



APCN×TSN 2025

23rd Asian Pacific Congress of Nephrology

Link the Future Kidney Health with **GIVE**

Dec. 5 Fri. ▸ Dec. 7 Sun. 2025
TaiNEX 2, Taipei Taiwan

Session Title: Multi-omic Approaches to Kidney Diseases

Organelle Communication in Kidney Diseases

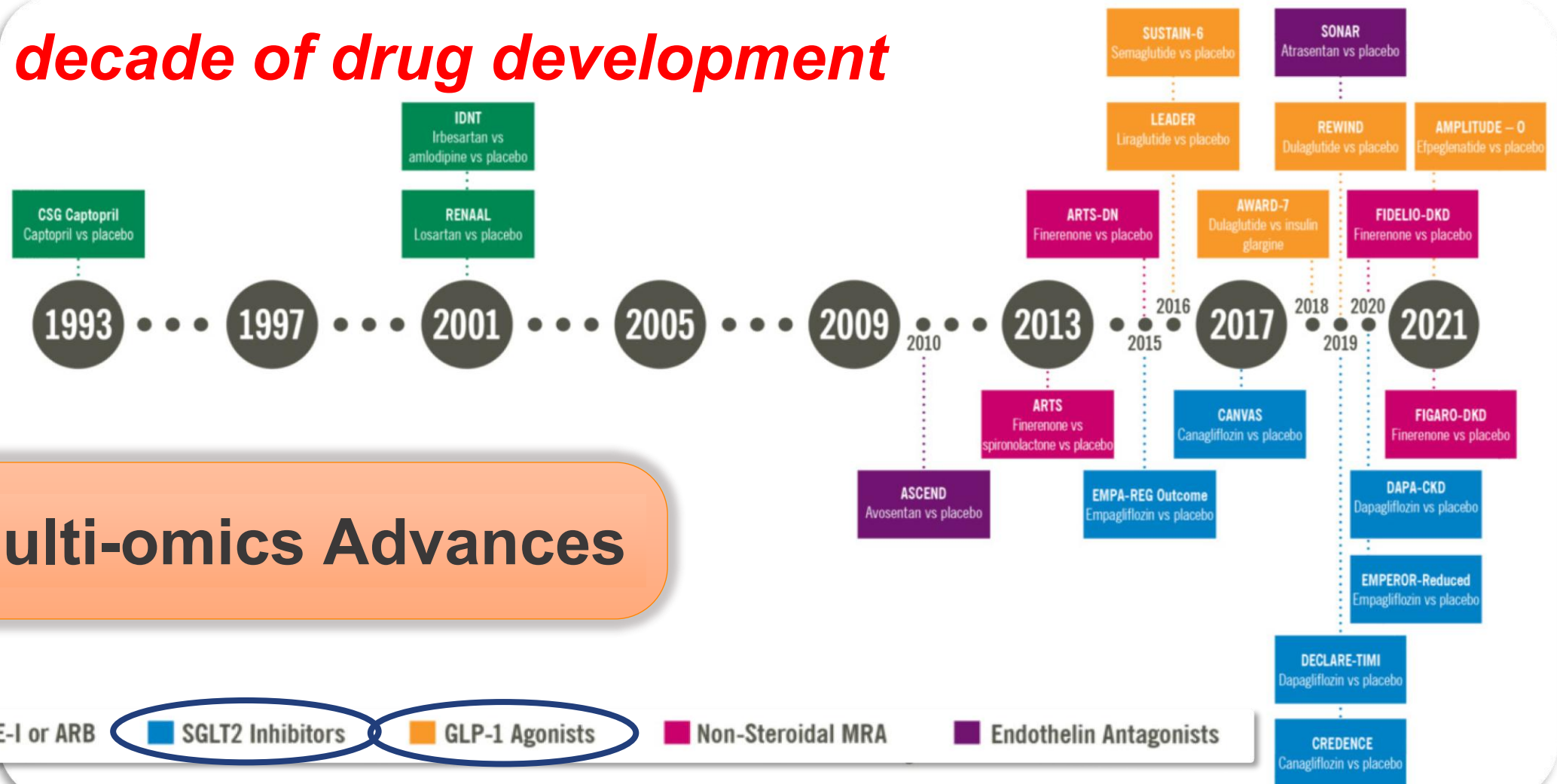
Reiko Inagi, PhD

Division of CKD Pathophysiology,
Graduate School of Medicine, The University of Tokyo



