



# Fibromyalgia and MEFV

Marie Kumerow

<http://lakescenterchiro.com/wp-content/uploads/2011/10/fibromyalgia41.jpg>

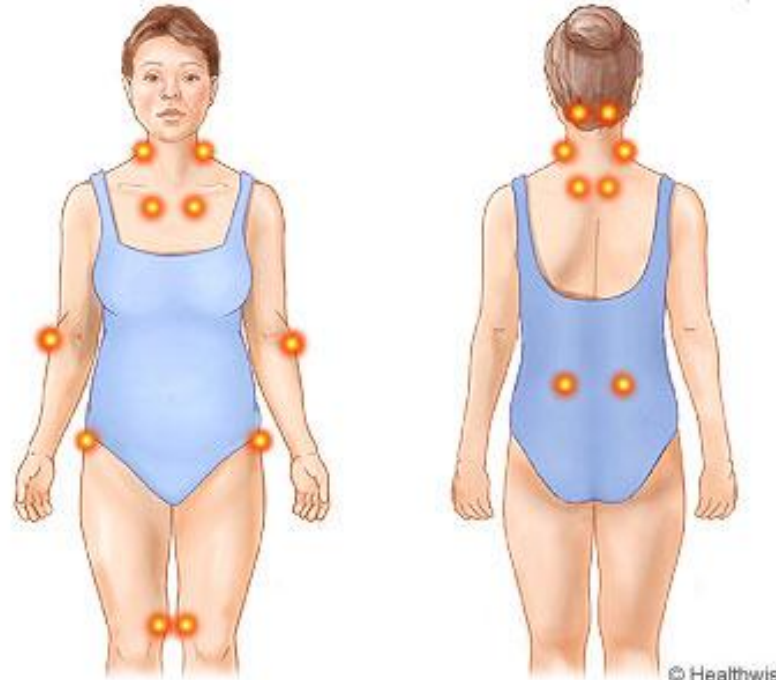
# What characterizes fibromyalgia?

## Symptoms

- Musculoskeletal pain, fatigue, pressure points, depression

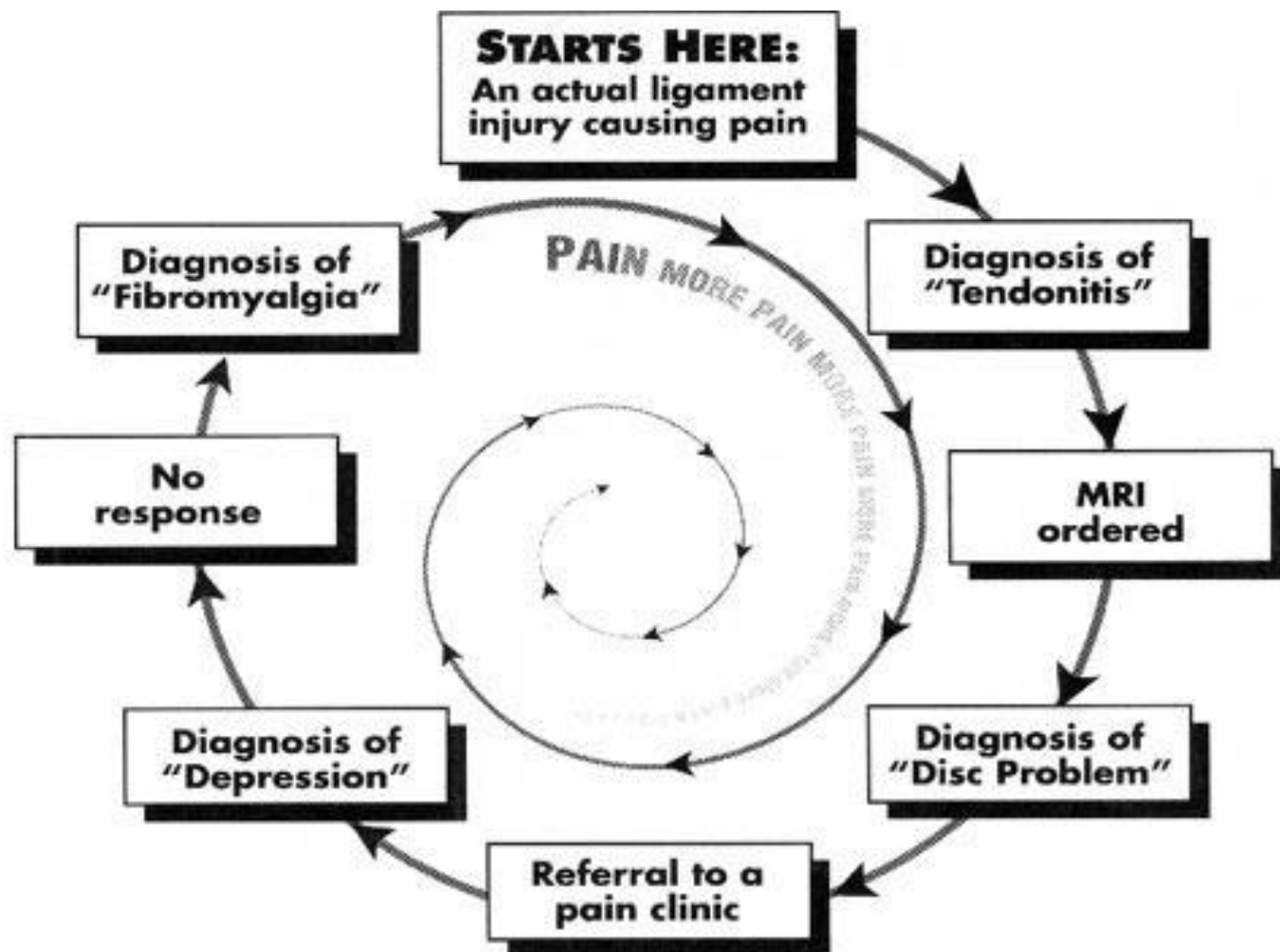
## Prevalence

- 2% general population affected
- 85% cases are in women



“...may be due to injury, emotional distress, or viruses that change the way the **brain perceives pain**, but the exact cause is unclear.” -FDA, 2008

# Diagnosis of Fibromyalgia



# Drug Treatments



2007



Consumer Health Information  
www.fda.gov/consumer

[www.fda.gov/consumer/updates/fibromyalgia062107.html](http://www.fda.gov/consumer/updates/fibromyalgia062107.html)

## Living with Fibromyalgia, Drugs Approved to Manage Pain

After meeting on the Internet in 1997, Lynne Matallana and Karen Lee Richards discovered they had a lot in common. They both had seen numerous doctors before being diagnosed with fibromyalgia, a chronic condition characterized by fatigue and widespread pain in muscles and joints. They both had trouble finding medical information and support for coping with the illness. Seven months after meeting, they started gathering with five other people with fibromyalgia who also wanted to bring awareness to the issue.



