

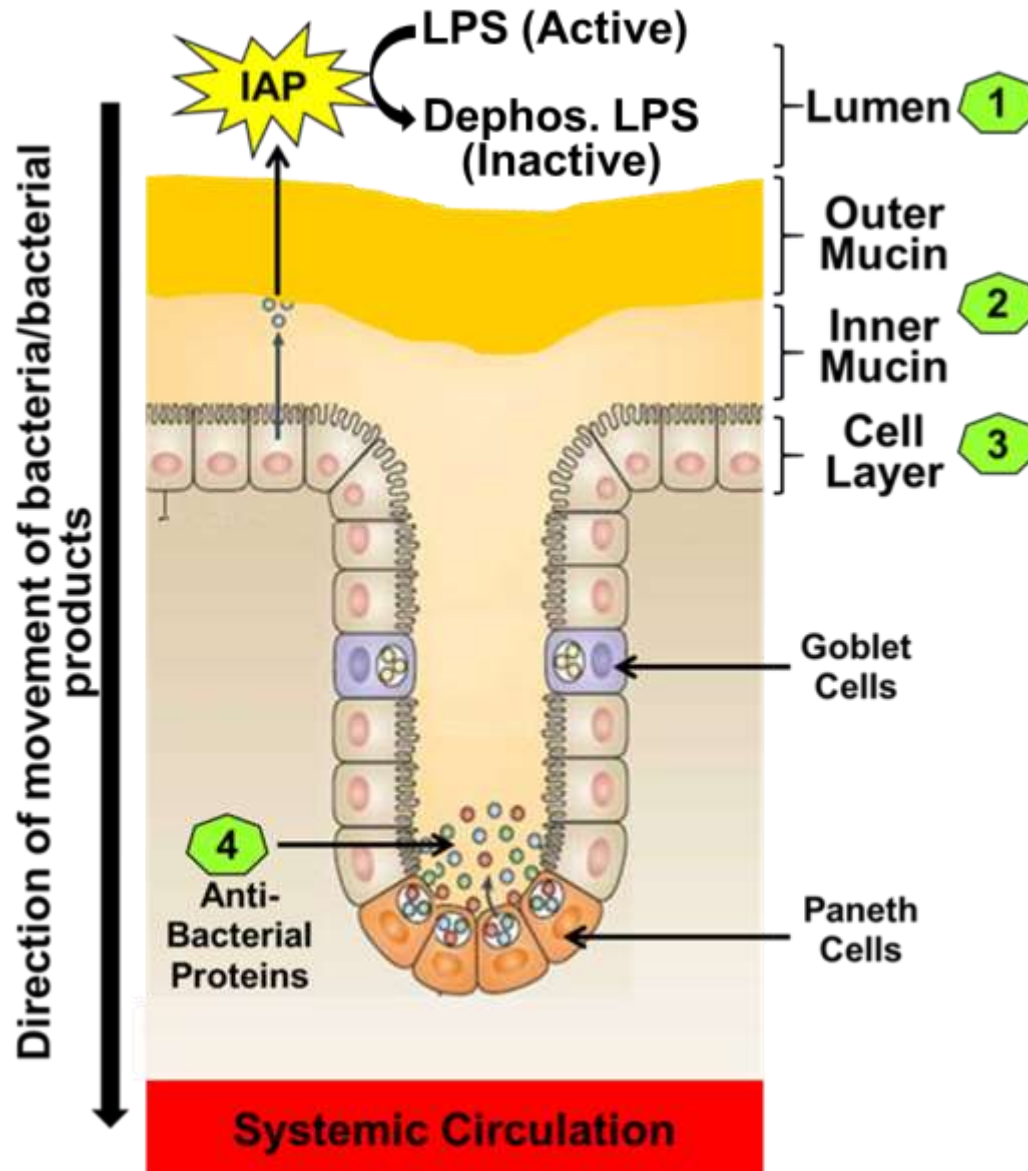
# Turmeric/Curcumin: Working to strengthen the “Barrier” to disease development

**Shobha Ghosh, PhD, FAHA**

Department of Internal Medicine, VCU Medical Center  
Hunter McGuire VA Medical Center, Richmond, VA