Renaissance of Nephrology

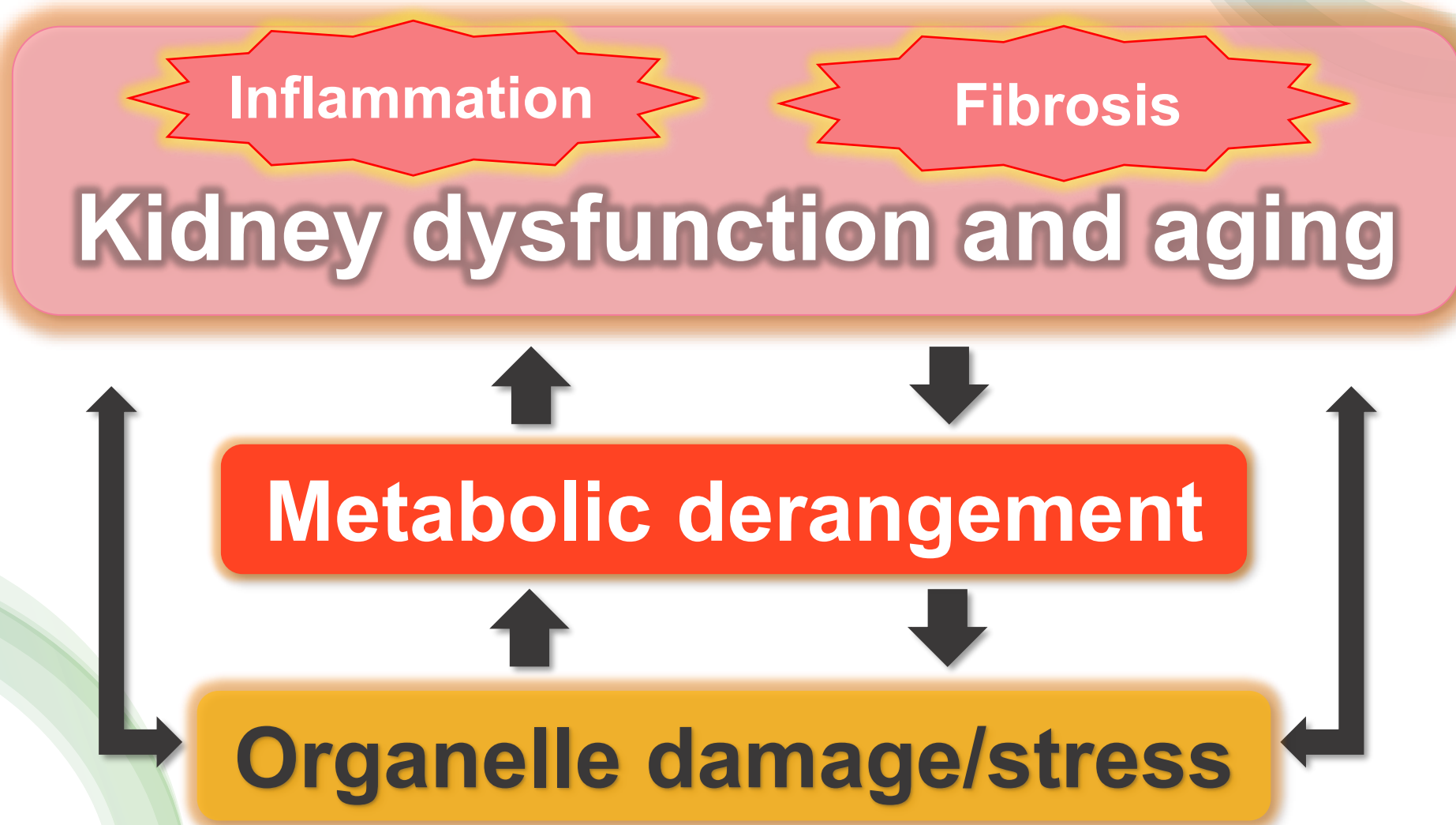
➤ A decade of drug development



➤ Multi-omics Advances

Pathophysiology of CKD

- *Key Molecular Mechanisms in Spotlight* -



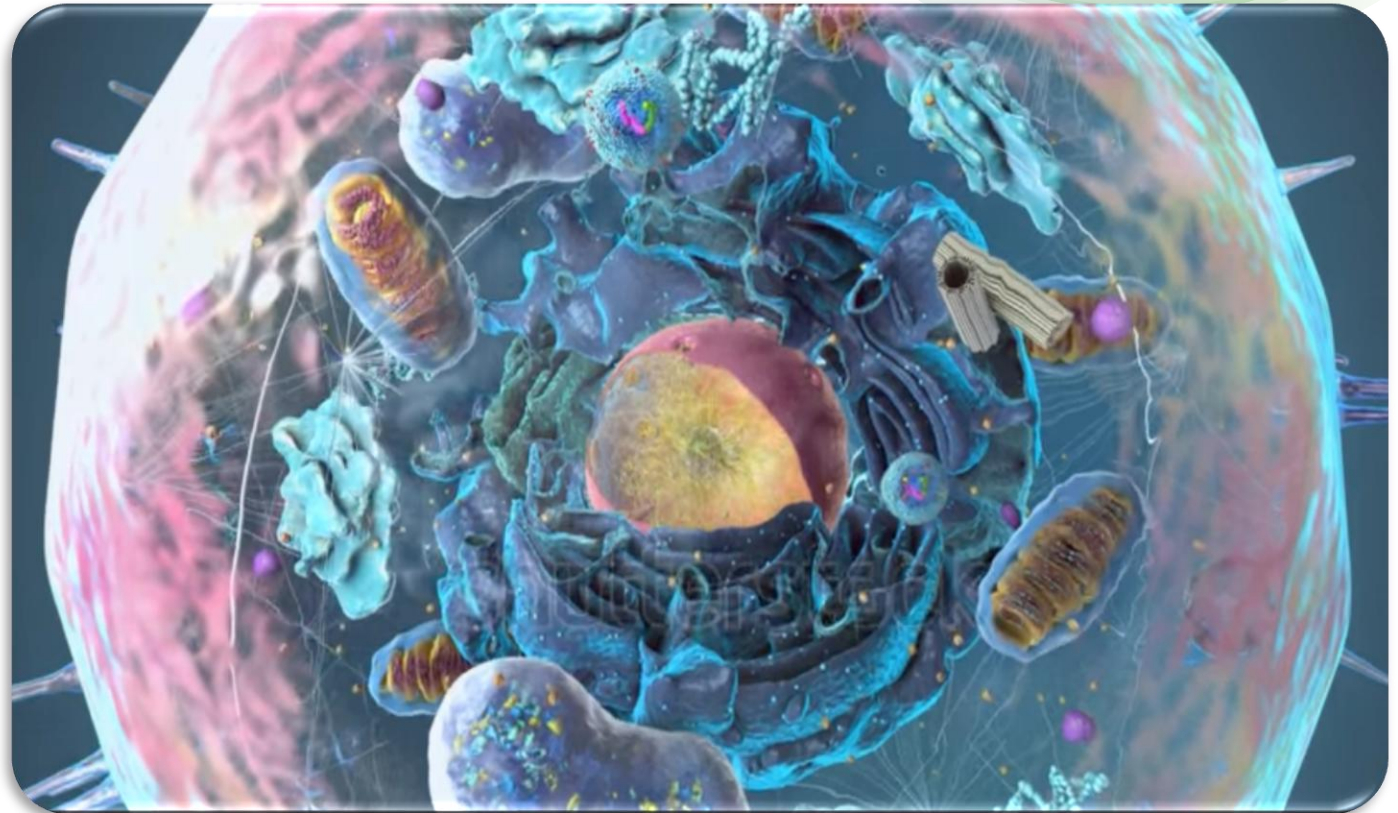
From Organelle Stress to Metabolic Derangement in CKD

◆ ER stress

- ↓ Proteostasis
- ↓ ER-mito lipid transfer

◆ Mitochondrial stress

- ↓ OXPHOS, ATP
- ↓ FA β -oxidation



<https://www.shutterstock.com/video/clip-1110802575-organelles-inside-eukaryote-eukaryotic-cell-focus-on>

From Organelle Stress to Metabolic Derangement in CKD

◆ ER stress

↓ Proteostasis

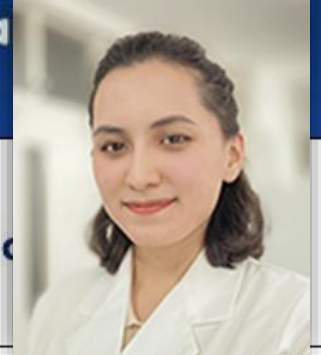
↓ ER-mito lipid transfer

◆ Mitochondrial stress

↓ OXPHOS, ATP

↓ FA β -oxidation

23rd ASIAN PACIFIC CONGRESS OF NEPHROLOGY APCN 2025 Link the Future Kidney Health with GIVE Dec.5-7 2025 Dec. 5 Fri. ▷ Dec. 7 Sun. 2025 TaiNEX 2, Ta APCN X TSN 2025 Oral Presentation No	
NO.	Oral 4-1
Title	Dissecting the Role of ATF6 α and ATF6 β in Podocyte Homeostasis and Injury Response
Room	Room 8 (602)
Presentation Time	Dec. 6 (Sat.) 9:30-9:39
Oral Communications	GN
First Author	MAIDINA SAIFUDING



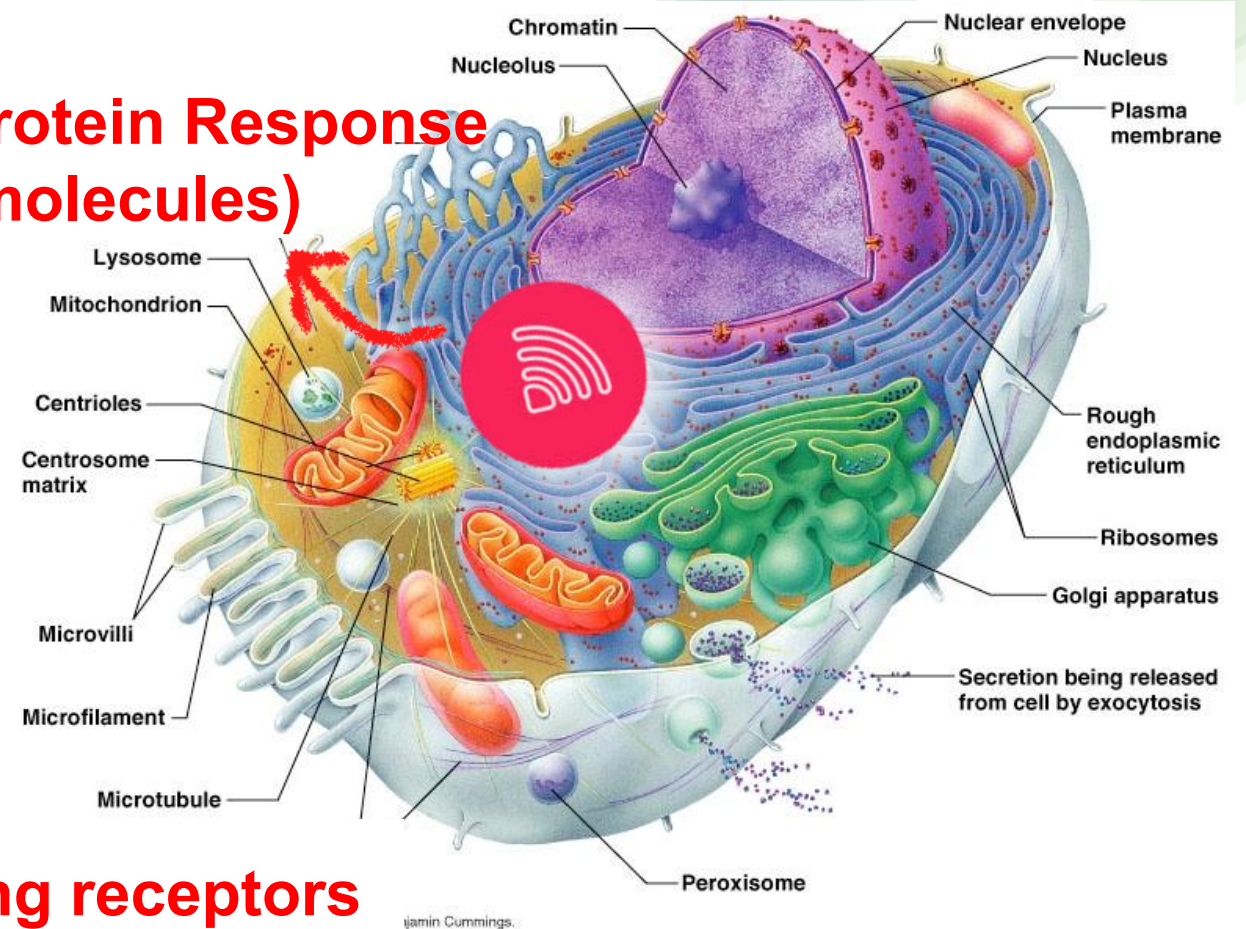
From Organelle Stress to Organelle crosstalk in CKD

