POST TRANSPLANT FSGS RECURRENCE

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INTRODUCTION

- Recurrence of FSGS in graft is 30-50% and is the cause for graft loss.
- Present with rapid nephrotic-range proteinuria with a median time to recurrence of 1.5 months.
- Proteinuria from native kidneys decreases significantly within 1 month of transplantation hence proteinuria detected more than 1 month after KT is most likely derived from the allograft.
- Rare in patients with genetic FSGS and those without nephrotic syndrome at onset.

RISK FACTORS

- Higher risk of recurrence: younger age of disease onset, white race ,rapid progression of initial disease [< 3 years] , living-related KT, history of recurrence in a previous kidney allograft, and native kidney nephrectomies .

- A family history of FSGS, histologic subtype in the native kidney, and choice of transplantation immunosuppressive therapy have not been shown to alter the risk of recurrence.

Recurrence of Focal Segmental Glomerulosclerosis after Kidney Transplantation in Adults

CJASN
Clinical Journal of American Society of Nephrology

Post-Transplant Glomerular Disease Project (TANGO)

Observational Multicenter International

2005 to 2015

Kidney transplant recipients
n = 11,742

Risk Factors for recurrence

	Hazard Ratio
Old age	1.37 *per decade* *(1.09-1.56)*
White race	2.14 *(1.08-4.22)*
BMI	0.89 per Kg/m² *(0.83-0.95)*
Native kidney nephrectomy	2.76 *(1.16-6.57)*

Recurrence of FSGS

32% *(n = 57)* Recurrent FSGS → 39% *(22 of 57)* Graft loss

Median IQR: 5 years

Response to treatment of recurrent FSGS

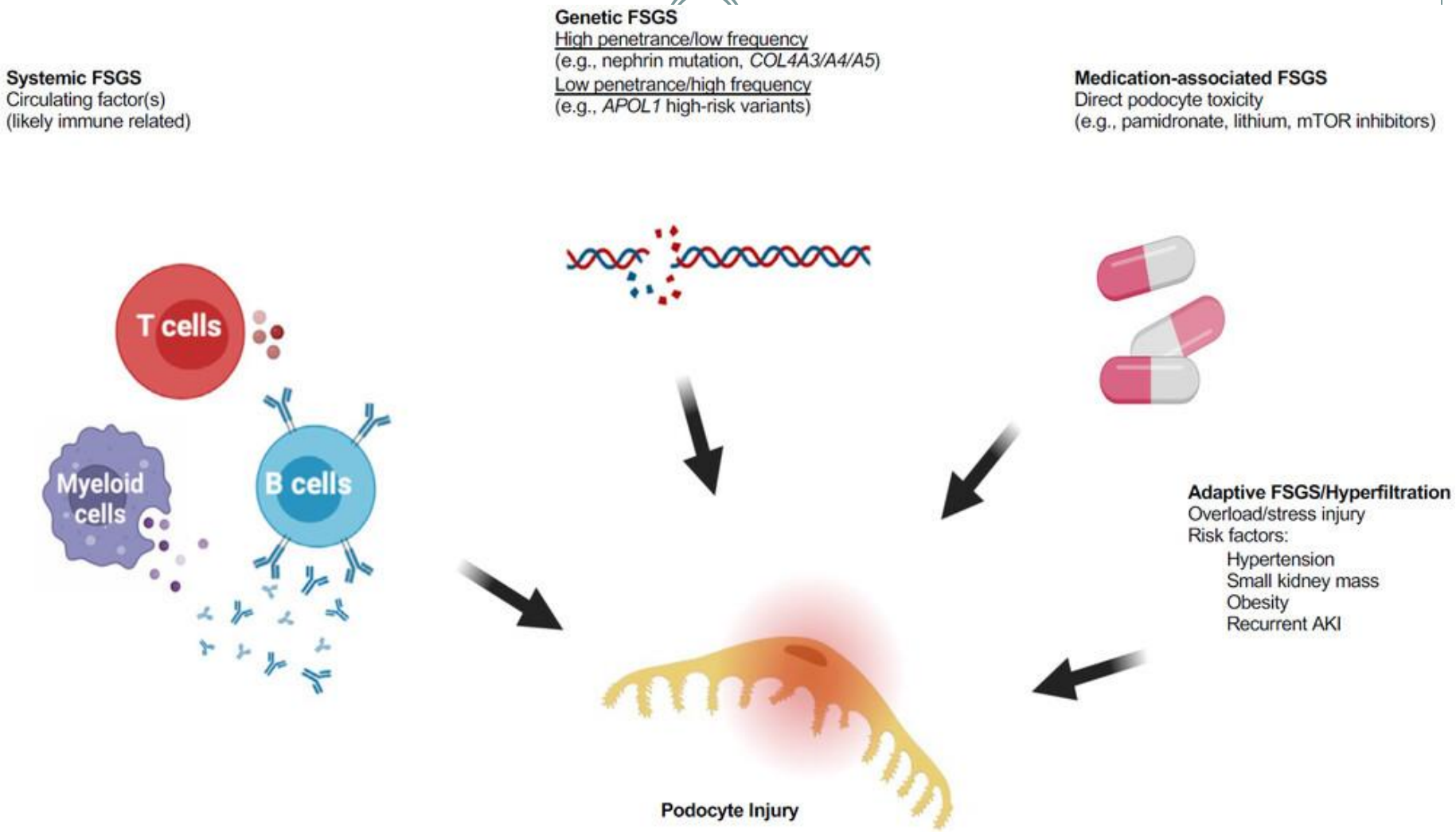
81% *(n = 61)* Plasmapheresis ± Rituximab were the most frequent treatments

