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Effects of metabolic-bariatric surgery on intestinal permeability and MASLD - a rodent model

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Combined Therapies, The Dawn of a New Era

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Nothing to disclose

„Leaky Gut“ associated with obesity

MASLD/MASH associated with increased gut permeability

Impact of MBS on intestinal permeability?

Kapil et al. Gastroenterol Hepatol. 2016
Mouries et al. Hepatol. 2019
Wilbrink et al. Obes. 2020

Study Design

PILOT - Intervention groups and study design

Goal → MASH + Fibrosis



N=5
+Mtx

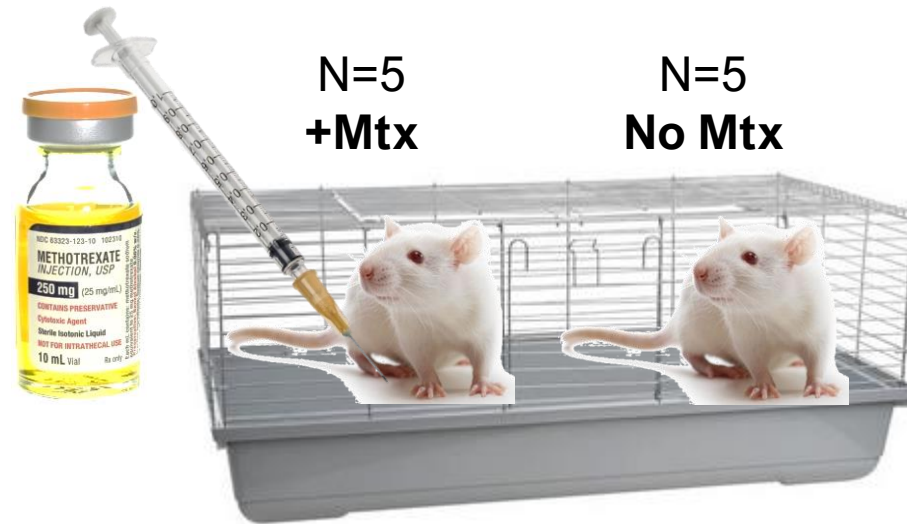
N=5
No Mtx

- ALIOS
- 8 wks

No Folate



ALIOS = 60 e% Fat, 17 e% Protein, 2 e% Cholesterol, 150 g/kg Fructose



N=5
+Mtx

N=5
No Mtx

- ALIOS
- 8 wks

Folate (10 mg/kg chow)

Study Design

Pilot



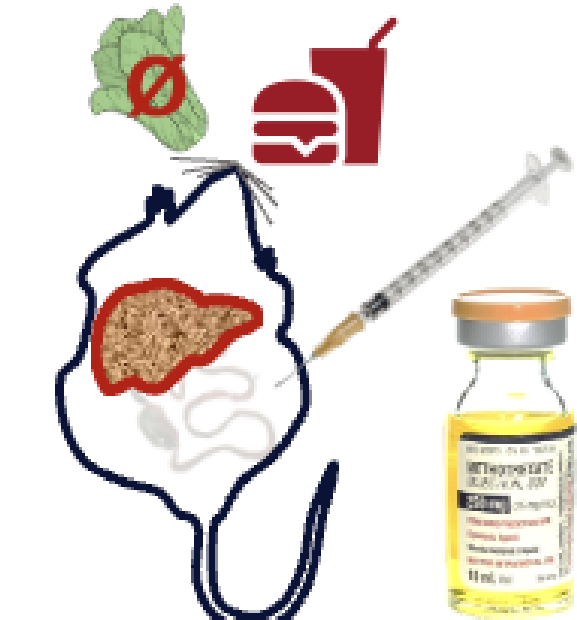
**ALIOS
No Folate
+Mtx**

8 Weeks

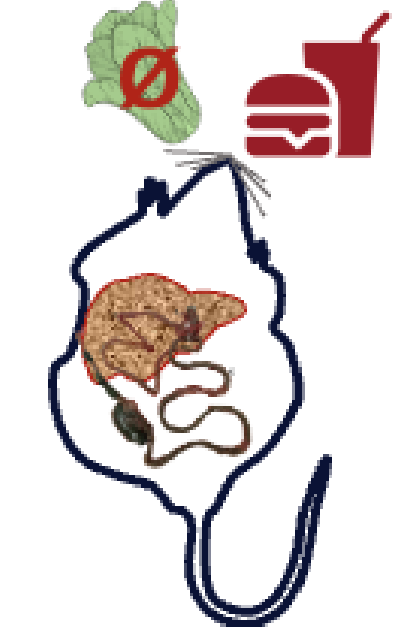
(n=5/Group)

