso-$Gb_3$, globotriaosylsphingosine.

| | | | |
|---|---|---|---|
| Fabry disease | *GLA* | α-Galactosidase | A risk of renal dysfunction exists in heterozygous female donors; living related transplantation is possible in donors who do not have the mutation |

**Ryszard Grenda**
Klinika Nefrologii, Transplantacji Nerek i Nadciśnienia Tętniczego Instytutu „Pomnik Centrum Zdrowia Dziecka" w Warszawie

Forum Nefrologiczne
2009, tom 2, nr 4, 227–231

ISSN 1899–3338

VIA MEDICA
www.fn.viamedica.pl

# Nawrót glomerulopatii po przeszczepieniu nerki

| Udokumentowany czynnik zwiększonego ryzyka | Czynniki o sprzecznym znaczeniu | Udokumentowany czynnik zmniejszonego ryzyka |
|---|---|---|
| Nawrót choroby w poprzednim przeszczepie | Płeć | Genetyczne tło (izolowanej) choroby kłębuszków |
| Szybki (< 3 lat) rozwój schyłkowej niewydolności nerek w przebiegu pierwotnej choroby | Obecność rozplemu mezangium w biopsji własnych nerek | „Syndromiczny" zespół nerczycowy u dzieci (tło genetyczne; uszkodzenie wielonarządowe) |
| „Dziecięca" postać zespołu nerczycowego (początek w dzieciństwie) | Obecność czynnika przepuszczalności białka | |
| | Rodzinne pochodzenie przeszczepu | |
| | Dobór HLA | |
| | Długość dializoterapii przed kwalifikacją do transplantacji | |
| | Rodzaj immunosupresji | |
| | Usunięcie własnych nerek przed transplantacją | |

# Increased glomerulonephritis recurrence after living related donation

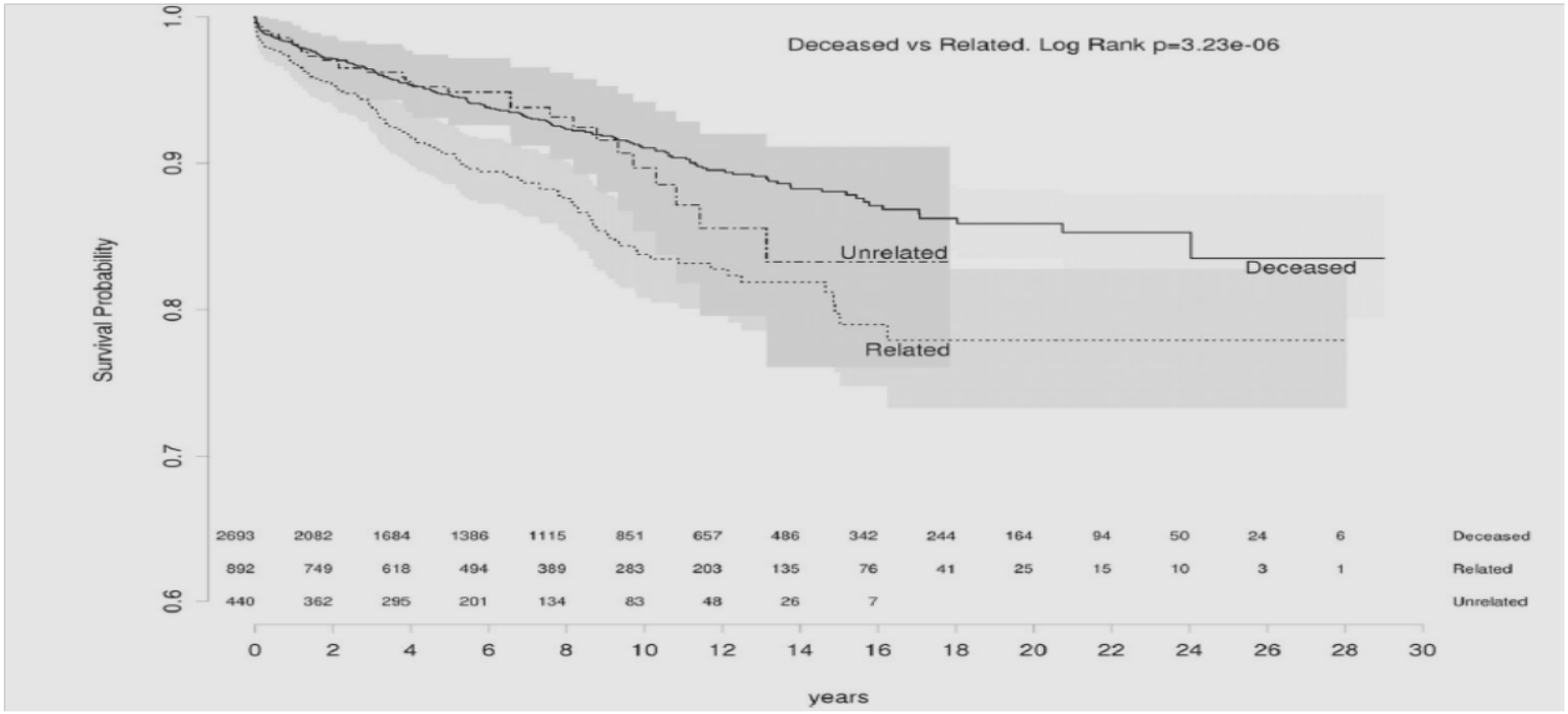
Kennard *et al. BMC Nephrology* (2017) 18:25