# Gut Barrier: Our body's "ADT" Sign (Prevents invasion of unwanted things)



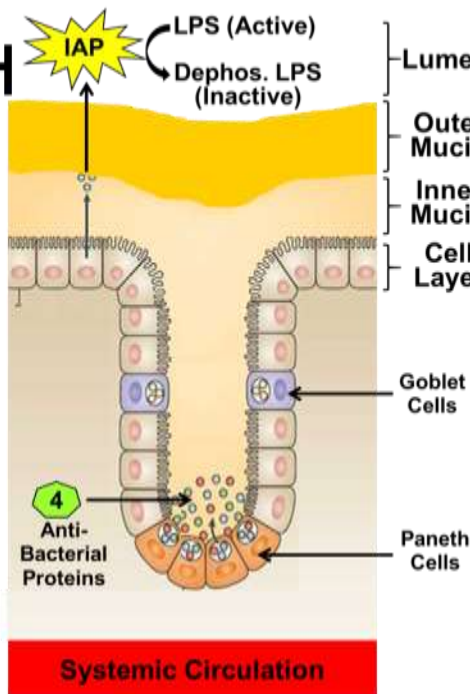
# How Western Diet (WD) causes all the diseases by affecting the gut barrier function



**WD**

**WD decreases IAP  
but  
Curcumin  
increases IAP!!!**

**↓ Activity**



**Disrupts**



**WD**

**WD is high in  
Fat and  
Cholesterol  
but low in  
fiber**

**↑ MΦs  
↑ Inflammation  
↑ Permeability**

**↑ LPS**

**↑ MΦ infiltration  
into adipose  
tissue**

**↑ MΦ Activation**

**↑ MΦ infiltration  
into artery wall**

**↑ T2DM**

**↑ Atherosclerosis**

# Oral supplementation with curcumin reduces diabetes and Heart Disease

LDLR<sup>-/-</sup> Mice



Fed a High Fat High Cholesterol (WD) for 16 weeks

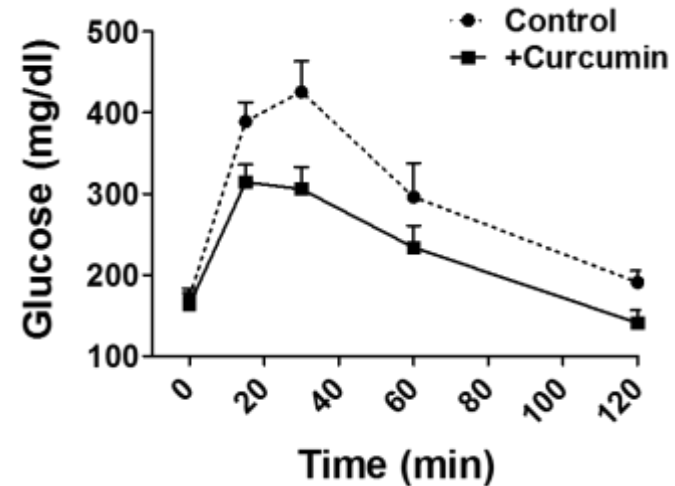
Glucose Tolerance Tests  
(Test for Diabetes)



Mice  
Sacrificed

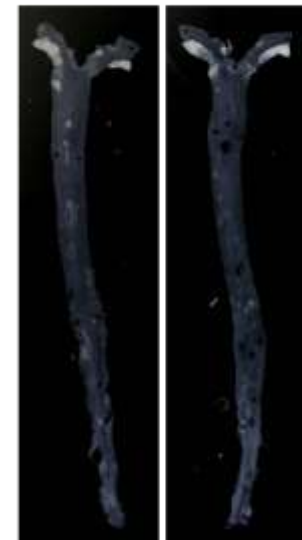
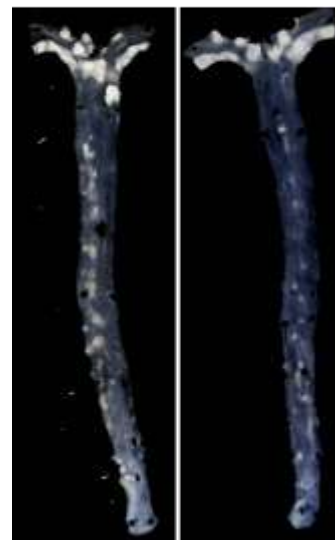