21%	36%	43%
(n = 13)	*(n = 22)*	*(n = 26)*
Complete Remission	Partial Remission	No Response

Conclusions: Idiopathic FSGS recurs post-transplant in one-third of cases, increas by five-fold the risk of graft loss. Response to treatment significantly improves outcomes t achieved in only half of the cases.

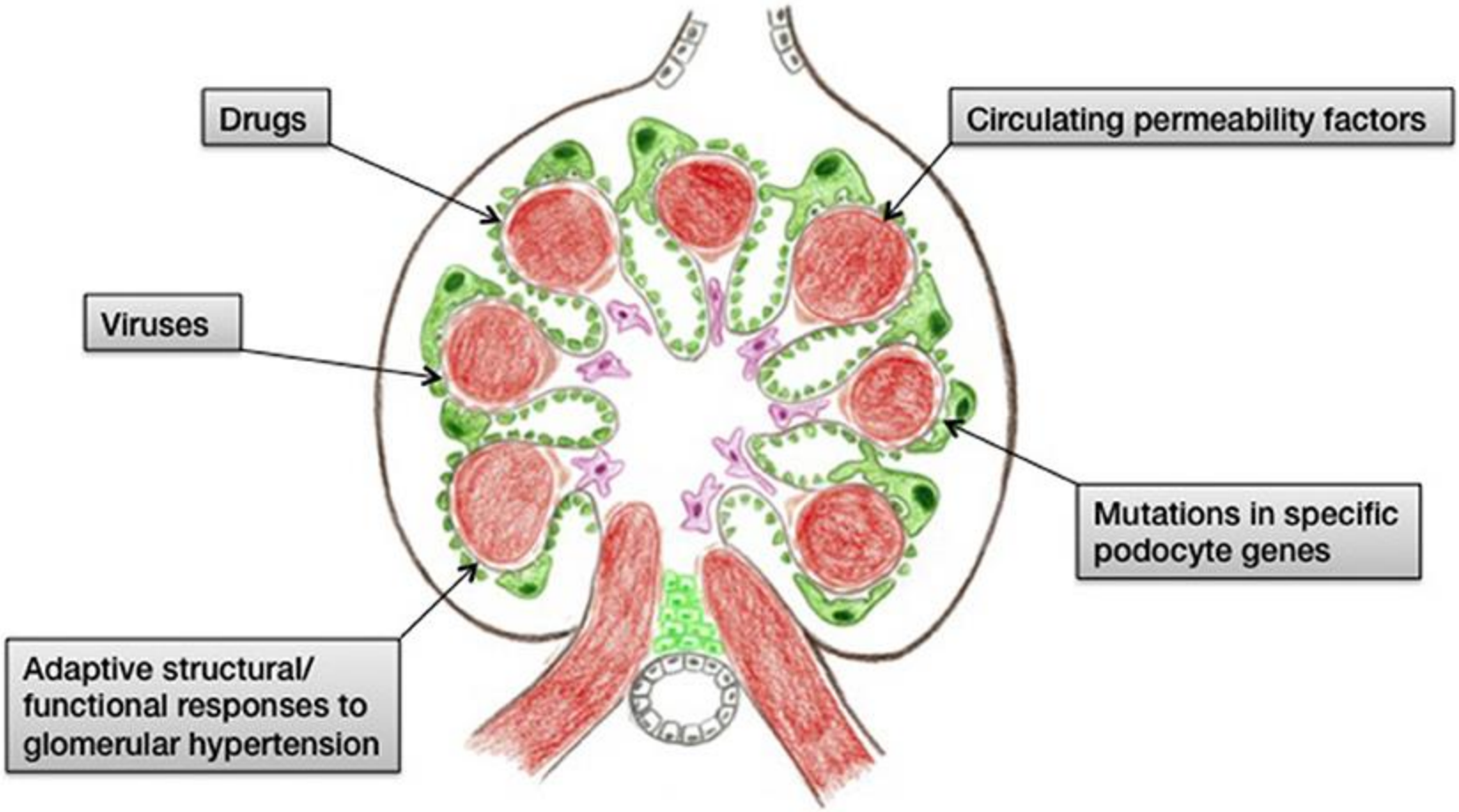
Audrey Uffing, Maria José Pérez-Sáez, Marilda Mazzali, et al. ***Recurrence of Focal Segmental Glomerulosclerosis after Kidney Transplantation in Adults.*** CJASN doi: 10.2215/CJN.08970719. Visual Abstract by Edgar Lerma, MD, FACP, FASN