Organelle
stress



Organelle
crosstalk

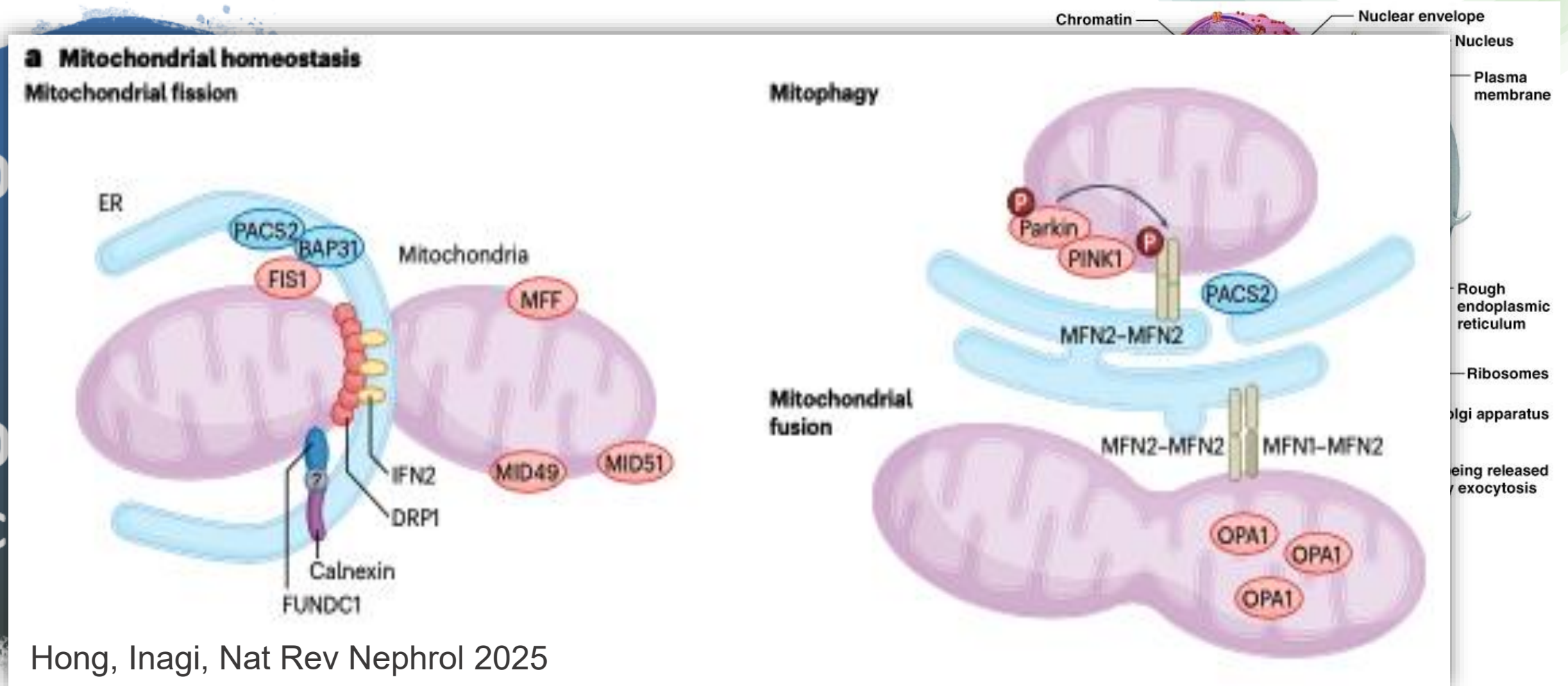
◆ Unfolded Protein Response (sensor molecules)



◆ ER signaling receptors

◆ ER tethering molecules

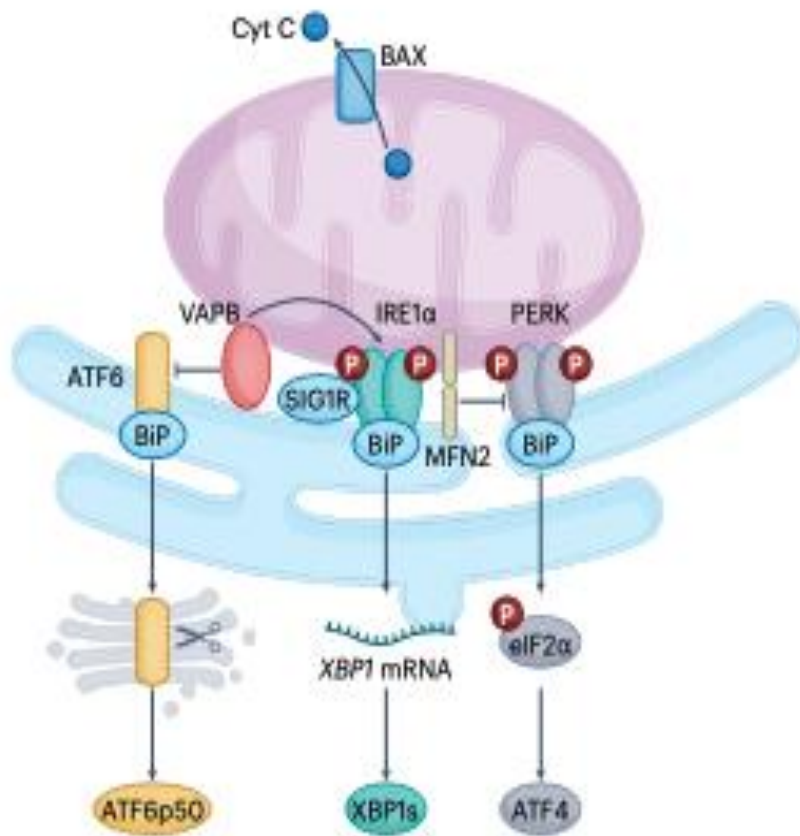
From Organelle Stress to Organelle crosstalk in CKD



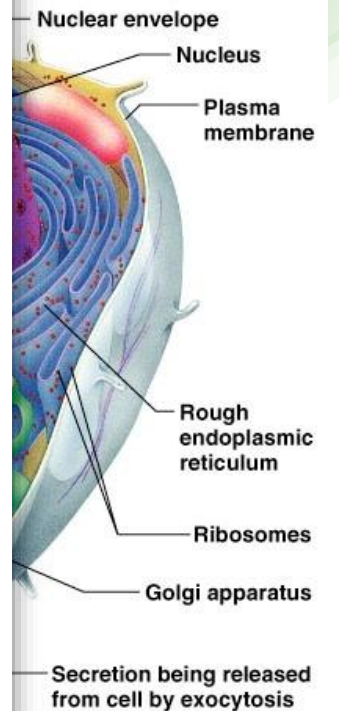
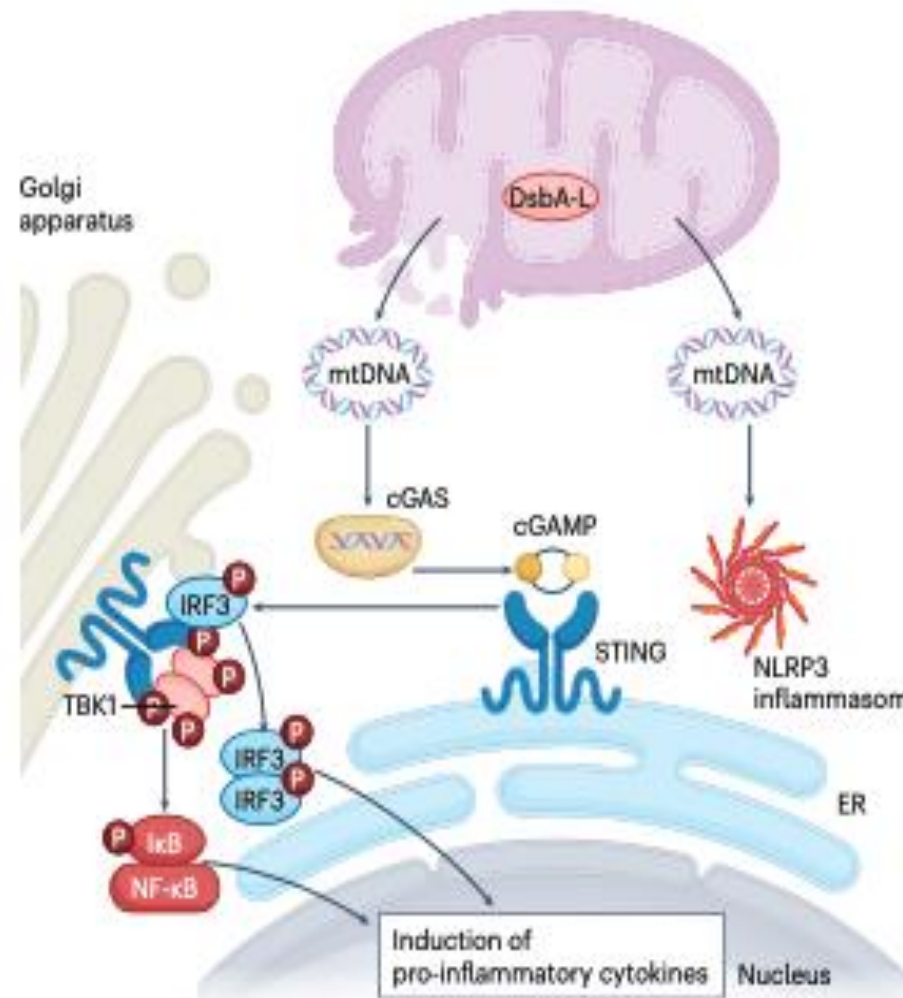
◆ ER tethering molecules

