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# Biliary Signature of a Bacterial Pathogen

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*Listeria monocytogenes*

# The Deadly Deli

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## Nation

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### Listeria fear prompts largest U.S. meat recall

By Anita Manning, USA TODAY

PHILADELPHIA — This weekend's recall of more than **27 million pounds** of turkey and chicken sandwich meats is the latest, and largest, in a series of food recalls that suggest routine testing for the bacteria listeria is needed, consumer advocates say.



A row of Wampler foods trailers sit in a lot at the Pilgrims Pride meat processing plant in Franconia, Pa. on Monday.

By Chris Gardner, AP

Wampler Foods, owned by Pilgrim's Pride, launched a recall last week when listeria was detected on a product sample taken by the

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**intel inside**  
pentium 4  
TIPS FOR CONSUMERS

- Brands involved: Wampler Foods, Golden Acre, Reliance and a variety of others.
- Products included: Turkey and chicken sandwiches at deli counter packages of sliced deli meats. Turkey sandwiches — only cooked products.
- Time and plant affected: Meat produced at the Pilgrim's Pride processing plant in Franconia, Pa., facility from May 1, 2007, to the date of the recall.

Internet zone

# The Deadly Deli

## Listeria Hysteria at Jamba Juice

● Wed, 12/06/2006 - 4:10pm by [FitSugar](#) **ONLINE**

1,146 Views - 5 comments

Consumers in the U.S. Southwest are being warned that Jamba Juice Co. smoothies containing strawberries may be contaminated with the potentially deadly *Listeria monocytogenes* bacterium (commonly known just as Listeria), which can cause potentially deadly infections in children, the elderly and other people with weakened immune systems. It is also known to cause still births and miscarriages in pregnant women.

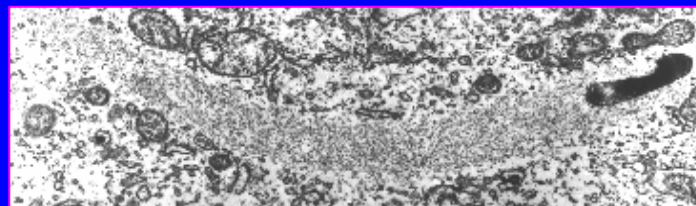
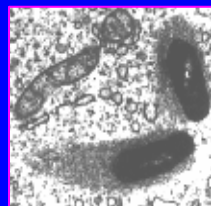
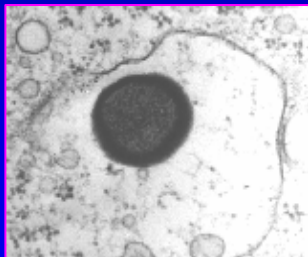
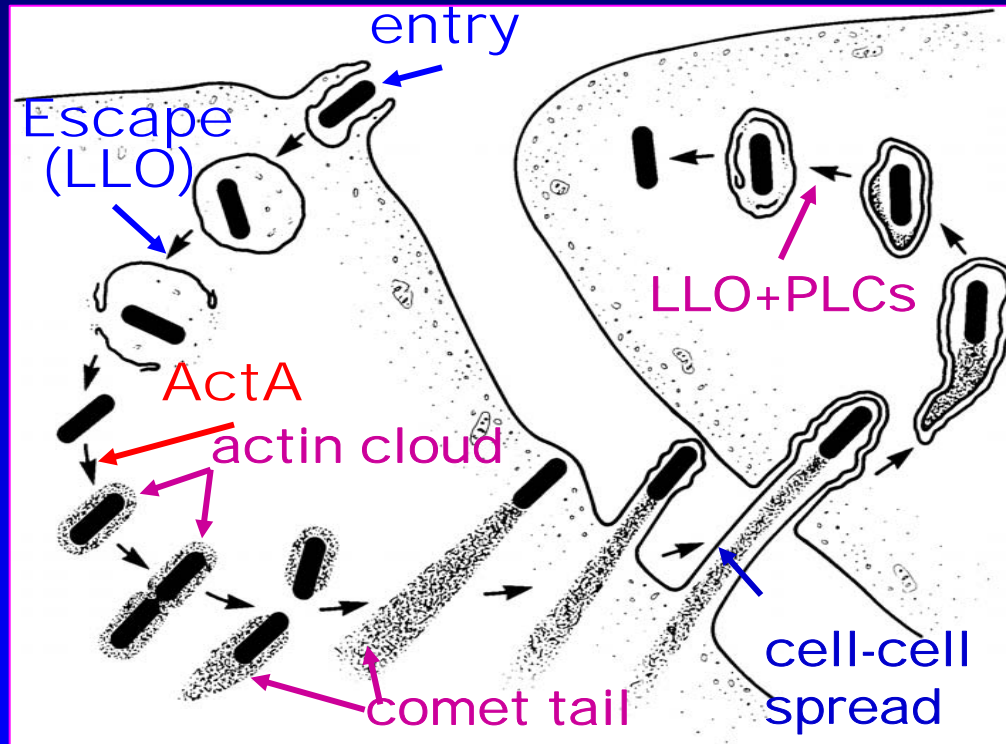
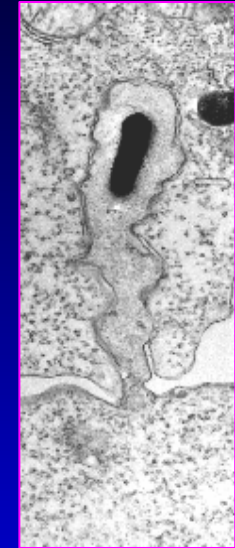
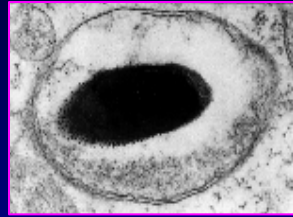


