



# Functional Bowel Disorders

Some Lessons from Sexual Medicine

Arun Chaudhury

GIM Foundation, Little Rock, USA

*Thank you Dean (Prof.) Bhattacharyya & Mr. Chatterjee*

*Shri Ramakrishna Institute of Medical Sciences (SRIMS)*

*Sanaka Educational Trust*

*Malandighi, Durgapur, India*

# Disclaimer

- No Conflict of interest
- No funding with vested interest

# What are functional bowel disorders

## Commonest gastrointestinal problems

Affects people worldwide across all cultures

Chronic timeline

Rome IV

Gwee et al. Second Asian Consensus on Irritable Bowel Syndrome. [J Neurogastroenterol Motil.](#) 2019 Jul 1;25(3):343-362.

*Douglas Drossman*

*Robert Spiller*

*Satish SC Rao*

*Many other authors*

## Cardinal symptoms

Upper & Lower GI specific symptoms

Vomiting/Nausea

Constipation/Diarrhea

Bloating

Pain

# Semantic Classification

- Irritable Bowel Syndrome
  - Constipation (IBS-C)
  - Diarrhea (IBS-D)
  - ALTERNATING (mixed) (IBS-M)

Symptoms occurring for last 6 months, at least 3 days/week, variable complaint of abdominal pain, with alteration of bowel habits and form/appearance of stool

- Functional constipation
- Functional diarrhea
- Functional dyspepsia
- OVERLAP symptoms (upper GI, cholestasis)
- Rumination syndrome
- Narcotic bowel syndrome

# Obtain detailed **HISTORY**

- Establish empathetic doctor patient relationship
- Nonjudgmental, unrushed environment of discussion
- **LISTEN**
- Description of symptoms
- Duration of symptoms (sudden arising of symptoms like an abdominal lump should raise suspicion for Crohn's disease; High suspicion for colon cancers if age >50 years)
- Medical conditions (Hypothyroidism, Scleroderma, Liver diseases, Pancreatic diseases)
- Past surgical conditions (Lithogenic bile, cholecystectomy, CBD exploration)
- Cancer chemotherapy
- Drug history (Prescription drugs: long term use of CCBs can cause diverticulosis; *Circulation, 2019;*)
- Drugs of abuse like opioids, alcohol, cannabis, tobacco in all forms)
- Drug or food allergy

# Obtain **DIETARY** history

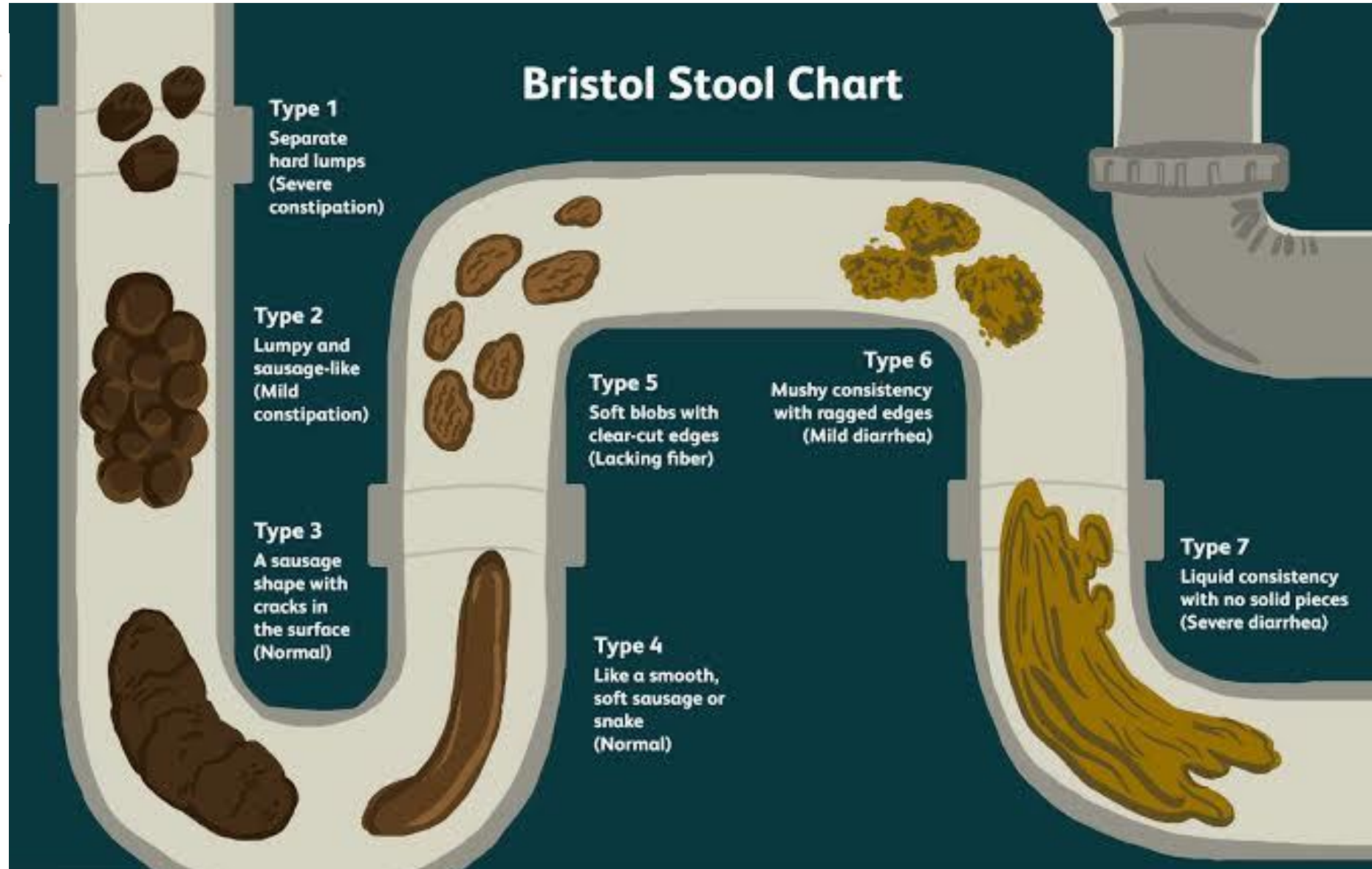
- Eating pace
- Time of meals
- Aerophagia
- Drinking water during meals
- Lying down after meals
- Cold vs warm water
- Chemical composition of food)

# Obtain **RESTROOM** history

- Patient's attribution to excessive gassiness can actually be normal passage of gas
- Squatting vs. commode
- Floating stools
- Impaction of soft stools



# Bristol Stool Scale



# History of stress

*Gas gives me tension, tension gives me gas*

*I am passing “buckets” of gas*

*---Chaudhury, personal case series, 2019*

- Personal life stress (Bereavement, divorce, work life balance, physician burnout, excessive travel)
- Very carefully, obtain MENTAL HEALTH history, including generalized anxiety, depression, bulimia/anorexia, strange eating practices (pica, etc), panic disorder, post-traumatic stress, dysfunctional coping, sleep disturbances, sexual abuse, childhood abuse

# Review of Systems (ROS)

- ROS may not reveal any abdominal findings but be alert about other body systems – may reflect nutritional deficiencies
- Perform routine physical examination (For example, look out for anemia, skin symptoms in celiac disease)

# Preliminary Investigations

## Keep to a minimum

CBC

TSH

Fasting Blood Glucose

Stool electrolyte

Erythrocyte sedimentation rate

C-reactive protein

fecal lactoferrin

fecal calprotectin

- serologic tests for celiac disease: IgA tissue transglutaminase
- tests for bile acid diarrhea
- <sup>75</sup>selenium homotaurocholic acid test
- serum fibroblast growth factor 19 & 7 $\alpha$ -hydroxy-4-cholesten-3-one
- tests for Giardia infection, *H. pylori*

# Management Strategies

- Drug therapies
- Dietary therapies: Water, knowledge of food chemistry, PORTION SIZE during meals, teeth brushing, microbiome acclimatization?
- Assess for nutritional deficiencies
- Behavioural therapy ("biofeedback"); Hypnotherapy; Mindfulness
- Psychological therapies

# Drug Therapies

*GO SLOW*

## For Diarrhea

- Loperamide (mu opioid agonist)
- Eluxadoline

## For Constipation

- Fibers (psyllium, isabgol): advocate natural fibers in diet
- Lactulose
- Senna
- Lubiprostone
- Naloxegol

## For Flatulence

- Lovastatin lactone
- BEANO

## For Pain

- Low-dose psychogenic medications (TCA, etc)
- Well-informed on pharmacology

## For Dysbiosis

- Antibiotics (rifaximin )

## For Upper GI symptoms (GERD, NERD, biliary reflux)

- PPIs

Pair drugs with symptoms: for example, be cautious in prescribing for IBS alternating phenotype

Szigethy et al  
2018

# Personalize the prescription

- Flatulence after high-carbohydrate, high-lipid meals: use pancreatic enzymes

# Dietary therapies

- Identify and avoid offending food, with attention to potential nutritional issues
- Careful with sodas
- FIBERS: OKRA & PRUNE
- Phytochemicals (ginger, shogaol)
- Advocate eating rinds of vegetables (cucumber, kheera, water-melon; rind rich source of L-citrulline)  
(Chaudhury, patent protected, 2019)
- Cultural issues with fibers
- Identify non-offending FODMAP components: discuss that some gassiness is normal physiology
- Prebiotics (inulin, chicory, flaxseed) & Probiotics (Lactobacillus acidophilus; *may induce mu-opioid agonist on mucosa, Nat. Med*)





## **About beano®**

beano® products work to prevent gas naturally before it occurs. The natural enzymes found in beano® work to prevent gas by breaking down the complex carbohydrates found in many foods such as beans, vegetables and whole grains making eating the foods you love more enjoyable.



# FODMAP

## Fermentable

Process through which gut bacteria ferment undigested carbohydrate to produce gases.



## Oligosaccharides

Fructans & GOS - found in foods such as wheat, rye, onions, garlic and legumes/pulses.



## Disaccharides

Lactose - found in dairy products like milk, soft cheeses and yogurts.



## Monosaccharides

Fructose - found in honey, apples, high fructose corn syrups, etc.



And

## Polyols

Sorbitol and Mannitol - Found in some fruit and vegetables and used as artificial sweeteners.