Surgery groups

ALIOS+ MTX- B9



ALIOS - B9

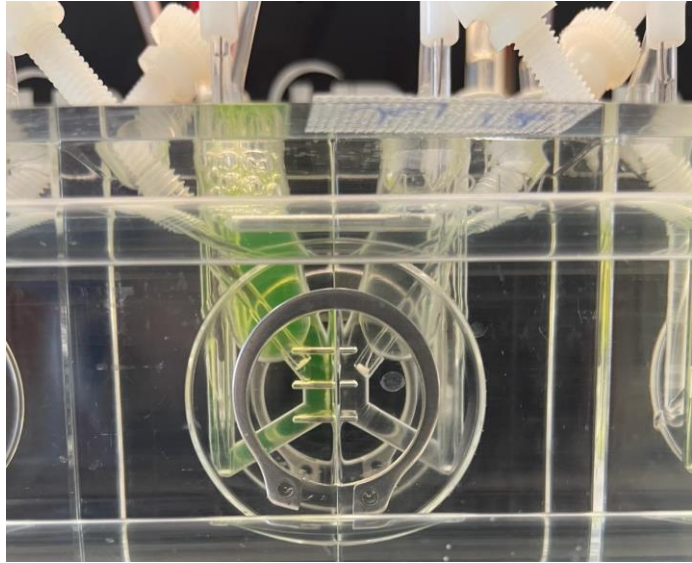
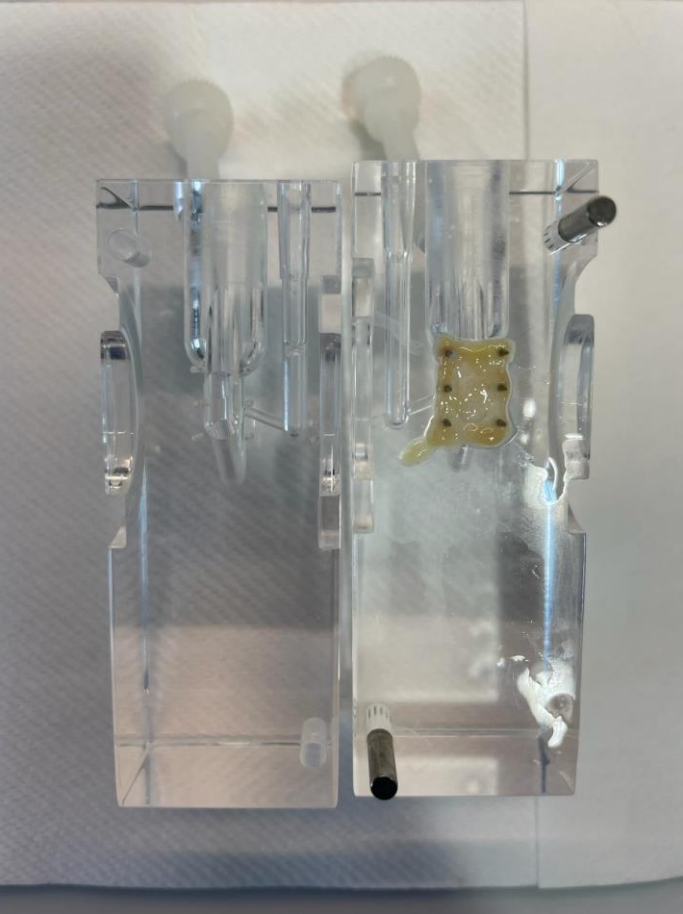


OAGB vs Sham surgery (n=5/group)