# Spectrum of Listeriosis

- Mild **fever** and malaise
- Mild to severe **gastritis**
- Severe **meningitis** in newborns
- Bacteremia and **sepsis** in newborns
  - **Osteomyelitis** and arthritis
    - **Endocarditis**
  - Asymptomatic carriage
- Age-dependent (young and old)
- More frequent in **pregnancy**
- Immune status is critical

# *L. monocytogenes* Intracellular Life Cycle

Tilney and Portnoy



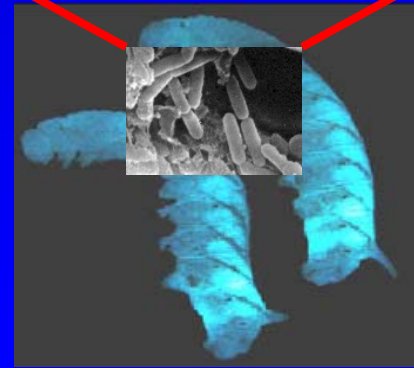
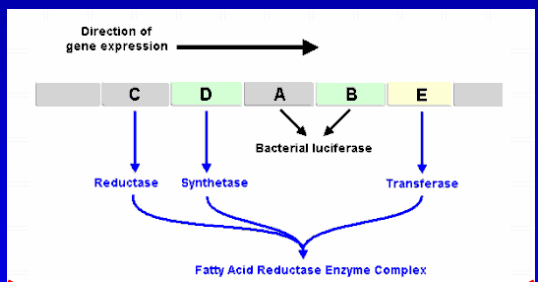
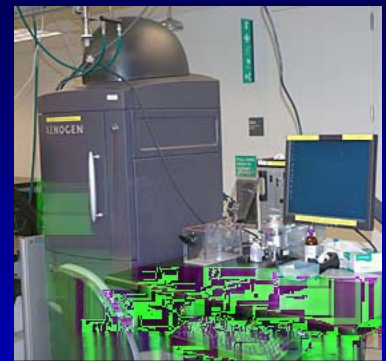
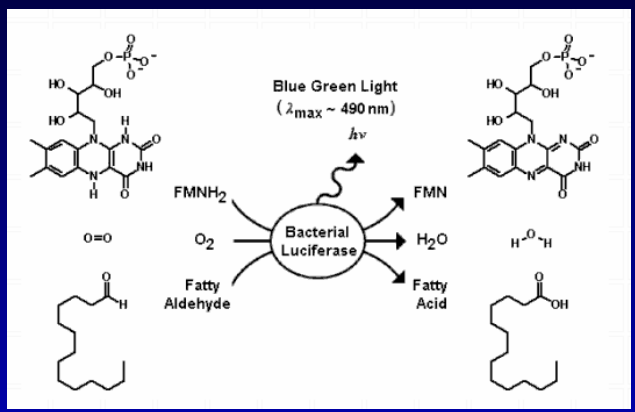
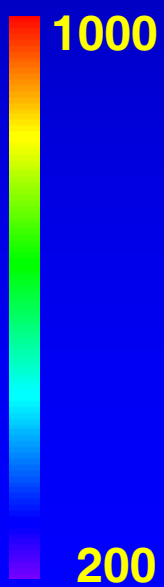
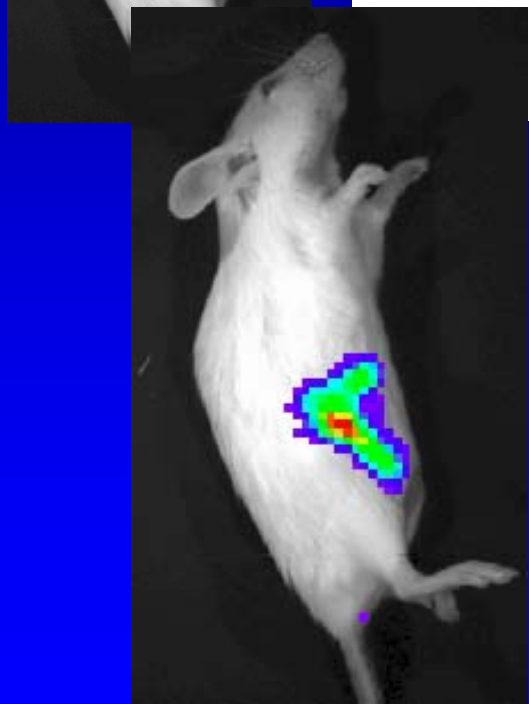
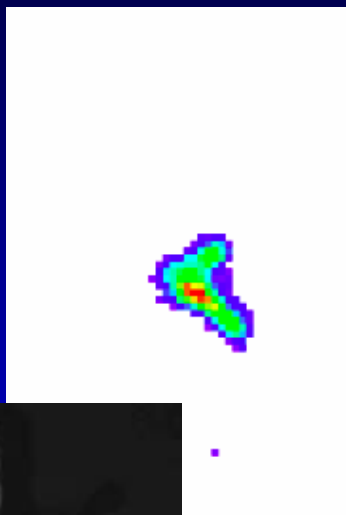
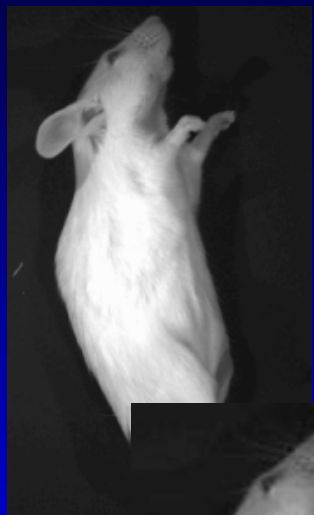
# Organs Infected by *L. monocytogenes*

