

# Targeting Glycolysis Reduces Inflammation in a Murine Model of Rheumatoid Arthritis and Crohn's Disease

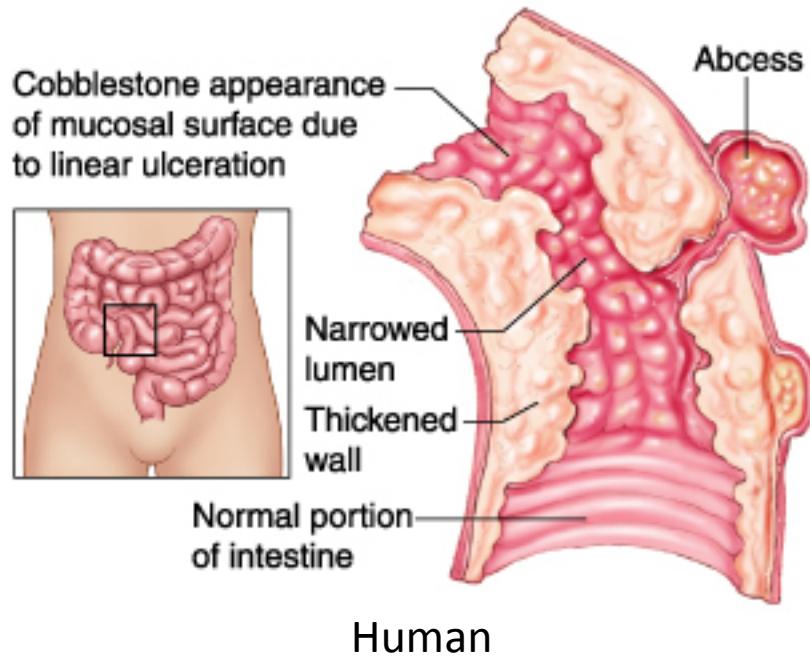
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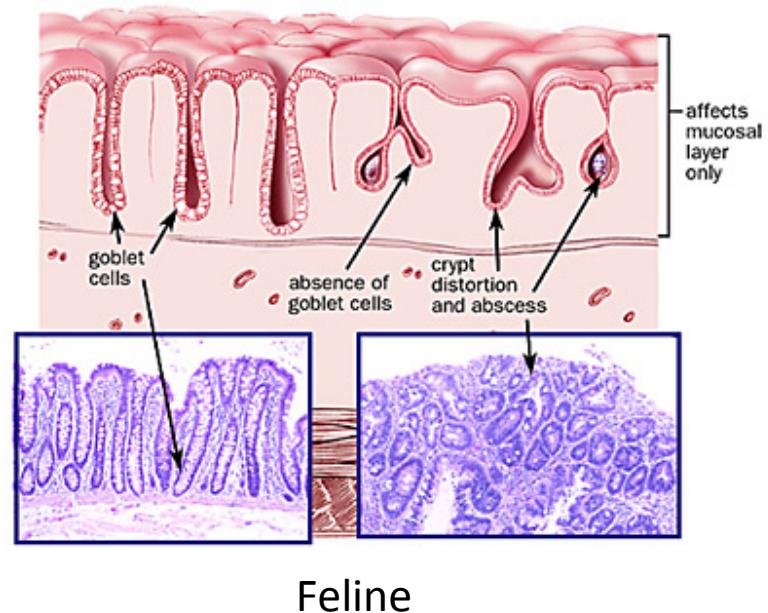