BMC Nephrology

A. L. Kennard[1†], S. H. Jiang[1,2†] and G. D. Walters[1,2,3,4*]

**Table 1** Chracteristics of GN Patients by donor category

| | Deceased | Related | Unrelated | Total |
|---|---|---|---|---|
| GN Patients | 4956 | 1576 | 704 | 7236 |
| Other Patients | 6201 | 1686 | 900 | 8787 |
| Total | 11157 | 3262 | 1604 | 16023 |



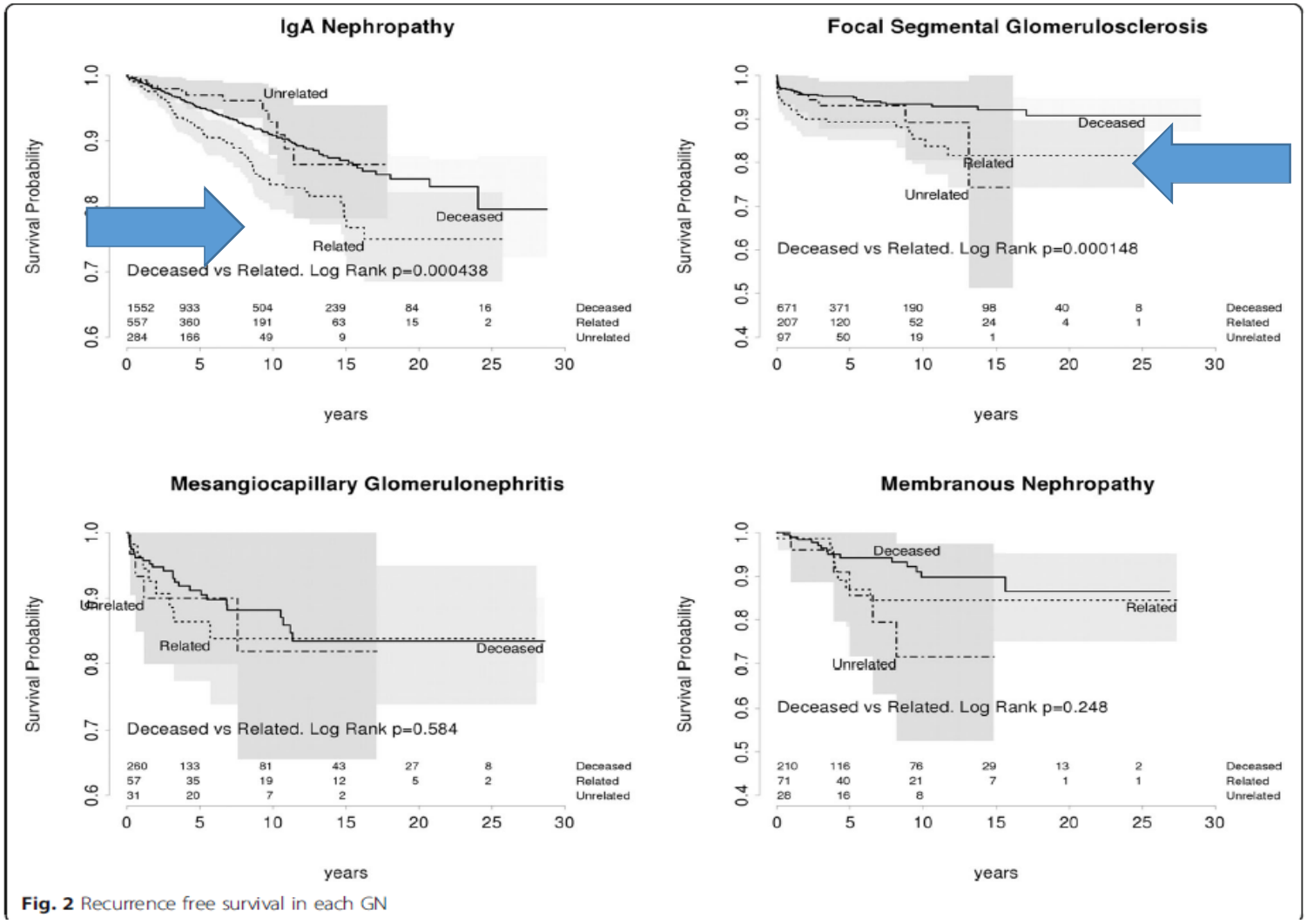



**Fig. 2** Recurrence free survival in each GN

**Conclusions:** We identified a significant increase in the risk of glomerulonephritis recurrence in IgA Nephropathy and Focal Segmental Glomerulosclerosis in living related donors compared to a deceased donors.

## Recurrence of nephrotic syndrome in kidney grafts of patients with congenital nephroptic syndrome of the Finnish type : Role of nephrin

Patrakka J, Ruotsalainen V, Reponen P et al..