2008



2009

[http://www.sandmedia.com/what/examples/PfizerLyrica\\_sm/PfizerLyrica\\_sm-poster.jpg](http://www.sandmedia.com/what/examples/PfizerLyrica_sm/PfizerLyrica_sm-poster.jpg)

<http://www.fogmagazine.com/wp-content/uploads/2008/07/simba.jpg>

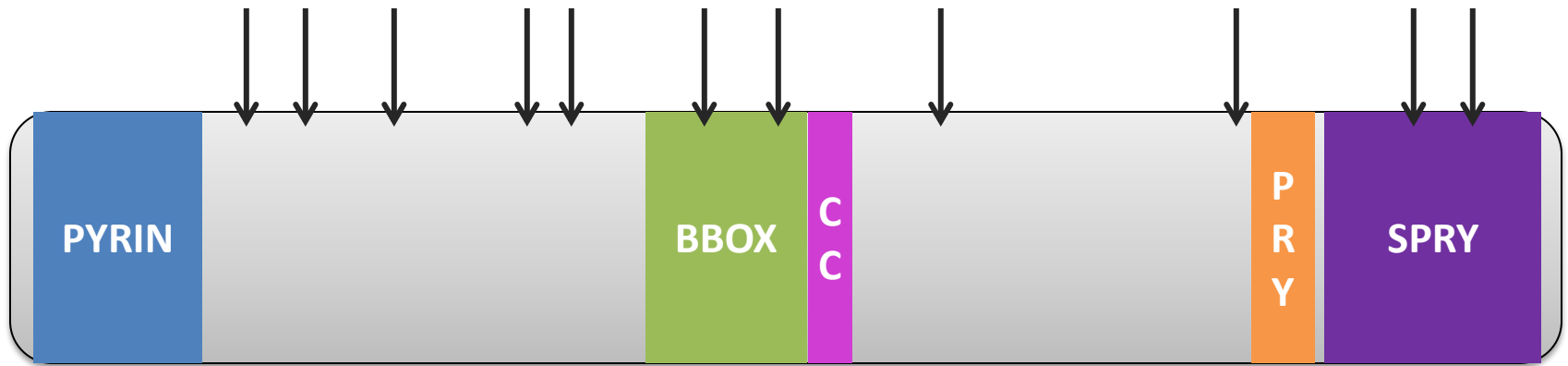
<http://www.hopkinsarthritis.org/wp-content/uploads/2011/04/savella.gif>

# Alternative Treatments

- Massage, acupuncture, chiropractics, exercise programs, **weight loss**, herbal medicines and dietary supplements
- **Vegetarian or vegan diet**

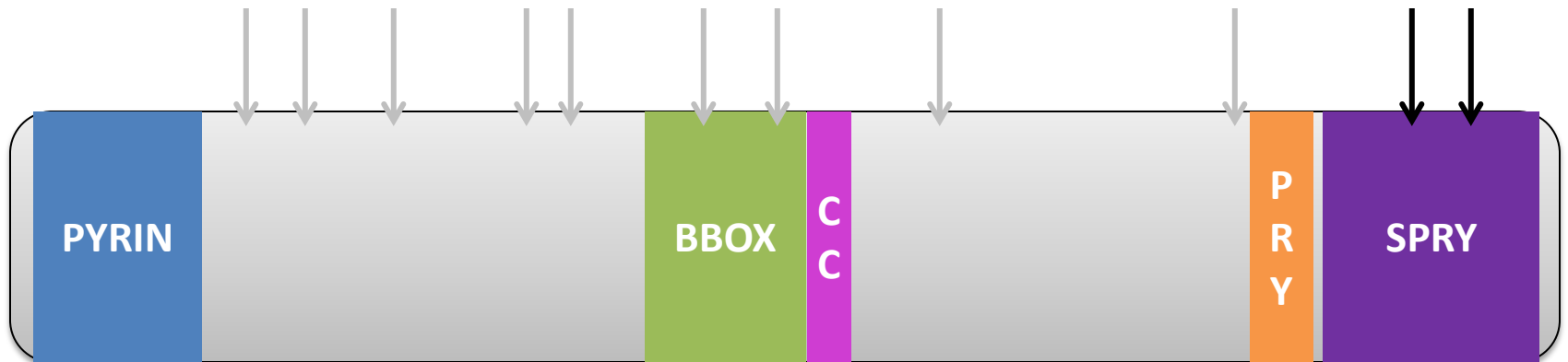


# Fibromyalgia correlated to MEFV Gene



- “Mediterranean fever” gene named for association with Familial Mediterranean Fever Syndrome (FMF).
- FMF symptoms include intense joint attacks, abdominal pain, pleura and pericardium inflammation, and fever.

