



# Disruption of peritoneal membrane barrier function by prolonged exposure to Peritoneal Dialysis fluids is restored with 2-deoxy-glucose (2-DG) administration



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O39

*Oral Presentations: Dialysis-Glomerular Diseases*

*October 21<sup>st</sup>, 8:30 - 10:00, Hall Alexandros II*

HELLENIC SOCIETY  
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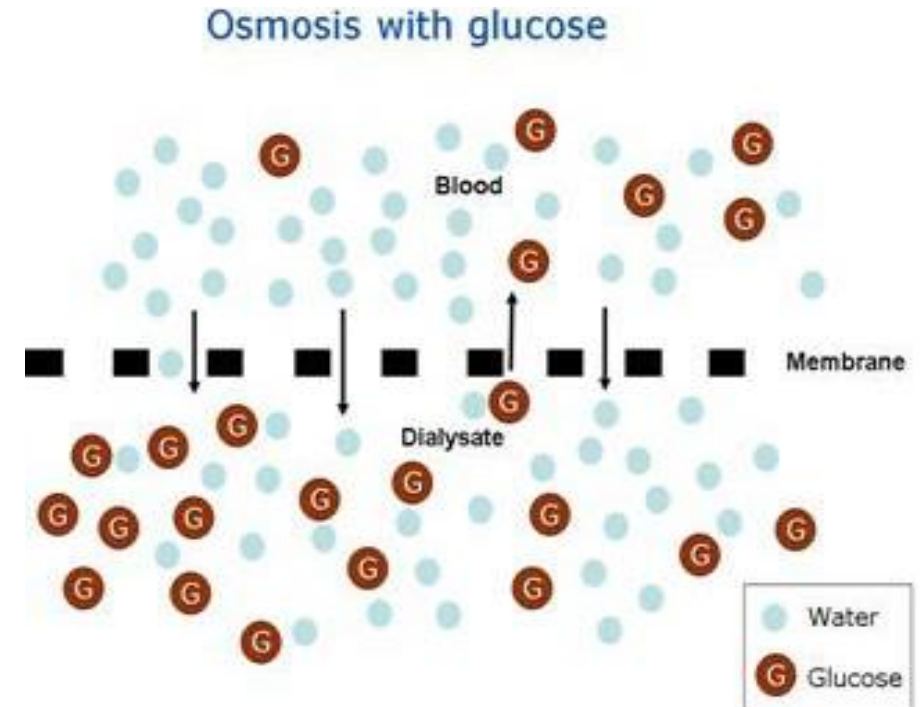
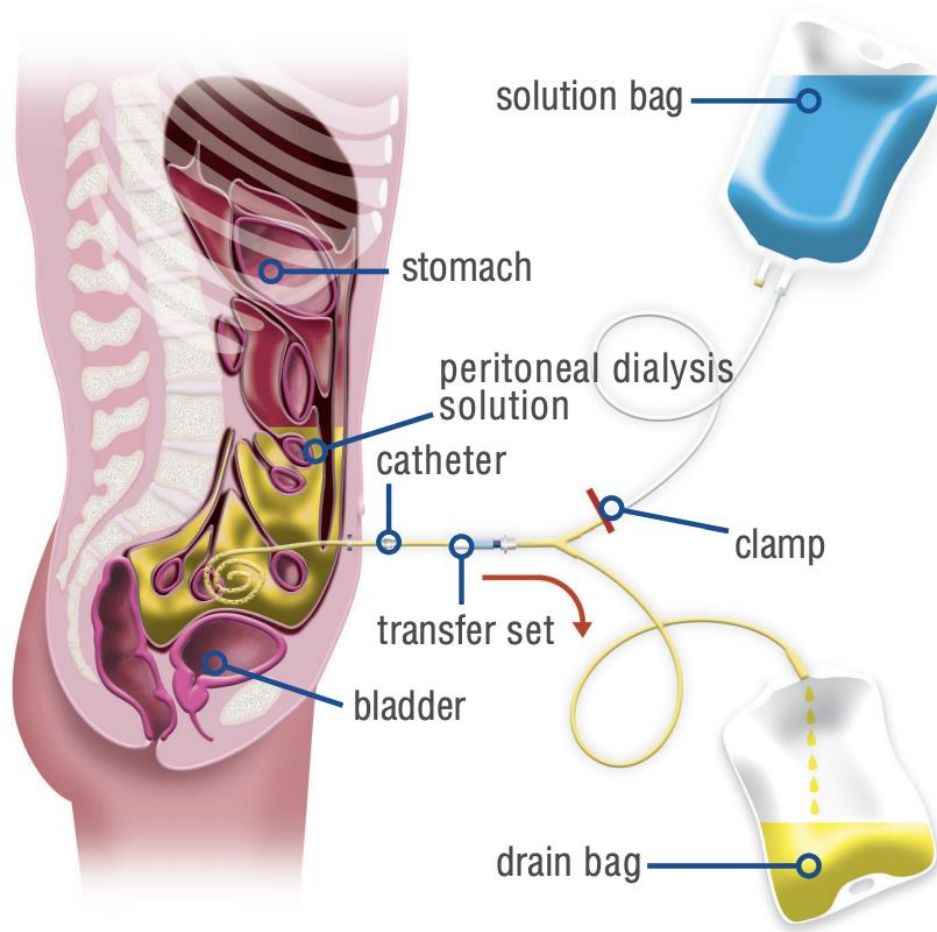
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October 19-22, 2023