Wolters Kluwer Health | Lippincott Williams & Wilkins

**Transplantation**

THE OFFICIAL JOURNAL OF THE TRANSPLANTATION SOCIETY

2002; 73(3): 394-403

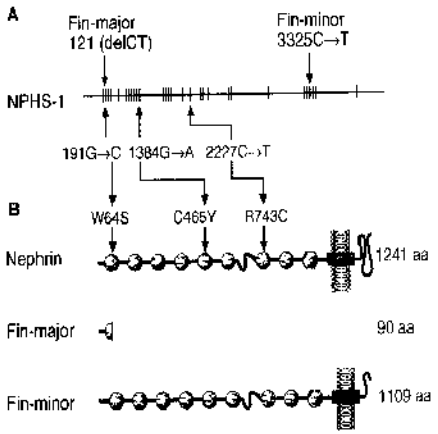



**TABLE 4. Circulating antibodies against glomerular structures and nephrin as detected by indirect immunofluorescence (IF) against fetal glomerulus and ELISA for anti-nephrin antibodies**

| Patient group | IF positive | ELISA | |
|---|---|---|---|
| | | Anti-nephrin antibodies (>114 U/mL) | Binding inhibited by solubilized nephrin |
| NPHS1 patients with recurrent nephrotic syndrome | 8/9 (89 %) | 5/9 (56%) | 4/5 |
| Other NPHS1 patients | 11/27 (41%) | 2/27 (7%) | 0/2 |
| Other kidney tx patients | 8/31 (26%) | 2/31 (6%) | 1/2 |
| Heart and liver tx patients | 7/47 (15%) | 3/47 (6%) | 0/3 |

Pediatr Nephrol (2014) 29:2309–2317
DOI 10.1007/s00467-014-2781-z

EDUCATIONAL REVIEW

# Congenital nephrotic syndrome and recurrence of proteinuria after renal transplantation

Christer Holmberg · Hannu Jalanko

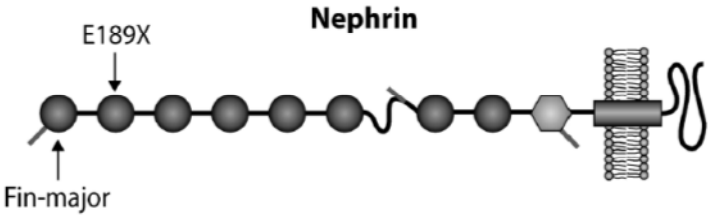



Table 2 Treatment and outcome of the last six Finnish CNS patients with recurrence of proteinuria and nephrotic syndrome after RTx

| Patient | Mutation | dgn | RTx, age | Re-nephrosis (no) | Time after RTx (mo) | Therapy | Outcome (+ time since last remission in bold) |
|---|---|---|---|---|---|---|---|
| 1<br>UTI, polyoma, rejections | Fin-major homozygote | at birth | 1y 7mo | 1) | 51 | MP, Cyclo, PE | **Remission 7y 7mo** |
| 2 | Fin-major homozygote | at birth | 2y 4mo | 1)<br>2)<br>3)<br>4)<br>5)<br>6) | 4, 5<br>12<br>23<br>26<br>31<br>40 | MP, Cyclo, PE<br>MP, Cyclo, PE<br>MP, Cyclo, PE<br>MP, Cyclo, PE, ACE<br>MP, Cyclo, PE, ACE<br>MP, **Rituxi x4**, ACE | Remission<br>“<br>“<br>“<br>“<br>**Remission 6y** |
| 3 | Fin-major homozygote | at birth | 1y 1mo | 1)<br>2) | 40<br>42 | MP, Cyclo, PE<br>ACE<br>MP, **Rituxi x4**<br>ACE | Remission after 1mo<br>**Remission 5y 6mo** |
| 4 | Fin-major homozygote | at birth | 2y 10mo | 1)<br>2) | 4<br>5<br>20 | MP, PE, **Rituxi x4**<br>Cyclo<br>MP, PE, *Bortetsomibi x4*<br>**Rituxi x1** | Remission after 12mo<br>still γ-glob. infusions<br>**Remission 3y 7mo** |
| 5<br>H1N1 | Fin-major homozygote | at birth | 1y 4mo | 1)<br>2) | 32<br>60 | MP, Cyclo, PE<br>**+Rituxi x2**<br>+ACE<br>*+Bortetsomibi x4*<br>**+Rituxi x1**<br>MP, **Rituxi x4**<br>ACE | U-prot:<br>1.5 g/l<br>Transplant nephropathy, HD |
| 6 | Fin-major homozygote | at birth | 1y 8mo | 1) | 13<br>14 | MP, Cyclo, PE<br>**Rituxi x2** | Remission after 11mo<br>**Remission 4y 6mo** |