- Intestine
- Lymph nodes
  - Liver
- Spleen
- Brain
- CNS
- Bones
- Heart

How can one hope to monitor  
all of these in every animal?



# In Vivo Bioluminescence Imaging (BLI)



Xenogen Corp.  
Alameda CA, USA

*Photobacterium luminescens*



# 1 LD<sub>50</sub> (4×10<sup>4</sup> CFU)

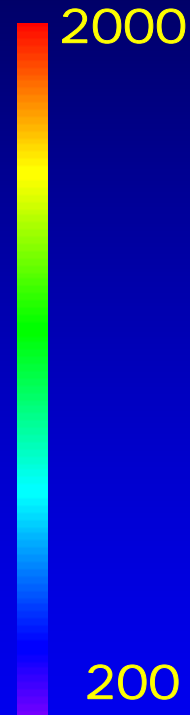
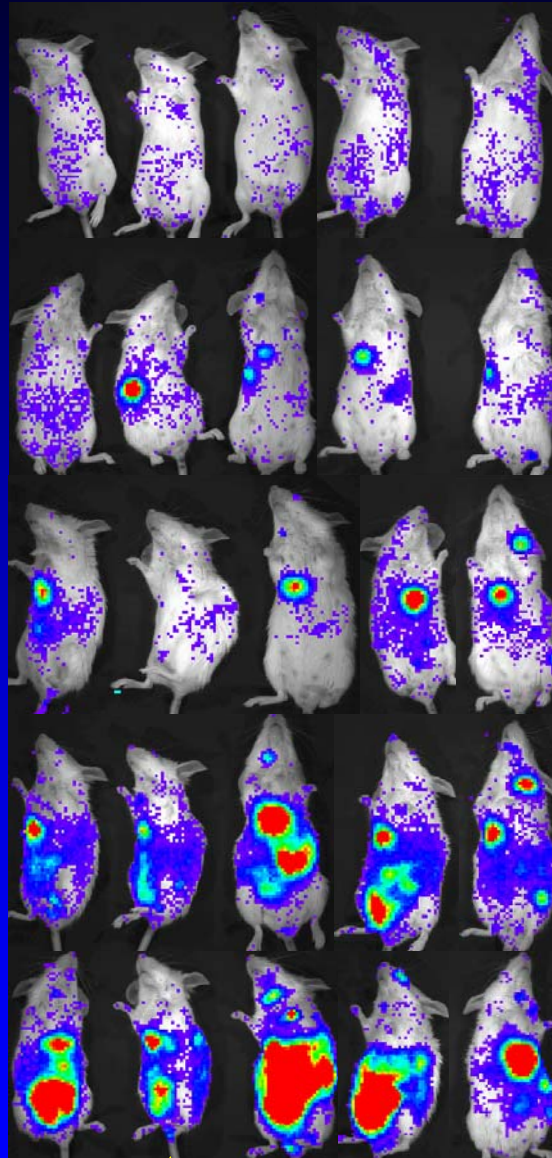
Day 1