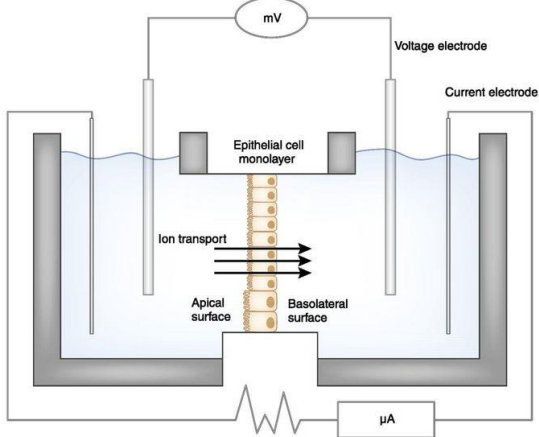
Methods

- Histology
 - Liver - CRN Criteria
 - Intestine (Jejunum, Ileum, Colon): *Claudin-1*, *Occludin*, ZO-1
- Ussing chamber
 - Transepithelial resistance TEER
 - Permeability assessment with probe molecules
 - Fluorescein isothiocyanate (FITC)-dextran 4kDA,
 - Lucifer yellow (LY) 457 Da

Ussing Chamber



The Ussing Chamber can be used to measure ion transport between the two sides of an epithelial cell membrane by polarized cells.



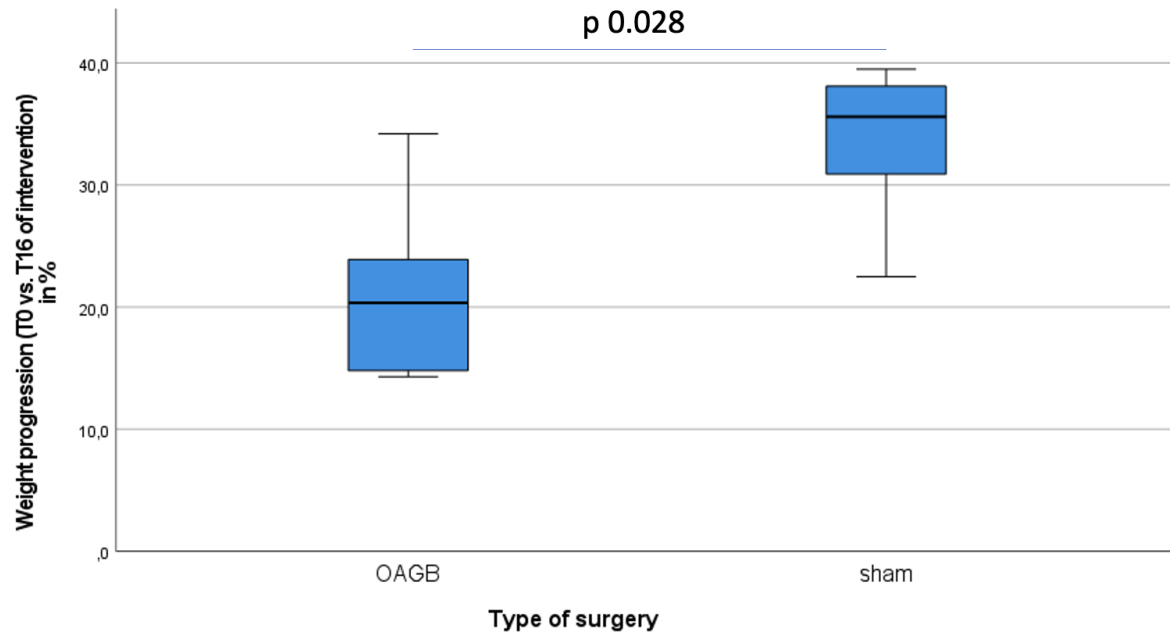
Melanie P. Hoenig, and Mark L. Zeidel CJASN 2014;9:1272-1281