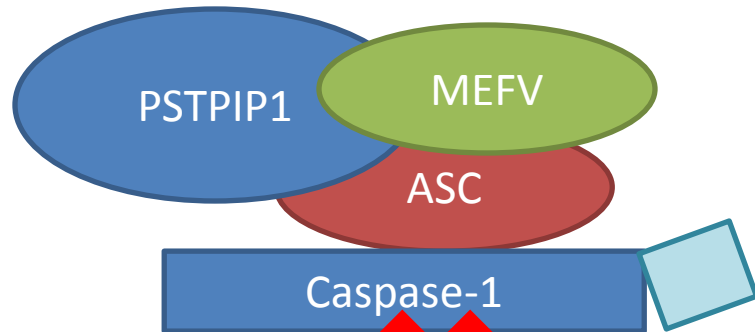
# MEFV Gene inhibits inflammatory response genes



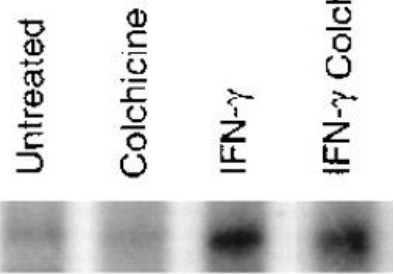
ASC

actin

PSTPIP1

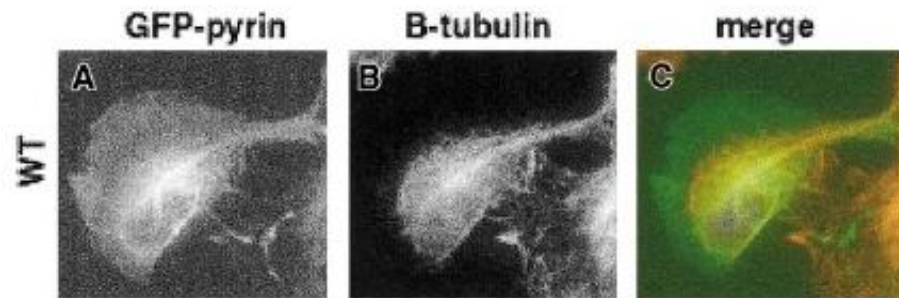
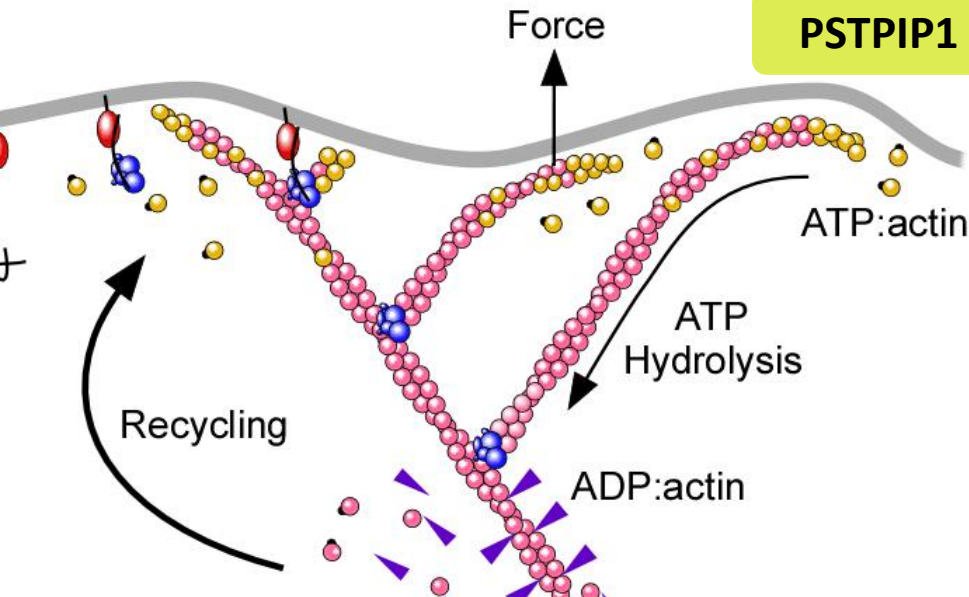
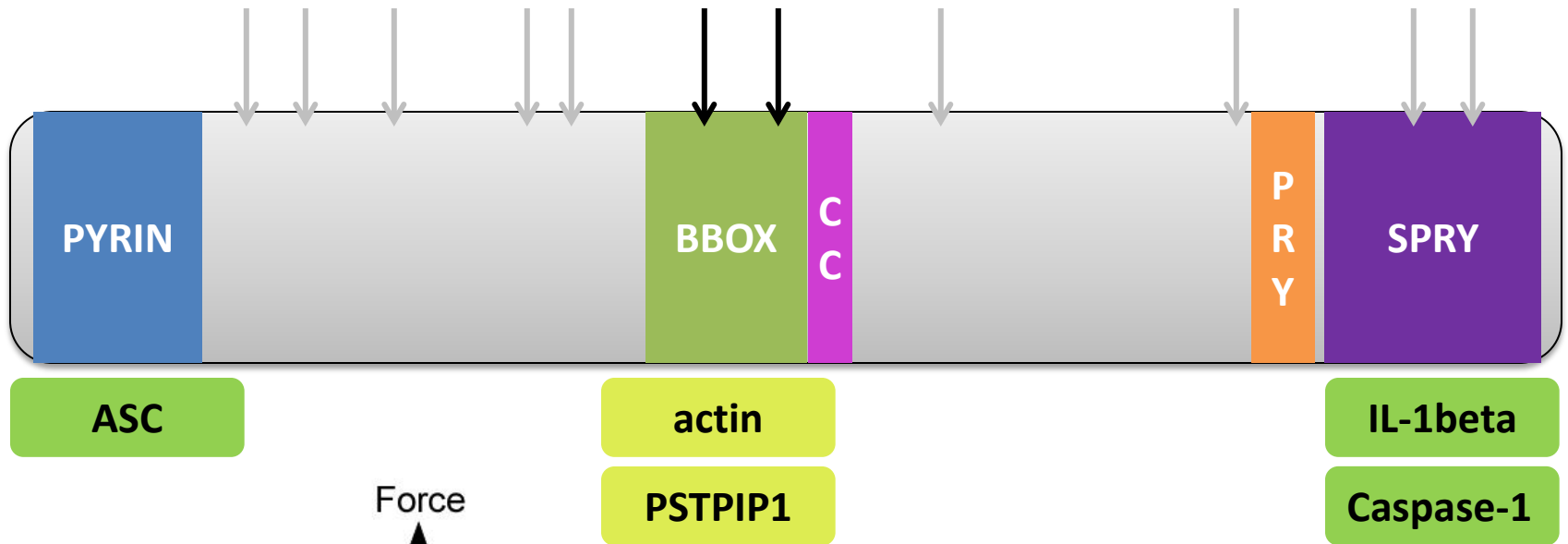