Fodmap diet increase effluent of ileostomy

*Barrett JS, et al. Dietary poorly absorbed, short-chain carbohydrates increase delivery of water and fermentable substrates to the proximal colon. Aliment Pharmacol Ther. 2010 Apr; 31(8):874-82.*

Murray K. Differential effects of FODMAPs (fermentable oligo-, di-, mono-saccharides and polyols) on small and large intestinal contents in healthy subjects shown by MRI. *Am J Gastroenterol. 2014 Jan; 109(1):110-9.*



## HIGH FODMAP FOODS AND

## LOW FODMAP ALTERNATIVES

Vegetables	Artichoke, asparagus, cauliflower, garlic, green peas, mushrooms, onion, sugar snap peas	Aubergine/eggplant, bean(green), bok choy, capsicum (bell pepper), carrot, cucumber, lettuce, potato, tomato, zucchini
Fruits	Apples, apple juice, cherries, dried fruit, mango, nectarines, peaches, pears, plums, watermelon	Cantaloupe, grapes, kiwi fruit (green), mandarin, orange, pineapple, strawberries
Dairy and alternatives	Cow's milk, custard, evaporated milk, ice cream, soy milk (made from whole soybeans), sweetened condensed milk, yoghurt	Almond milk, brie/camembert cheese, feta cheese, hard cheeses, lactose-free milk, soy milk (made from soy protein)
Protein sources	Most legumes/pulses, some marinated meats/poultry/seafood, some processed meats	Eggs, firm tofu, plain cooked meats/poultry/seafood, tempeh
Breads and cereal products	Wheat/rye/barley based breads, breakfast cereals, biscuits and snack products	Corn flakes, oats, quinoa flakes, quinoa/rice/corn pasta, rice cakes (plain), sourdough spelt bread, wheat/rye/barley free breads
Sugars/sweeteners & confectionery	High fructose corn syrup, honey, sugar free confectionery	Dark chocolate, maple syrup, rice malt syrup, table sugar
Nuts and seeds	Cashews, pistachios	Macadamias, peanuts, pumpkin seeds, walnuts

Courtesy: Monash University

# FODMAP +BEANO = You may have these foods

## ***Food Groups***

### **Grains**

Bagels  
Barley  
Breakfast cereals  
Granola  
Oat bran  
Pasta  
Rice bran  
Rye  
Sorghum grain  
Wheat bran  
Whole wheat flour  
Whole grain breads

### **Vegetables**

Beets  
Broccoli  
Brussels sprouts  
Cabbage  
Cauliflower  
Corn  
Cucumbers  
Leeks  
Lettuce  
Onions  
Parsley  
Peppers, sweet

### **Beans**

Black-eyed peas  
Bog beans  
Broad beans  
Chickpeas  
Lentils  
Lima beans  
Mung beans  
Peanuts and peanut butter  
Pinto beans  
Red kidney beans  
Seed flour (sesame, sunflower)  
Soybeans and soy milk

# Histamine Containing Food

Sausage  
Dried Fish  
Preserved Fish (caviar)  
Seafood  
Hard and Soft Cheese  
  
Ketchup  
Tomato Juice  
Eggplant  
  
Vinegar and Alcohol



Nausea  
Vomiting  
Abdominal Pain  
Diarrhoea

Personalize  
prescription: Use  
H2-blockers

Why **FUNCTIONAL**?

# Seeking for TANGIBLE PATHOPHYSIOLOGY

- Visual pathology
- Biomarkers?
- Molecular Medicine

Challenges in obtaining full-thickness bx



## Gut & its challenges: Capturing the ethos for FBD/FGID

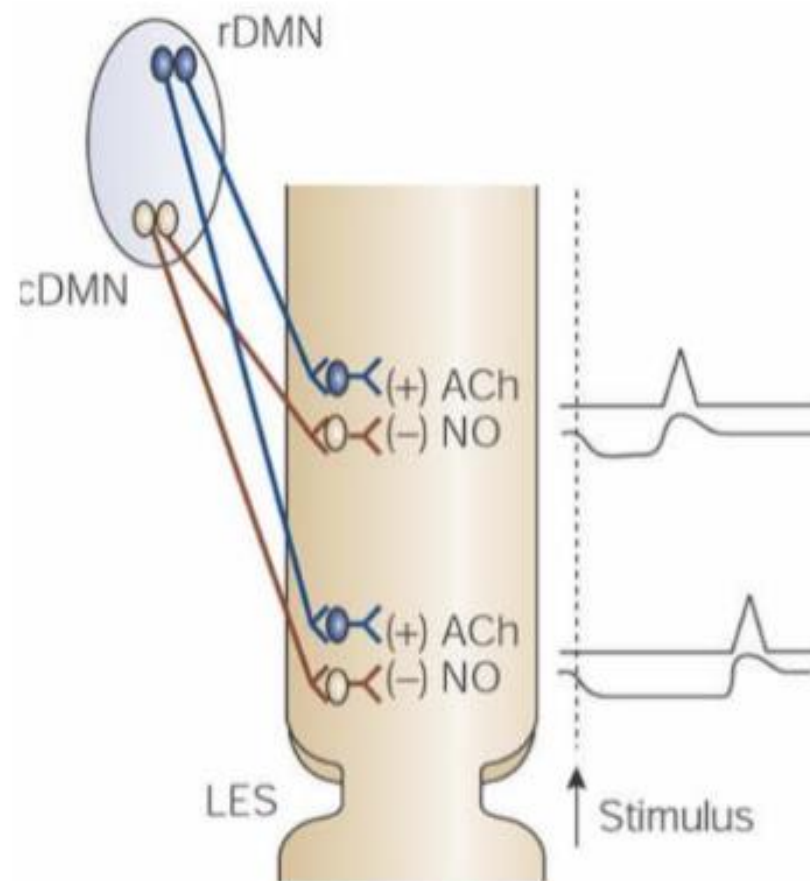


1. Vat
2. “Trapped” in the long tube: food & gas
3. Stochastic, difficult to assay chemical space



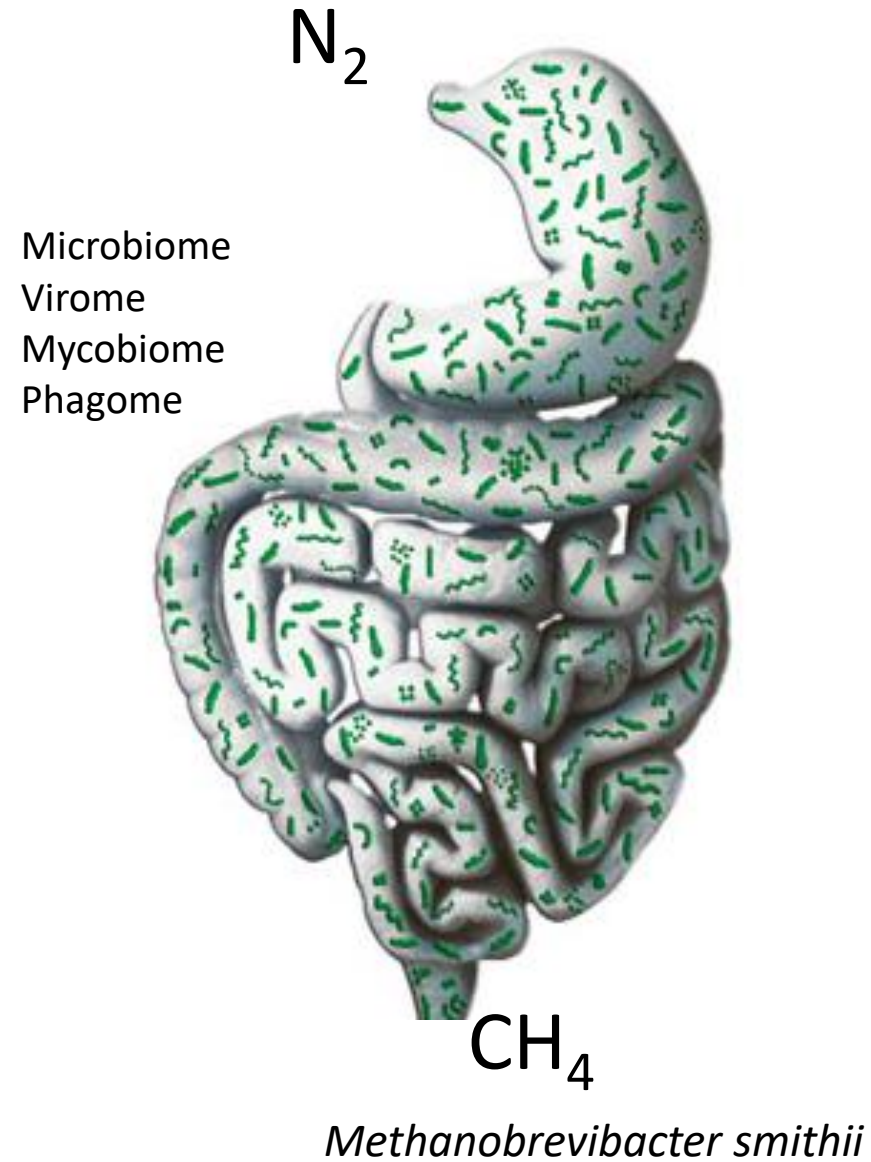
## Ascending Excitation, Descending Inhibition

Accommodation of bolus



Goyal and Chaudhury, 2008

# Can Pathophysiology of FBD discerned?



Complex Defects in motility

Stasis

Intraluminal  
secretion/swelling

Microbial fermentation

Stretch/Mechanical  
activation of wide  
dynamic range receptors  
(WDR)