# Screening for *NPHS2* Mutations May Help Predict FSGS Recurrence after Transplantation

J Am Soc Nephrol **22:** 579–585, 2011

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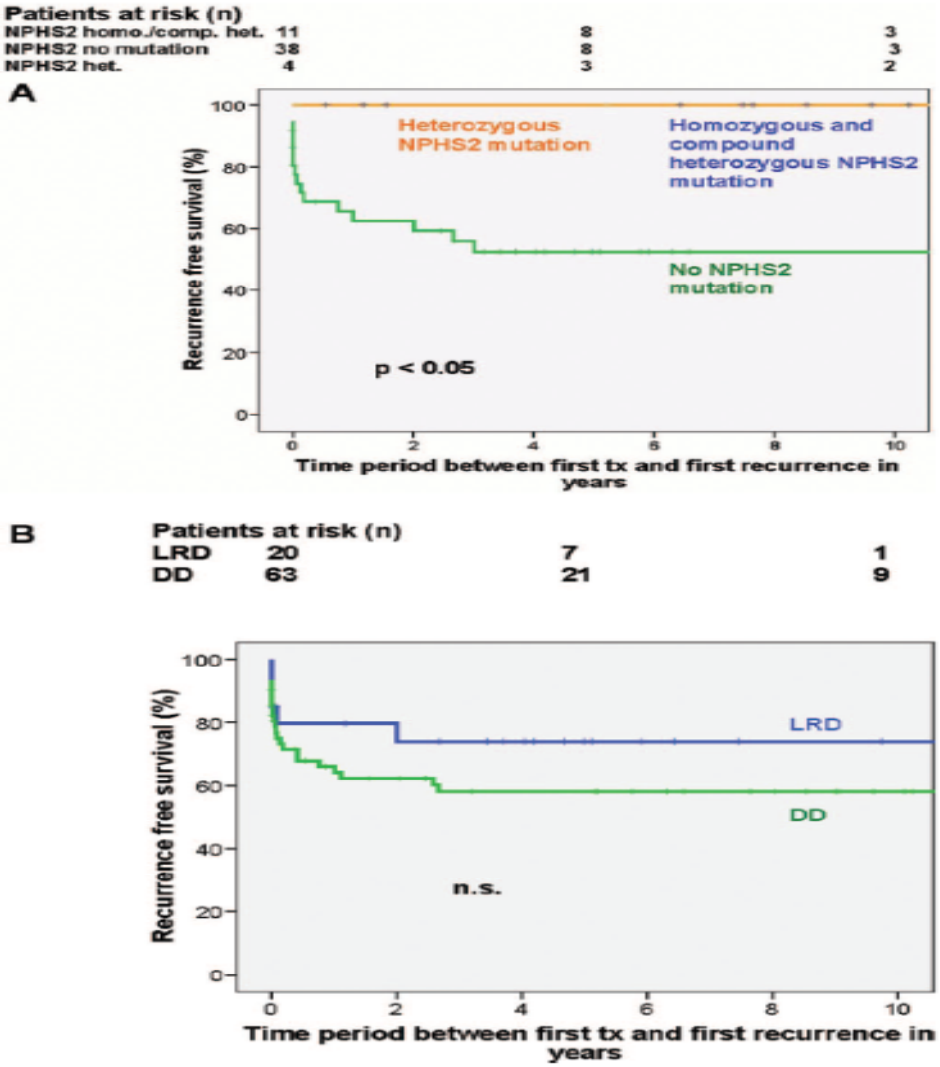
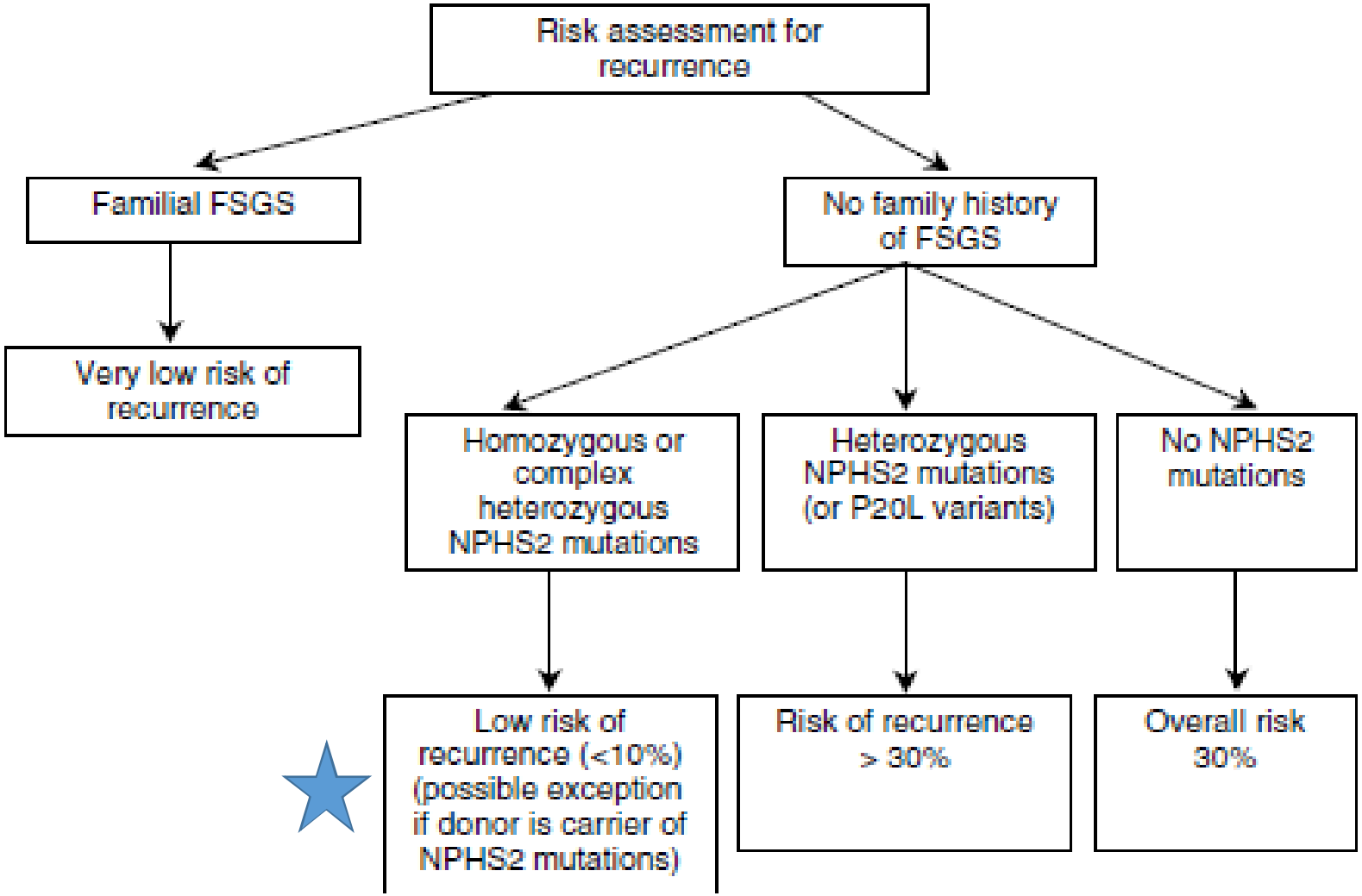
None of the 11 patients with homozygous or compound heterozygous *NPHS2* mutations developed recurrent FSGS compared with 45% of patients without mutations. These data suggest that genetic testing for pathogenic mutations may be important for prognosis and treatment of FSGS both before and after transplantation.