IL-1 $\beta$



IL-1 $\beta$

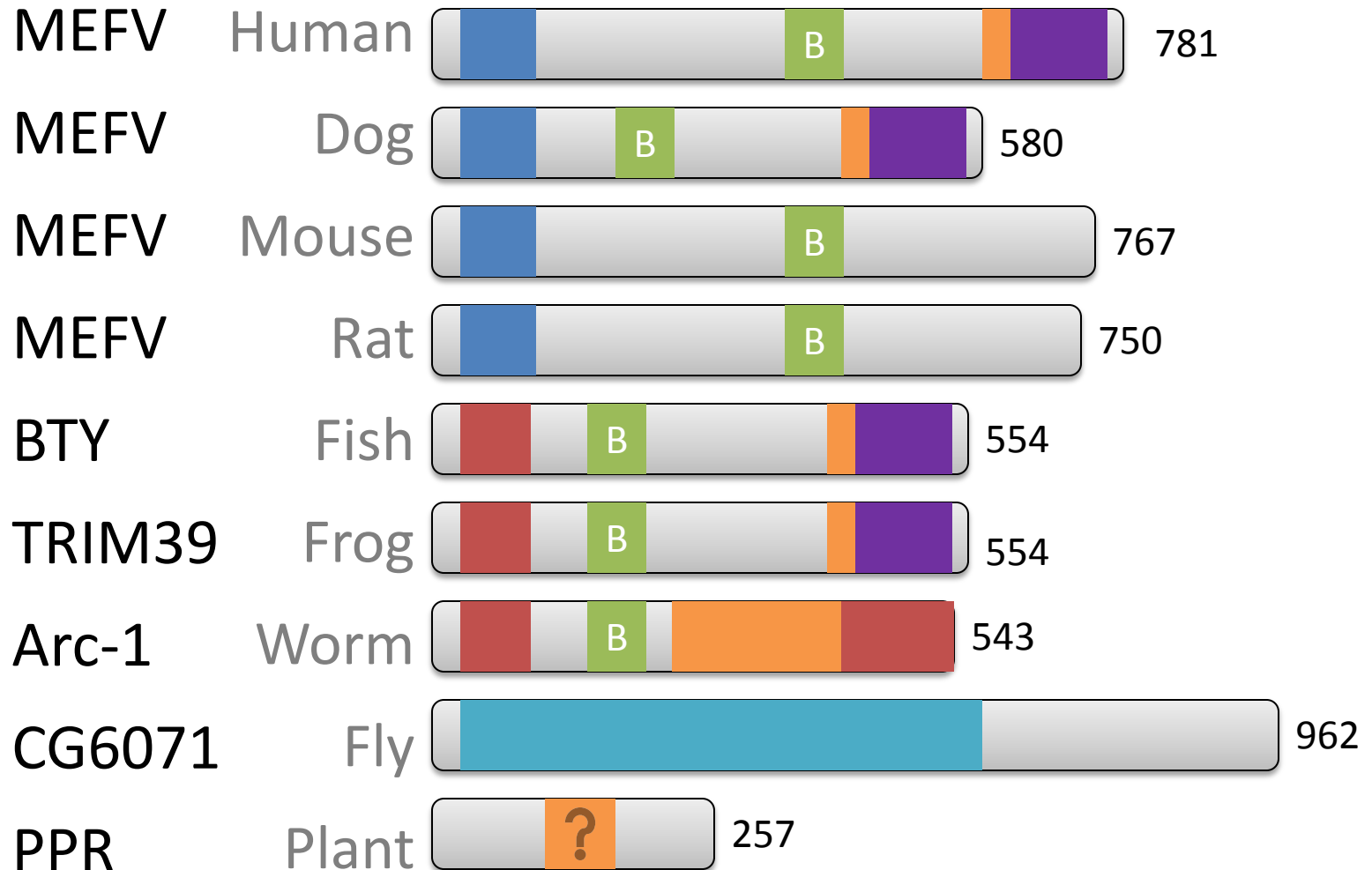
# Where does MEFV protein bind actin?



Mansfield et al. 2001

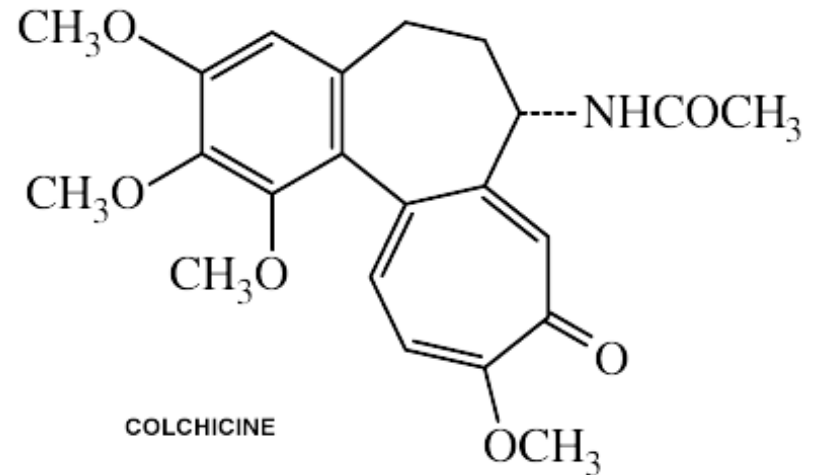


# Actin binding domain is well conserved



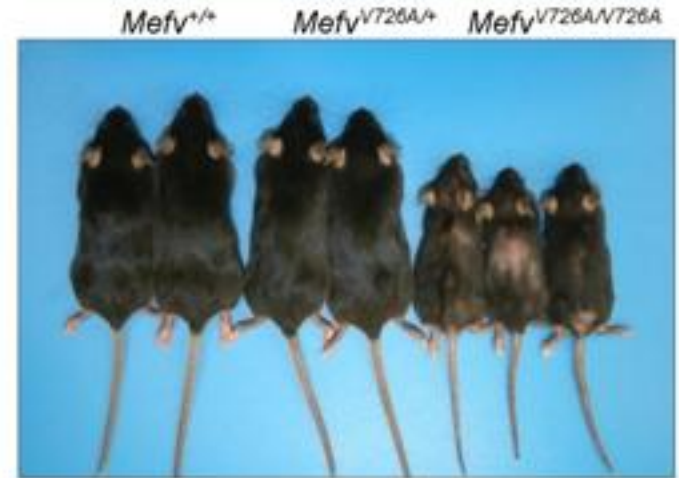
# How can you target actin?