CJASN

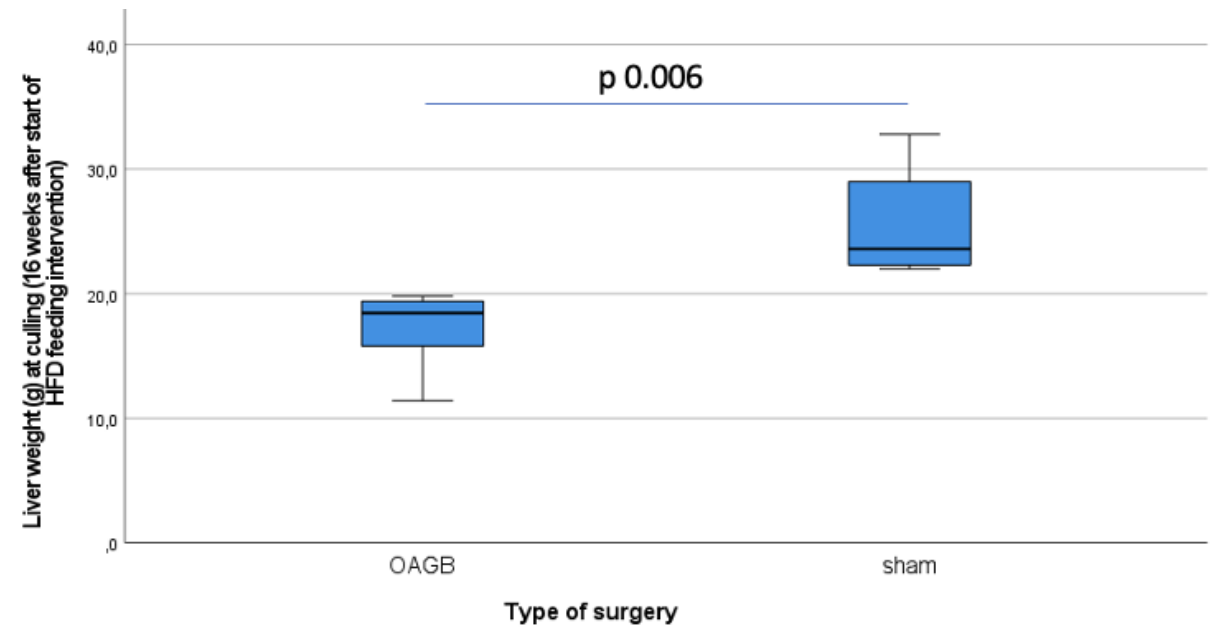
©2014 by American Society of Nephrology
 Hanson PJ, Moran AP, Butler K. Innate Immun 2011; 17: 269-82.
 Kapil S, Duseja A, Sharma BK, et al. J Gastroenterol Hepatol 2016;31:213-21.