# New Insights into the Pathogenesis and the Therapy of Recurrent Focal Glomerulosclerosis

**Flavio Vincenti[a,*] and Gian Marco Ghiggeri[b]**

*American Journal of Transplantation 2005; 5: 1179–1185*



Pediatr Nephrol (2014) 29:2309–2317
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EDUCATIONAL REVIEW

# Congenital nephrotic syndrome and recurrence of proteinuria after renal transplantation

Christer Holmberg · Hannu Jalanko

**Table 3** Treatment and outcome of CNS patients with NPHS2 and recurrence of proteinuria and nephrotic syndrome after RTx (29, 41–45)

| Patient no | Nucleotide change | Exon | Coding sequence | Age at RTx | Proteinuria after RTx | Proteinuria | Treatment | Outcome |
|---|---|---|---|---|---|---|---|---|
| 1 | 413G>A<br>413G>A | 3 | R138Q<br>R138Q | 9 y | 10 d | 2–3 g/l | PE<br>Cyclo | Good |
| 2 | 413G>A<br>413G>A | 3 | R138Q<br>R138Q | 4.5 y | 300 d | 2–3 g/l | PE<br>Cyclo | Good |
| 3 | 412C>T<br>412C>T | 3 | R138X<br>R138X | 3.1 y | 4 y | TP/Cr<br>5.5 g/g | PE | Stable |
| 4 | 948delT<br>948delT | 8 | L347X<br>L347X | 4.5 y | 7 d | 2.4 g/l | MP -pulses | Good |
| 5 | 412C>T<br>412C>T | 3 | R138X<br>R138X | | 2 y | | | |
| 6 | 413G>A<br>IVS4-1,G>T | 3<br>5 | R138Q<br>Split | 7 y | 10 y | 10.7 g/m$^2$ | Switch from sirolimus to CsA | Good |

*RTx* renal transplantation, *y* year, *d* day, *PE* plasma exchange, *Cyclo* cyclophosphamide, *MP* methylprednisolone, *CsA* cyclosporine A, *TP* total protein, *Cr* creatinine, *CNS* congenital nephrotic syndrome

## Key summary points

- Severe proteinuria and NS are very rare in primary CNS patients after RTx
  - The most probable etiology is NPHS1 with a gene mutation leading to absence of nephrin, as occurs in Fin-major homozygotes
  - In the majority of these patients, anti-nephrin antibodies are detectable after RTx
  - Sometimes NS can develop after RTx in patients with *NPHS2* mutations, but the mechanisms are still elusive
  - The best treatment options known today are MP, cyclophosphamide, and plasma exchange alone or combined with Rituximab