- Small molecule colchicine activates actin polymerization by microtubule depolymerization
- Used as a drug in Familial Mediterranean Fever and Gout

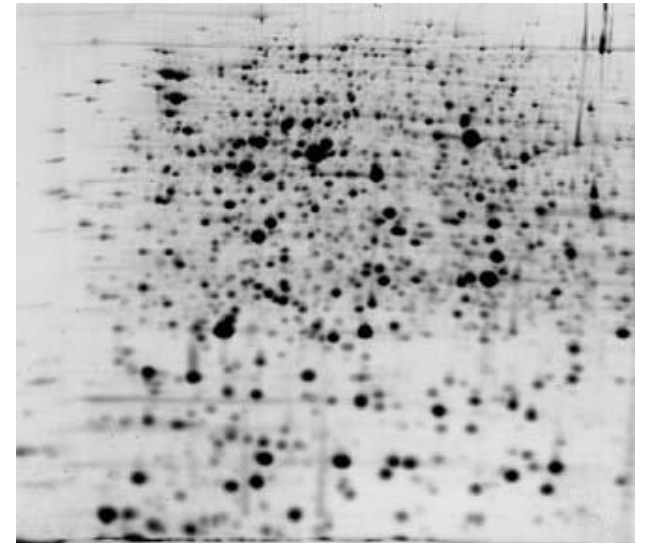


# Hypothesis

Colchicine will show decreased levels of interleukin inflammatory response relative to SNRI treatment.



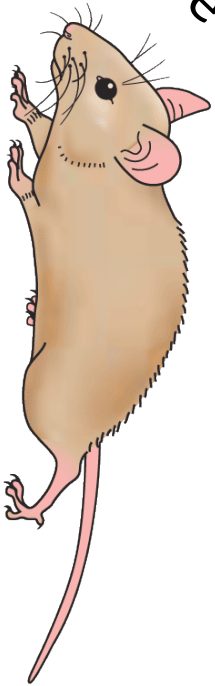
Che et al. 2003



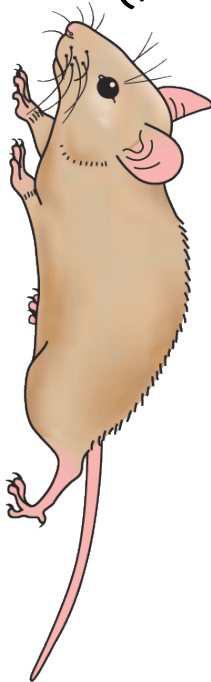
# How does colchicine affect fibromyalgia?

Is SNRI or colchicine more effective treatment?