**GAS**

**BLOATING**

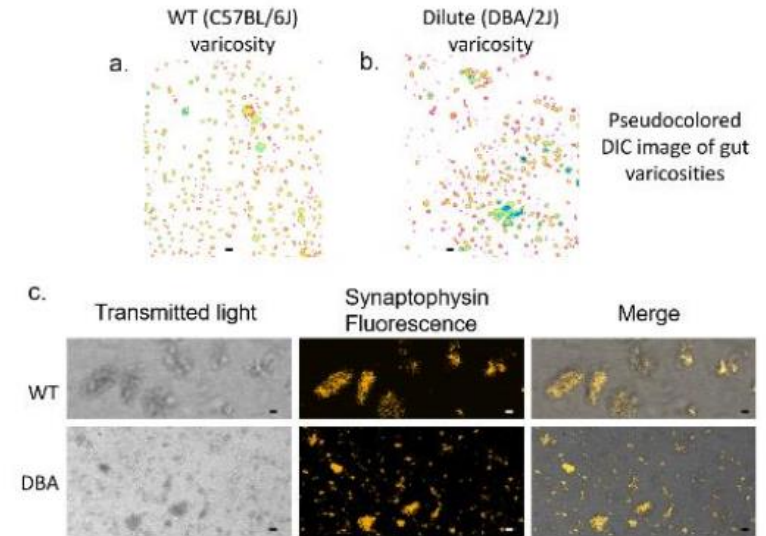
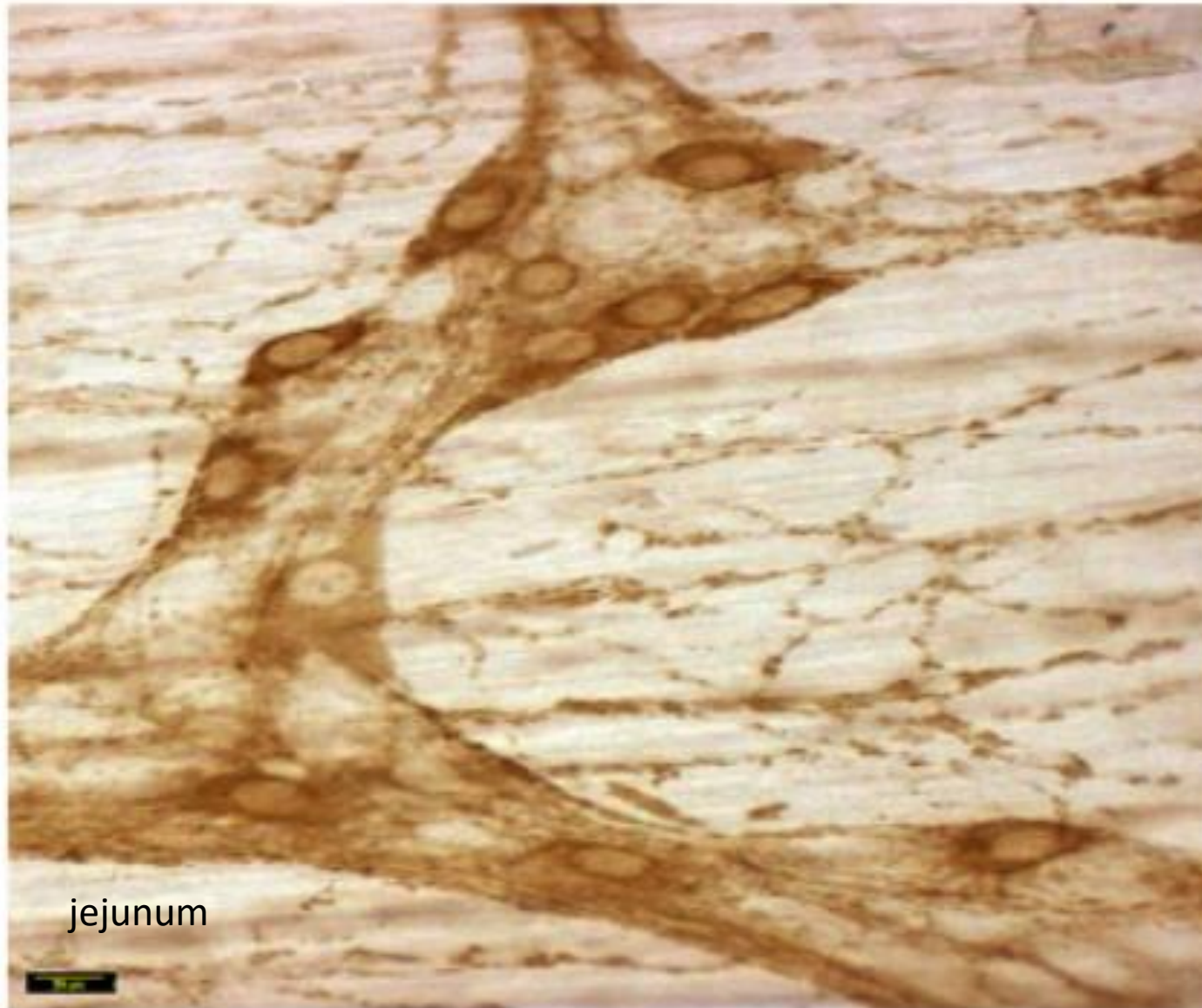
**DYSBIOSIS**

**PAIN**

Goyal & Chaudhury, Esophageal Pain, 2009

Chaudhury & Mashimo, Current Diagnosis  
and Treatment in Gastroenterology)

# The Main Actor: Nitroergic Neurons

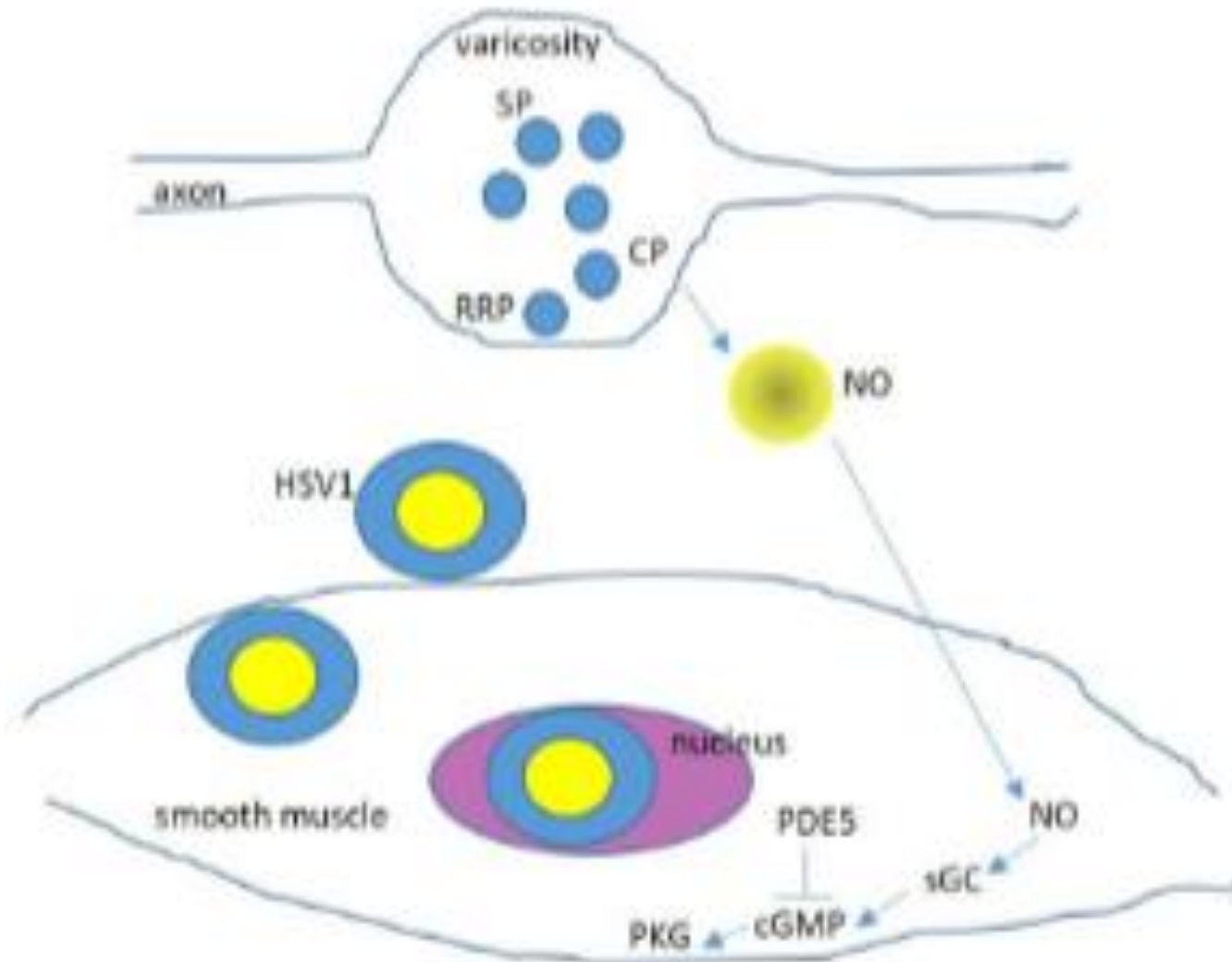


Chaudhury et al 2011, 2012

nNOS alpha

Chaudhury, Zanoni, et al. Frontiers in Medicine, 2014

# Nitergic neuromuscular junction



Pathology arising from multiple defects in junctional neuro-smooth muscle neurotransmission