# Immune-Mediated Diseases

- Crohn's Disease – symptoms of abdominal pain, diarrhea and weight loss



## *Inflammatory Bowel disease(IBM)*



- Rheumatoid Arthritis– symptoms of painful joint swelling and deformity



Figure 1



Figure 2

Human

Immune mediated erosive polyarthritis



\*

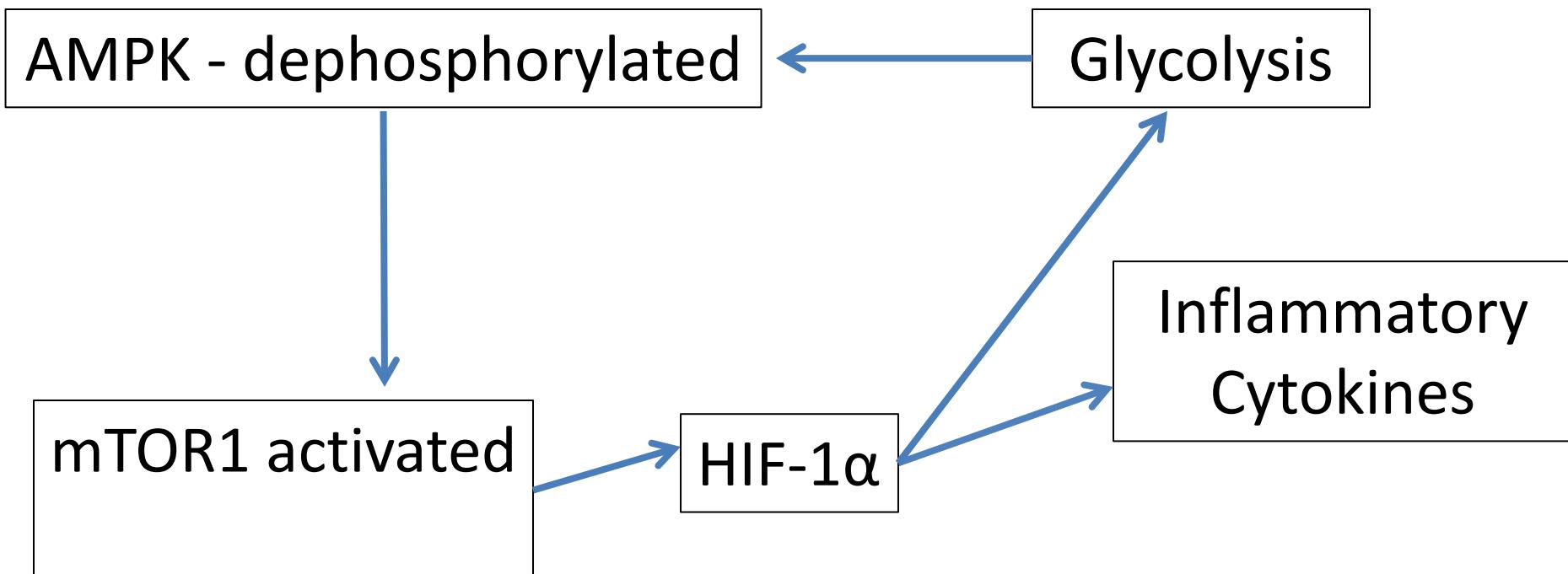


Canine

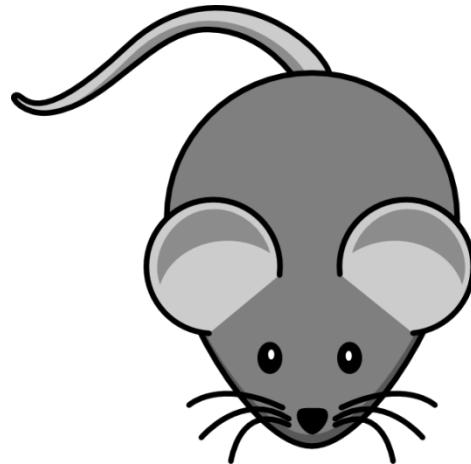
\* VET 403: "Imaging of Joint Disorders" Dr. Kathryn Phillips

# Warburg Effect

- Metabolic switch: Ox. Phos. → Glycolysis
- Glycolytic metabolism: possible targets within the pathway to reduce inflammation