Day 2

Day 3

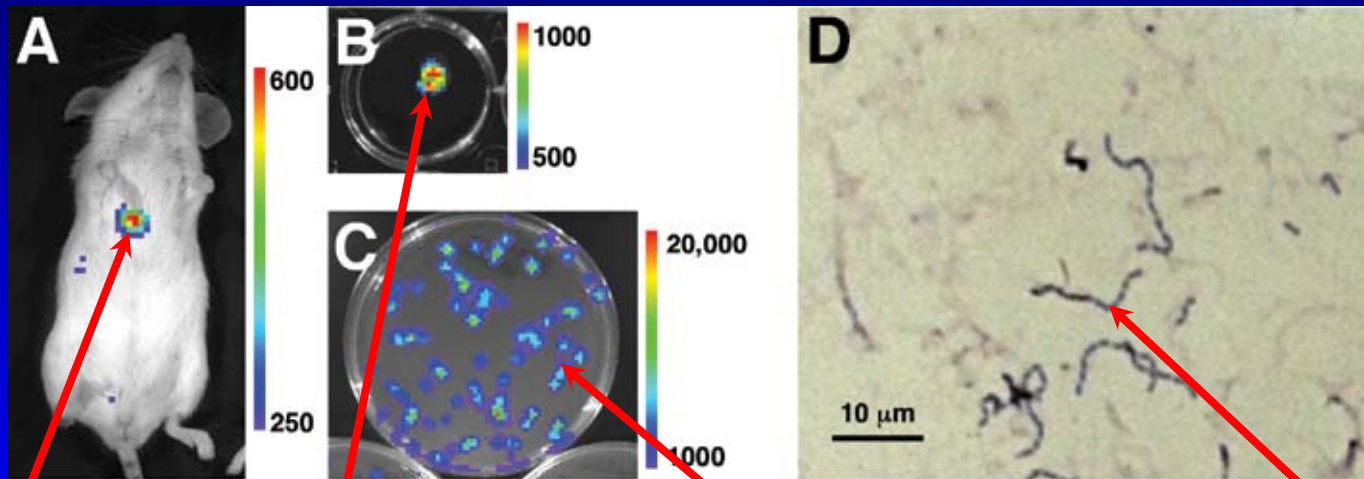
Day 4

Day 5



Survived

# Localization of Focal Signal to the Gall Bladder Lumen



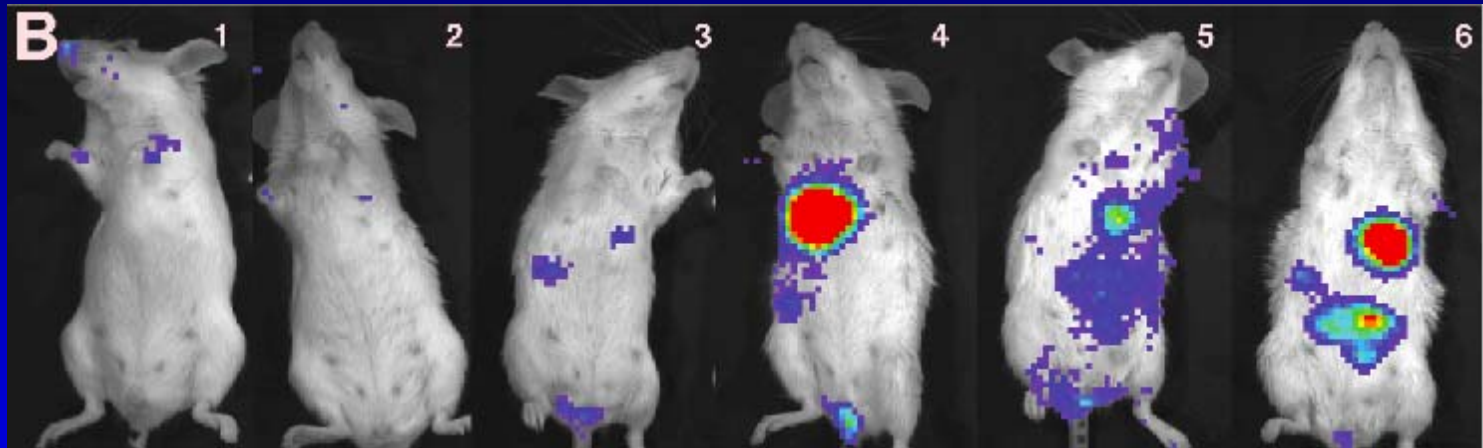
1. BLI Signal

2. Excised gall bladder

3. Colonies from  
lumen on a petri  
dish

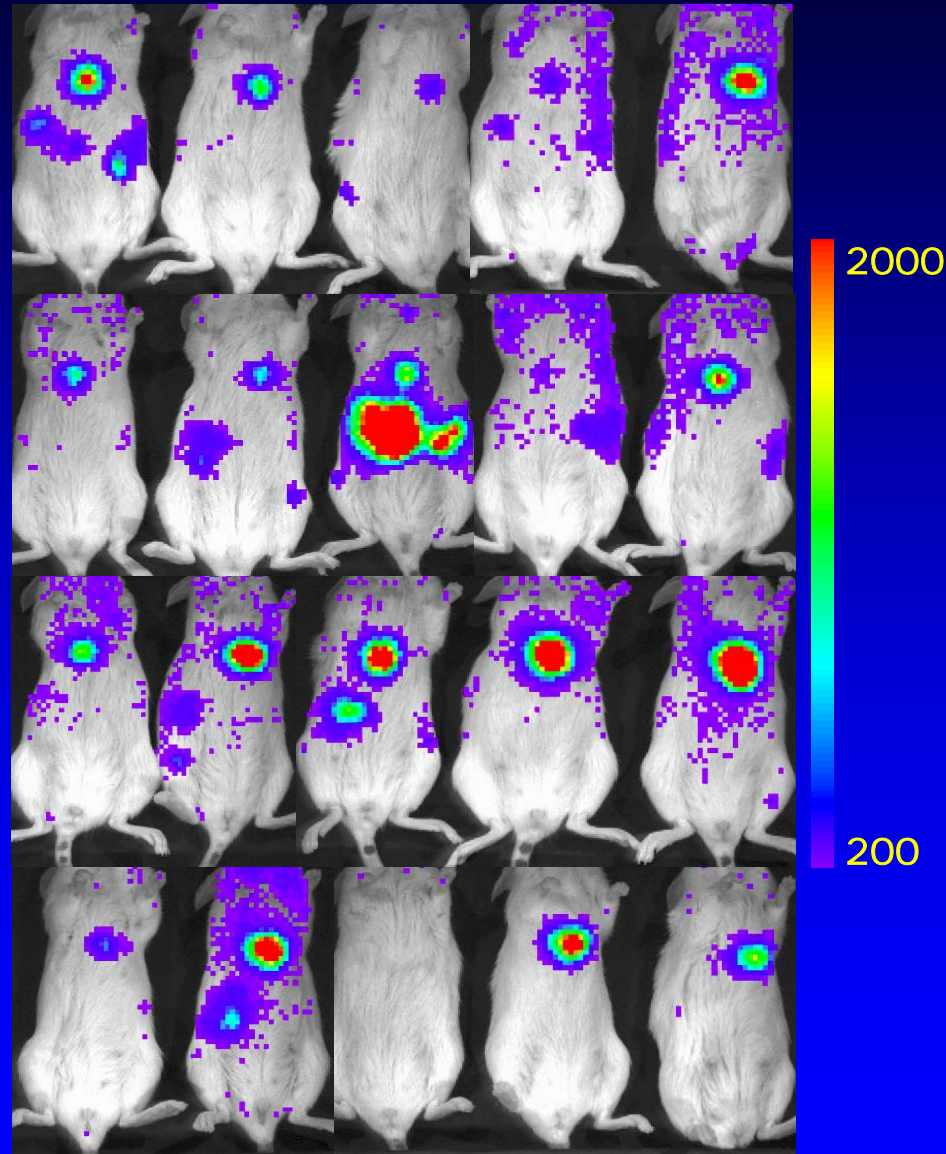