TAK

# Excellent long-term outcome of renal transplantation in cystinosis patients

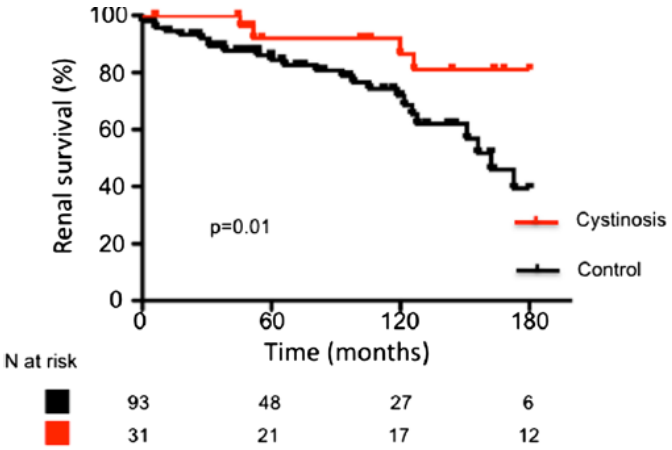
Cohen *et al. Orphanet Journal of Rare Diseases* (2015) 10:90

ORPHANET JOURNAL OF RARE DISEASES

Camille Cohen[1,2], Marina Charbit[3,2], Bernadette Chadefaux-Vekemans[4,2], Magali Giral[5], Valérie Garrigue[6] Michèle Kessler[7], Corinne Antoine[8], Renaud Snanoudj[1,2], Patrick Niaudet[3,2], Henri Kreis[1,2], Christophe Legendre[1,2] and Aude Servais[1,2*]

**Table 1** Clinical and demographic data of patients

| | cystinosis ($n = 31$) | control ($n = 93$) | |
|---|---|---|---|
| Male / Female | 16/15 | 59 / 34 | |
| Age at ESRD (years) | 18.8 (7.7-35.0) | 19.8 (4.0-32.0) | $p = 0.07$ |
| Age at transplantation (years) | 20.4 (7.1-36.5) | 21.8 (13.6-32.0) * | $p = 0.03$ |
| Patient <19 yearsold ($n$=) | 15 (48.4 %) | 12 (12.9 %) * | $P < 0.001$ |
| Time from dialysis to transplantation (years) | 1.3 (0.12-8.0) | 1.6 (0.1-19.0) | $p = 0.1$ |
| Preemptive transplantation ($n$=) | 9 (29.0 %) | 12 (13.0 %) | $p = 0.06$ |
| Transplantation rank | 1 ($n = 25$); 2 ($n = 6$) | 1 ($n = 75$); 2 ($n = 17$) | |
| BMI (kg/m$^2$) | 19.0 (14.3-28.7) | 19.9 (14.0-25.0) | $p = 0.4$ |
| Diabetesmellitus ($n$=) | 3 (9.7 %) | 2 (2 %) | $p = 0.1$ |
| Initial graft data | | | |
| Living kidney donation ($n$=) | 9 (29.0 %) | 26 (28.6 %) | $p = 1$ |
| Deceased donor age (years) | 30.0 (0.6-64.0) | 37.0 (10.0-62.0) * | $p < 0.05$ |



# Five years results after intrafamilial kidney post-transplant in a case of familial hypomagnesemia due to a claudin-19 mutation

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Patricia de Fátima Lopes[1]
Jorge Paulo Strogoff de Matos[1]
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J Bras Nefrol. 2014;36(3):401-415.