Dissect aorta and prepare for  
en face analyses  
(Test for Heart Disease)



No Curcumin

+ Curcumin

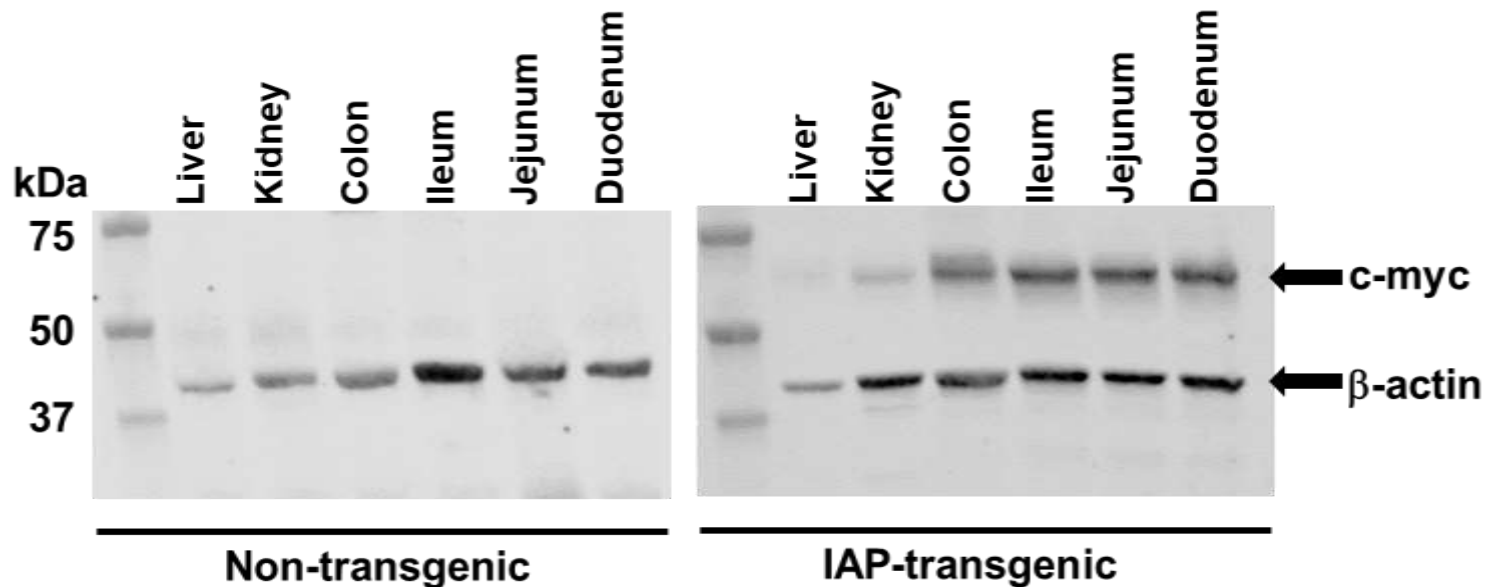


[Ghosh et al PLoS One 9:e108577 \(2014\).](https://doi.org/10.1371/journal.pone.0108577)