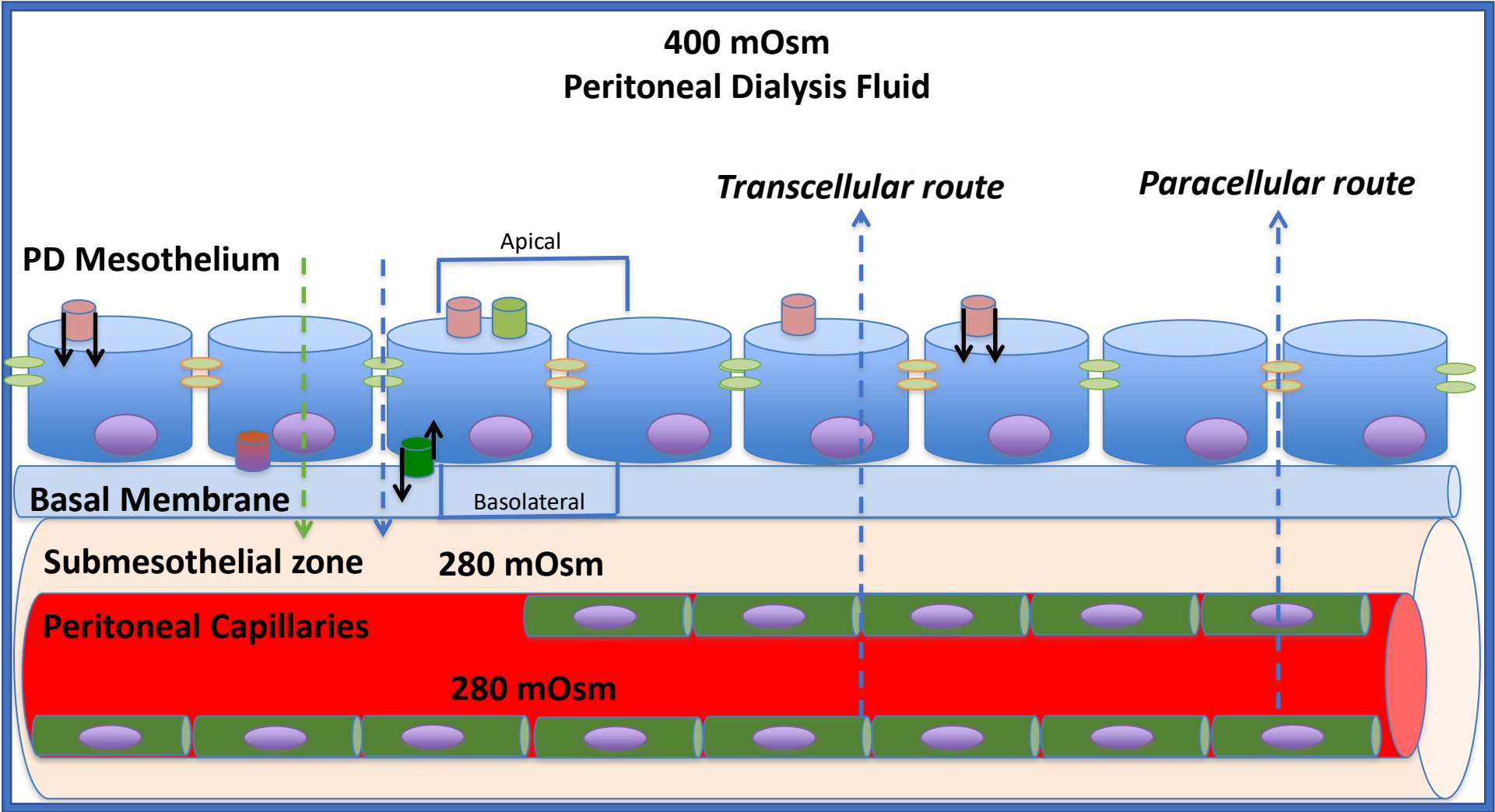
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# Peritoneal Dialysis (PD)



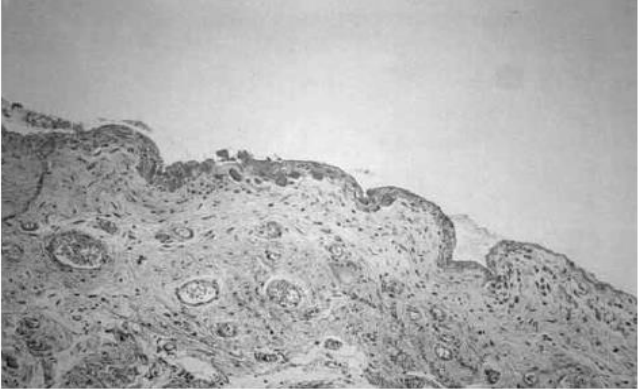
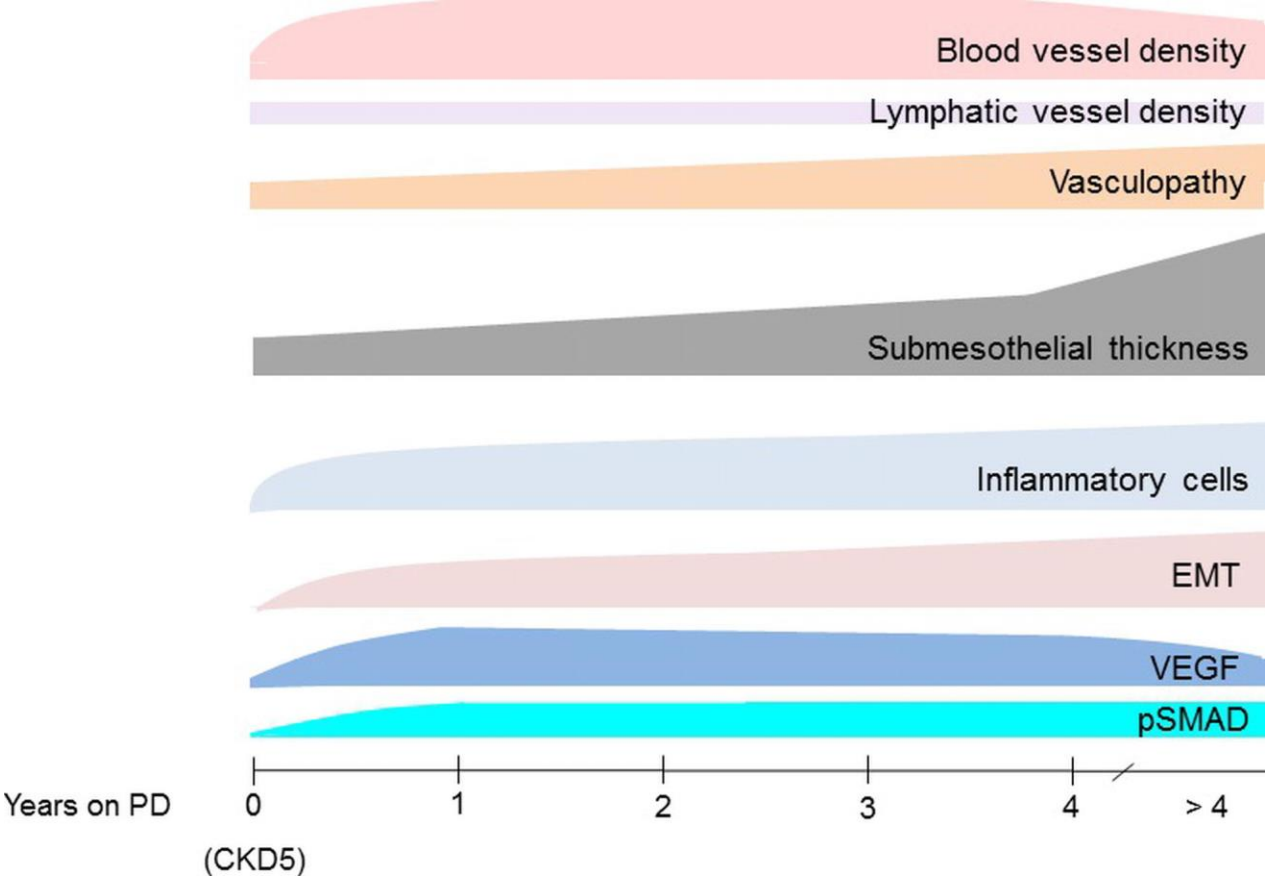
# Solute and water transport mechanisms in PD