Chaudhury et al, Frontiers in Pathology, 2018

Chaudhury, AJP Cell Physiology, 2016

Chaudhury, Nature, 2013

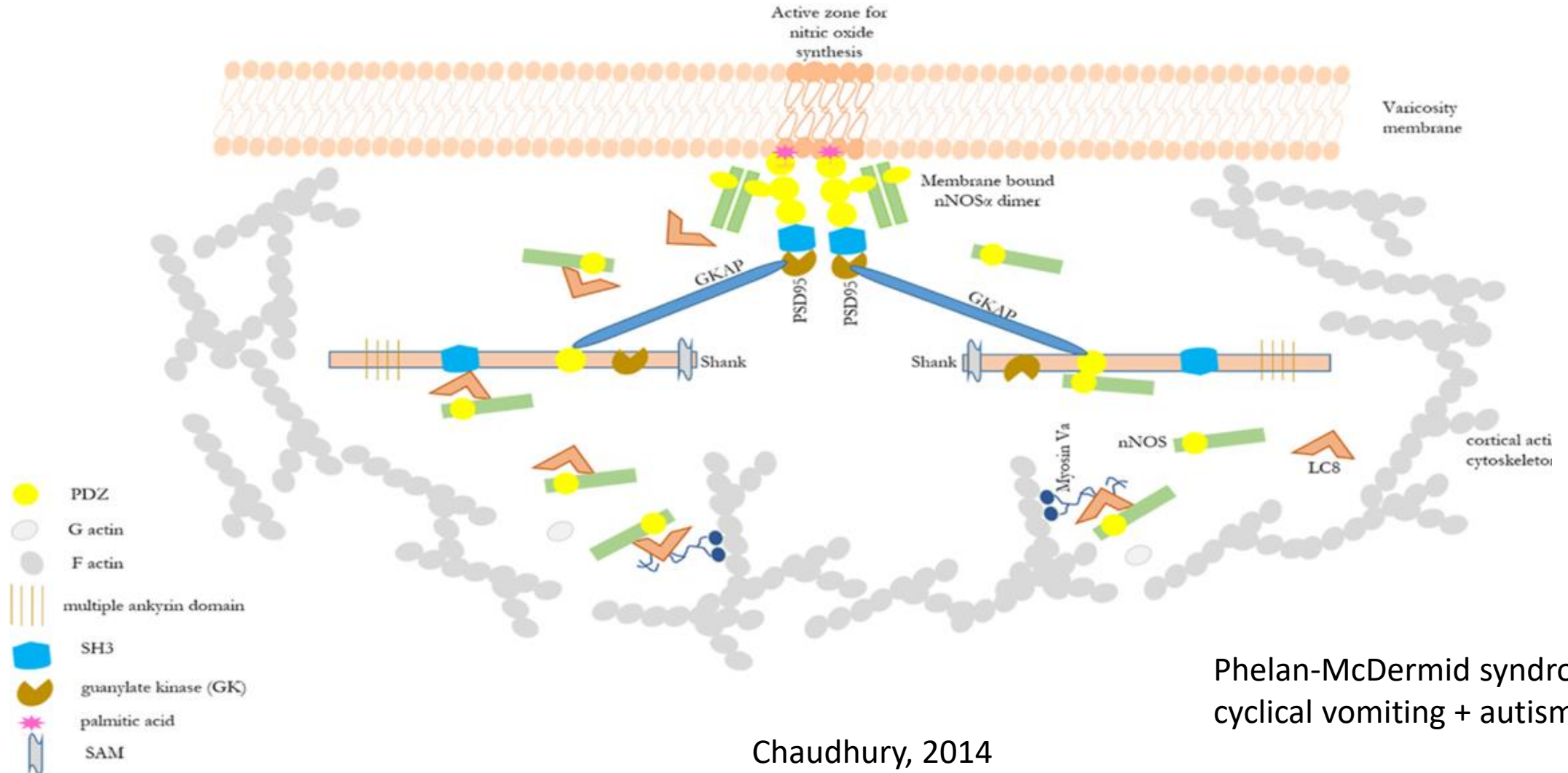
Chaudhury, Frontiers Med, 2014

Chaudhury, Gastroenterology, 2015, 2013

Chaudhury et al, Front Physiol 2016



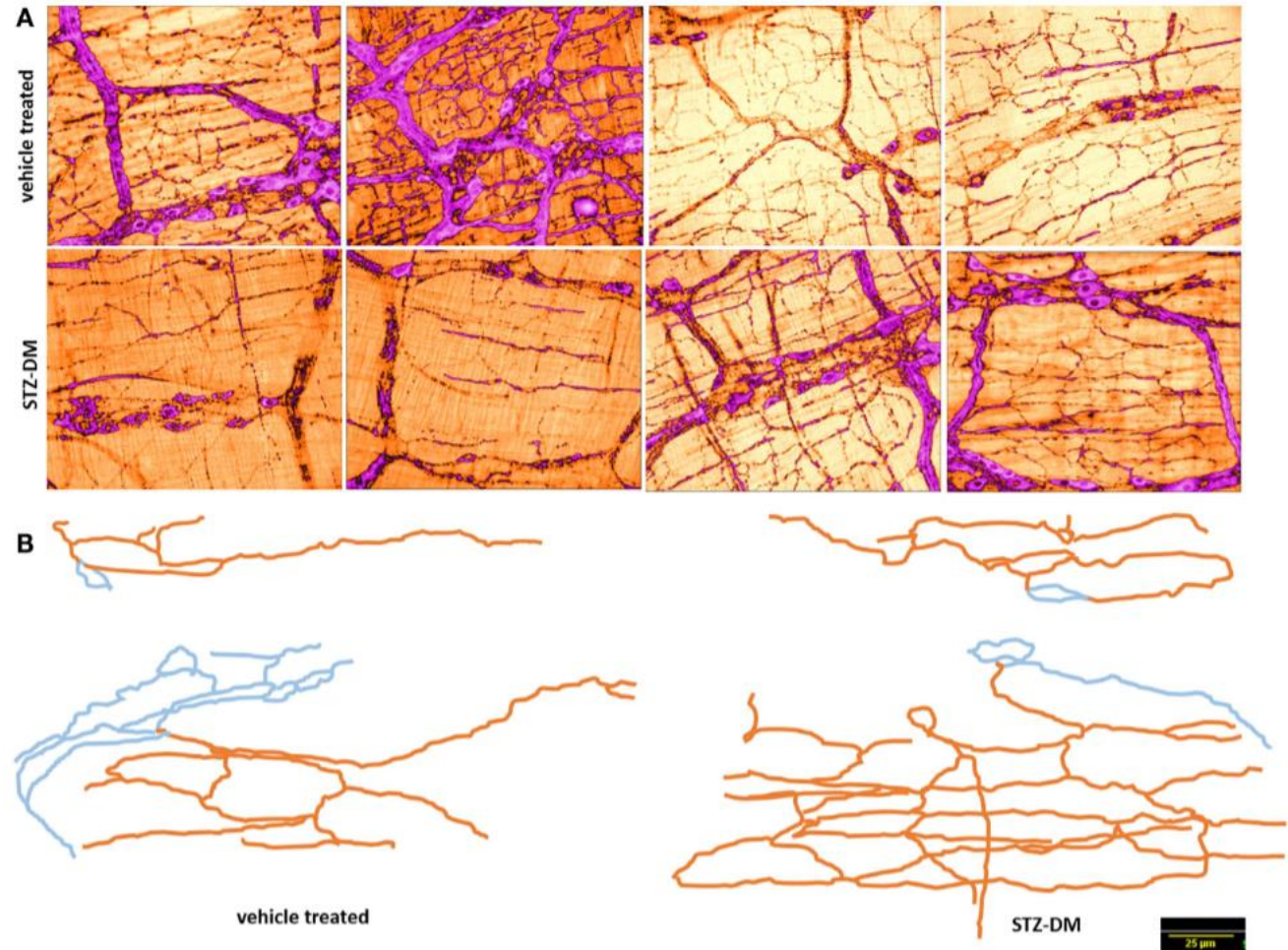
# Transit of nNOS in the nitrenergic nerve terminal may be very complicated



Phelan-McDermid syndrome:  
cyclical vomiting + autism

Chaudhury, 2014

# Nitrergic axons have normal ramification through muscle in diabetes

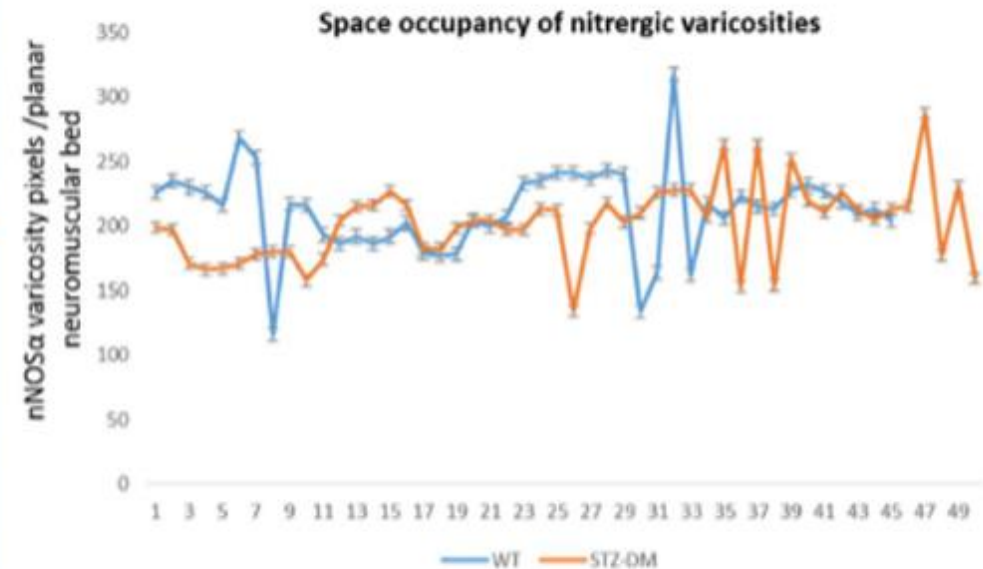
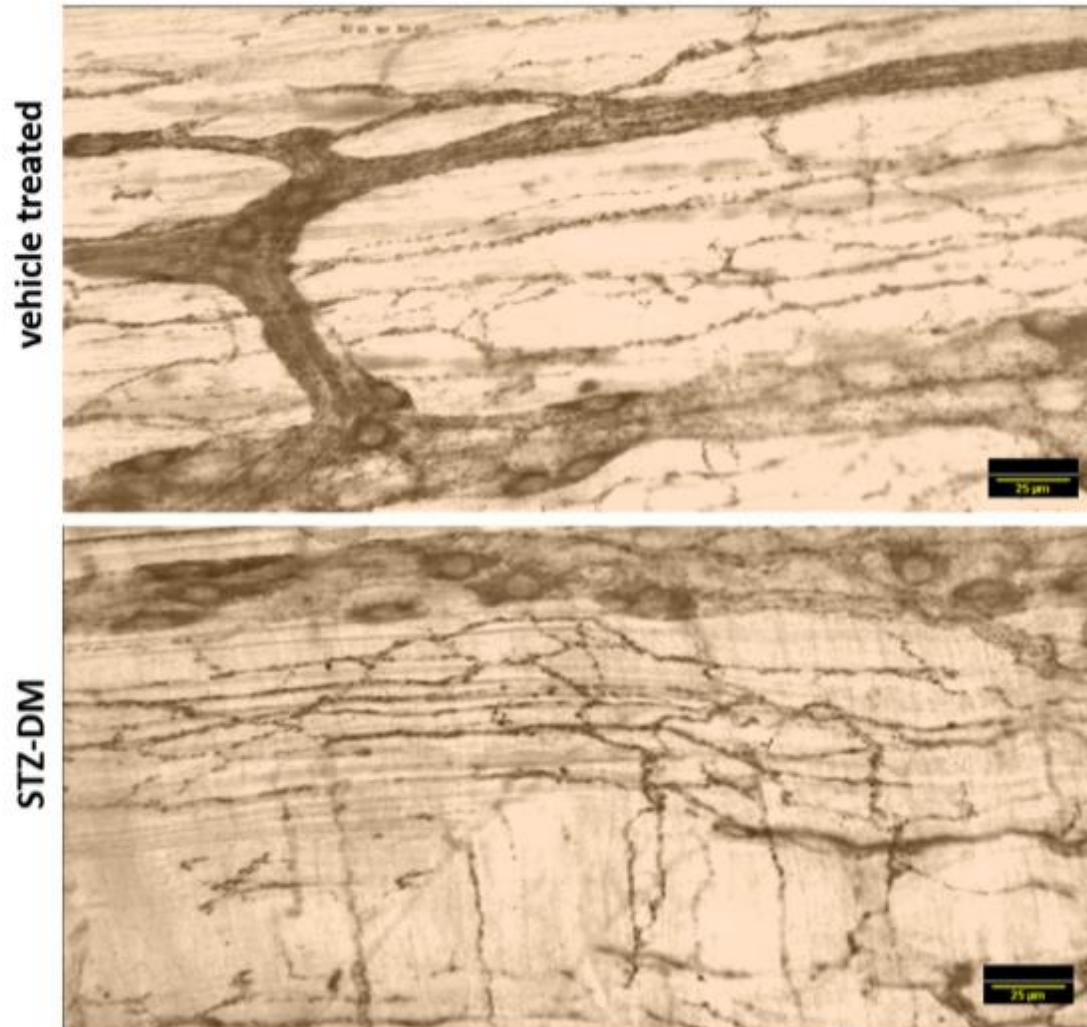