From Organelle Stress to Organelle crosstalk in CKD

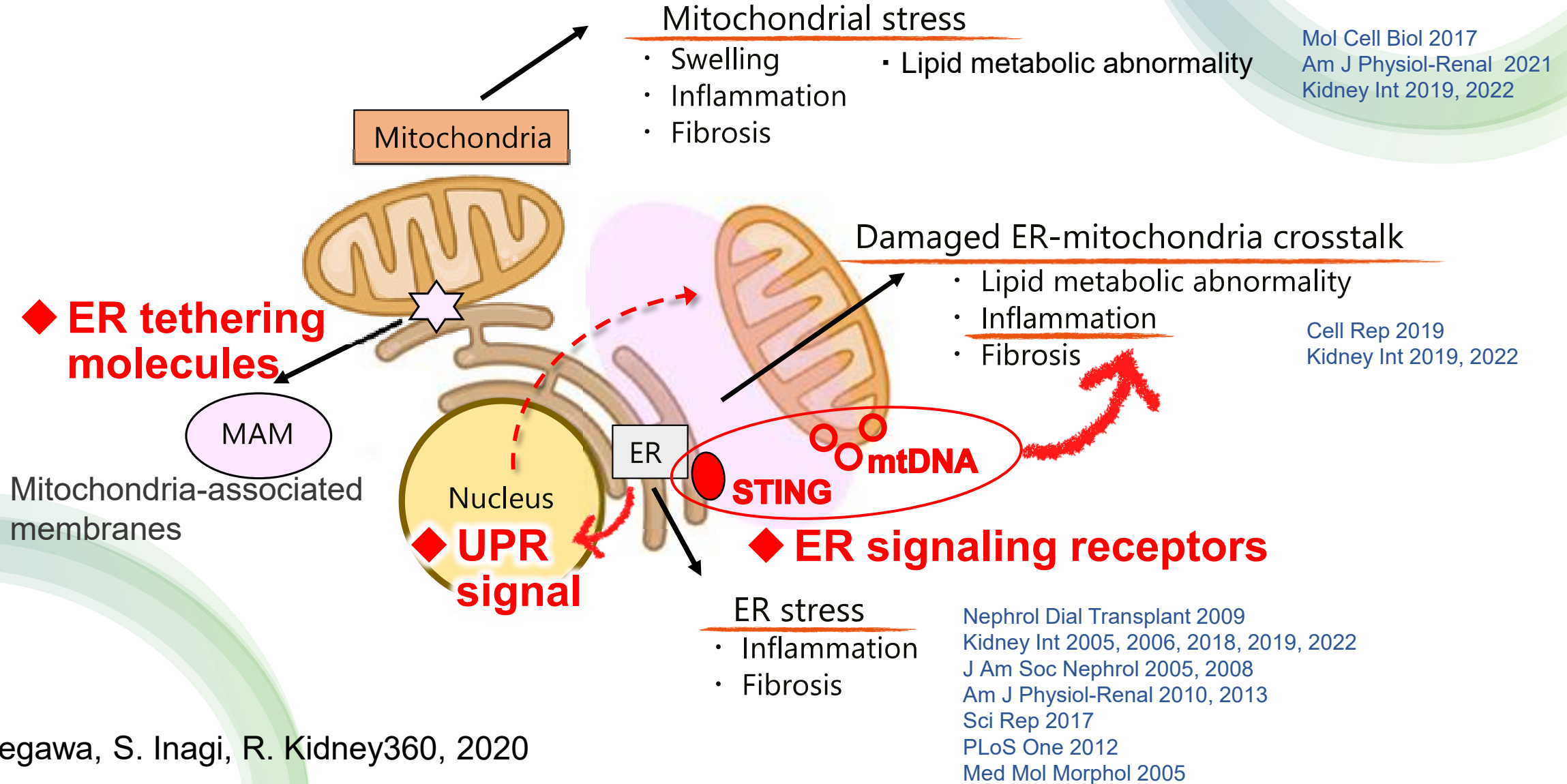
b Unfolded protein response



c Inflammation

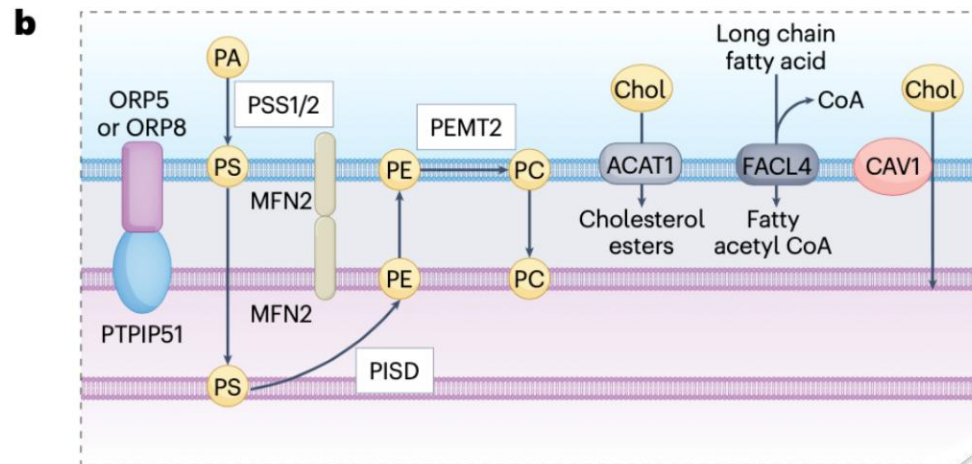
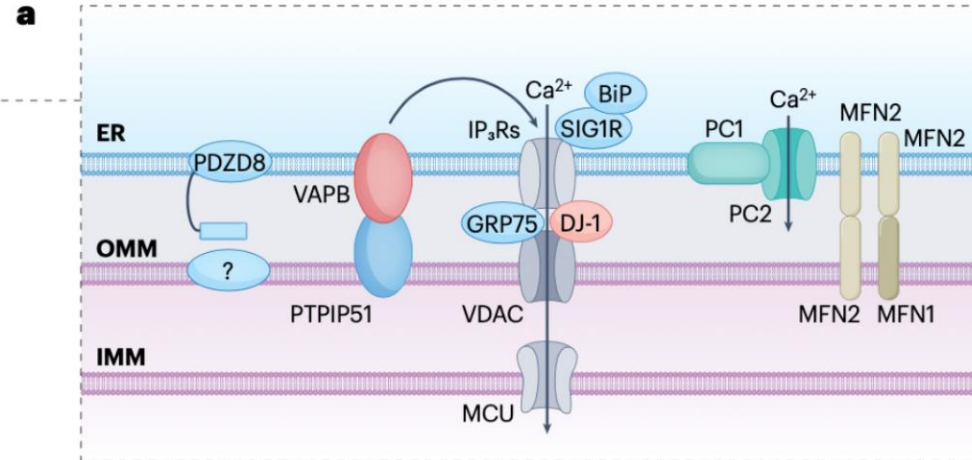
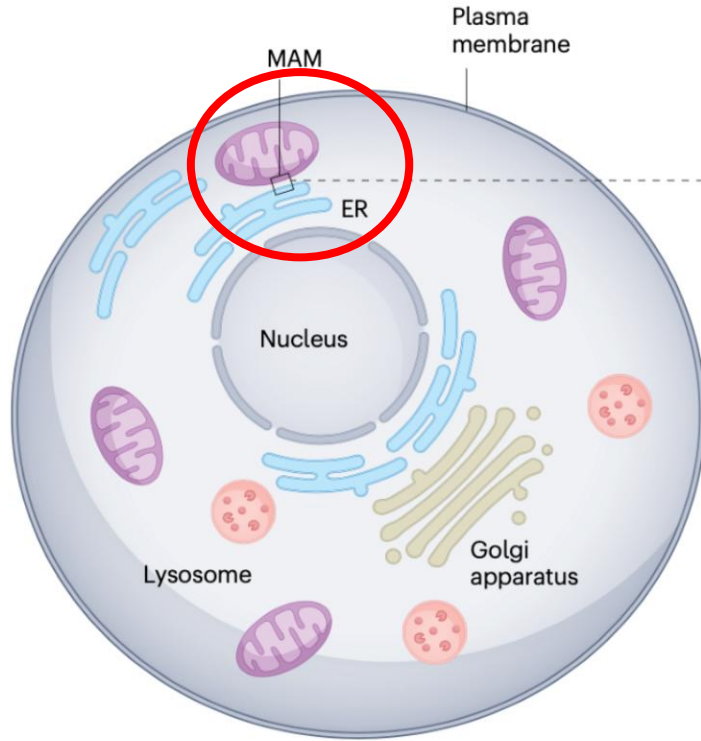