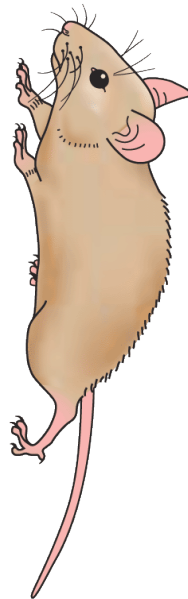
MEFV<sup>+/+</sup> Mouse



MEFV<sup>+/+</sup> Mouse  
w/ colchicine



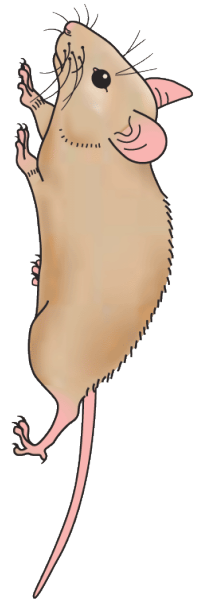
MEFV<sup>-/-</sup> Mouse



MEFV<sup>-/-</sup> Mouse w/  
colchicine



MEFV<sup>-/-</sup> Mouse w/  
SNRI



# Levels of active IL-1 are lower in colchicine treatment

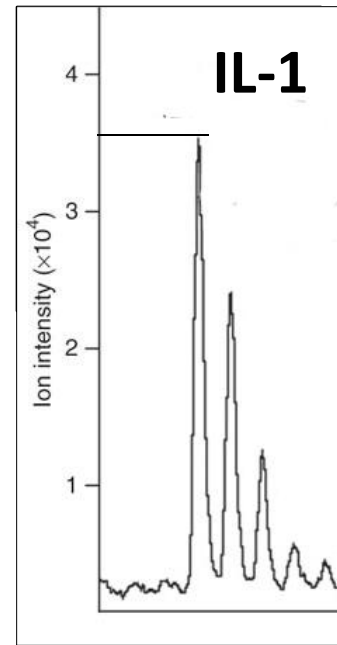
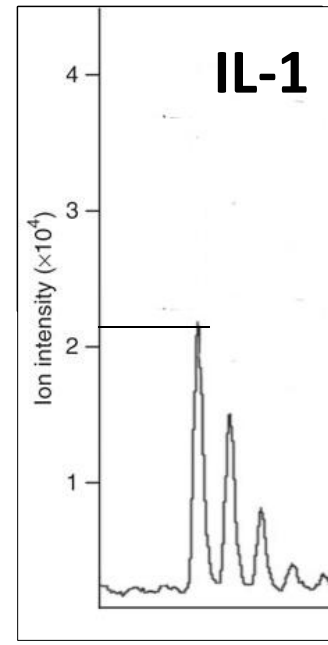
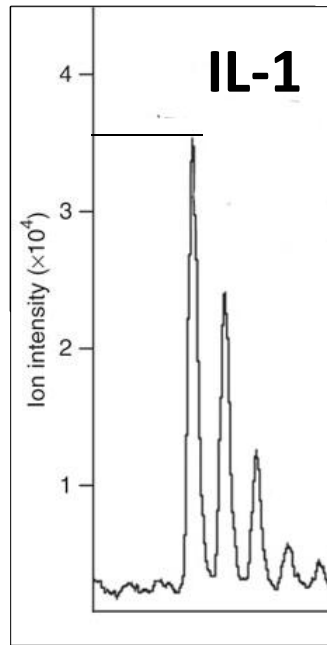
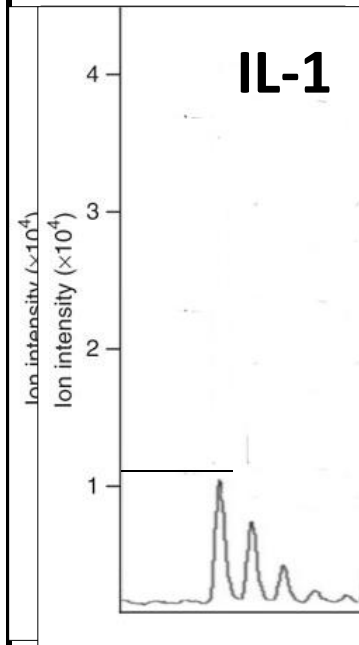
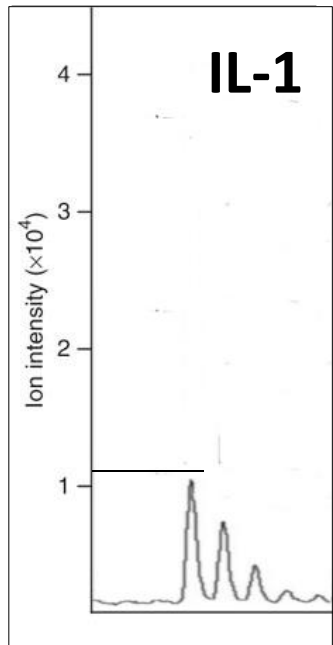
MEFV<sup>+/+</sup> Mouse

MEFV<sup>+/+</sup> Mouse  
w/ colchicine

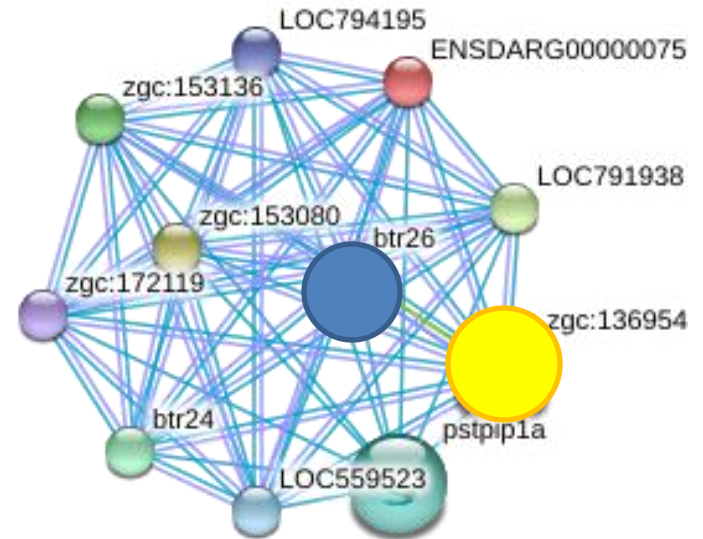
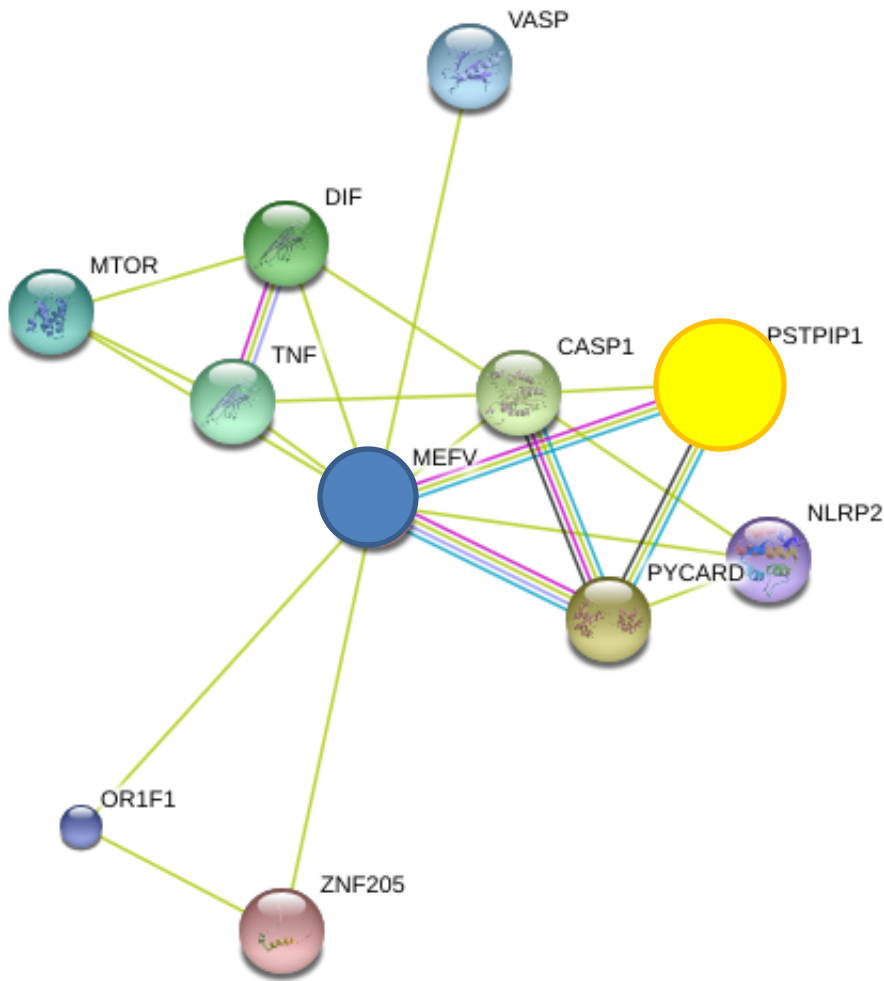
MEFV<sup>-/-</sup> Mouse