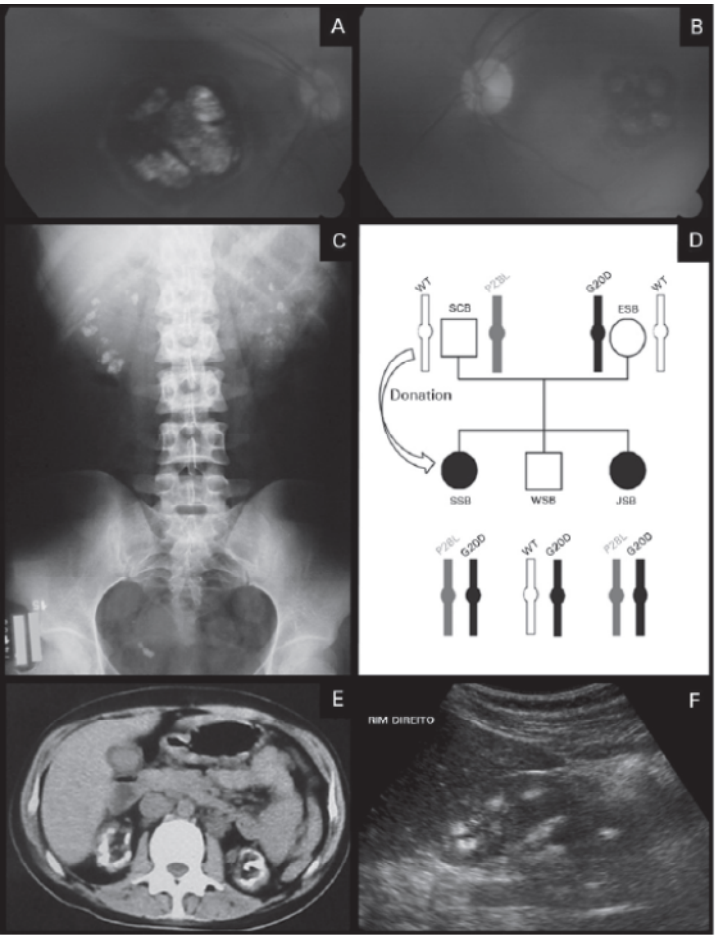


**TABLE 1** BLOOD AND URINARY TESTS BEFORE AND FIVE YEARS AFTER THE TRANSPLANTATION

| | SSB | | SCB | | JSB | | |
|---|---|---|---|---|---|---|---|
| | before | after | before | after | before | after | Unit |
| Urea | 320 | 33 | 31 | 34 | 27 | 37 | mg/dL |
| Creatinine | 12.6 | 1.2 | 0.9 | 0.7 | 1.1 | 0.9 | mg/dL |
| Calcium | 9.0 | 9.2 | 9.4 | 8.5 | 9.0 | 8.9 | mg/dL |
| Magnesium | 1.5 | 1.9 | 1.7 | 1.9 | 0.5 | 1.2 | mg/dL |

(SSB) are the initials to the kidney recipient, (SCB) to the donor and (JSB) to the youngest daughter.

In conclusion, after five years of donation the renal graft function remained stable without recurrence of metabolic disturbances or nephrocalcinosis. Besides, donor single kidney $Mg^{2+}$ and $Ca^{2+}$ homeostasis associated to monoallelic status did not affect the safety and the usual living donor post-transplant clinical course.

# Panel genów do oceny u potencjalnego żywego dawcy nerki, z ograniczeniem kierunku badań– stosownym do odmiany choroby podstawowej u biorcy

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Wiley Periodicals Inc.



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# Screening of Living Kidney Donors for Genetic Diseases Using a Comprehensive Genetic Testing Strategy

C. P. Thomas[1,2,3,*], M. A. Mansilla[4], R. Sompallae[4], S. O. Mason[4], C. J. Nishimura[4], M. J. Kimble[4], C. A. Campbell[1,4], A. E. Kwitek[4,5], B. W. Darbro[2,6,7], Z. A. Stewart[8] and R. J. H. Smith[1,2,4,6,9,*]

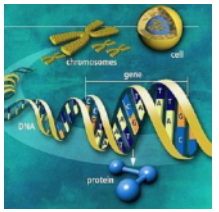
**Table 1:** Genes implicated in genetic renal diseases and screened by targeted genomic enrichment and massively parallel sequencing

| Gene | Accession number | Locus/ alternative name | Exon count |
|---|---|---|---|
| ACTN4 | NM_004924 | | 21 |
| AE1 | NM_000342 | SLC4A1 | 20 |
| AGTR2 | NM_000686 | | 3 |
| AGXT | NM_000030 | | 11 |
| AHI1 | NM_001134830 | JBTS3 | 27 |
| ALMS1 | NM_015120 | | 23 |
| APOL1 | NM_001136540 | FSGS4 | 6 |
| APRT | NM_000485 | | 5 |
| AQP2 | NM_000486 | | 4 |
| ARL13B | NM_001174150 | JBTS8 | 10 |
| ARL6 | NM_001278293 | BBS3 | 8 |
| ATP6V0A4 | NM_020632 | ATP6N1B | 22 |
| AVPR2 | NM_000054 | | 3 |
| BBS1 | NM_024649 | | 17 |
| BBS2 | NM_031885 | | 17 |
| BBS4 | NM_001252678 | | 15 |
| BBS5 | NM_152384 | | 12 |
| BBS7 | NM_018190 | | 18 |
| BMP4 | NM_001202 | | 4 |
| BSND | NM_057176 | | 4 |
| CaSR | NM_000388 | | 7 |
| CC2D2A | NM_001080522 | JBTS9 | 38 |
| CD2AP | NM_012120 | | 18 |
| CEP290 | NM_025114 | JBTS5, MKS4, NPHP6 | 54 |
| CLCN5 | NM_000084 | CLC5 | 12 |
| CLCNKA | NM_004070 | | 20 |
| CLCNKB | NM_000085 | | 20 |
| CLDN16 | NM_006580 | HOMG3 | 5 |
| CLDN19 | NM_001123395 | HOMG5 | 4 |
| CNNM2 | NM_017649 | HOMG6 | 8 |
| COL4A1 | NM_001845 | | 52 |
| COL4A3 | NM_000091 | | 52 |
| COL4A4 | NM_000092 | | 48 |
| COL4A5 | NM_000495 | | 51 |
| COQ2 | NM_015697 | | 7 |
| CREBBP | NM_001079846 | | 30 |
| CTNS | NM_001031681 | | 13 |
| CUL3 | NM_001257197 | | 15 |
| DHCR7 | NM_001163817 | | 9 |
| EGF | NM_001178130 | HOMG4 | 23 |
| EYA1 | NM_000503 | | 18 |
| FGF23 | NM_020638 | | 3 |
| FN1 | NM_002026 | | 46 |
| FRAS1 | NM_001166133 | | 42 |
| FREM2 | NM_207361 | | 24 |
| GATA3 | NM_001002295 | | 6 |
| GLA | NM_000169 | | 7 |
| GLI3 | NM_000168 | | 15 |
| GLIS2 | NM_032575 | NPHP7 | 6 |
| GPC3 | NM_001164617 | | 9 |
| GRHPR | NM_012203 | | 9 |
| HNF1B | NM_000458 | | 9 |