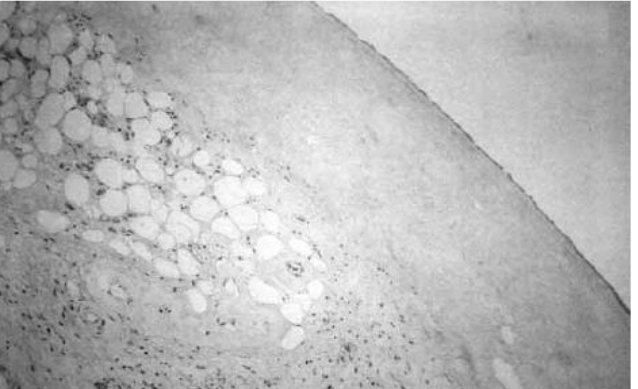
- TJs
- AQP1
- ENaC
- Na<sup>+</sup>/K<sup>+</sup> ATPase
- SGLTs
- GLUTs

Schematic Representation of Peritoneal Cavity filled with Peritoneal Dialysis Fluid

# Structural and functional alterations of the peritoneal membrane



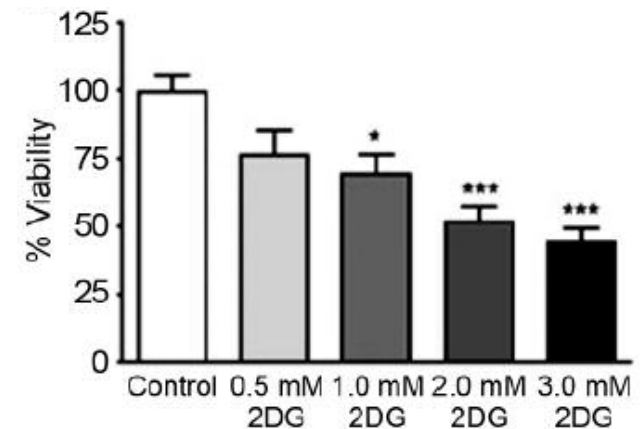
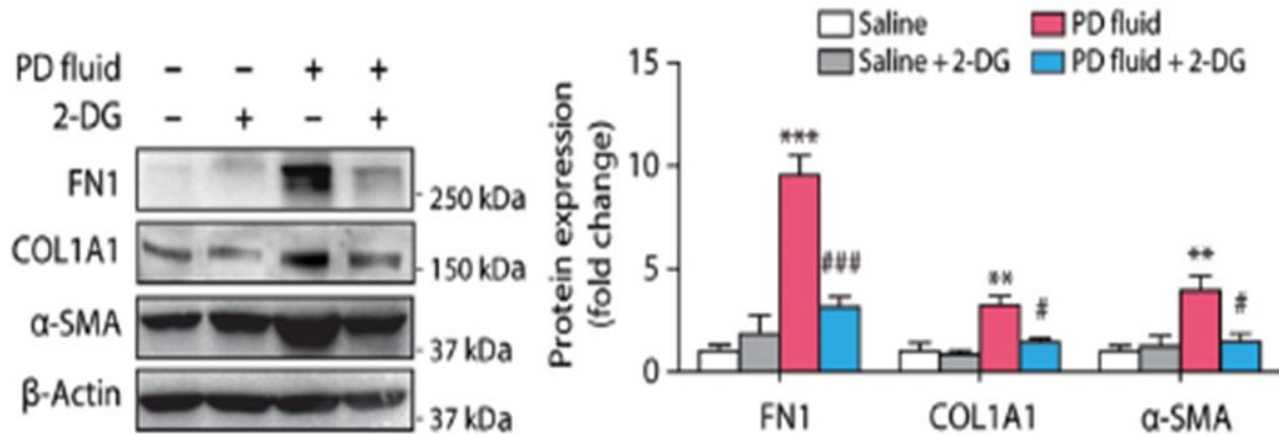
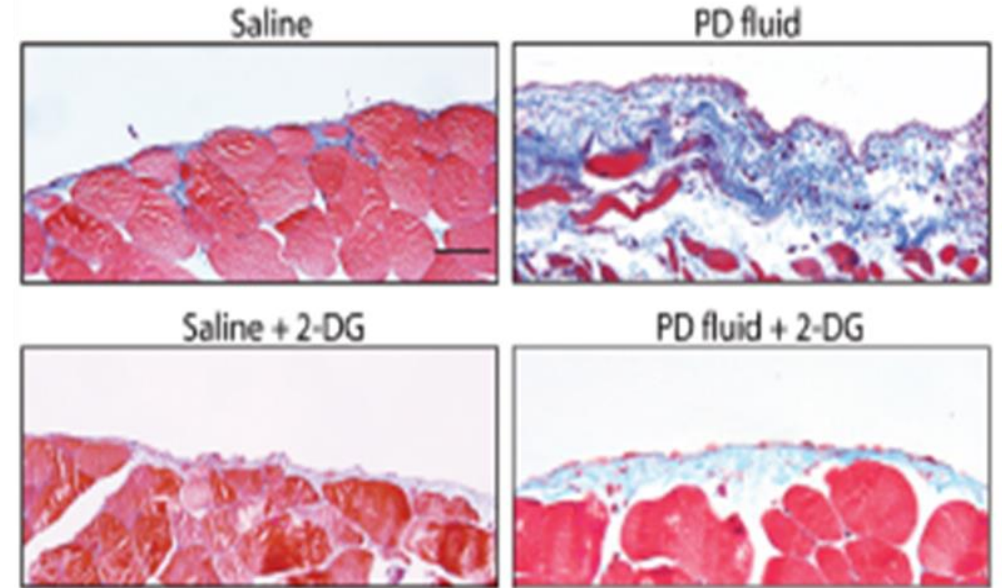
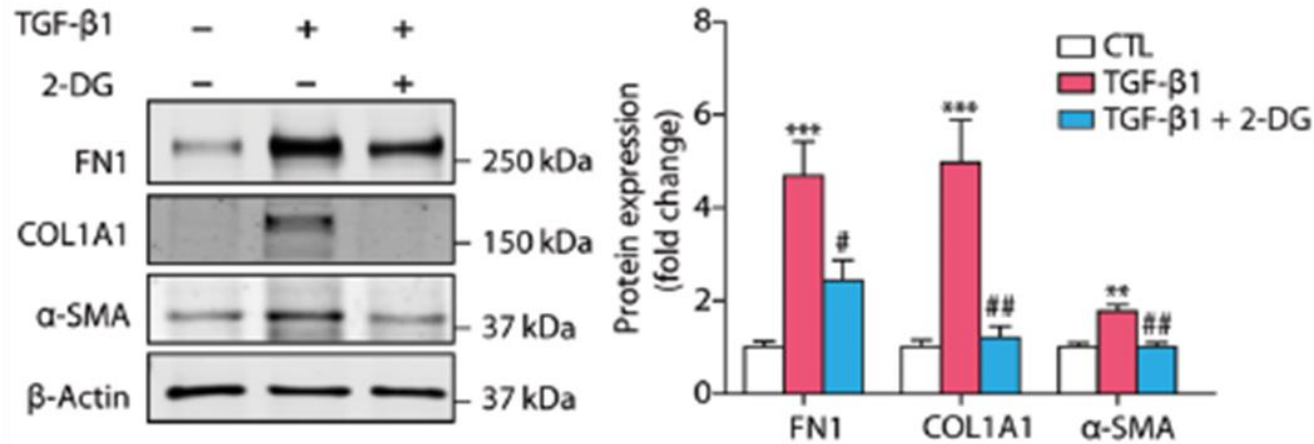
**Fig. 1 -** Mesothelial thickening with cellular swelling and activation; submesothelial layer with neoangiogenesis and increased collagen deposition. Hematoxylin and Eosin 100 x.