# Methods



TNF $\Delta$ ARE

Rx with 3-  
bromopyruvate



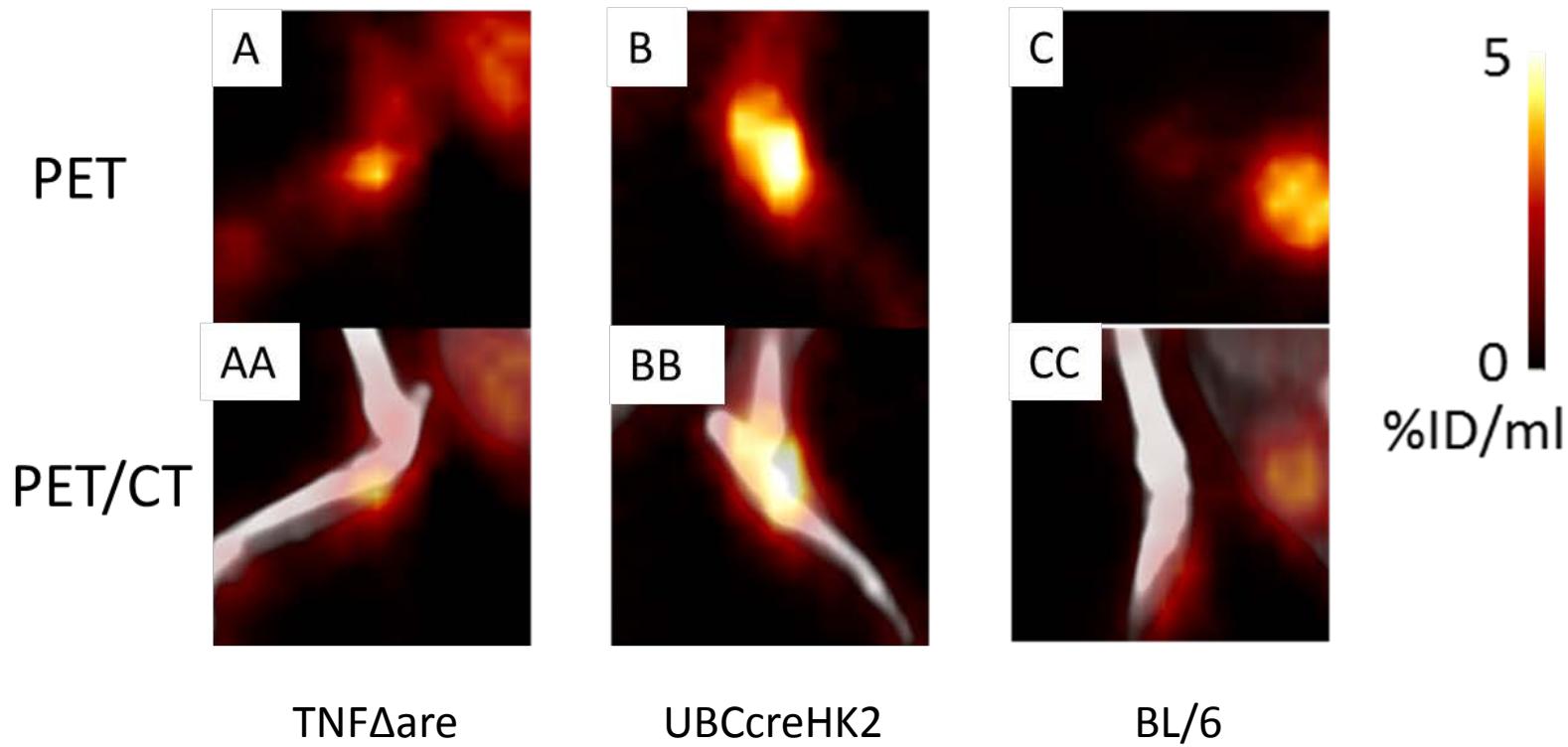
UBCcreHK2 $^{F/F}$

Rx with tamoxifen

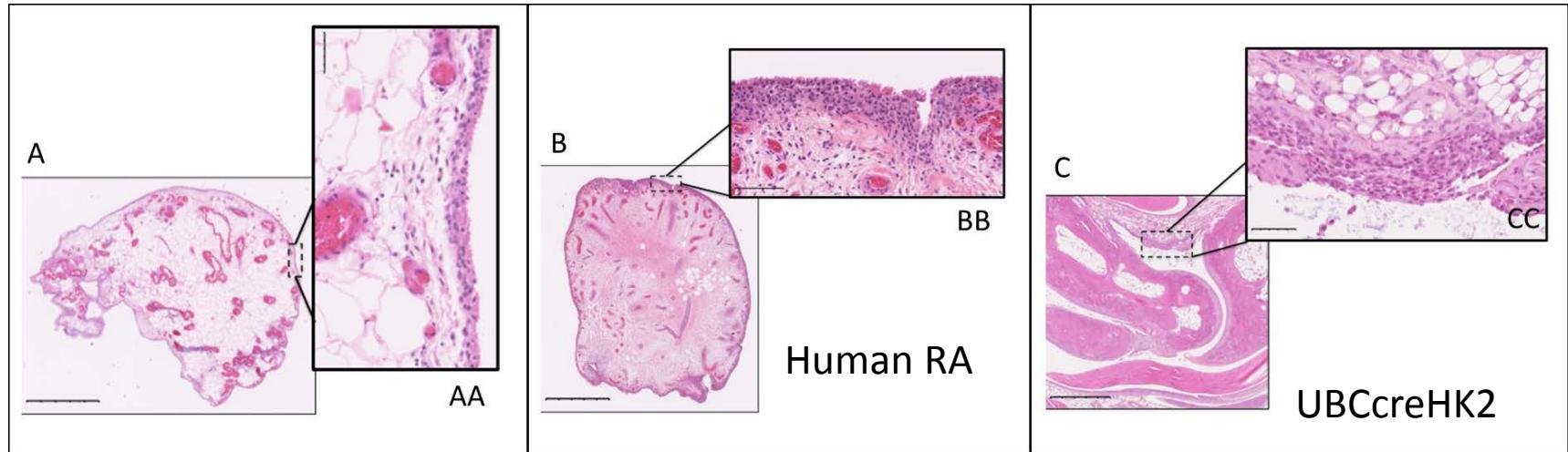
Rx with K/BxN  
serum

Evaluate by PET  
scan, histology,  