MEFV<sup>-/-</sup> Mouse w/  
colchicine

MEFV<sup>-/-</sup> Mouse w/  
SNRI

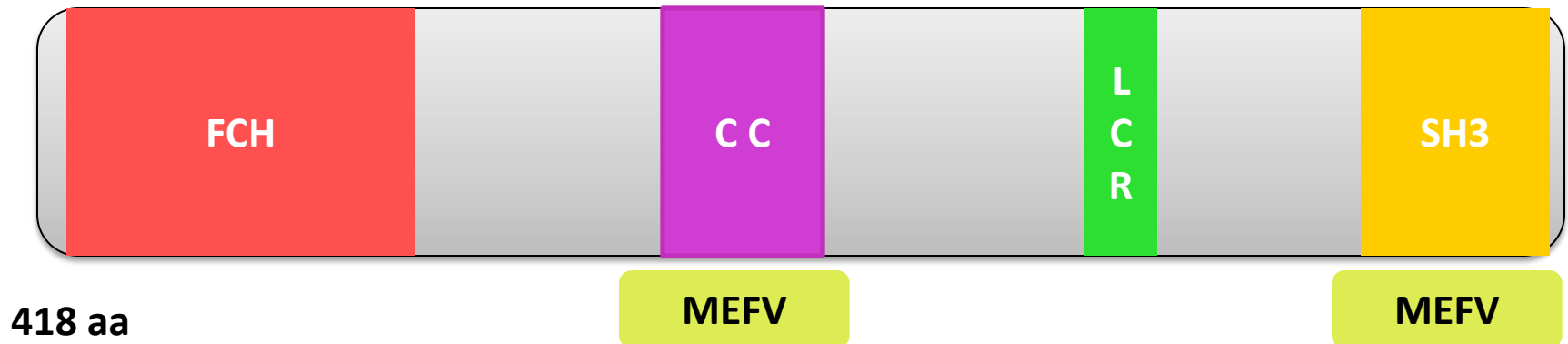


# Conservation of protein interaction



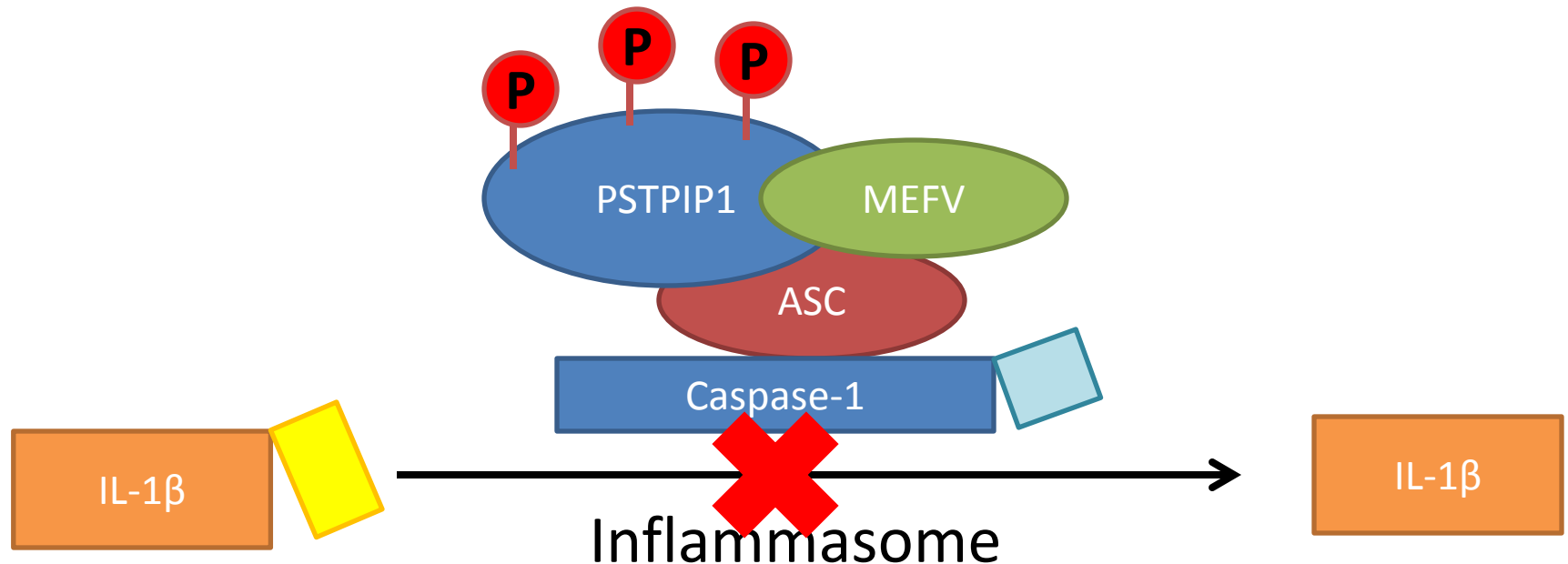
# What is PSTPIP1?

- Scaffold protein and regulator of actin cytoskeleton
- Known interactor with MEFV
- PAPA syndrome



# How does PSTPIP1 interact with MEFV protein?

- Mutations in PSTPIP1 protein create a dominant negative effect on the predicted inhibition by MEFV protein.