Chaudhury et al. Frontiers in Medicine, 2014

**Control**

**Diabetes**

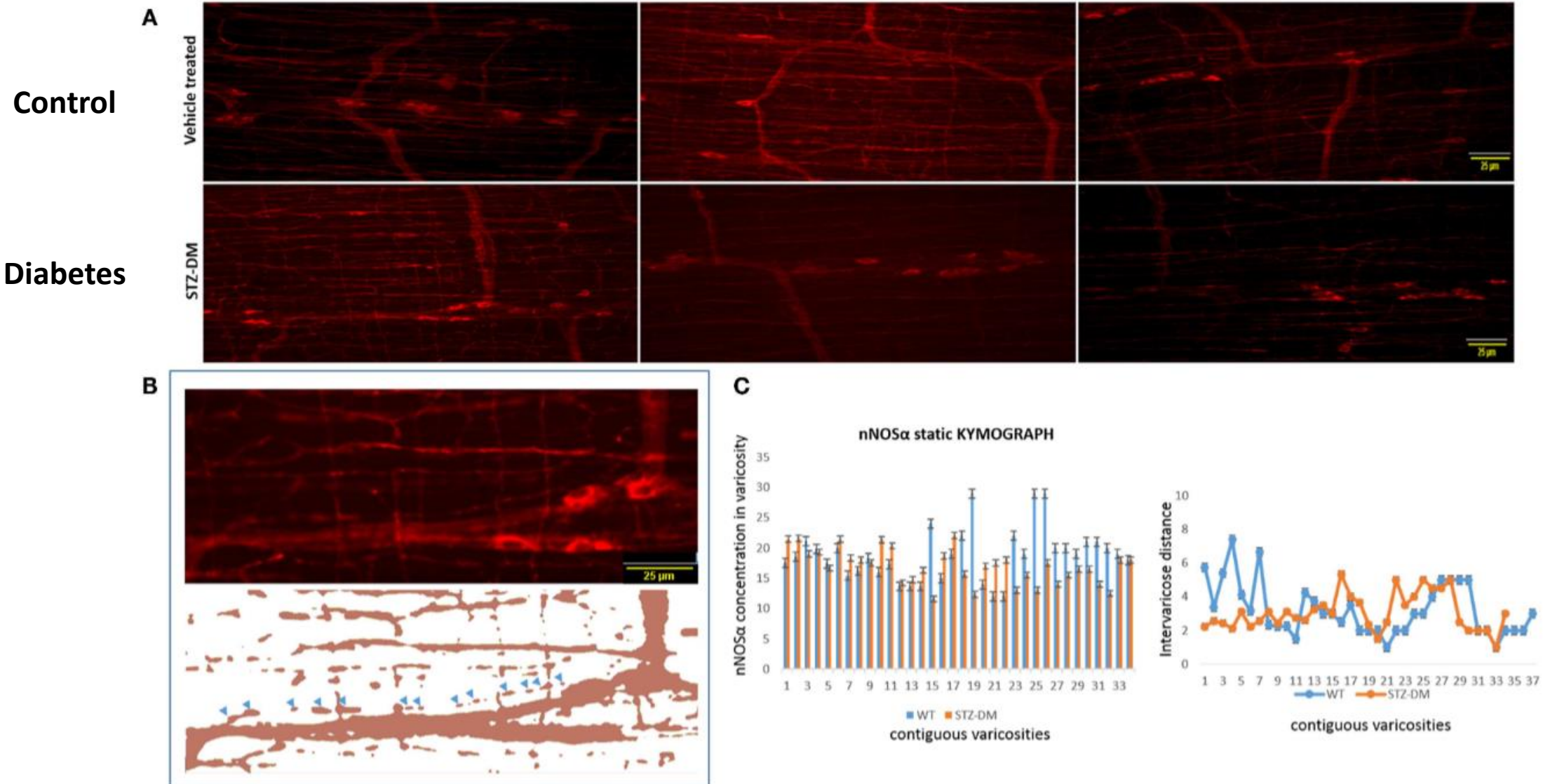
# Distribution of nitrenergic varicosities are comparable in control and diabetes



Chaudhury et al. Frontiers in Medicine, 2014



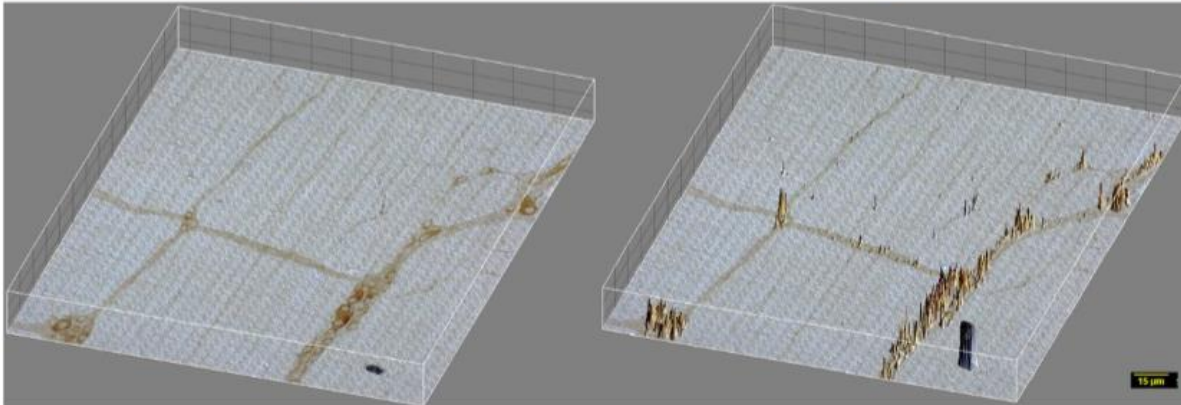
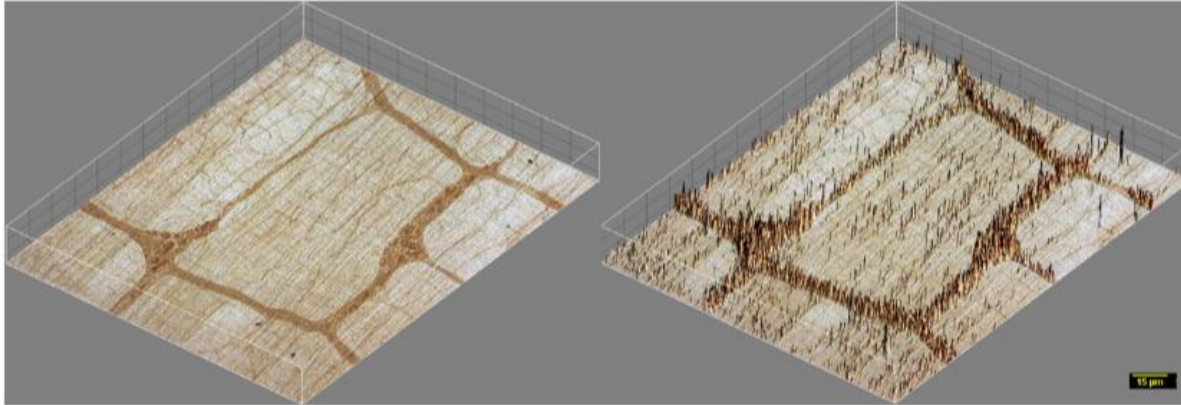
# Axonal transport of nNOS $\alpha$ is comparable in control and diabetes





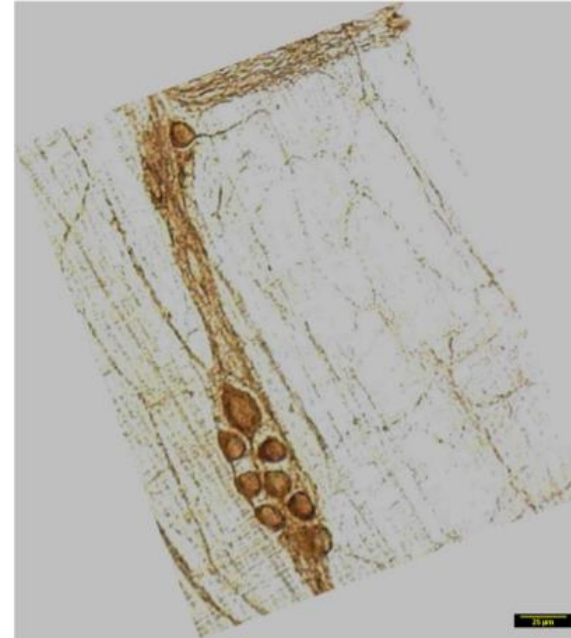
# However, **Myosin Va** is deficient in diabetes

Control



Diabetes

Control



Diabetes



# Natural inhibitors of nNOS beneficial in stroke

**nNOS + PIN → Inhibition of nitric oxide(NO) production**

Jaffrey & Snyder, 1996

**PIN (protein inhibitor of nNOS) -> 8kDa....also dynein light chain (DLC8)**

Dynein is retrograde axonal transporter

I asked, whether DLC8 can act as anterograde transporter of nNOS $\alpha$

LC8 is also light chain of Myosin Va

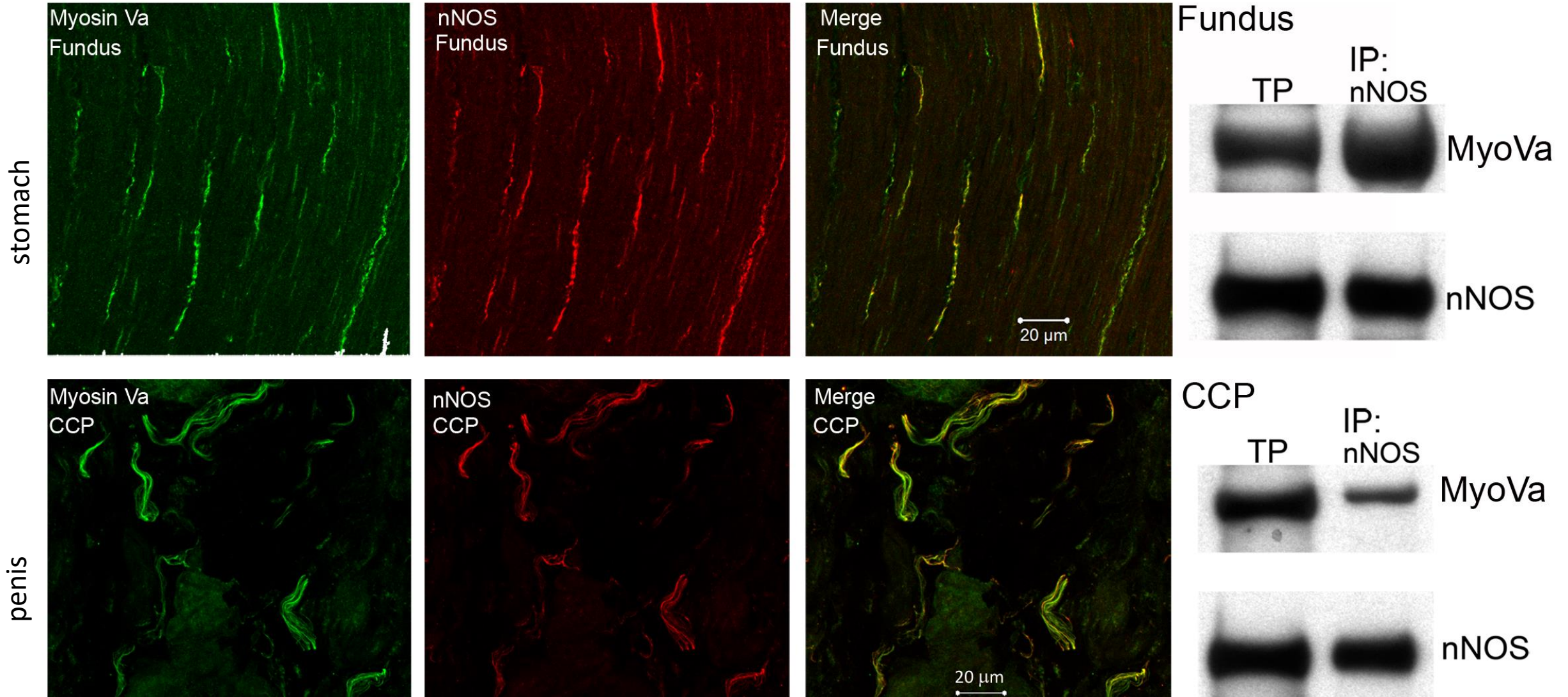
Chaudhury et al, AJP Gastrointestinal Liver, 2011