Results

Body weight progression at week 16

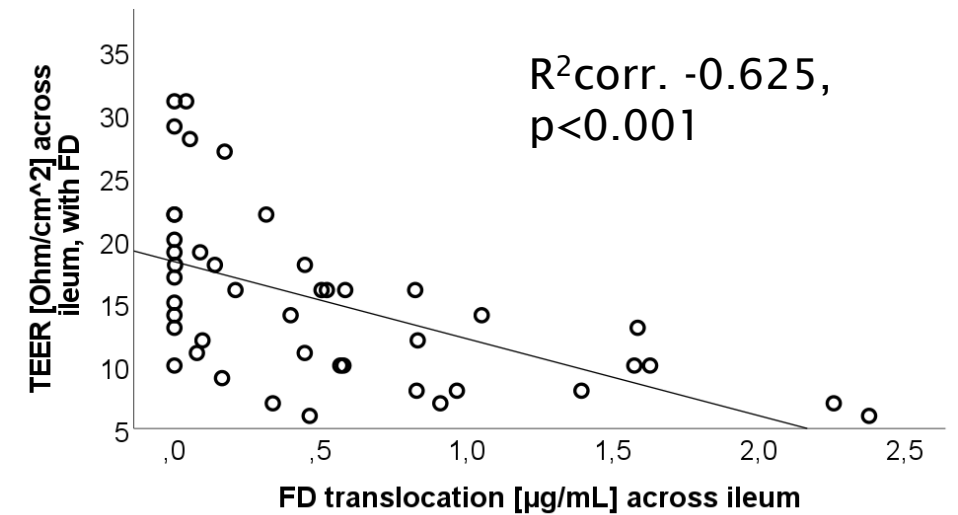