**Fig. 2 -** Disappearance of mesothelial layer. Submesothelial collagen thickening > 50 microns. Neoangiogenesis with vascular sclerosis. Fibrous tissue infiltrating the adipose layer. Hematoxylin and Eosin 100 x.

Bartosova M et Schmitt CP. *Front. Physiol* 2019; 9:1853  
 Bertoli SV, et al. *Int J Artif Organs* 2005; 28: 112-116

# Inhibition of hyper-glycolysis by 2-Deoxy-glucose (2-DG)



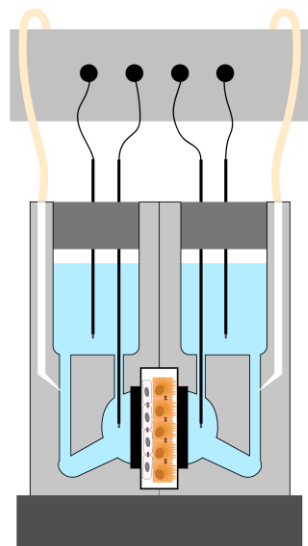
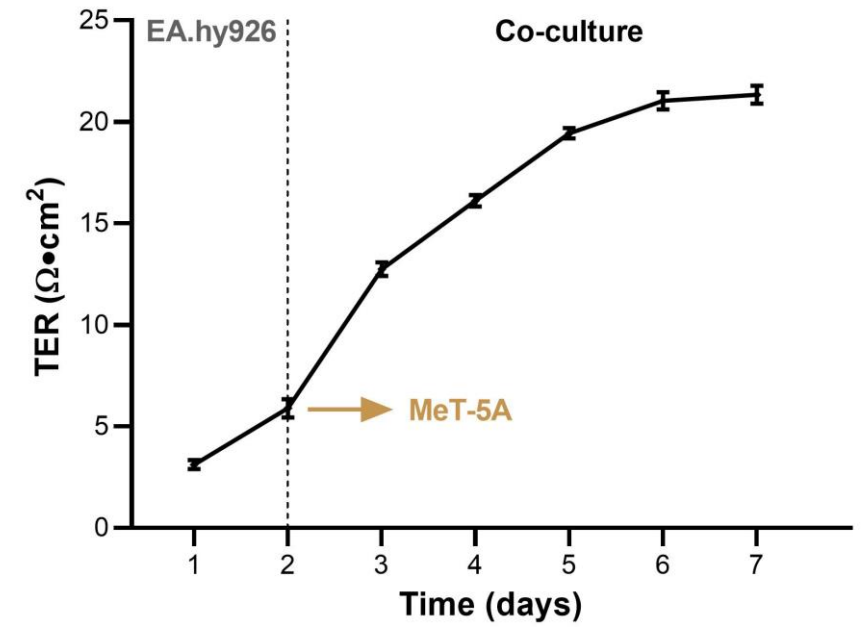
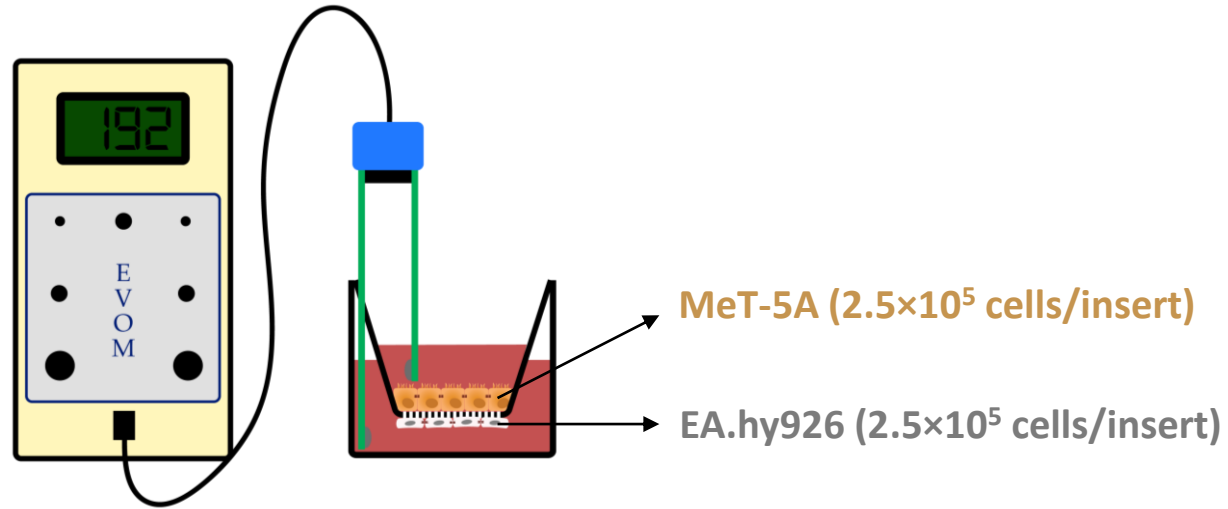
# Aim of the study

We assessed whether administration of 2-DG with several PD fluids of different composition affects the permeability of mesothelial and endothelial barrier of the peritoneal membrane.