Chaudhury et al, AJP Gastrointestinal Liver, 2012

# **The Myosin Va story**

Myosin generates force and streams substances through the cytosol

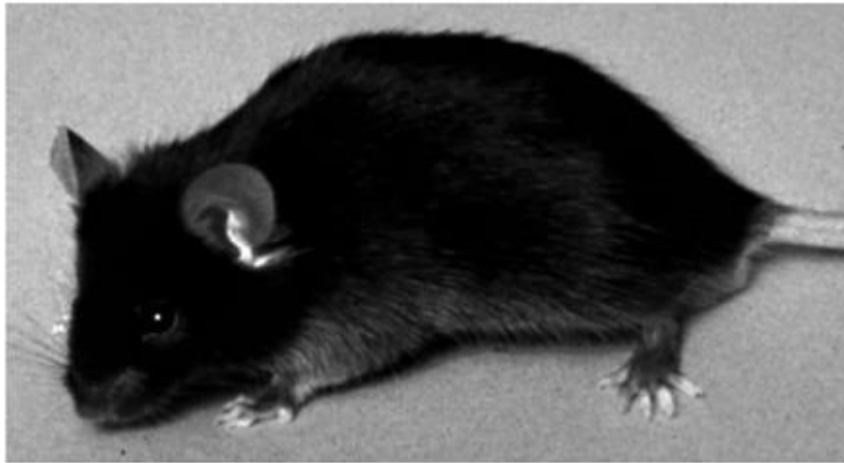
# Myosin Va binds nNOS in stomach and penis





“Dilute” mice: Deficiency of myosin Va leads to lightening of coat color

C57BL/6J

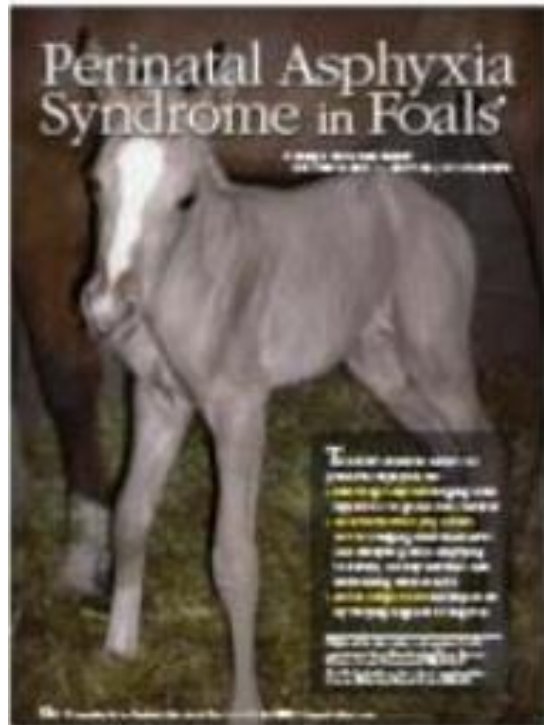


Myosin Va in  
melanosomes

DBA/2J



'Dilute'