Organelle stress and organelle crosstalk link to kidney cell dysfunction



Inter-organelle communication orchestrated by organelle zones

MAM: the inter-organelle hub for lipid synthesis and remodeling



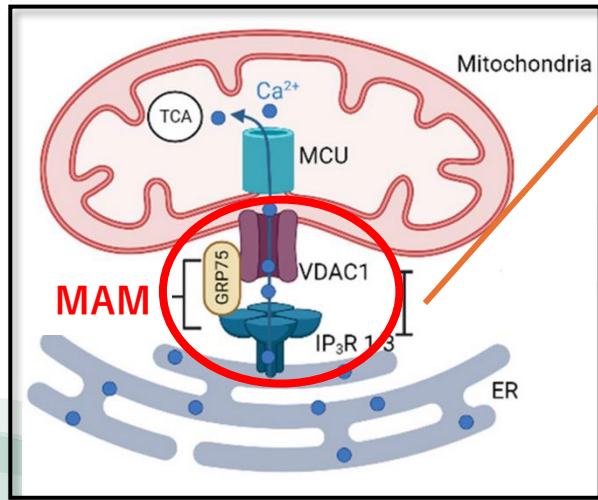
Hong, YA. Inagi, R.
Nat Rev Nephrol, 2025

Lysophosphatidylcholine (LPC) reduces **ER-mitochondria contact site** in tubular cells



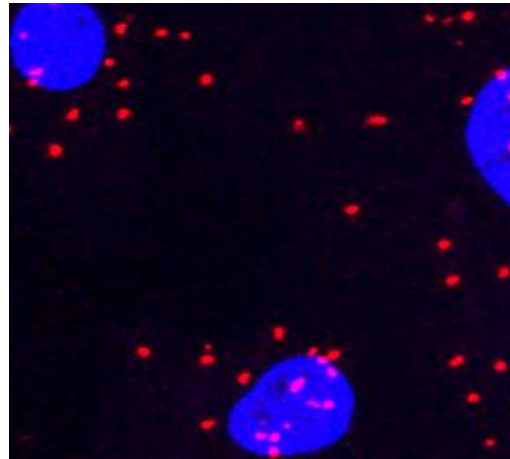
Proximity ligation assay:
between IP3R (ER) and VDAC (mitochondria)

Mitochondria-associated
ER membranes (MAM)

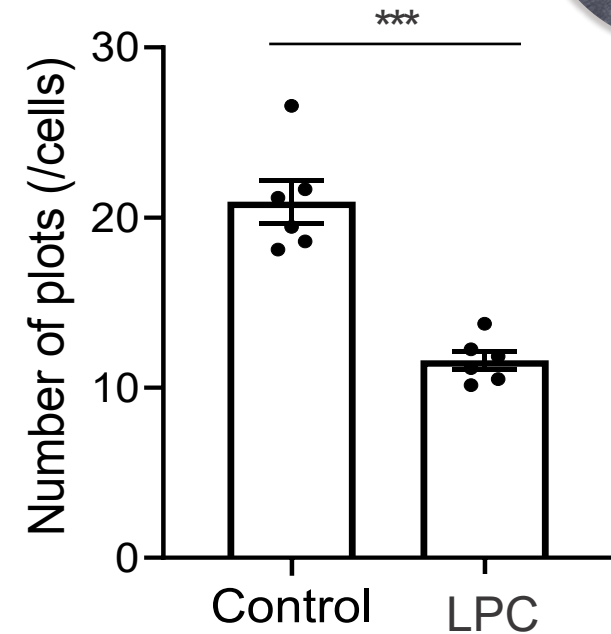
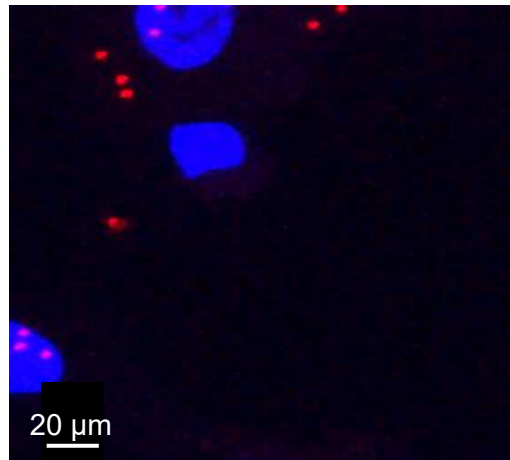