RT PCR

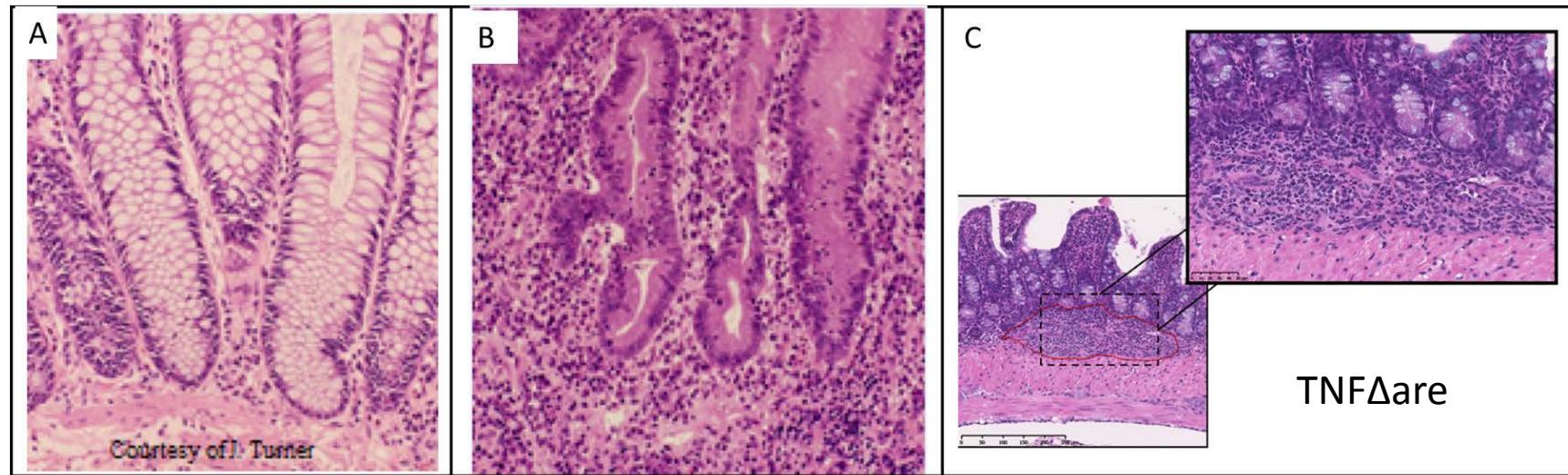
# PET/CT with $^{18}\text{F}$ -FDG



# Comparison of Human and Murine Tissues



Normal Human

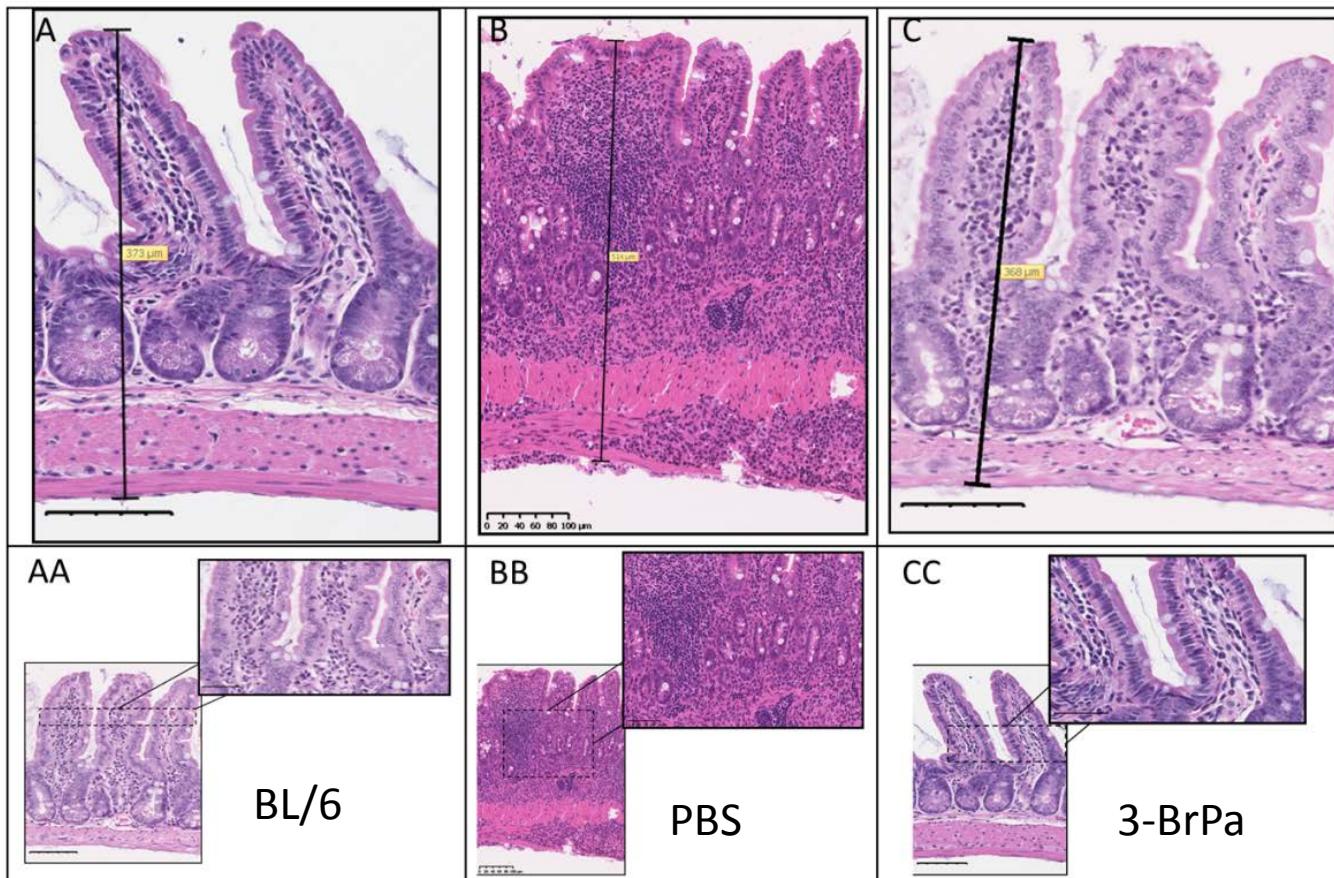


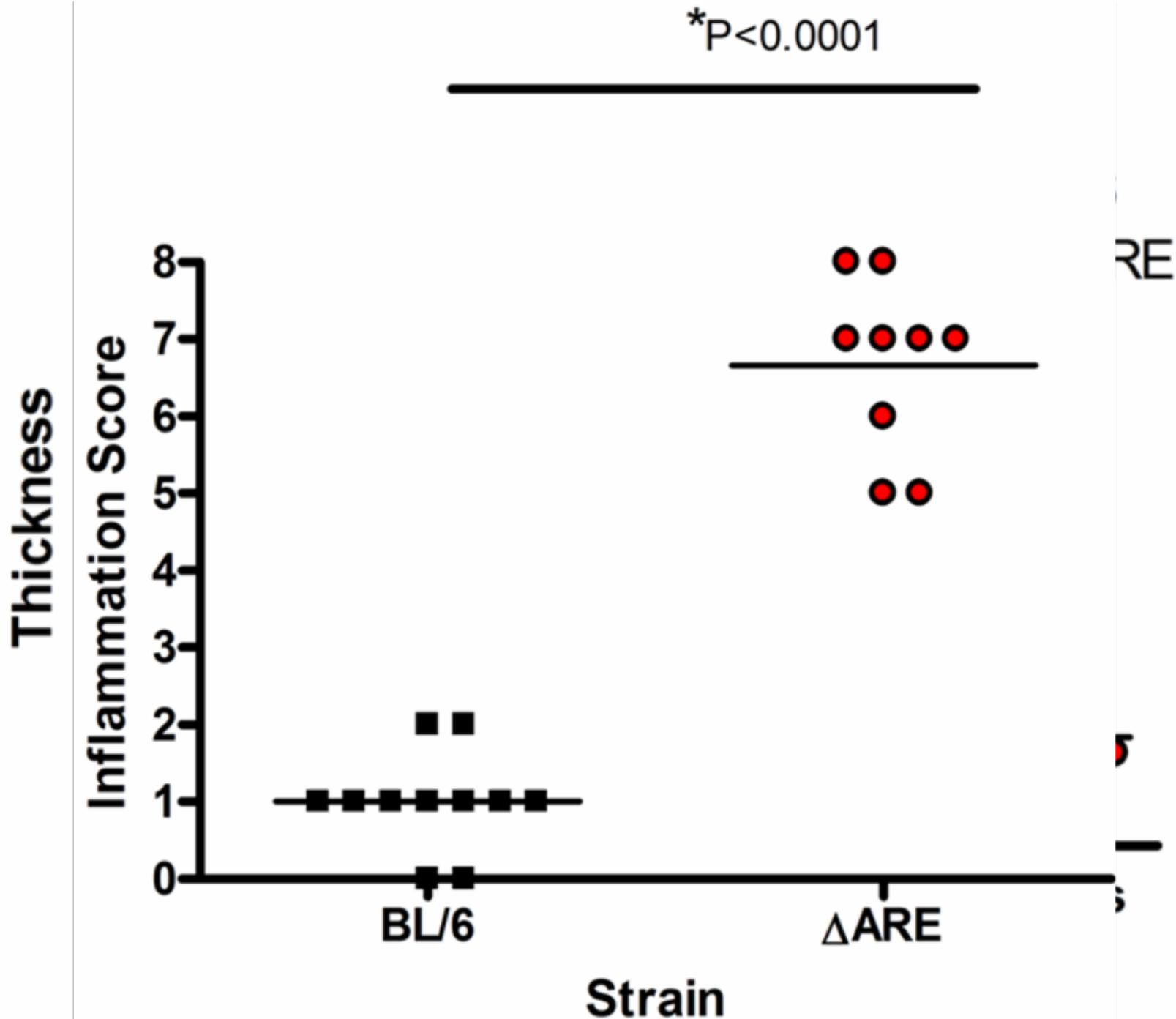
Normal Human