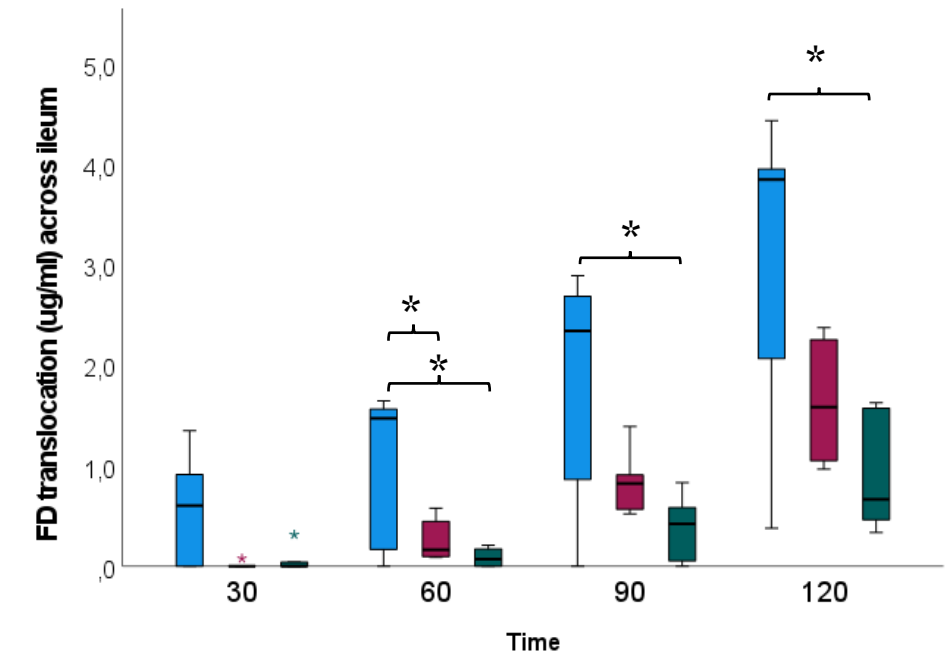
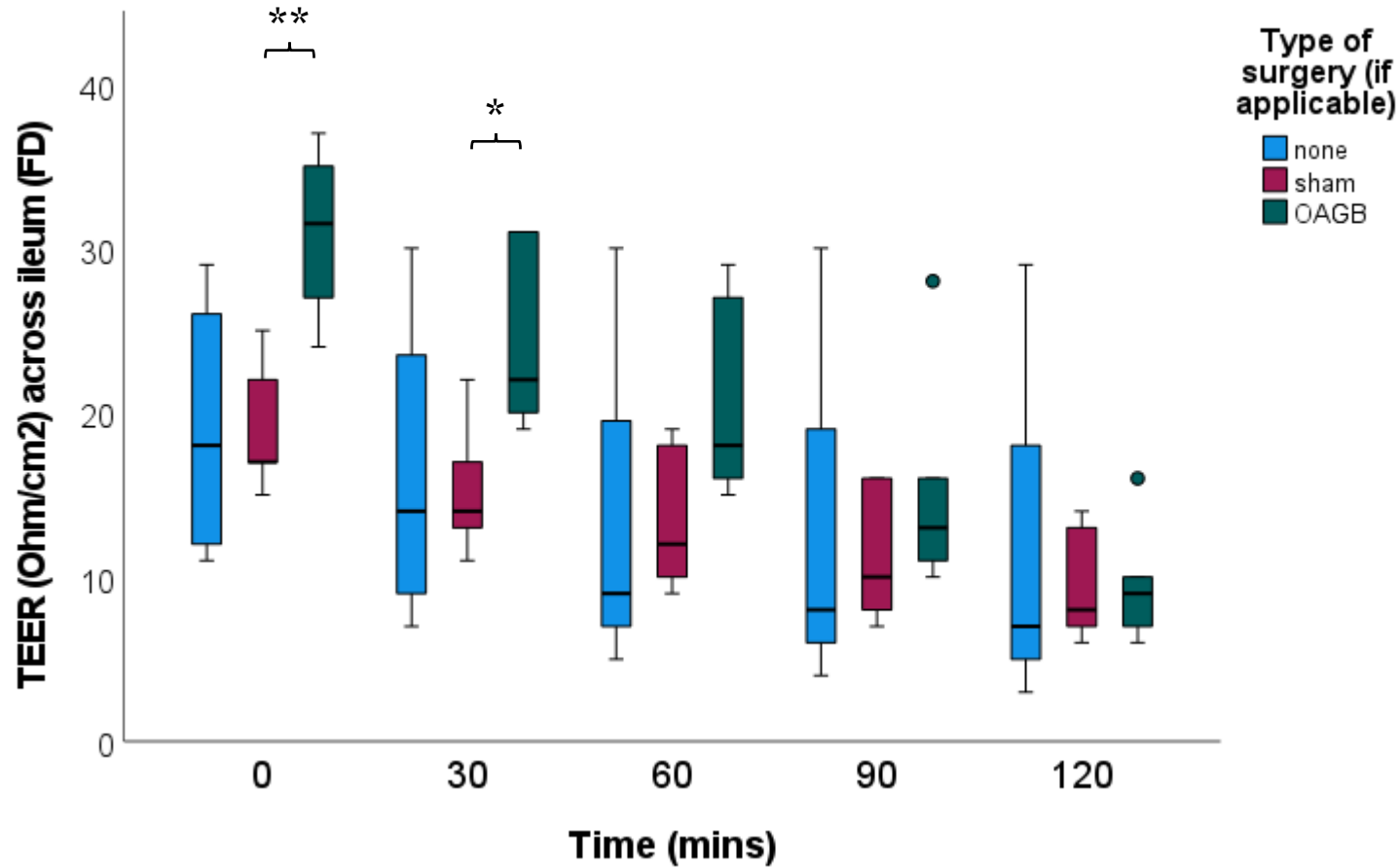