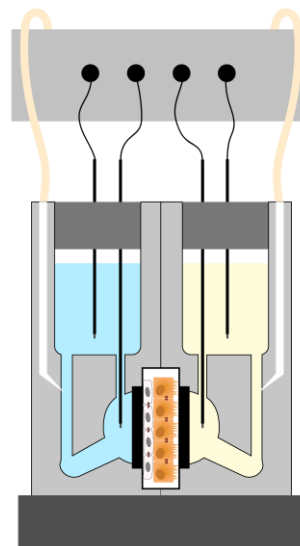
2-DG effect was assessed by monitoring:

- Transmembrane resistance ( $R_{TM}$ )
- FITC-dextran (10 kDa) diffusion
- mRNA expression levels of *CLDN-1* to *-5*, *ZO1*, *SGLT1*, and *SGLT2* genes

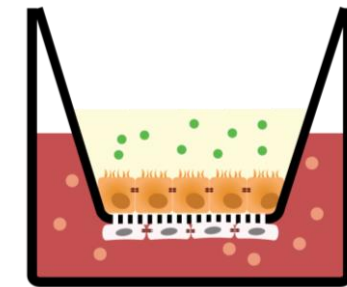
# Materials & Methods



30 min



4 hours



*CLDN-1 to -5*  
*ZO1*  
*SGLT1*  
*SGLT2*

# Materials & Methods

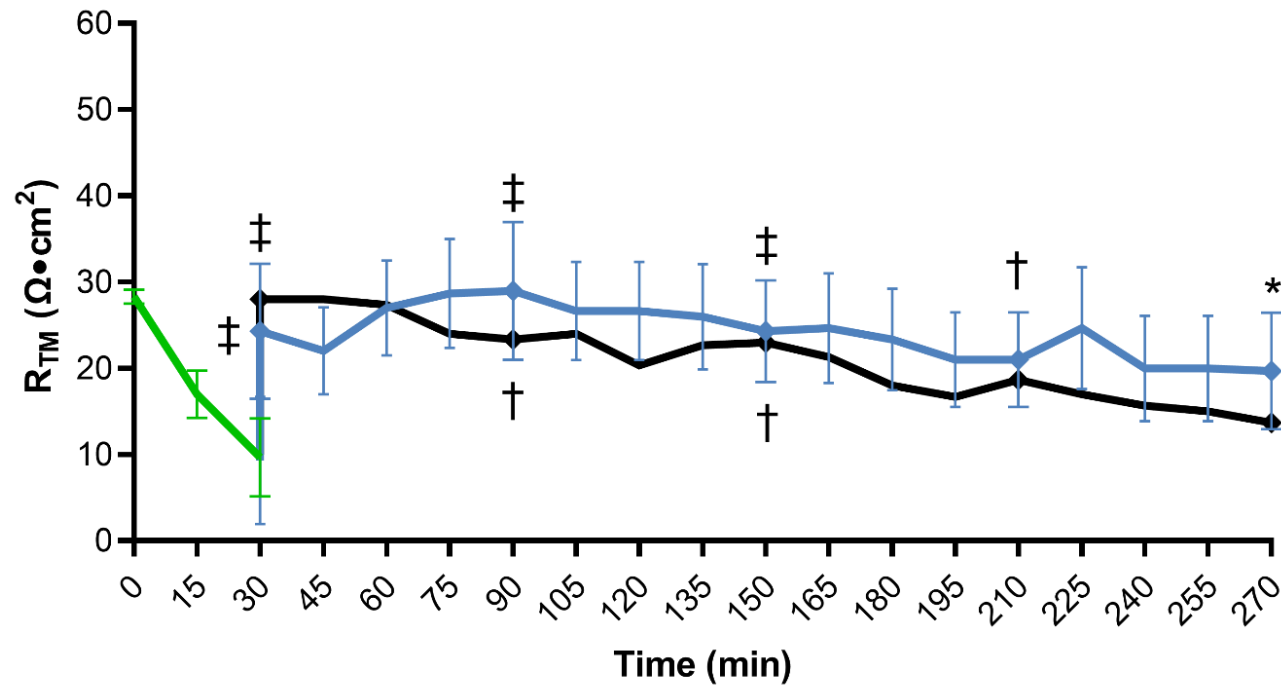
	Conventional PDF (CPDF)	Bicarbonate-buffered PDF (BPDF)	Lactate-buffered PDF (LPDF)
<b>Solution (manufacturer)</b>	<b>Dianeal (Baxter Healthcare)</b>	<b>BicaVera (Fresenius Medical Care)</b>	<b>Balance (Fresenius Medical Care)</b>
<b>Osmotic agent (% w/v)</b>	Dextrose (2.5%)	Glucose (2.3%)	Glucose (2.3%)
<b>Bag</b>	Single chamber	Double chamber	Double chamber
<b>pH</b>	5.0-6.5	7.4	7.0
<b>Osmolarity (mOsm/L)</b>	396	401	401
<b>Buffer solution (mmol/L)</b>	Lactate (40)	Bicarbonate (34)	Lactate (35)
<b>Ca<sup>2+</sup> (mmol/L)</b>	1.75	1.75	1.75
<b>Na<sup>+</sup> (mmol/L)</b>	132	134	134
<b>Mg<sup>2+</sup> (mmol/L)</b>	0.25	0.5	0.5
<b>Cl<sup>-</sup> (mmol/L)</b>	96	104.5	101.5
<b>Glucose (mmol/L)</b>	126	126.1	126.1



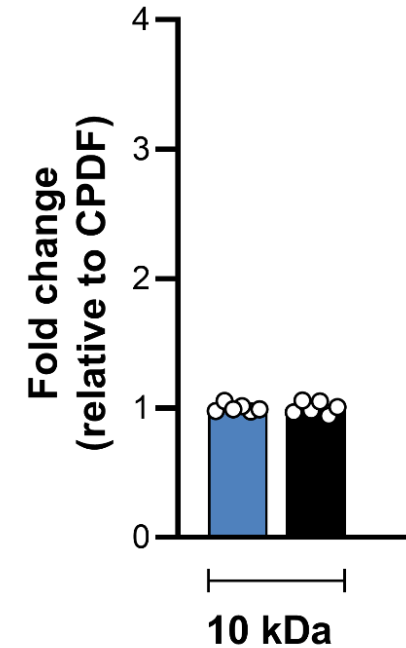
# Results (1/4)