Ulcerative Colitis

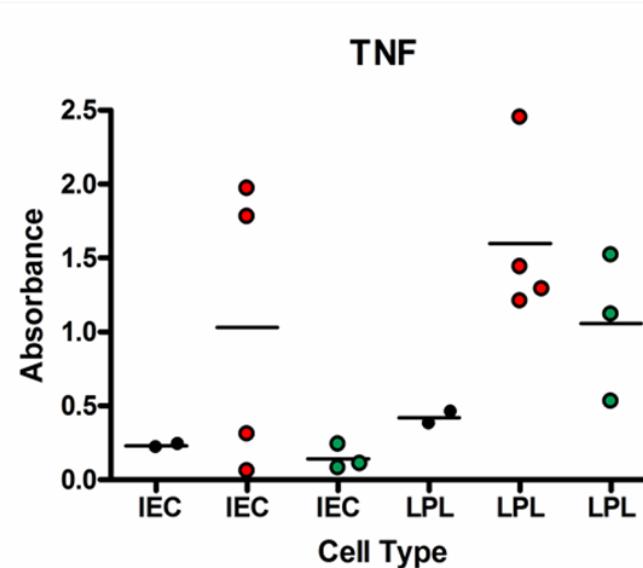
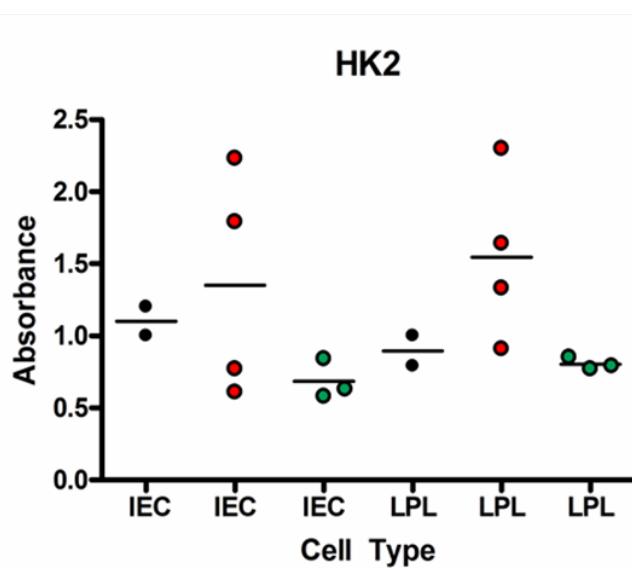
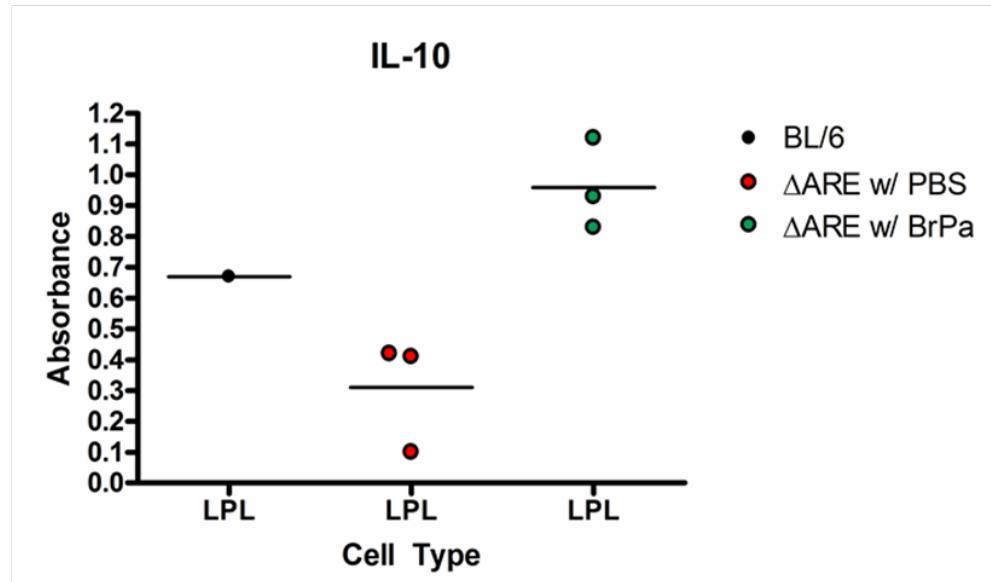
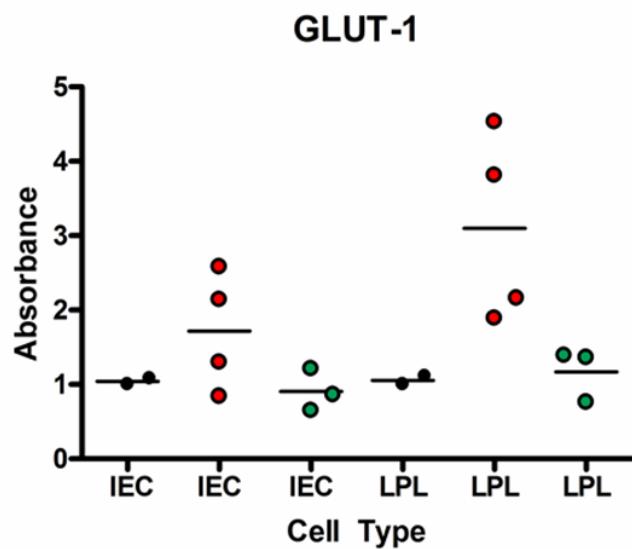
TNF $\Delta$ are

Ileum Histology Scoring Criteria				
Score	0	1	2	3
<b>Tissue Full Thickness</b>	< 450 $\mu$ m	>450 $\mu$ m	>600 $\mu$ m	>800 $\mu$ m
<b>Acute Inflammation (PMN)</b>	Normal	Focal	Multiple focal	Diffuse aggregate or crypt abscesses
<b>Chronic Inflammation (MN)</b>	Normal	Focal	Aggregate	Diffuse aggregate
<b>Other Inflammation</b>	Normal	Loss of goblet cells; bulging villi	N/A	N/A





# RT-PCR



# Conclusions

- Both murine models showed similar cellularity and inflammatory changes to the diseases they are meant to represent
- Glycolysis is increased under inflammatory conditions and inhibition of components of the pathway such as HK2 could be effective treatment strategies

# Acknowledgements

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- UCD SVM STAR Program