**Table 1:** Continued

| Gene | Accession number | Locus/ alternative name | Exon count |
|---|---|---|---|
| HOGA1 | NM_138413 | DHDPSL | 7 |
| IFT80 | NM_001190241 | | 21 |
| INF2 | NM_001031714 | FSGS5 | 22 |
| INPP5E | NM_019892 | JBTS1 | 10 |
| INVS | NM_014425 | NPHP2 | 17 |
| IQCB1 | NM_001023570 | NPHP5 | 15 |
| KAL1 | NM_000216 | | 14 |
| KCNJ1 | NM_153766 | ROMK1 | 3 |
| KLHL3 | NM_001257194 | | 15 |
| LAMB2 | NM_002292 | | 32 |
| LMX1B | NM_001174146 | | 8 |
| MKKS | NM_170784 | BBS6 | 6 |
| MKS1 | NM_001165927 | | 18 |
| MYH9 | NM_002473 | | 41 |
| NEK8 | NM_178170 | NPHP9 | 15 |
| NLRP3 | NM_001079821 | | 11 |
| NPHP1 | NM_000272 | JBTS4 | 20 |
| NPHP3 | NM_153240 | | 27 |
| NPHP4 | NM_001291593 | | 27 |
| NPHS1 | NM_004646 | | 29 |
| NPHS2 | NM_001297575 | | 7 |
| NR3C2 | NM_000901 | | 9 |
| OCRL1 | NM_000276 | | 24 |
| OFD1 | NM_003611 | JBTS10 | 23 |
| PAX2 | NM_000278 | | 10 |
| PHEX | NM_000444 | | 22 |
| PKD1 | NM_000296 | ADPKD-1 | 46 |
| PKD2 | NM_000297 | ADPKD-2 | 15 |
| PKHD1 | NM_138694 | | 67 |
| PLCE1 | NM_001165979 | NPHS3 | 32 |
| REN | NM_00537 | | 10 |
| RET | NM_020630 | | 19 |
| RPGRIP1L | NM_001127897 | JBTS7, NPHP8, | 25 |
| SALL1 | NM_001127892 | | 3 |
| SALL4 | NM_020436 | | 4 |
| SCNN1A | NM_001038 | | 13 |
| SCNN1B | NM_000336 | | 13 |
| SCNN1G | NM_001039 | | 13 |
| SIX1 | NM_005982 | | 2 |
| SIX2 | NM_016932 | | 2 |
| SIX5 | NM_175875 | | 3 |
| SLC12A1 | NM_000338 | NKCC2 | 27 |
| SLC12A3 | NM_000339 | NCCT | 26 |
| SLC26A4 | NM_000441 | | 21 |
| SLC34A1 | NM_001167579 | NPT2a | 9 |
| SLC34A3 | NM_001177316 | NPT2C | 13 |
| SLC3A1 | NM_000341 | | 10 |
| SLC4A4 | NM_001098484 | | 26 |
| SLC7A9 | NM_001126335 | | 13 |
| SMARCAL1 | NM_001127207 | | 18 |
| TCTN1 | NM_001082537 | JBTS13 | 15 |
| TMEM216 | NM_001173990 | JBTS2, MKS2 | 5 |
| TMEM237 | NM_001044385 | JBTS14 | 12 |
| TMEM67 | NM_001142301 | JBTS6, MKS3, NPHP11 | 29 |

# Podsumowanie




- Podłoże **genetyczne** chorób nerek ma znaczenie dla rokowania i ryzyka powodzenia transplantacji nerki; dotyczy to **zarówno mutacji obecnych u biorcy, jak i dawcy** przeszczepu
- **Mutacje** u biorcy, **jednoznacznie sprzyjające nawrotowi** choroby (np. aHUS) oraz mutacje powodujące wskazania do transplantacji **dwunarządowych** (wątroba/nerka; np. oksaloza) są **bezwzględnymi przeciwwskazaniami** do kwalifikacji żywego dawcy
- **Dawca spokrewniony z biorcą** u którego przyczyną niewydolności nerek jest choroba genetyczna o wysokim potencjale nawrotu powinien, nawet przy braku objawów klinicznych, **przejść skrining genetyczny** w kierunku podobnej mutacji
- Dodatkowym wskazaniem do badania przesiewowego u dawcy jest **potencjalna możliwość przeoczenia późniejszego rozwoju tej samej choroby**, co (przy zmniejszonej masie nefronów) może skutkować niewydolnością jedynej nerki u dawcy
- Istnieje także możliwość **„przeniesienia choroby”** wraz z nerką, co ogranicza jej przeżycie
- W pewnych okolicznościach **przeszczepienie prawidłowo zbudowanej nerki** - biorcy z dużym defektem mikrostruktury własnych nerek - **stymuluje rozwój glomerulopatii *de novo***, wywołanej produkcją swoistych przeciwciał przeciwko „nieznanym” organizmowi biorcy strukturom (nefryna, elementy błony podstawnej)