2-DG attenuated the CPDF-induced increase in the combined mesothelial and endothelial barrier electrical resistance

(A)



(B)



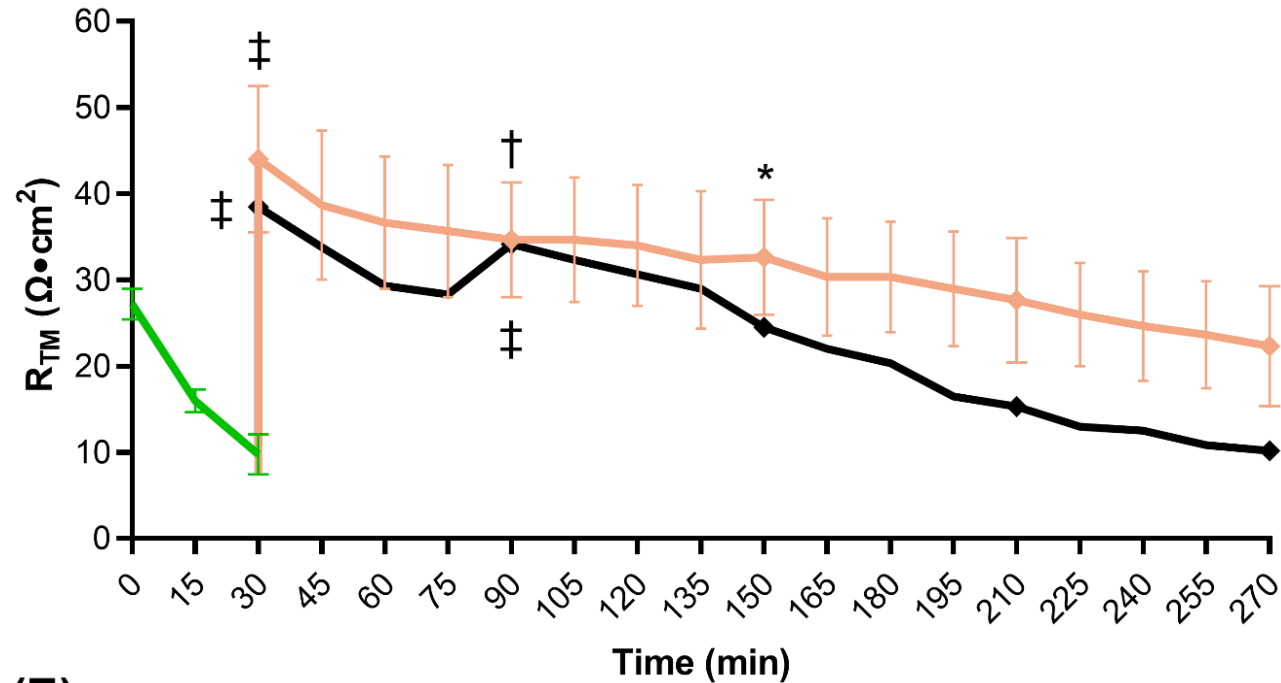
— KRB —◆— CPDF —◆— (+) 2-DG

\* $p < 0.05$ , † $p < 0.01$ , ‡ $p < 0.001$ ;  $n = 3-6$

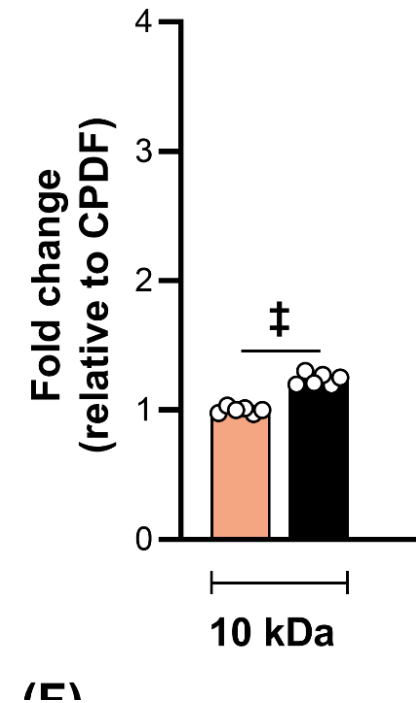
# Results (2/4)

2-DG attenuated the BPDF-induced increase in the combined mesothelial and endothelial barrier electrical resistance

(C)



(D)