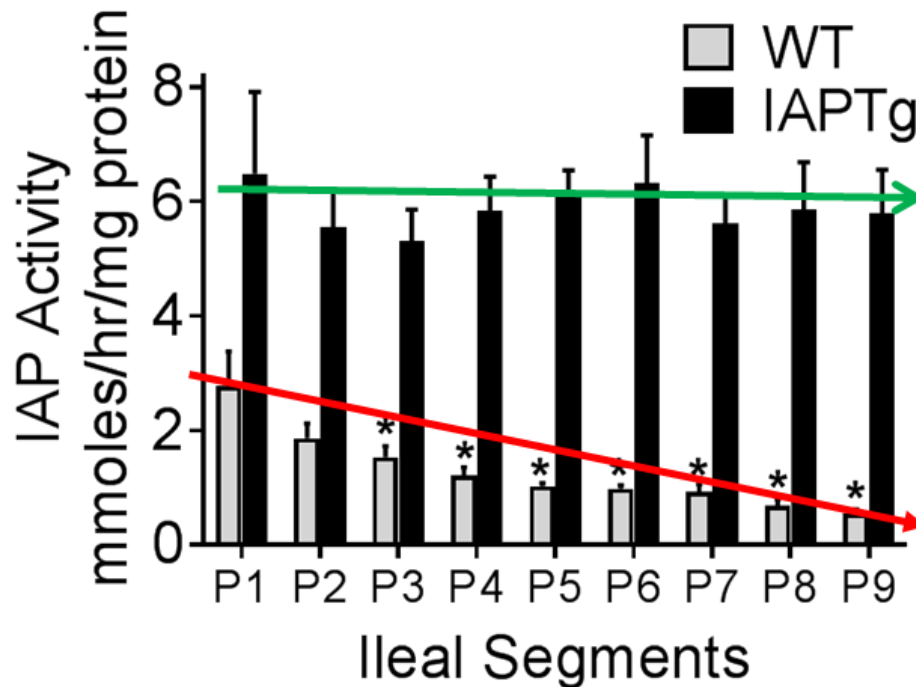
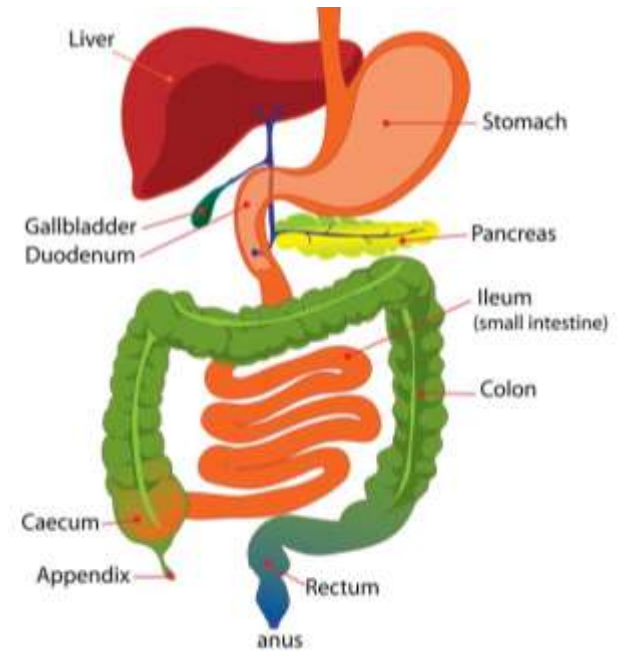
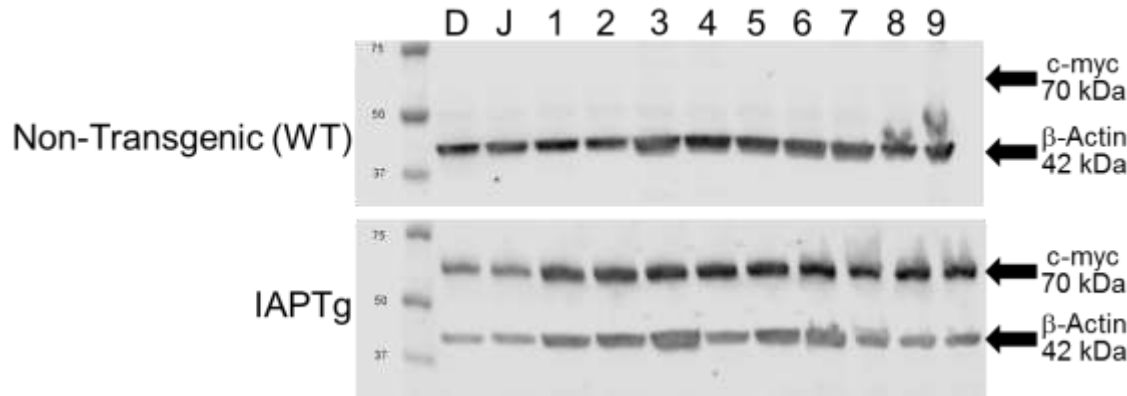
To bring this discovery to the clinic or for human use, we need to establish the underlying mechanism

## Development of IAP Transgenic mice

- Since curcumin increases IAP, we focused on this
- Human chimeric IAP gene – contains the catalytic domain of human placental IAP
- Introduced into mice such that it is expressed only in the intestine
- Question asked – can increasing IAP (that is increased by curcumin) alone can prevent disease development by protecting the barrier?

