

Claudin-7 dysregulation in pediatric EoE: A role for TGF- β 1 in esophageal epithelial barrier dysfunction

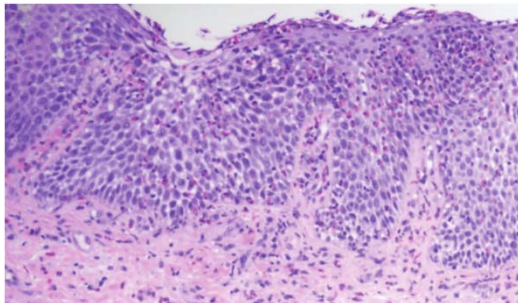
Joanne C. Masterson

University of Colorado, School of Medicine
Children's Hospital Colorado
Aurora, CO

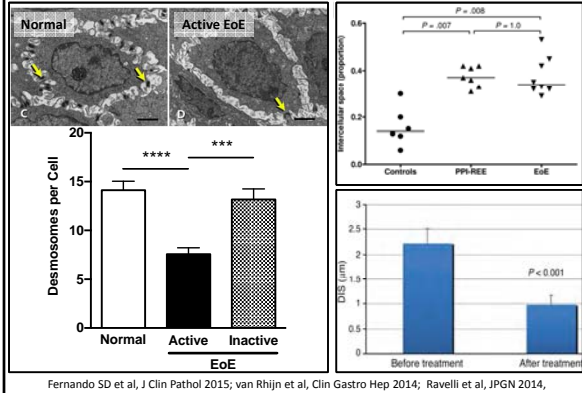


I have no disclosures.

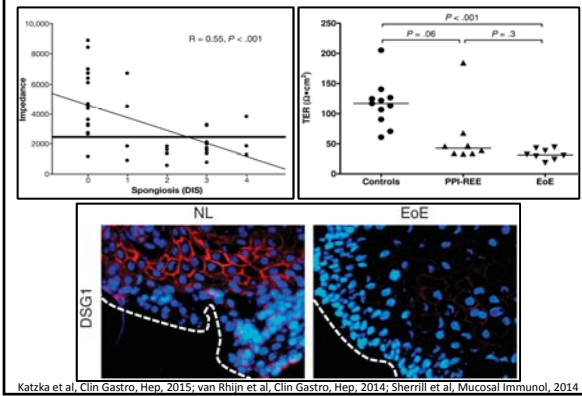
Eosinophilic Esophagitis: Histopathologic Features



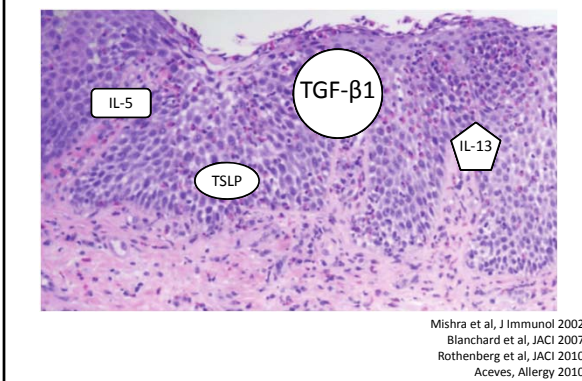
Barrier in EoE: Ultrastructural Features

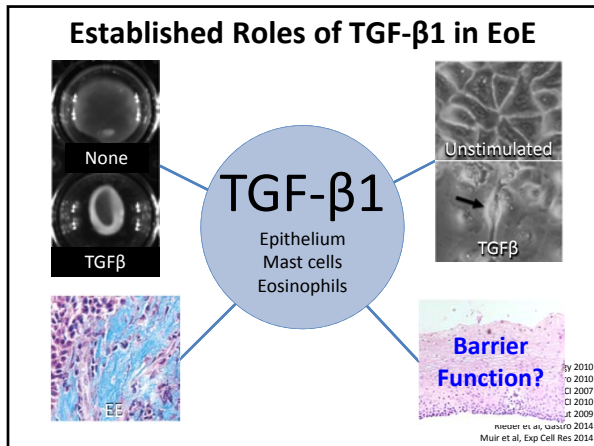


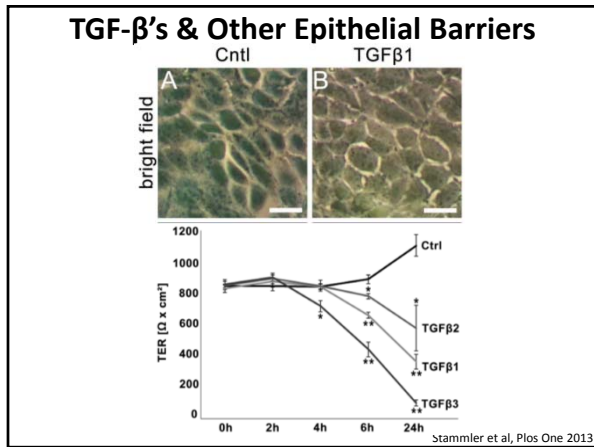
Barrier in EoE: Electrophysiological Assessment