<https://doi.org/10.1177/25152564231181020>

Control



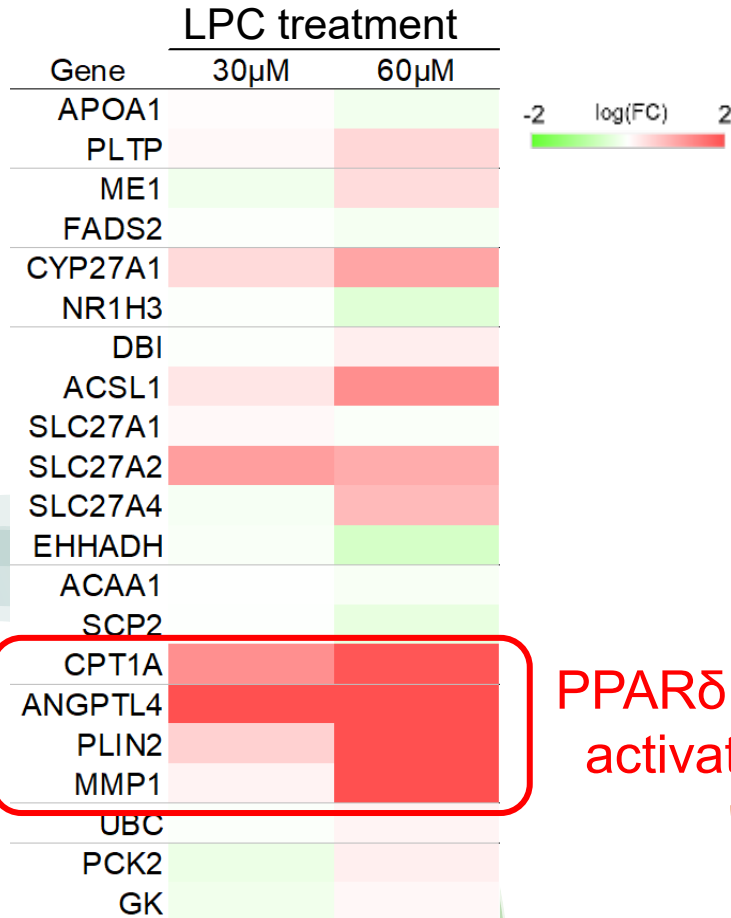
LPC



Yoshioka K, et al, Kidney Int. 2021

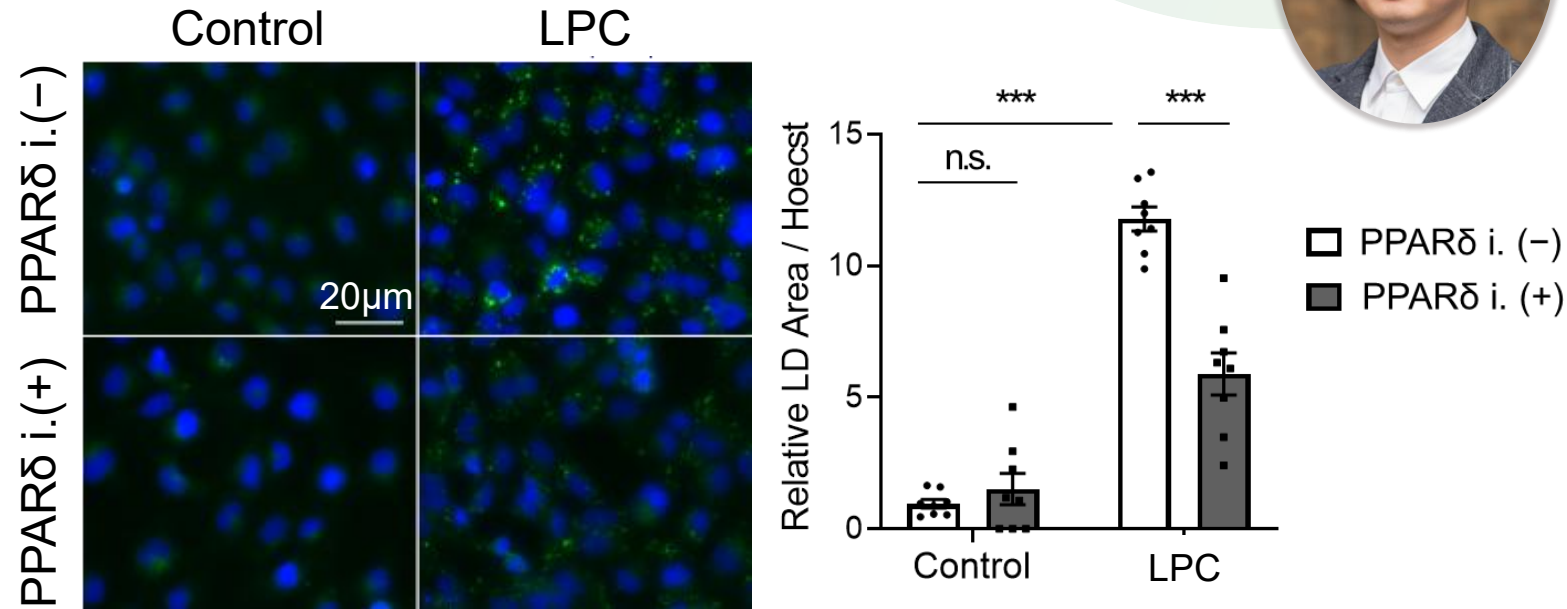
Lysophosphatidylcholine (LPC) induces proximal tubular lipotoxicity via PPAR δ activation

➤ Transcriptomic analysis (proximal tubular cells)