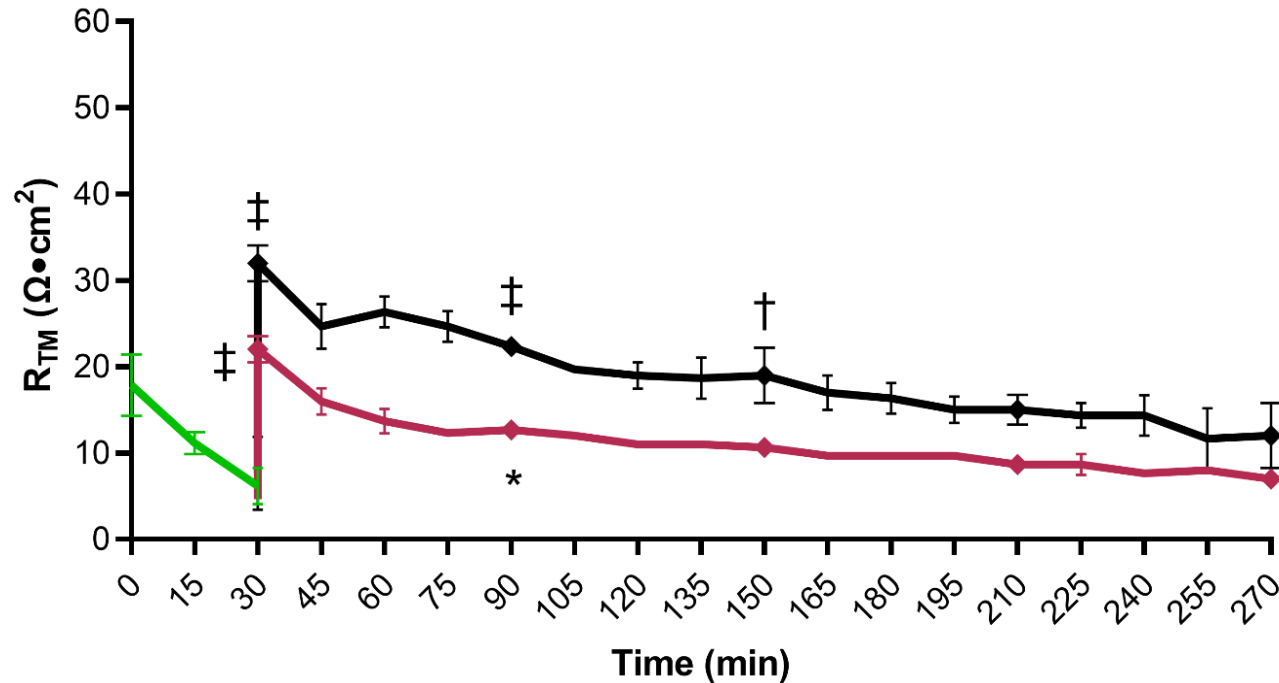
— KRB — BPDF — (+) 2-DG

\* $p < 0.05$ , † $p < 0.01$ , ‡ $p < 0.001$ ;  $n = 3-6$

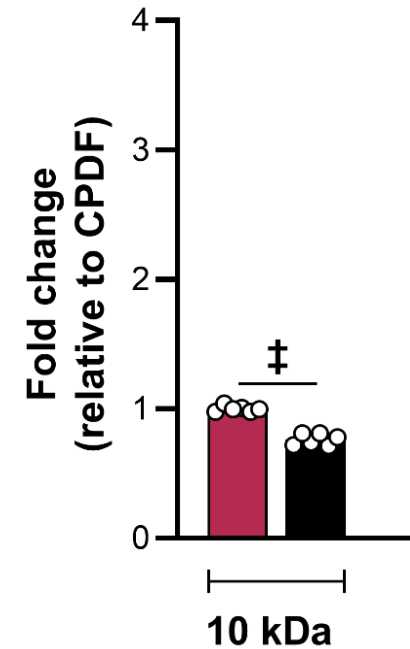
# Results (3/4)

LPDF supplementation with 2-DG enhanced the mesothelial and endothelial barrier function

(E)



(F)