Liver weight at week 16



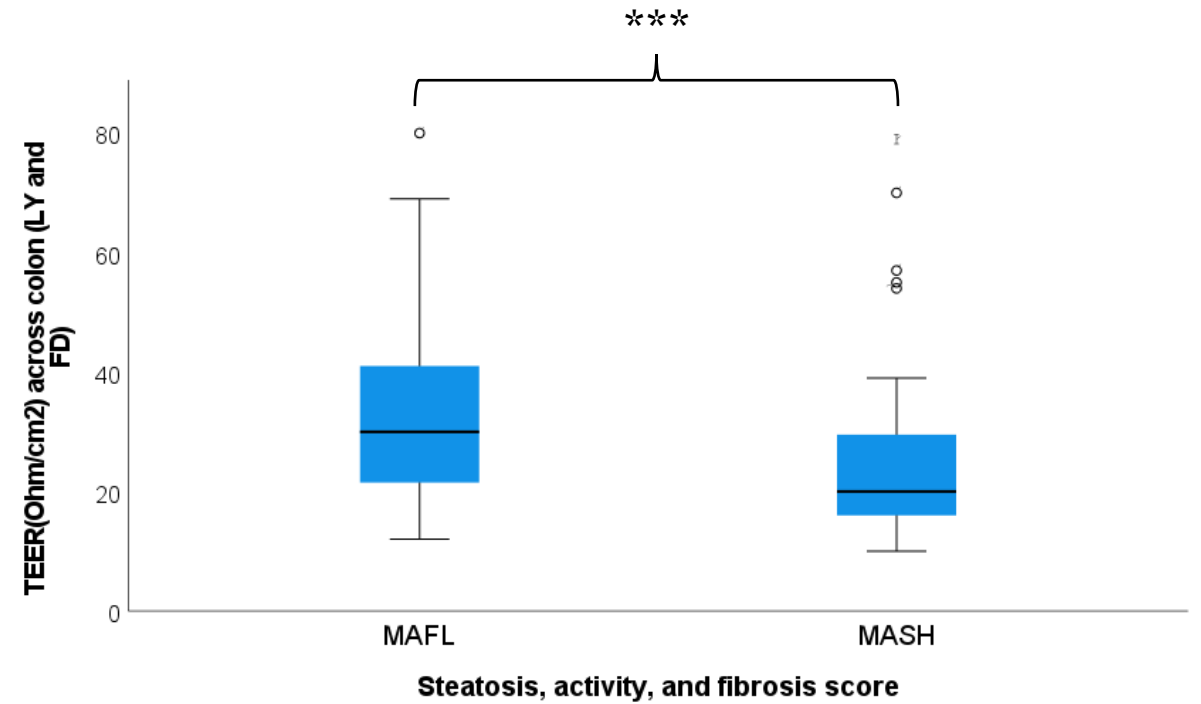
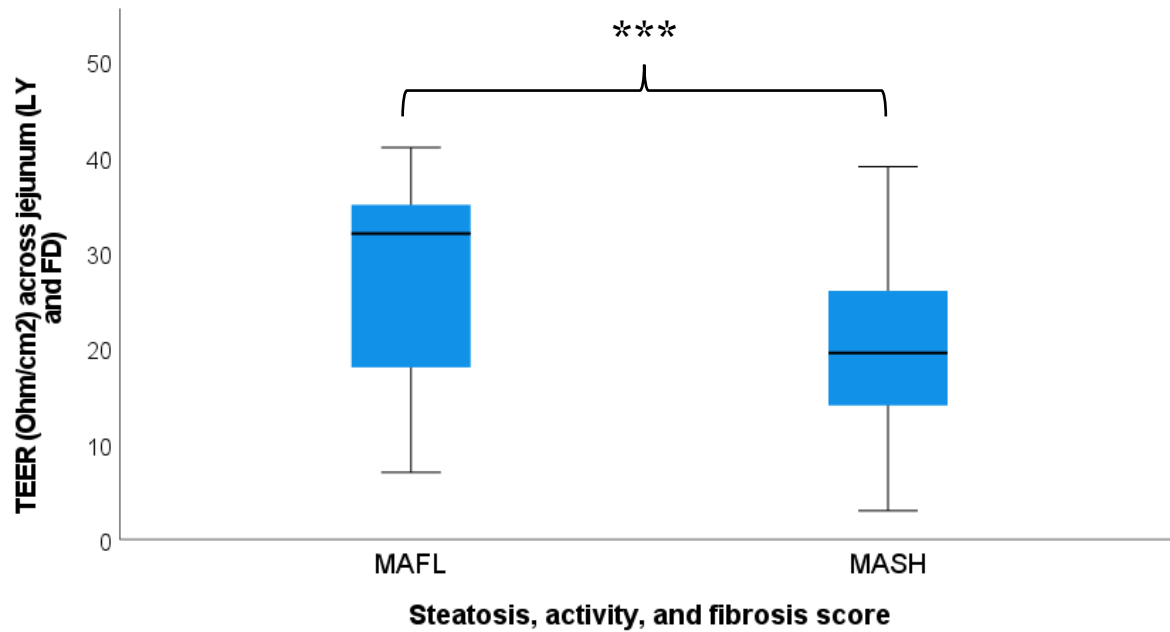
Results