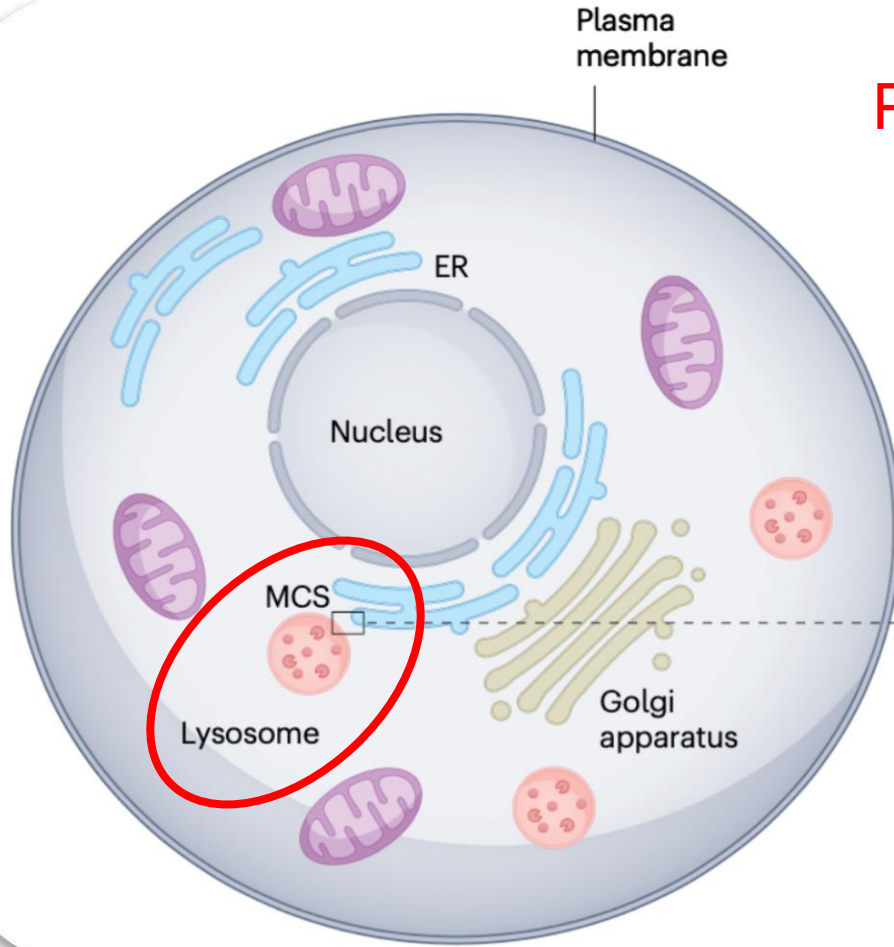
PPAR δ
activation

➤ Lipid droplet detection assay

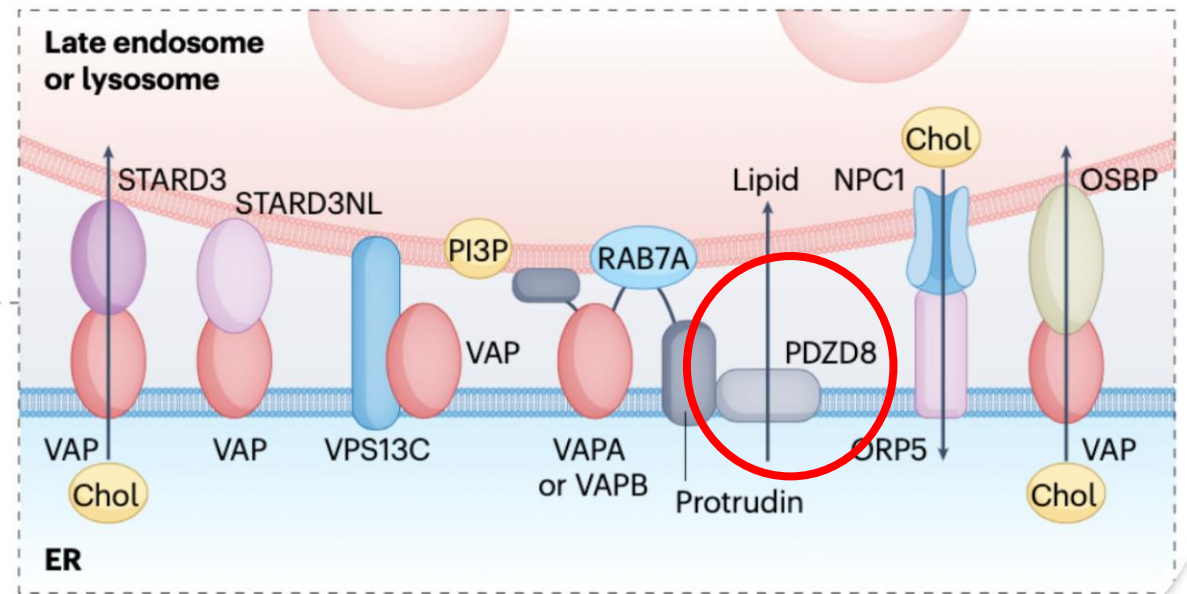


Lipid droplet accumulation
in proximal tubular cells → Lipotoxicity

Inter-organelle communication orchestrated by organelle zones



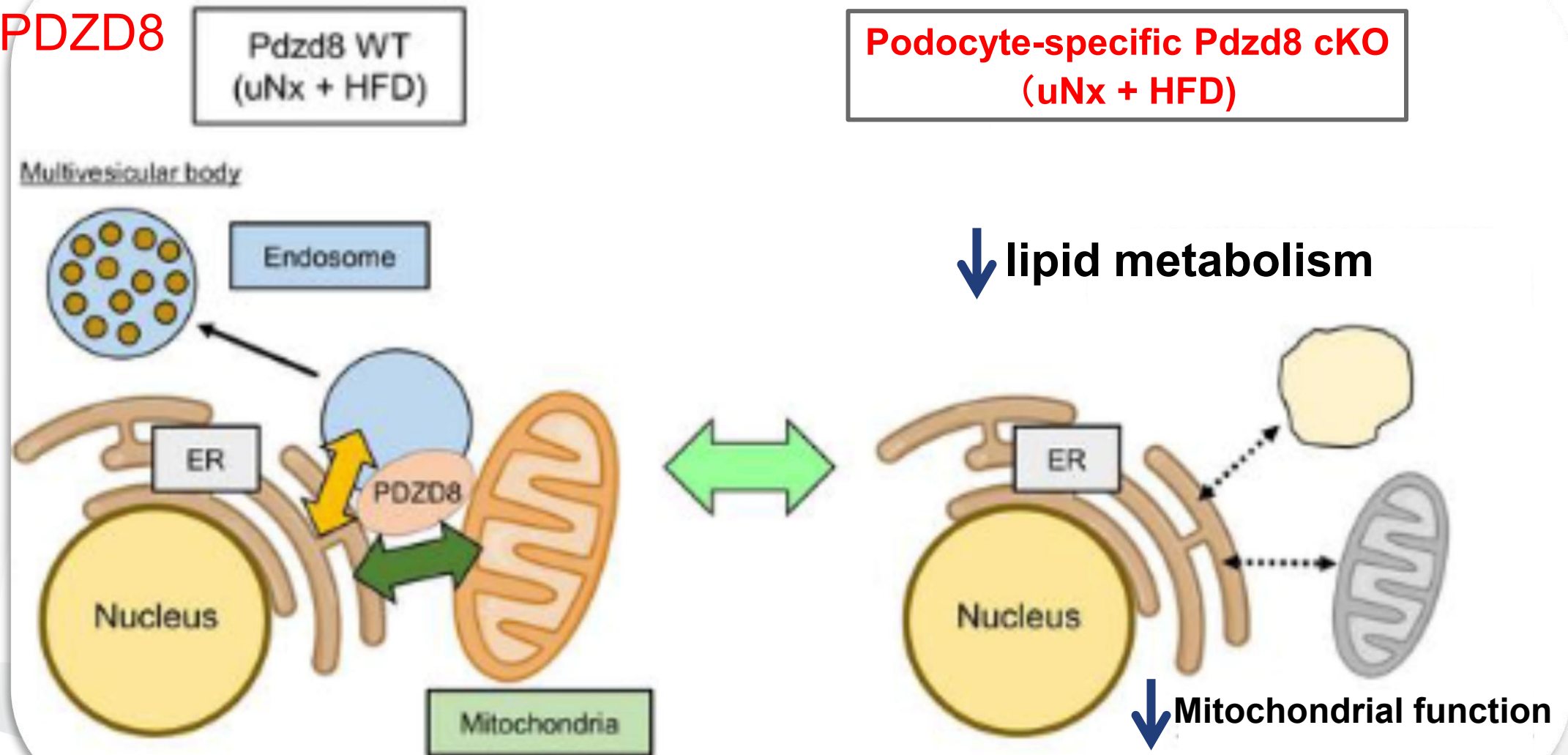
PDZD8: an ER-resident inter-organelle tether and lipid transfer protein at membrane contact sites



Organelle communication maintains mitochondrial and endosomal homeostasis during podocyte lipotoxicity

Hasegawa, S et al, JCI insight, 2024

◆ ER tethering protein PDZD8

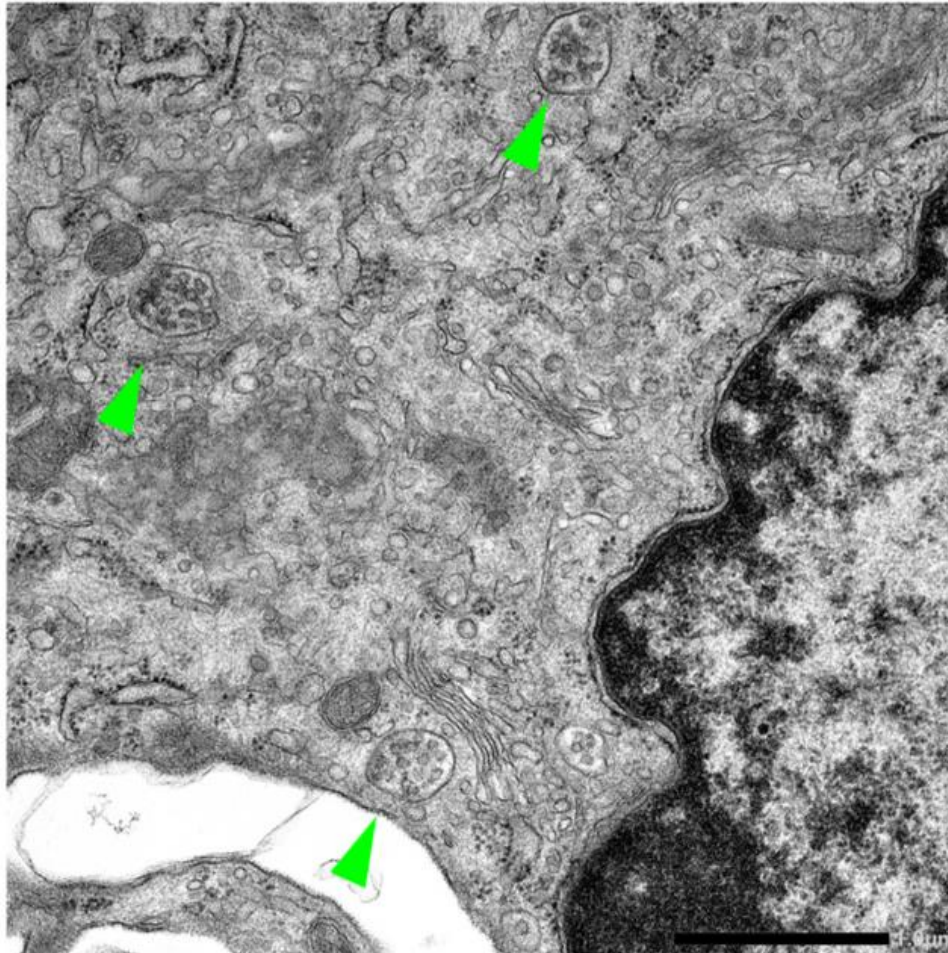


Organelle communication maintains mitochondrial and endosomal homeostasis during podocyte lipotoxicity

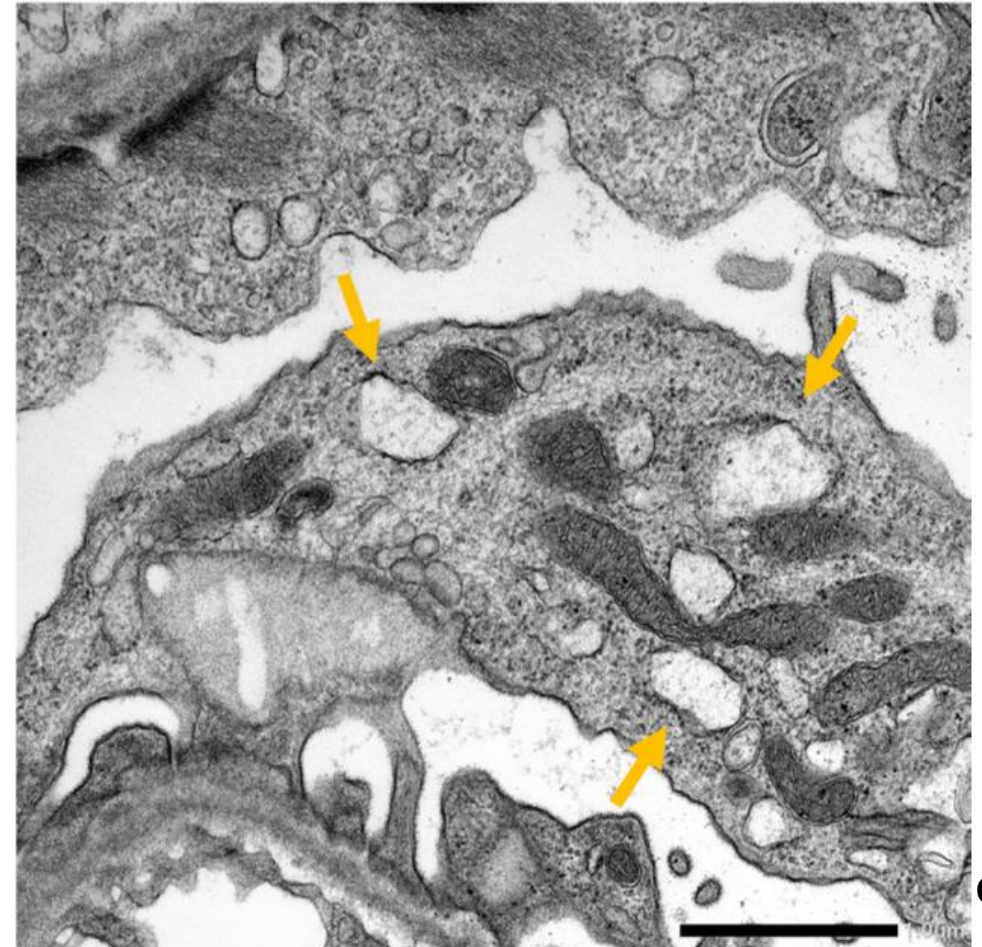
Hasegawa, S et al, JCI insight, 2024

◆ ER tethering protein P

UNx + HFD (WT)



UNx + HFD (cKO)