Underlying etiologies for the podocytopathy in FSGS patients

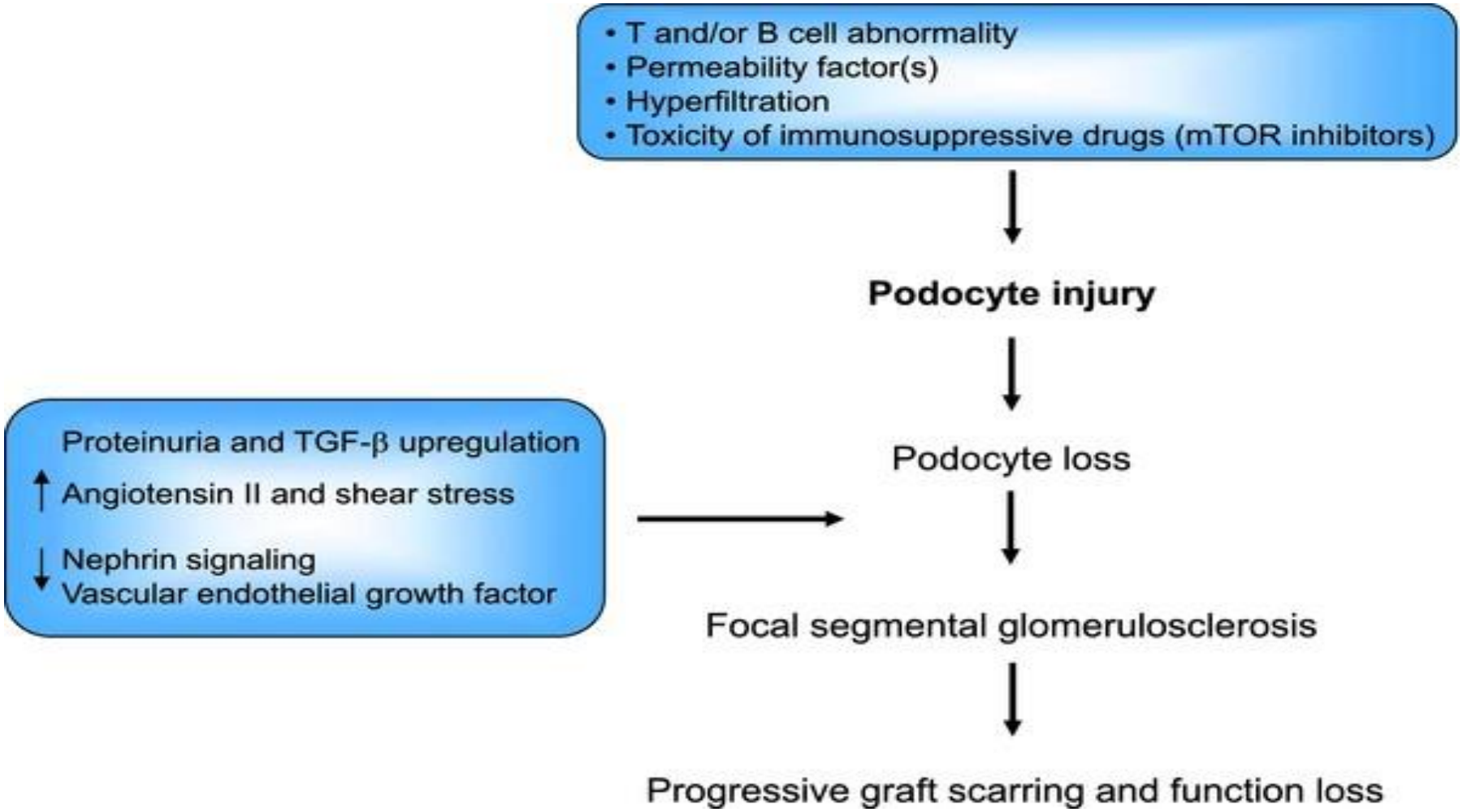


AKI, acute kidney injury; mTOR, mammalian target of rapamycin. Created with BioRender.com.