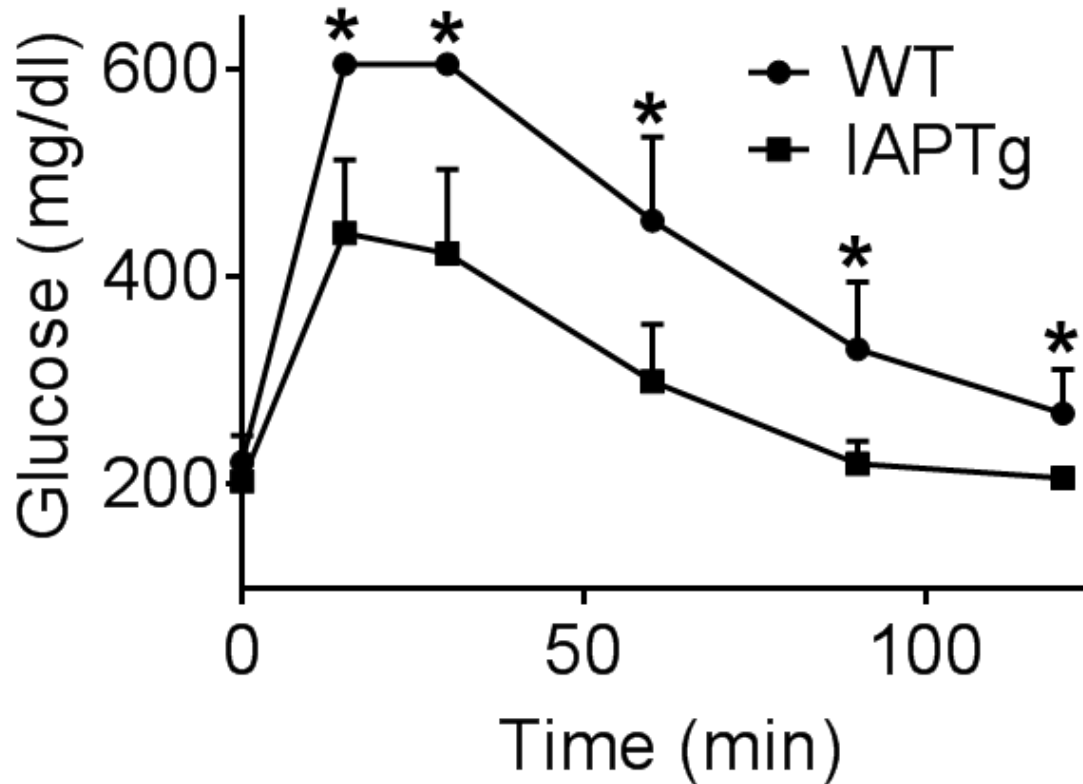


# IAP is uniformly expressed in IAP Transgenic mice



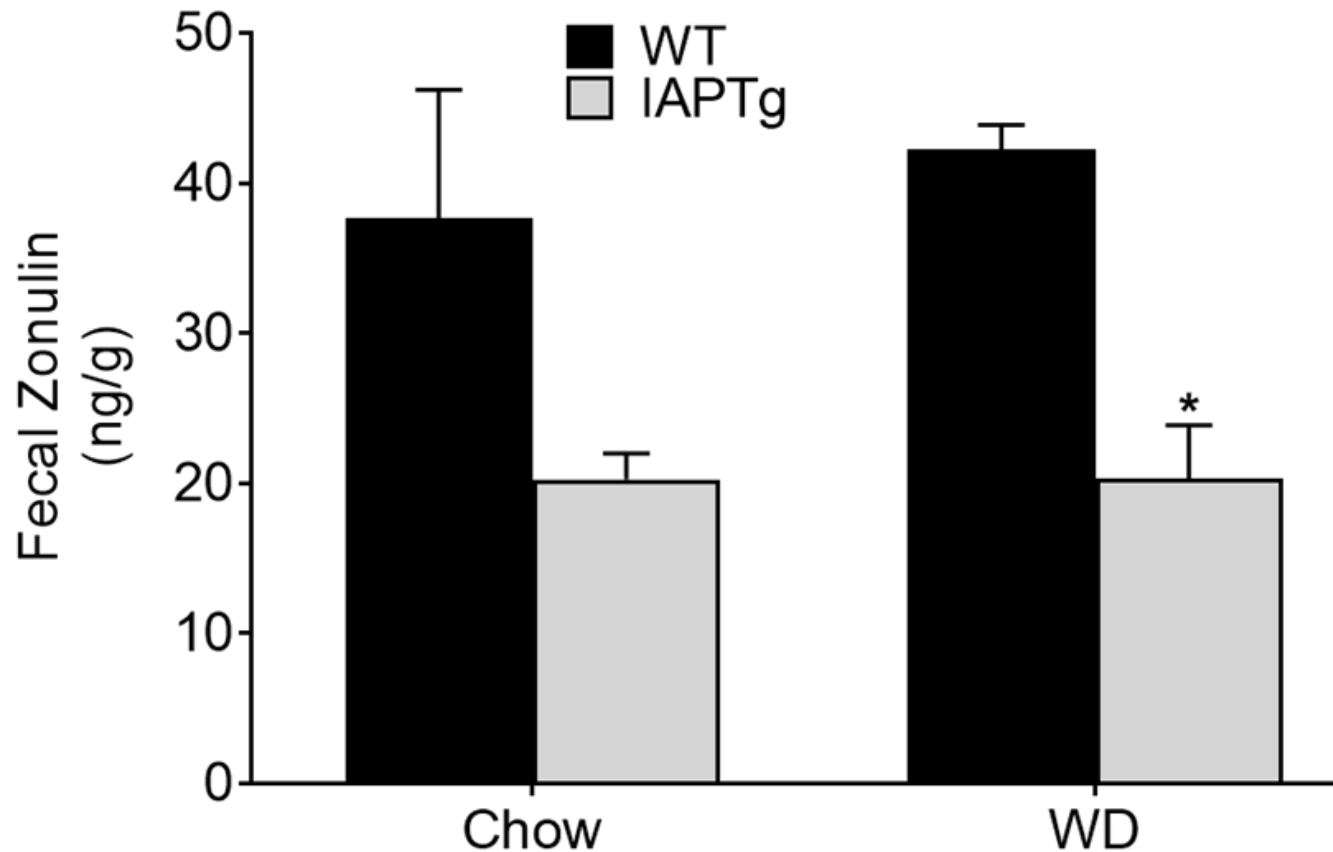
**Bacterial Load**  
 Duodenum ( $10^3$ /ml)  
 ↓  
 Colon (large intestine) ( $10^{11}$ /ml)

# Increased expression of IAP alone reduces diabetes





## Increased expression of IAP alone improves intestinal barrier function



(Fecal zonulin is clinically used to test for defects in gut barrier function)

Studies are in progress to determine the effects of increased IAP on heart disease

# Some important/beneficial aspects of IAP

## Animal Studies:

- Improves colitis, diabetes, chronic inflammation

## Human Studies:

- Intra-duodenal administration of IAP improves ulcerative colitis
- Pre-term babies have low IAP and are prone to Necrotizing enterocolitis
- Reduced fecal IAP activity associated with gut barrier dysfunction

While we can develop IAP tablets that can tolerate stomach acid, oral curcumin can easily have the same effect of increasing IAP in the intestine!!!

Studies in progress will establish how curcumin increases IAP production and these studies will help promote the use of curcumin for therapeutic purposes

(Since it is not effectively absorbed, its beneficial effects are always questioned)

Thank you for your attention

**Any Questions???**