4. Bacteria in the  
lumen by histology

# Oral Infection



# Frequency of Gall Bladder Signals

20 CD1 female mice given  $5 \times 10^5$  CFU of *Listeria*, imaged on Day 2



# Unusual Morphology of Intraluminal *L. monocytogenes*



Pauline Chu, Comparative Medicine

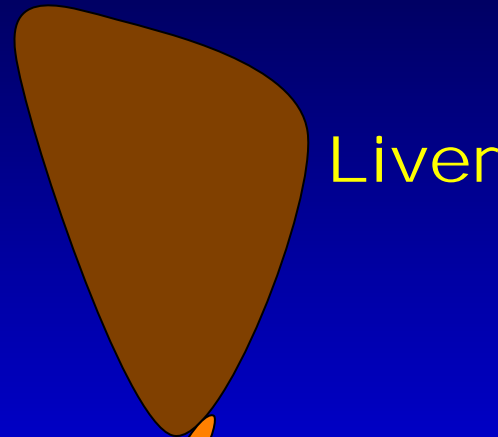


# Intraluminal *L. monocytogenes*





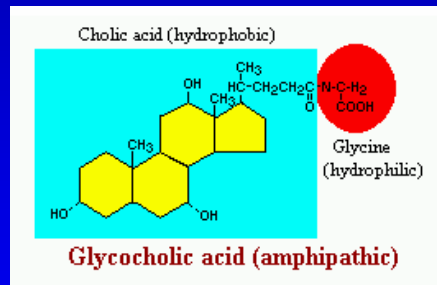
# The Gall Bladder



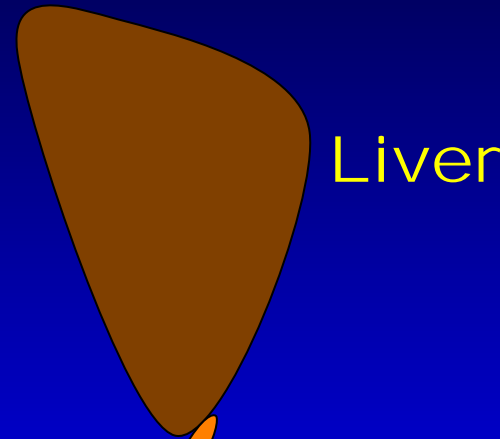
Bile duct

Gall Bladder

Intestine

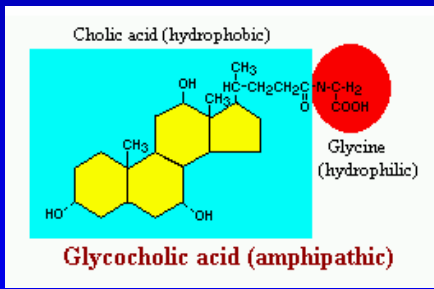
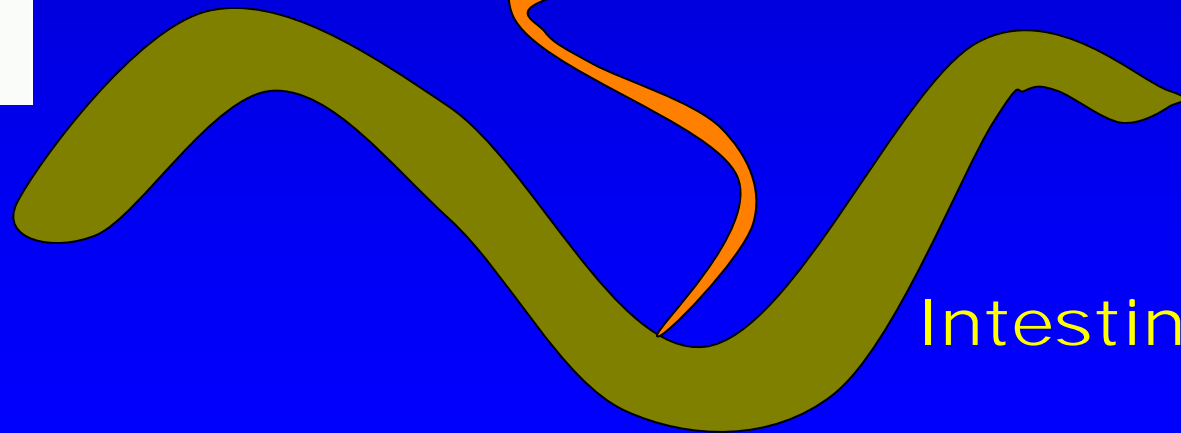