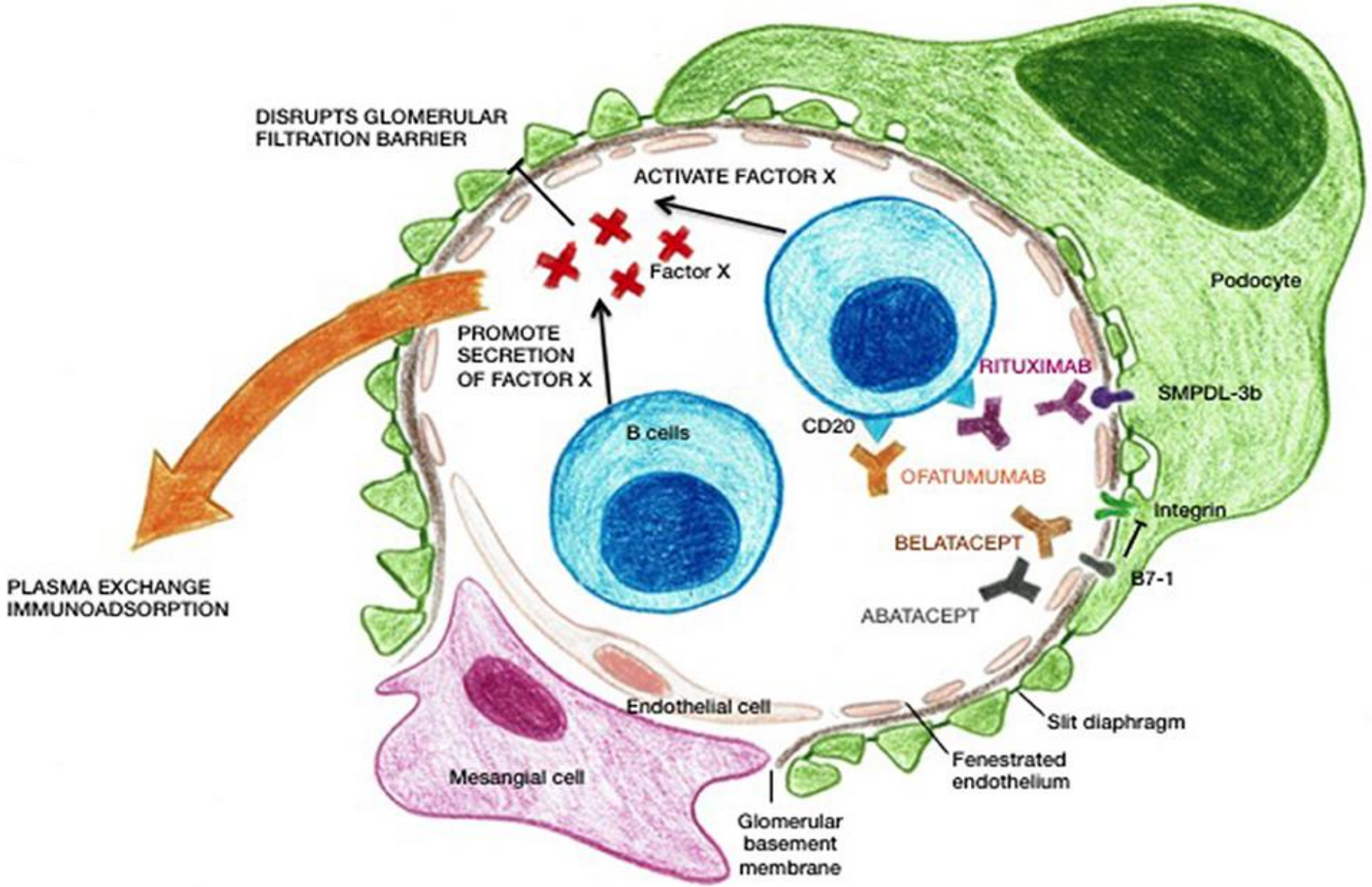
Post transplant recurrence - etiologies



MECHANISM OF RECURRENCE



THERAPUTIC TARGETS IN FSGS



TREATMENT OPTIONS

- PLASMAPHERESIS – most effective in removing circulating permeability factors.

- RITUXIMAB - Anti-CD 20 monoclonal antibody.
- OFATUMUMAB – fully human anti- CD 20 monoclonal antibody that depletes B – cells.

- BELATAOCEPT – co - stimulation blocker.
- ABATACEPT – selective T cell co stimualation blocker.

- LIPID APHERESIS – LDL apheresis.

RETRANSPLANT

- FSGS in the first KT are at very high risk (up to 75%) for recurrence in subsequent kidney allografts.
- Second KT should be delayed for 1–2 years ⇒ disappearance of the circulating factors responsible for the glomerular injury.
- A third KT in patients with two previous transplant losses due to recurrent FSGS should generally be avoided.
- Prophylactic plasmapheresis and rituximab do not appear to decrease the rate of recurrence after transplantation.

ESTABILISHED AND EMERGING THERAPIES FOR FSGS

Immunosuppression (primary FSGS):	Causative directed therapies:	Podocyte specific therapies:	Antifibrotic/ hemodynamic effect:
• Glucocorticoids • CNI • Anti-CD20 antibody • ACTH • MMF • Anti-CD20 antibody • Anti-CD40 antibody • Anti-C5 antibody • B-7 costimulatory inhibitor • mTOR inhibitor • Chlorambucil • Plasma exchange	• Antiviral agents • Obesity treatment • CoQ10 supplementation • APOL1 antagonist	• TRPC5/6 channel inhibitor • SLIT2 antagonist • Lipid modifying drug	• RAS inhibitors • SGLT2 inhibitor • Endothelin antagonist • CCR2 inhibitor • Janus Kinase-STAT inhibitor • Anti-TGF-ß antibody • p38 MAPK inhibitor • Anti-human TNF-α antibody • Pirfenidone • Nrf2 activator/NF-κB inhibitor