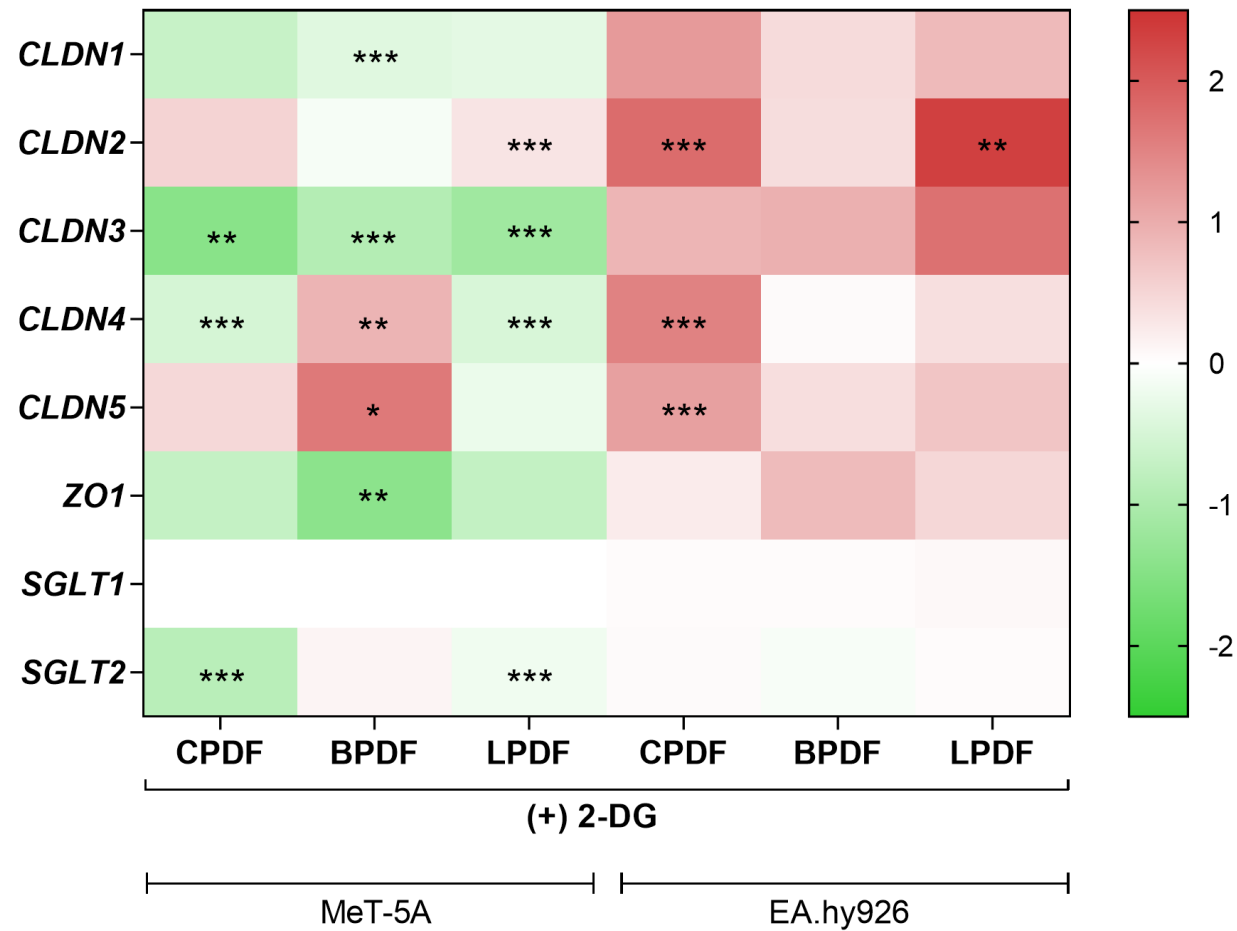


— KRB    ◆ LPDF    ◆ (+) 2-DG

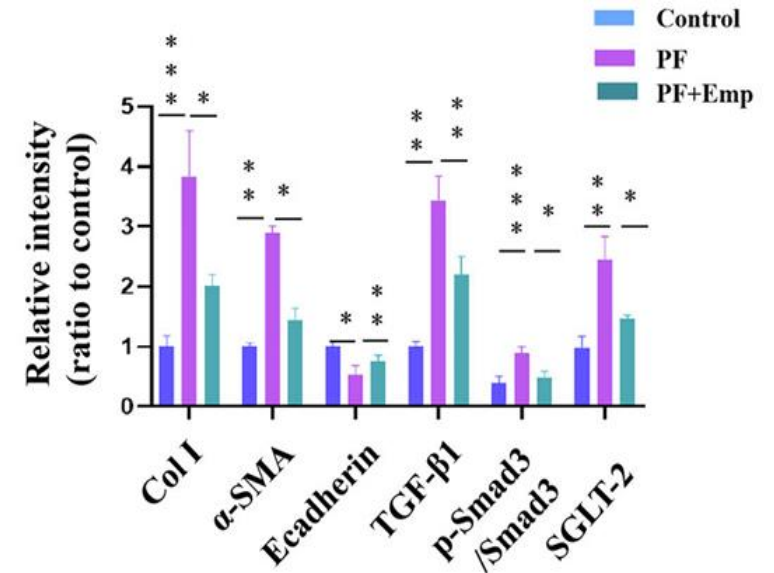
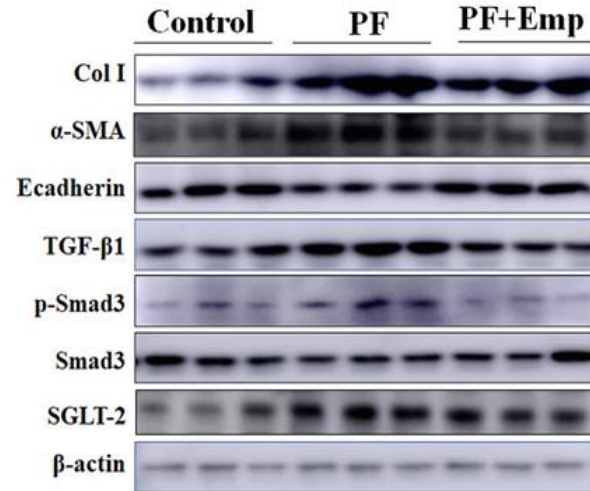
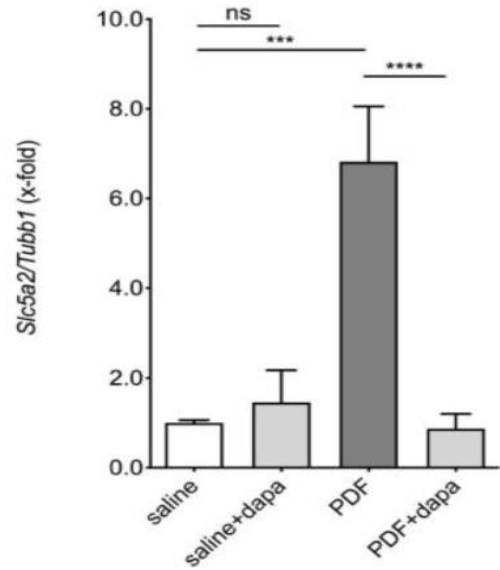
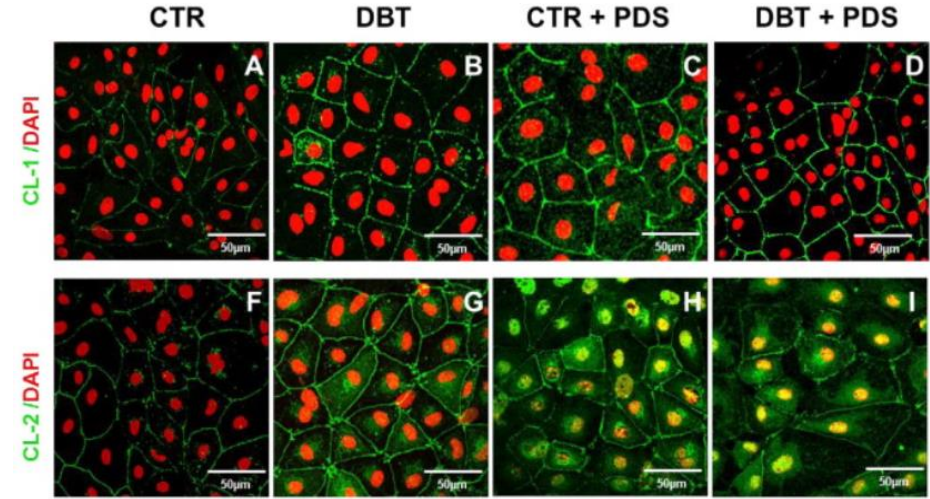
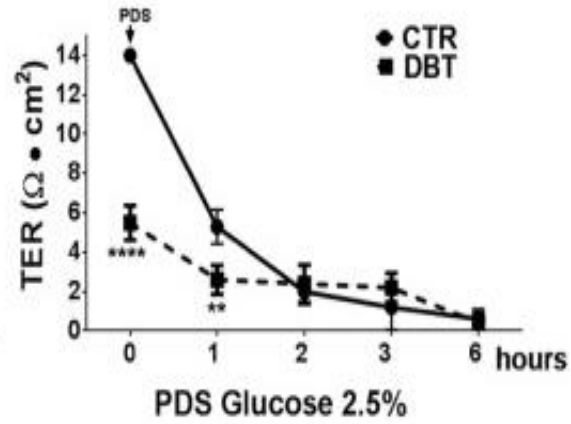
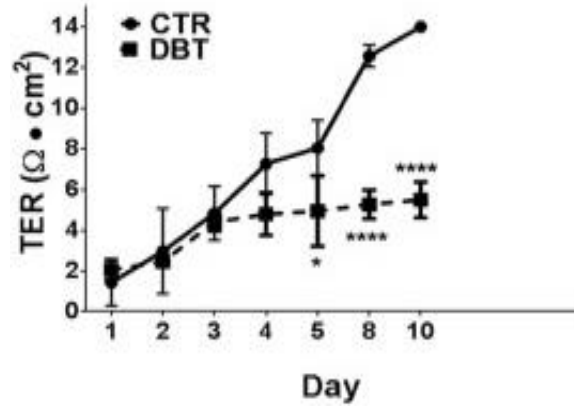
\* $p < 0.05$ , † $p < 0.01$ , ‡ $p < 0.001$ ;  $n = 3-6$

# Results (4/4)

Gene expression modulation after 2-DG administration was fluid- and cell-type depended



# Discussion



Debray-García Y, et al. *Life Sci.* 2016;161:78-89.

Balzer MS, et al. *Biomolecules.* 2020 Nov 19;10(11):1573.

Shentu Y, et al. *Int Immunopharmacol.* 2021 Apr;93:107374.

# Conclusions

- 2-DG improves functional permeability characteristics of the peritoneal membrane mesothelial and endothelial barrier.
- 2-DG administration restores gene expression changes of Tight junctions' components.
- Our promising results, along with the reported antifibrotic effect of 2-DG PDF supplementation warrant further studies.

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*Thank you for your attention!!!*



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