# Vegetarianism and inflammatory response

## Vegetarian diets

- Rich in antioxidants
- Low fat

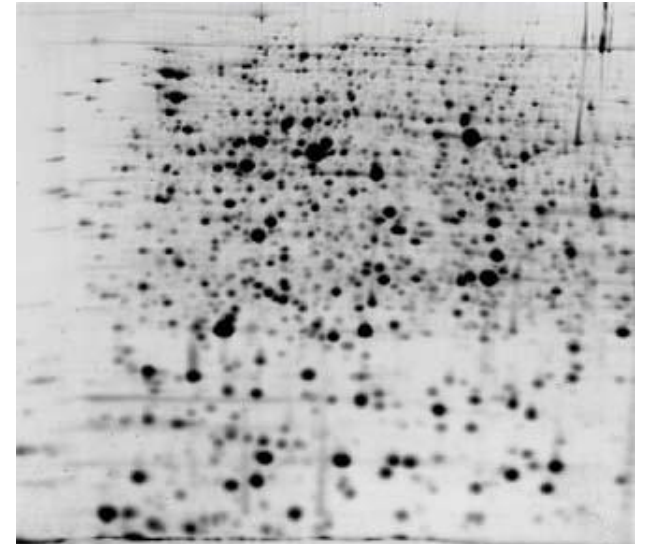


Studies on fibromyalgia and diet have shown decreased BMI associated with reduced symptoms.

IL-18 was associated with obesity.

# Hypothesis

Providing a low fat diet will reduce inflammatory response in mice with PSTPIP1 mutations.



# How can a low fat diet alter autoinflammation?

PTSPIP1 <sup>+/+</sup> Mouse



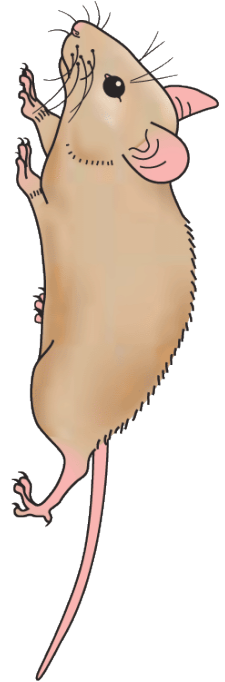
PSTPIP1 <sup>+/+</sup> Mouse  
Low fat diet



PSTPIP1 <sup>-/-</sup> Mouse

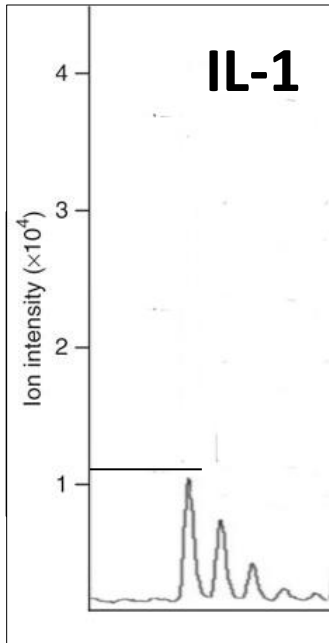


PSTPIP1 <sup>-/-</sup> Mouse  
Low fat diet

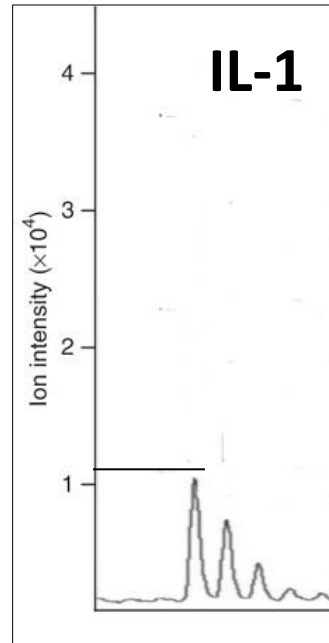


# A low fat diet decreases inflammatory response

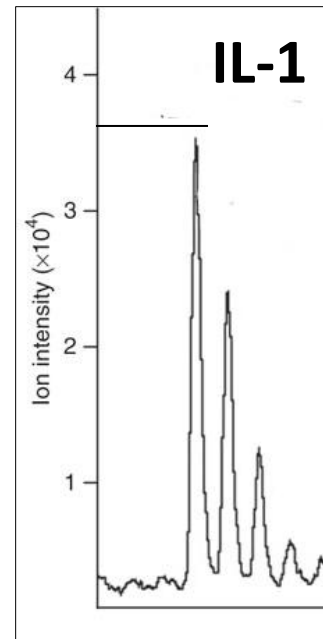
PTSPIP1 <sup>+/+</sup> Mouse



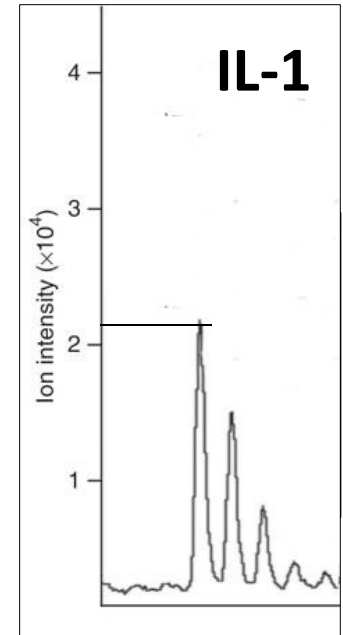
PSTPIP1 <sup>+/+</sup> Mouse  
Low fat diet



PSTPIP1 <sup>-/-</sup> Mouse



PSTPIP1 <sup>-/-</sup> Mouse  
Low fat diet



# Conclusions

- Colchicine treatment is likely to be effective in treatment of human fibromyalgia, where cytokines levels are high.
- A low fat, vegetarian diet should reduce inflammatory symptoms in fibromyalgia and other autoinflammatory diseases, including PAPA syndrome.



# Future Research

- More studies regarding whether being overweight is a symptom or cause of fibromyalgia.
- Human drug trials of colchicine for fibromyalgia.
- Global patterns of fibromyalgia – high rate of MEFV carriers from the Mediterranean Sea.