# The Gall Bladder



Bile duct

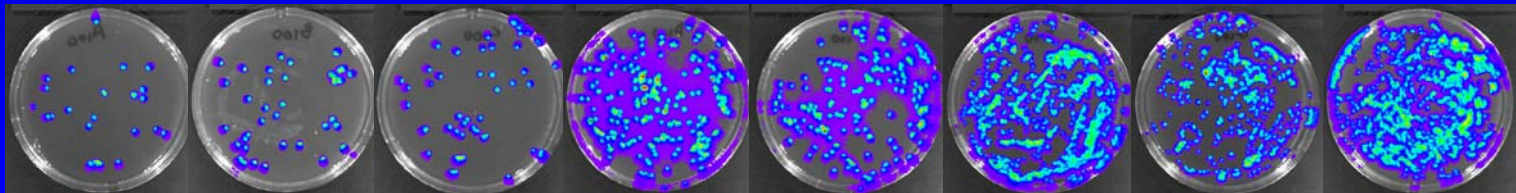
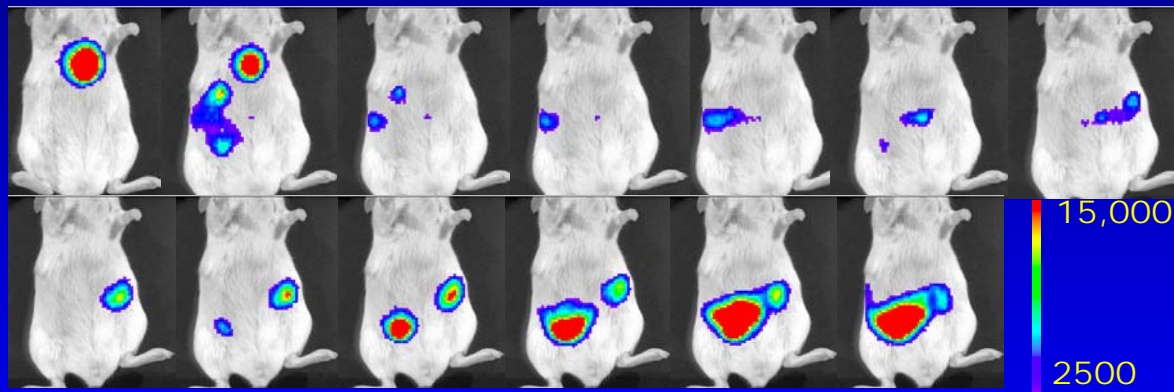
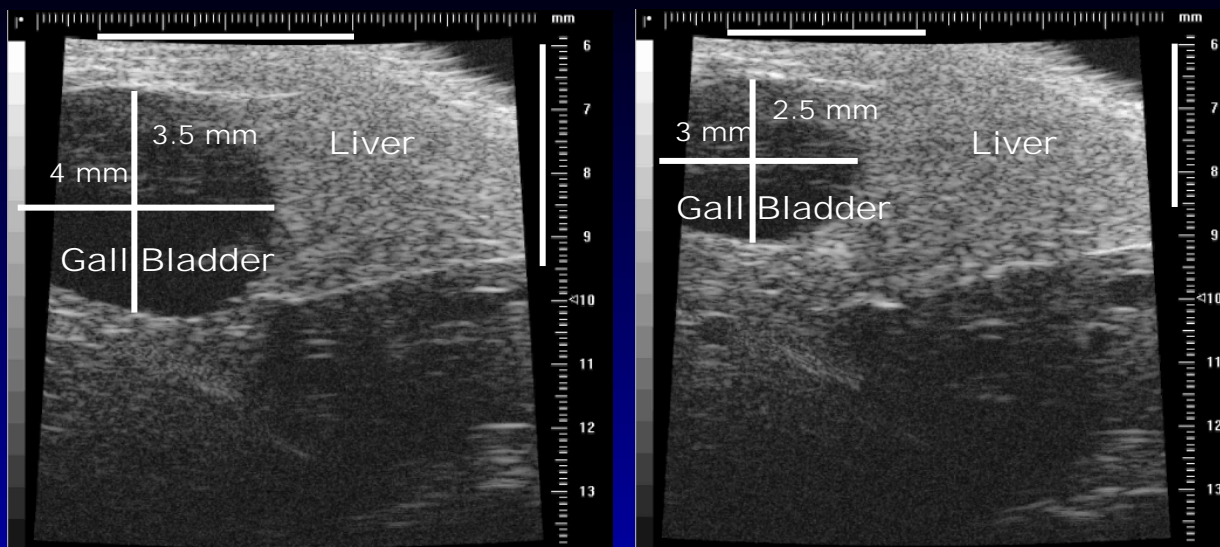
Gall Bladder