TEER and FD translocation terminal Ileum



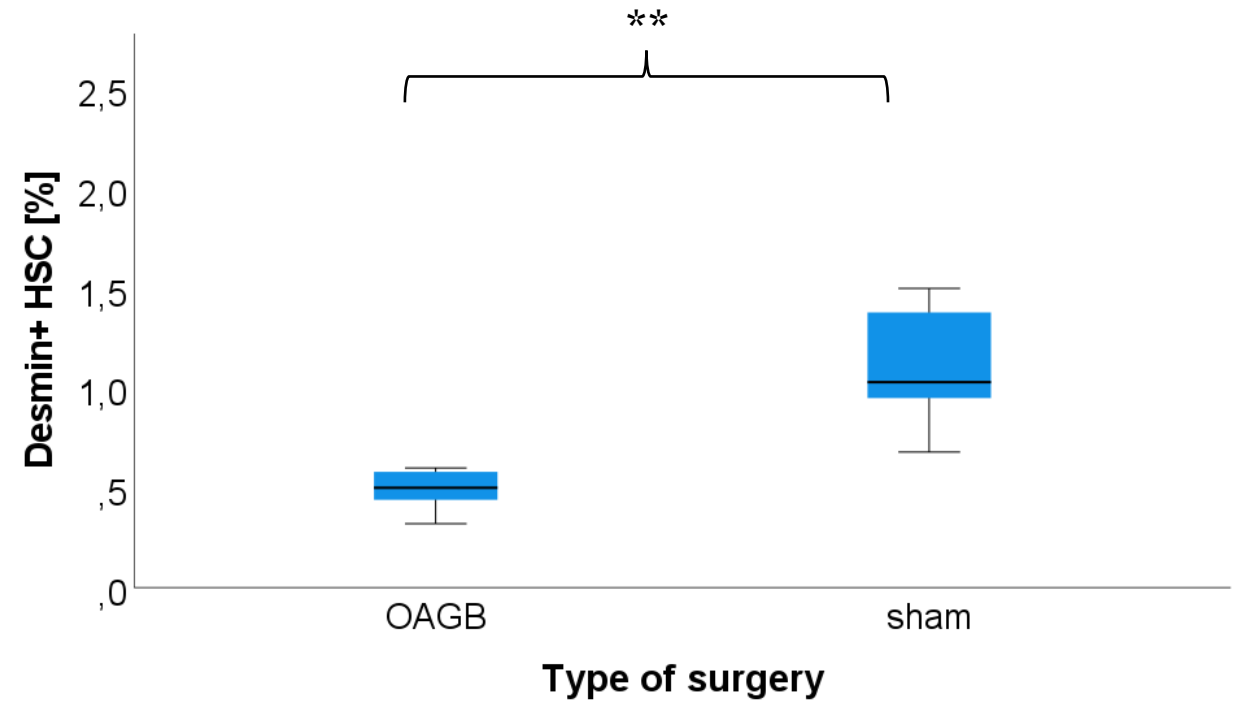
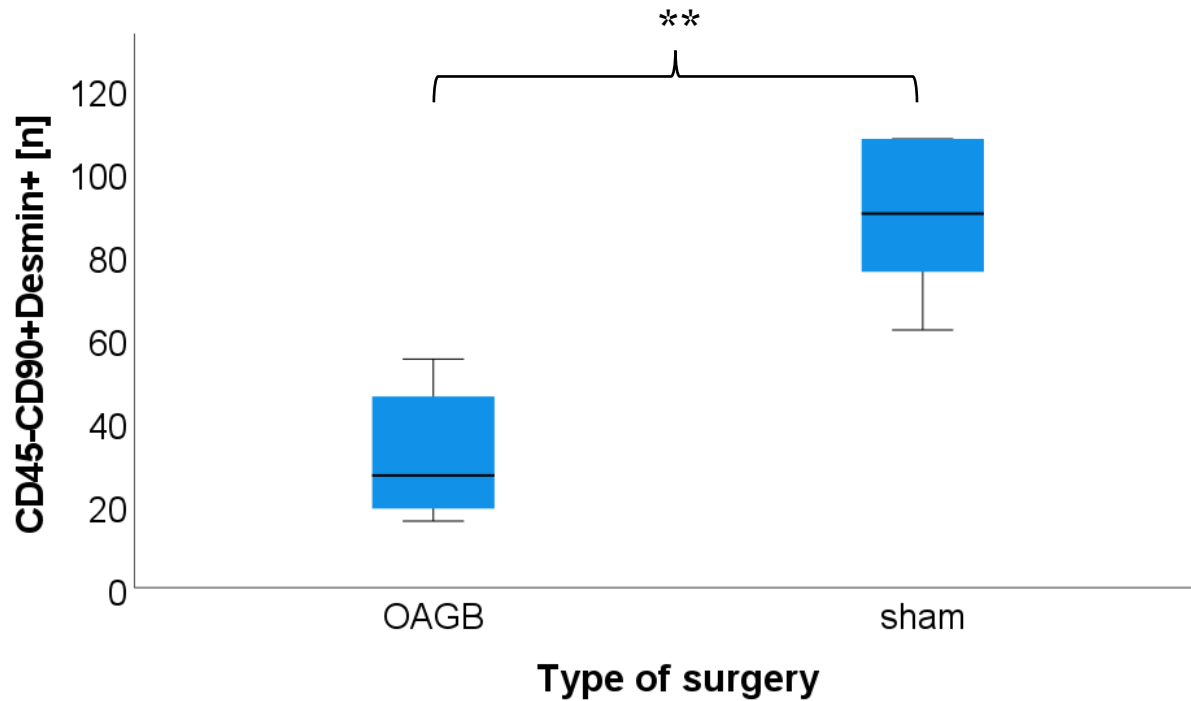
Results

TEER in MASL vs MASH



Results

Fibrosis markers after OAGB



Desmin and aSMA expressing Fibroblast precursors

% Desmin+ within CD45-CD90+ Fibroblast precursors

Desmin expressing HSC

% CD45-CD146-CD90- HSC

Conclusion

- Significant improvement of permeability in OAGB group
- Markers for fibrosis after OAGB decreased
- Higher permeability in rats with MASH (compared to MASLD)

- Histological workup of the liver to be performed
- Translational research in human model



Thank you for your attention

G. Prager
F. Langer
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N. Vock

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