Eosinophilic Esophagitis: Molecular Features







Hypothesis

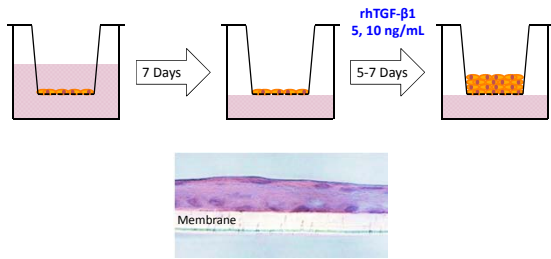
TGF- β 1 regulates esophageal epithelial barrier function

Aims

1. Determine whether TGF- β 1 alters esophageal epithelial barrier function *in vitro*
1. Determine the molecular target(s) through which TGF- β 1 may regulate esophageal epithelial barrier

Materials & Methods

- EPC2-hTERT cells \rightarrow 3D Air Liquid Interface (ALI)

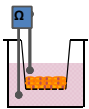


Sherrill et al, Mucosal Immunol 2014

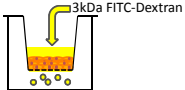
Materials & Methods

- *In vitro* Barrier Function Assays on 3D-ALI

- Barrier: Trans-epithelial electrical resistance (TEER)

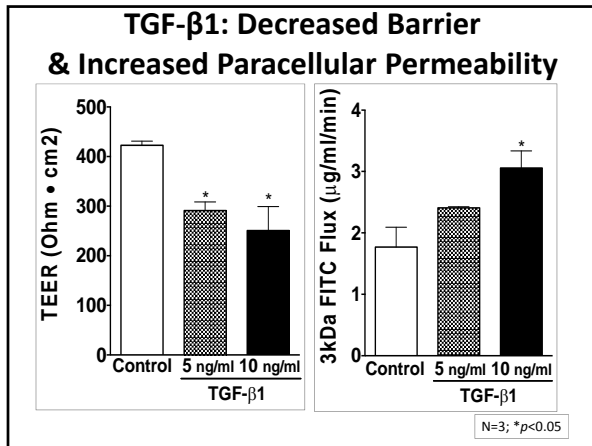


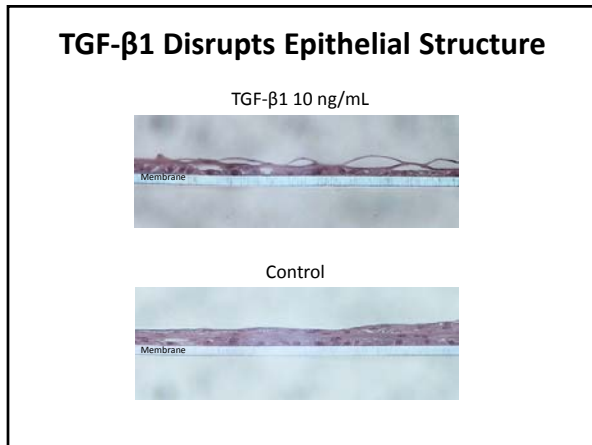
- Paracellular Permeability: 3kDa FITC Flux

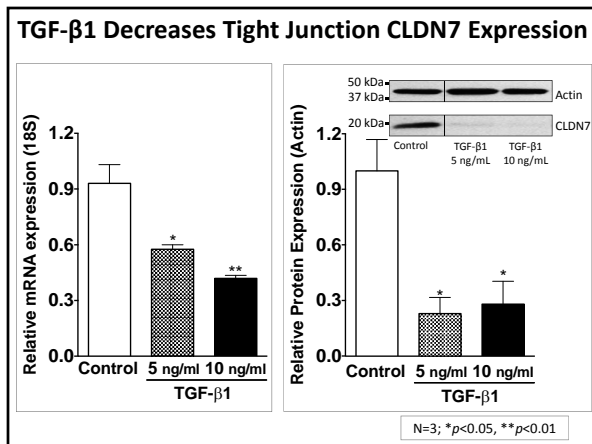


- Real time RT-PCR on 3D-ALI

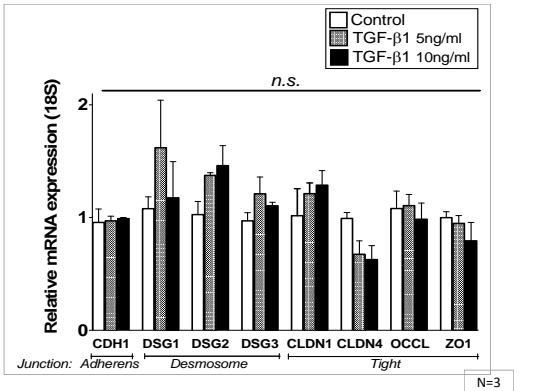
- Epithelial Junction Transmembrane Components