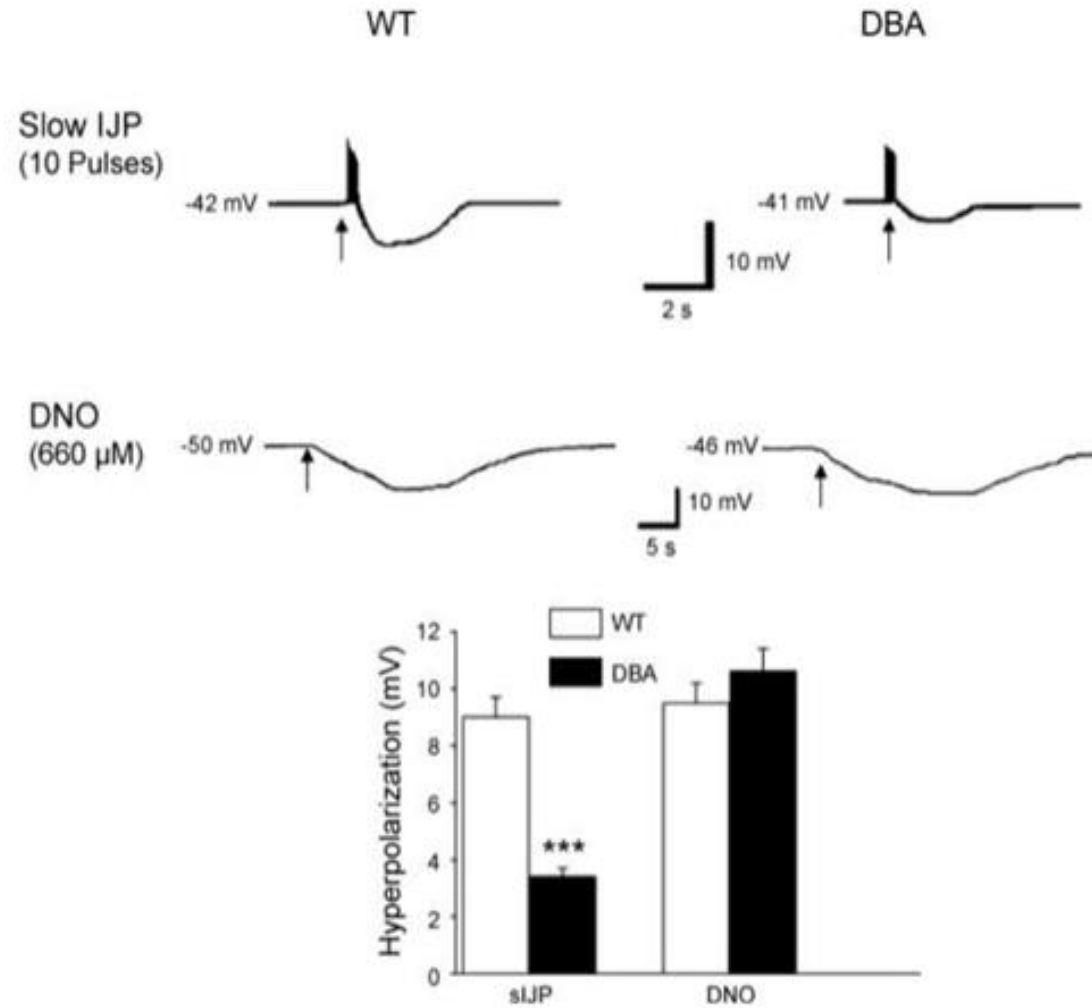


Lavender foal  
syndrome



Griscelli  
syndrome

# Nitrgenic Slow IJP reduced in DBA mice

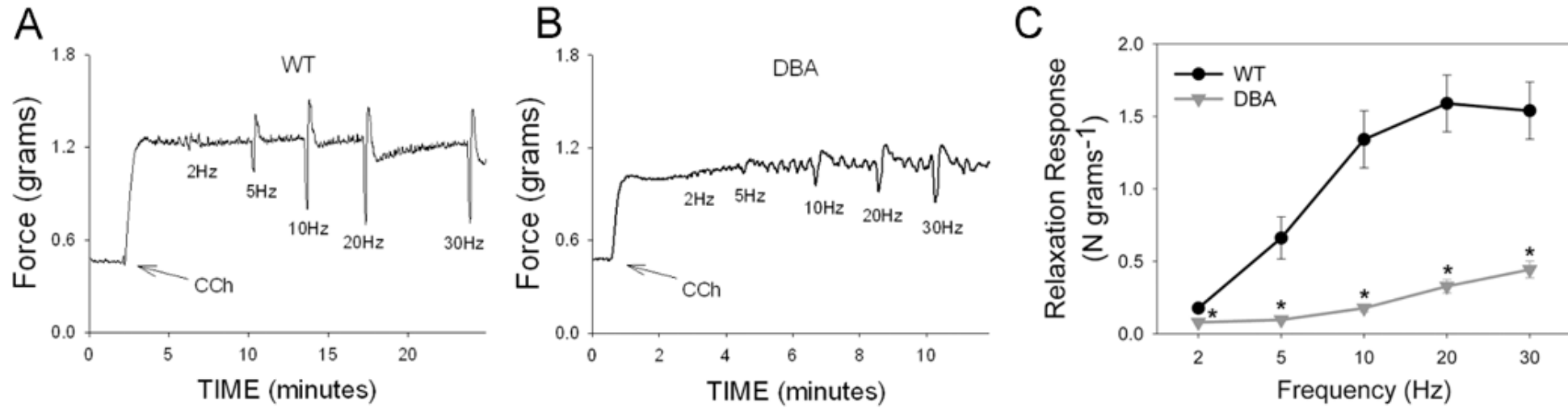


*Chaudhury et al 2011*

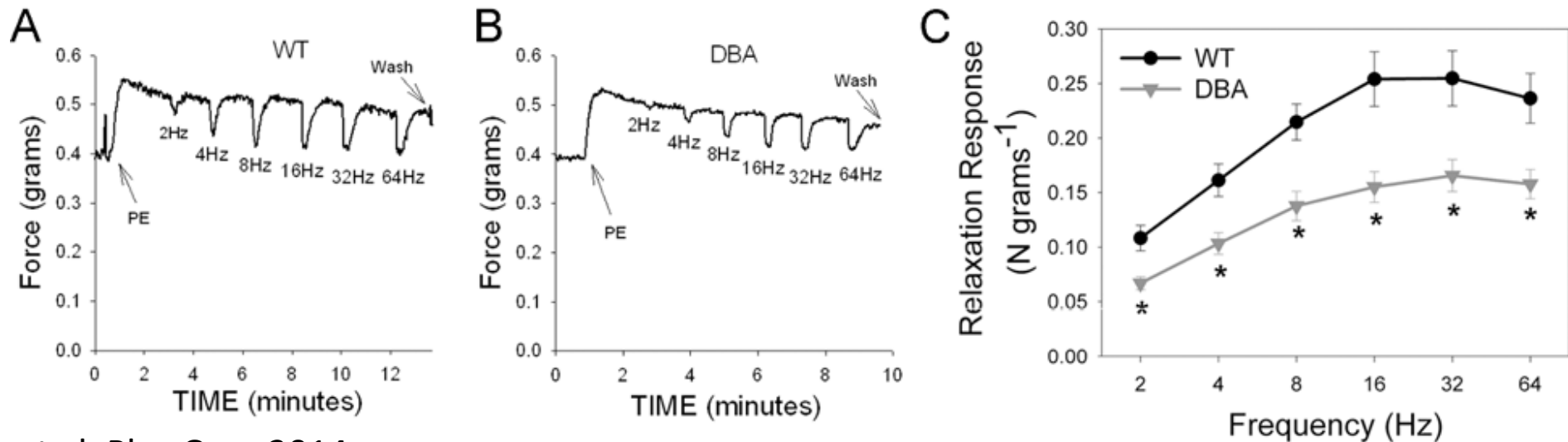


# Incomplete loss of cavernosal function in DBA mice

Fundus

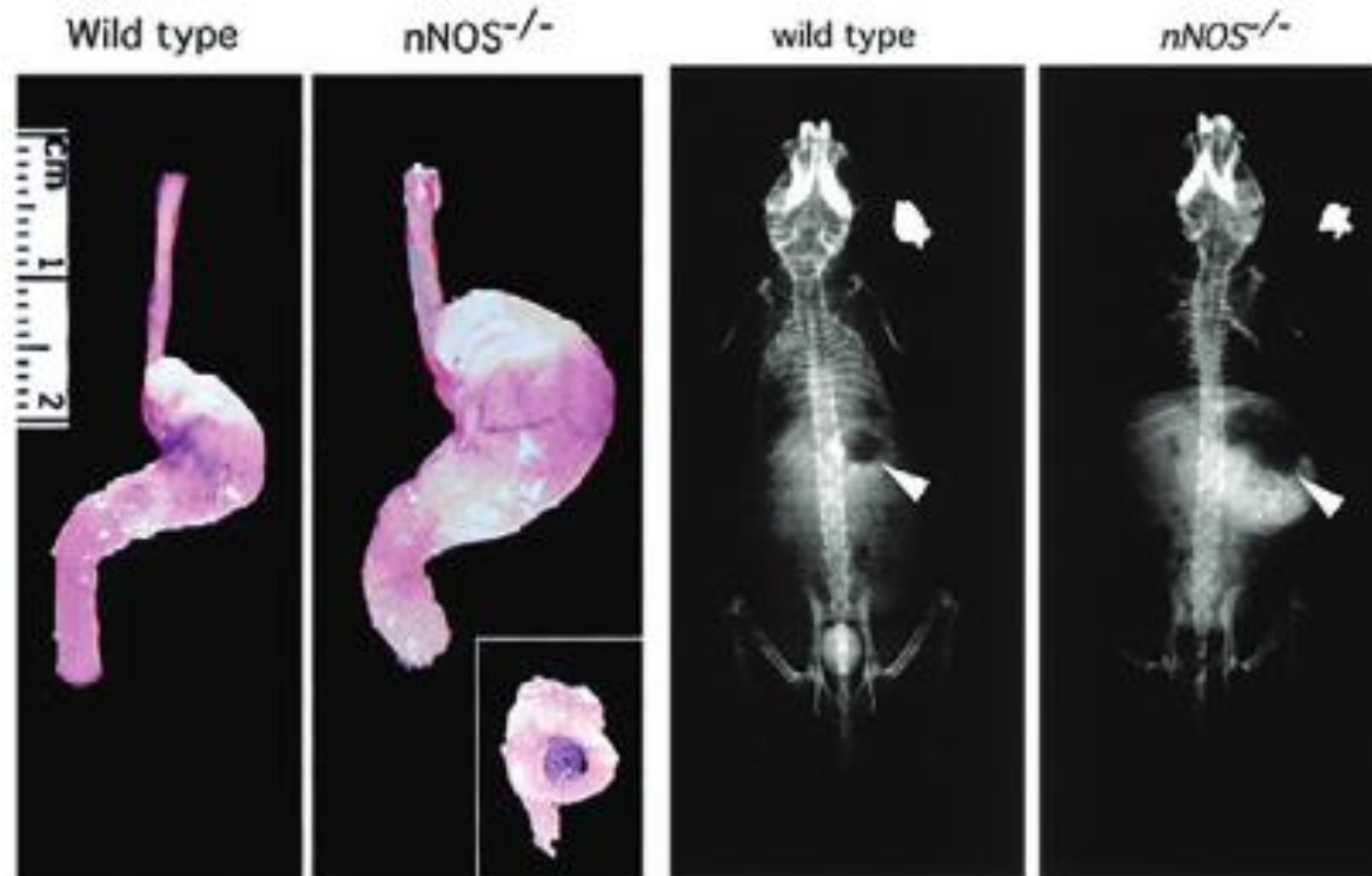


Corpora cavernosa



**Huge redundancy in nitrergic system**

# Sacrificial Project: creating a nNOS knockout



Double knockout  
(eNOS/nNOS) can  
still  
reproduce

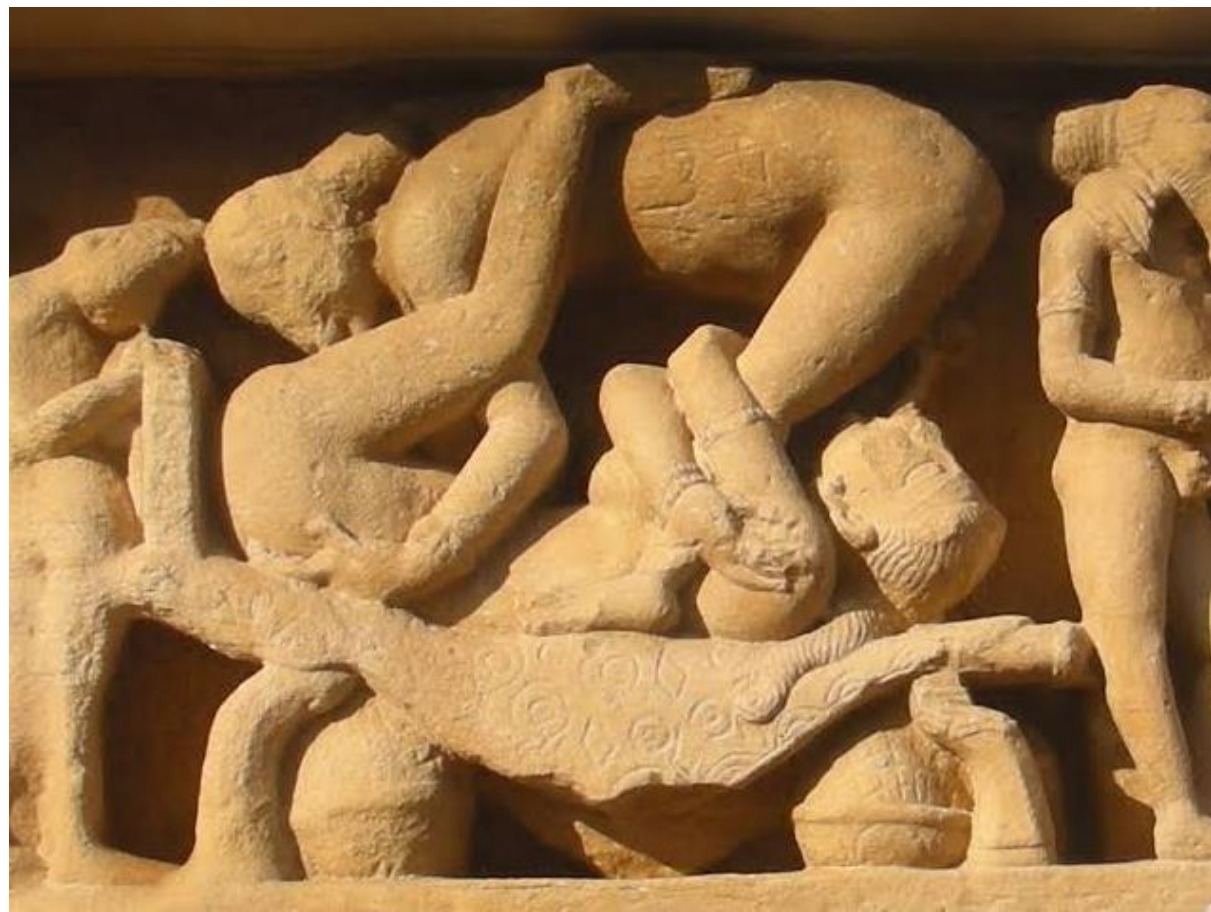
K Joseph Hurt, 2006

Hokfelt 1994

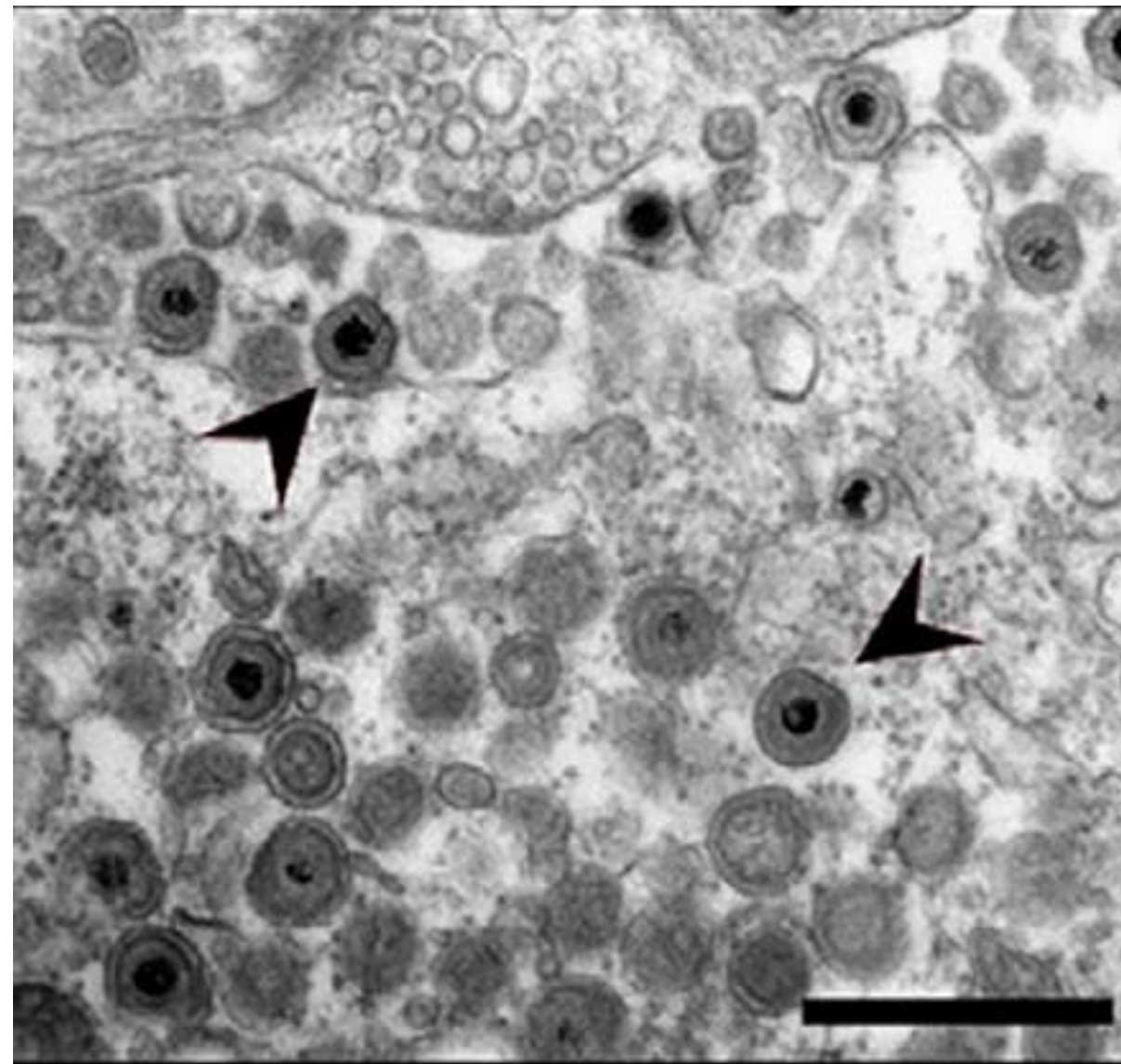
$nNOS\beta$

Mashimo et al 1996  
Chaudhury 2016

# Viral enteric myopathy: sexually acquired



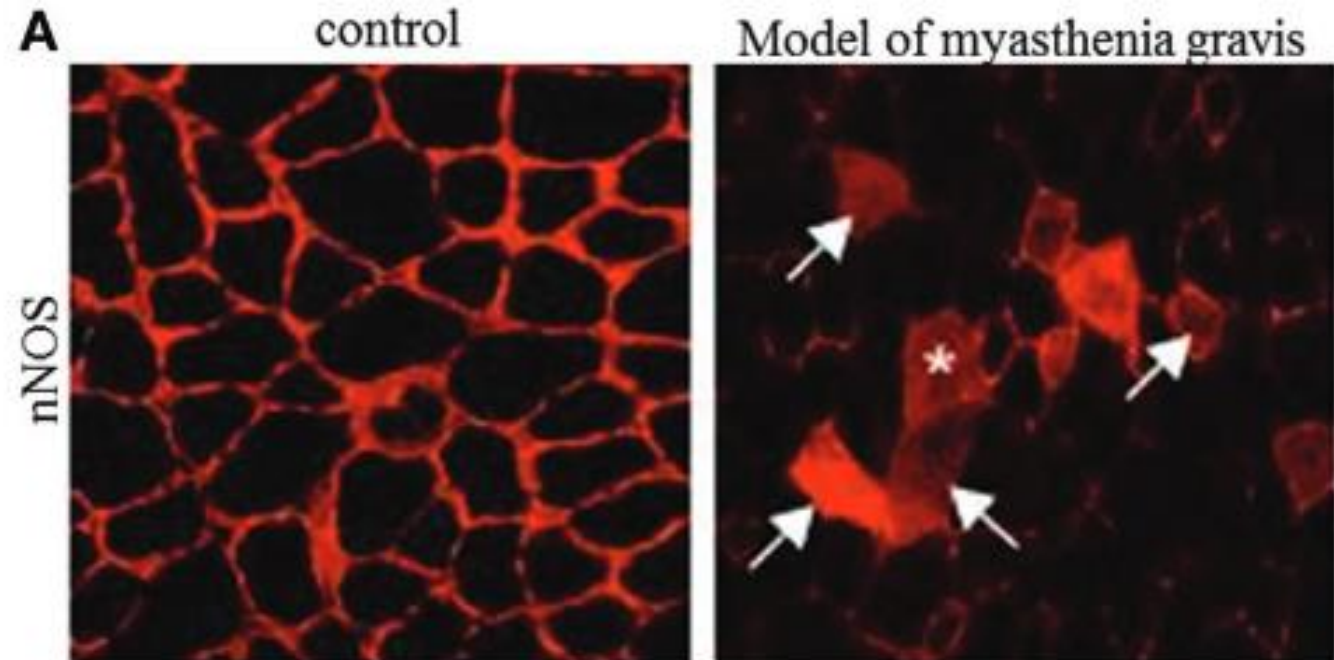
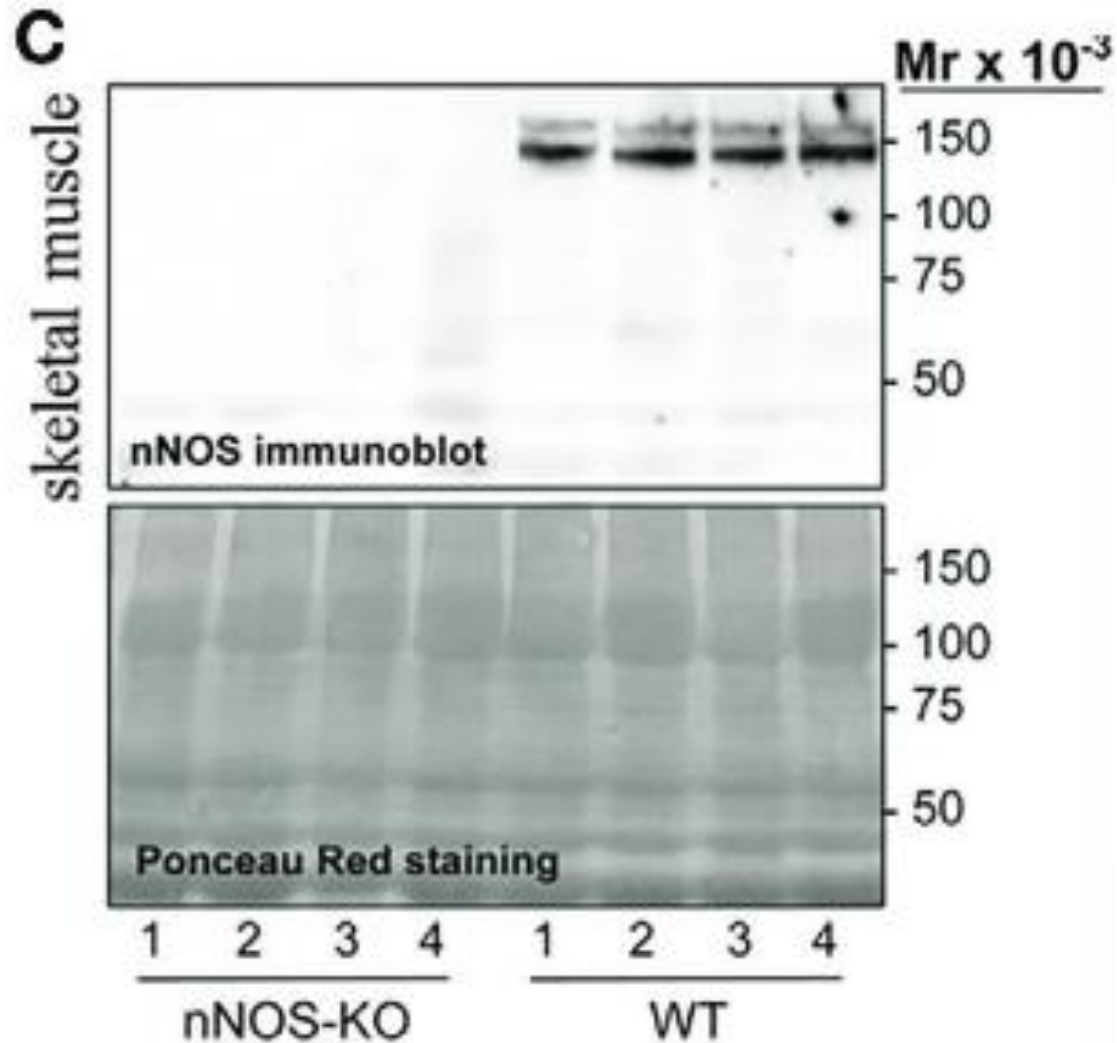
Khoury-Hanold et al 2016  
Chaudhury et al 2018



**HSV 2**



# Skeletal muscle biopsy as a surrogate for evaluation for enteric nNOS



Chaudhury et al 2015, 2016

# HIV Diarrhea: Slim Disease

VIP (vasoactive intestinal polypeptide) receptor facilitates HIV entry in gastrointestinal mucosa

Chaudhury 2015

# Novel Pharmacotherapy



Yartsa gunbu (cordyceps)

Himalayan Viagra

Androgen (cues from neurogenic impotence for genomic upregulation of nNOS)

Examine aphrodisiacs...?any useful targeted pharmacology

# Obtain sexual history for difficult cases of FBD

- Explicit consent prior to discussion
- Ask history of different sexual practices, sexual orientation
- Examine anogenital areas for evidence of MSM, proctitis, lesions
- Non-Judgemental, relaxing environment

Do not hesitate to obtain viral titers including for HIV



# Summary

Empathetically listen

Holistic & poised approach to management

Enhance health literacy & empower subjects

Be on the trail with them in their journey





AMITABH BACHCHAN

DEEPIKA PADUKONE

IRRFAN KHAN

RSE

MSM MOTION PICTURES, SARASWATI ENTERTAINMENT AND RISING SUN FILMS PRESENT

# SHOOJIT SIRCAR'S PIKU

MOTION 3E HI EMOTION



AMITABH BACHCHAN DEEPIKA PADUKONE IRRFAN KHAN MOUSHUMI CHATTERJEE RAGHUVIR YADAV ISSHI SENGUPTA