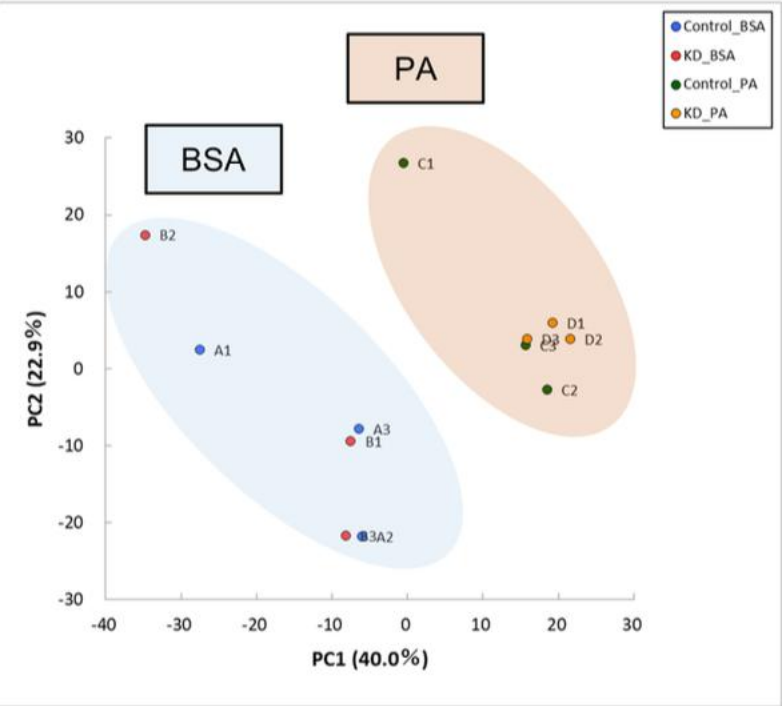


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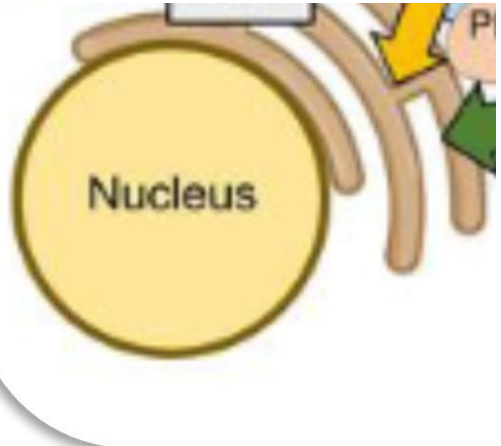
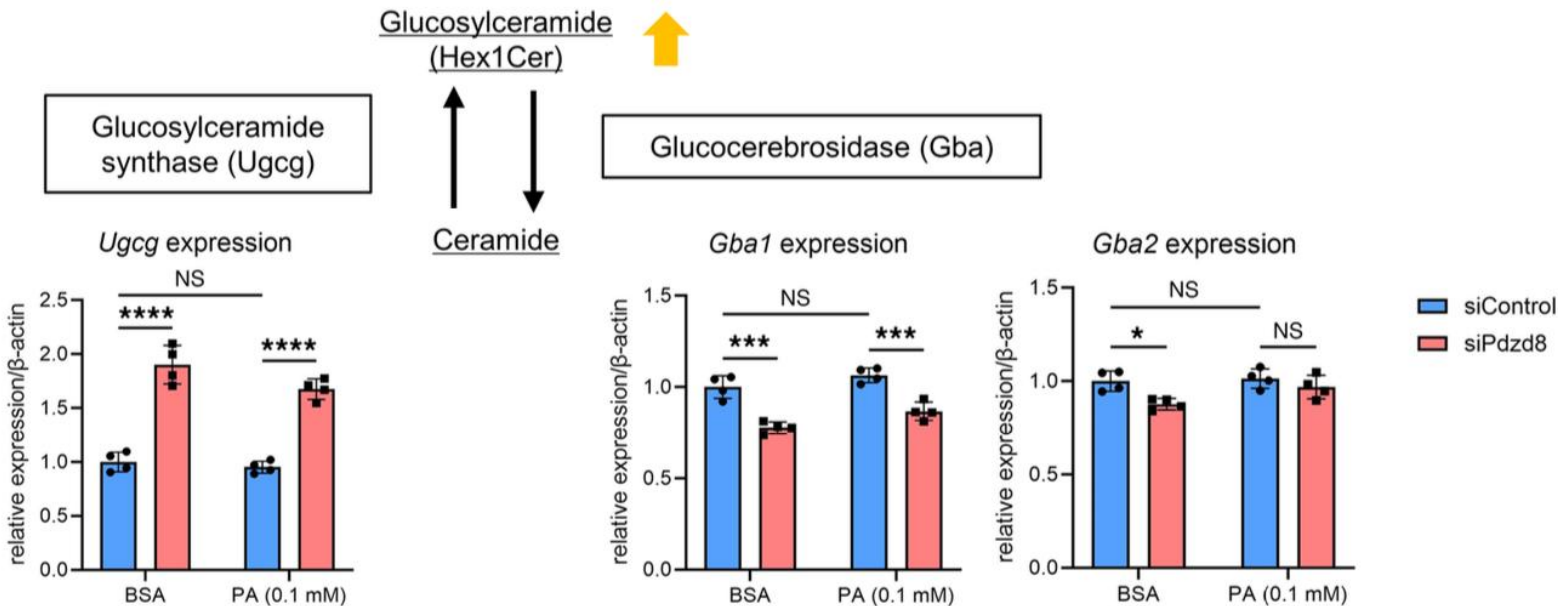


Hasegawa, S

Organelle communication maintains mitochondrial and endosomal homeostasis during podocyte lipotoxicity



Line	LipidMolec	Standardized Relative Area [§]											
		A1	A2	A3	B1	B2	B3	C1	C2	C3	D1	D2	D3
14	Hex1Cer(d18:2_24:0)	-1.499	-1.018	-0.270	0.988	1.675	0.582	-0.962	-0.529	-0.627	1.188	0.685	-0.211
15	GM3(d34:1)	-0.860	-0.614	-0.017	0.341	2.304	0.077	-1.522	-0.980	-0.403	0.336	0.602	0.736
16	Hex1Cer(d18:1_24:0)	0.070	-0.976	-1.049	0.992	2.065	0.162	-0.486	-1.269	-1.013	0.651	0.363	0.489
17	Hex1Cer(d18:1_22:0)	-0.701	-1.326	-0.694	1.043	1.476	0.017	-0.158	-1.162	-1.074	0.658	0.647	1.274
18	Hex1Cer(d17:1_24:0)	-0.424	-0.816	-1.038	1.391	1.126	0.248	-0.946	-1.319	-0.737	1.299	0.287	0.929
19	GM3(d42:2)	-0.686	-0.052	0.089	1.366	1.476	0.599	-1.800	-1.045	-1.053	0.056	0.277	0.771
20	GM3(d40:1)	-0.237	0.078	0.018	1.626	1.151	0.896	-2.018	-0.892	-1.090	0.100	0.311	0.058
21	Hex1Cer(d18:1_16:0)	-0.977	-0.707	-0.436	1.781	0.459	0.551	-1.271	-0.901	-0.991	0.656	0.656	1.182
22	Hex1Cer(d18:2_24:1)	-1.241	-1.138	-1.299	0.317	1.090	0.164	-0.131	-0.661	-0.670	1.173	1.120	1.275
23	Hex1Cer(d18:2_22:0)	-1.349	-1.417	-0.942	0.800	0.485	-0.122	-0.418	-0.272	-0.307	1.943	0.819	0.779
24	Hex1Cer(d18:1_20:0)	-0.426	-1.282	-0.324	-0.359	0.324	-0.171	-0.757	-0.767	-0.219	2.522	0.441	1.019
25	SPH(d18:2)	-0.150	-0.894	-0.618	1.493	-1.038	0.199	-1.280	-0.427	-0.352	1.132	1.789	0.147
26	DG(16:1_20:4)	-0.824	-0.937	-0.781	1.713	0.271	0.042	-0.251	-0.331	-1.187	1.885	0.750	-0.352
27	FA(26:0)	1.308	-0.743	-1.770	1.322	0.106	0.090	-0.607	-0.197	-1.111	1.033	0.980	-0.411
28	DG(14:0_14:0)	-1.481	0.649	0.706	0.396	-1.458	-0.190	-1.716	0.713	0.175	0.617	1.265	0.324



Take-home messages

- ◆ **Kidney cell phenotypic changes** are associated with metabolic dysregulation.
- ◆ **Organelle stress** alters metabolic homeostasis, contributing to kidney cell dysfunction.
- ◆ **Inter-organelle communication**, such as ER-mitochondria and ER-lysosome interactions, modulates kidney injury.
- ◆ **Targeting kidney metabolism** through organelle crosstalk offers new strategies to combat kidney damage.

Acknowledgements



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JSN welcomes back WCN after 1990 !!



Stay tuned !