TGF-β1 Effects on Epithelial Junctions

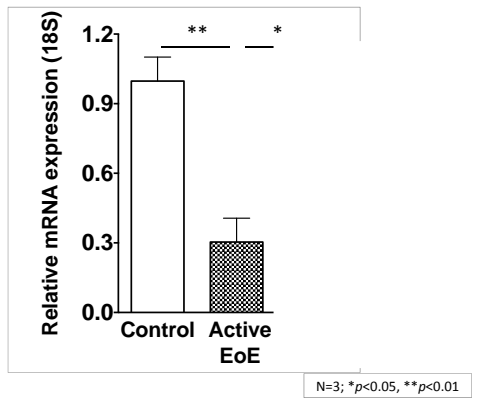


CLDN7 Expression in EoE Patients

Subject Characteristics

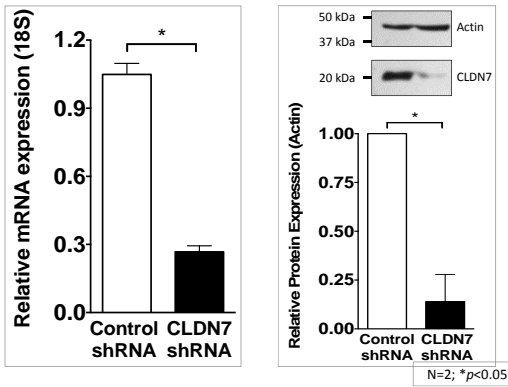
Group	N	Mean Age (yrs)	Symptoms	Mean Eos / HPF
Active EoE	10	10.1	Vomiting-4 Abdominal pain-6	46
Inactive EoE	6	9.1	None	2.8
Control	10	11.7	Abdominal pain-5 Diarrhea-3 Vomiting-2	0

CLDN7 is Decreased in Active EoE

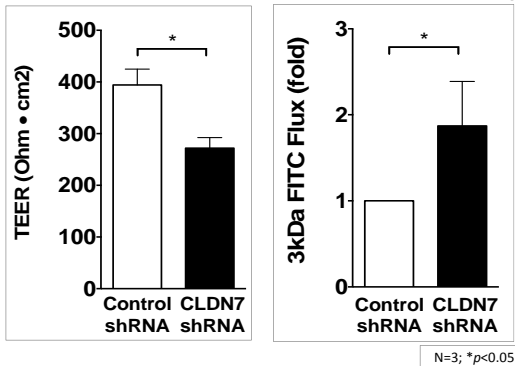


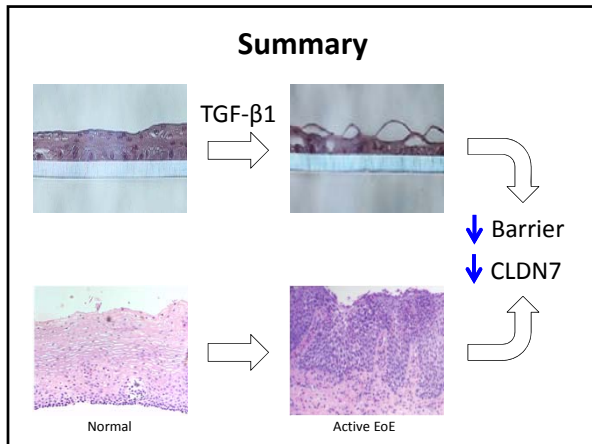
Independent of TGF- β 1,
can attenuated CLDN7 expression be
sufficient to decrease barrier function
in esophageal epithelial cells?

Generation of CLDN7 Knock-down Cells



CLDN7 KD: Decreased Barrier & Increased Paracellular Permeability





Conclusion

TGF-β1 participates in esophageal epithelial barrier dysfunction

Clinical Relevance

The findings of these studies implicate the utility of TGF-β1 targeting therapies in preserving & / or restoring esophageal epithelial barrier function

Acknowledgements



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C. Green

Thank You!!!