PRODUCED BY NP SINGH RONNIE LAHRI SNEHA RAJANI DIRECTED BY SHOOJIT SIRCAR EDITOR SUDHAKAR K. J. J. CHATURVEDI

CASTING BY KAMALJEET NEGI COSTUME DESIGNER ANUPAM KUMAR MUSIC BY CHANDRASEKHAR PRASAD PRODUCTION DESIGNER TILAK KAPREET EXECUTIVE PRODUCERS BHASKAR CHATTERJEE PRODUCED BY KUMAR THANKER

SARASWATI  
ENTERTAINMENT

[/msmmotionpicture](#)

[/pikufilm](#)

[/pikufilm](#)

[/pikufilm](#)







Can you  
**FART,**  
**LOUDER,**  
**LONGER**  
and  
**STRONGER?**

**WTF!**  
WHAT THE FART!  
**FART COMPETITION**  
(Surat Chapter)

Registration fees ₹100/-

**22<sup>nd</sup> SEPT. SUNDAY**  
**10:30 AM onwards**

Venue Partner  
*La Terraza*  
Surat Chapter

**Give it a try, Be a 'Pad'shah!**

For registration and more details contact us: **9825112421 | 9898998079**

Digital Partner  
**citytadka**  
www.citytadka.com

Image Courtesy : Hindustan Times, New Delhi 16<sup>th</sup> Sept 2019

<https://www.hindustantimes.com/it-s-viral/surat-to-host-india-s-first-fart-competition-there-will-be-trophies-too/story-pgThsrZBrYJQXWU26GKO1H.html>

Work in Progress

# Food and Consumer ( খাদ্য ও খাদক )



Seco-Iridoids

Extravirgin olive oil....mTOR downregulation/AMPK activation

**GERORETARDANT**

Can they be beneficial in constipation in elderly?

Xenohormesis

Bitter compounds and gut health



Flabelliferins





# What is the basis for multisystem involvement?

- 2 siblings from Ecuador, 11 and 14 yrs old
- Seizure disorders, pervasive neurodevelopmental disorder
- Achalasia
- Tuberculosis and recurrent fungal infections

Chaudhury, Pedroza, 2017

# Validation of work (amongst many)

[HOME](#)[BROWSE](#) ▾[EDITOR'S CHOICE](#)[VIRTUAL ISSUES](#)[ABOUT](#) ▾

Volume 176, Issue 2

Special Issue: Themed Section: Nitric Oxide 20 Years from the 1998 Nobel Prize. Guest Editor: Louis J Ignarro

Pages: 129-334

January 2019

[< Previous](#) | [Next >](#)

[☰ GO TO SECTION](#)

*Thank you*

*Mousumi Chaudhury*

*Sayan Biswas*

*Numerous colleagues & mentors across the globe*

*Friends of GIM Foundation*

*Wellcome*