# Questions at this Point

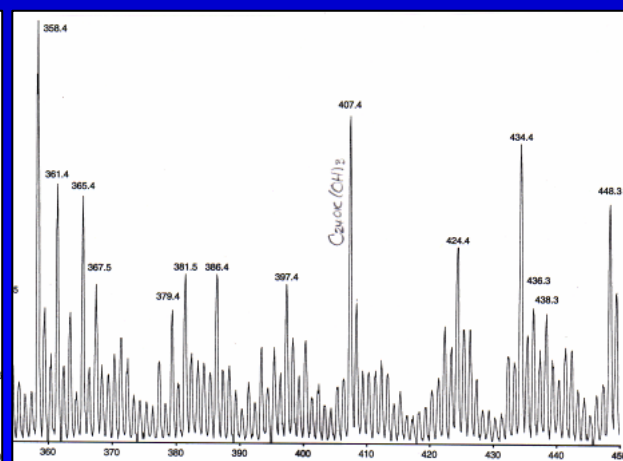
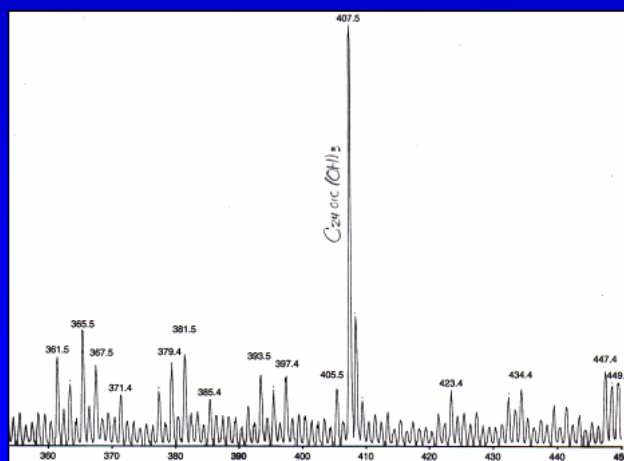
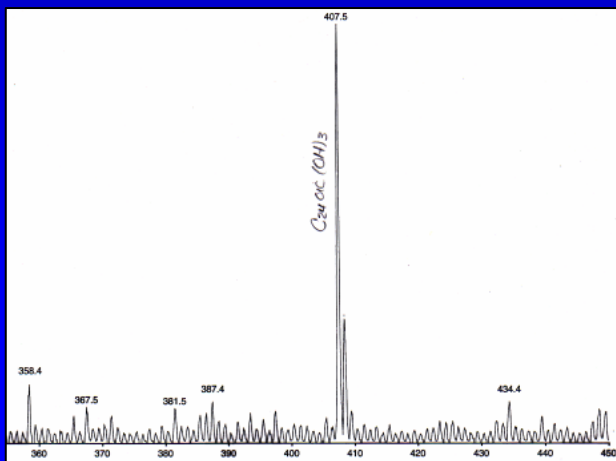
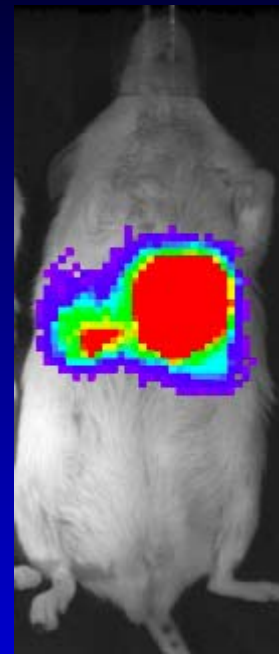
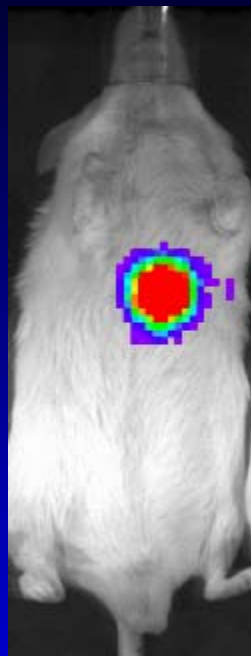
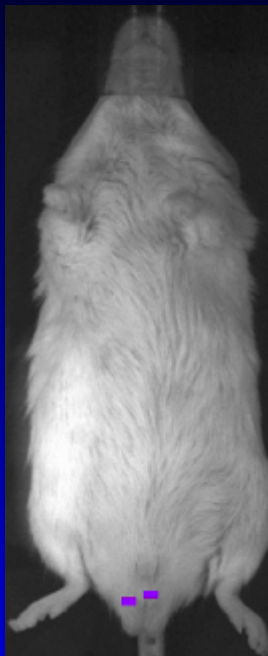
- What is the food source of the bacteria?
- Do they adhere to mucus, and if so, how?
- What genes are expressed?
- Does this process contribute to disease?
- What effects are seen on the tissue and contents of the organ?
- How do the bacteria mitigate the toxicity of the bile salts and other components of bile?

Can they ever GET OUT?



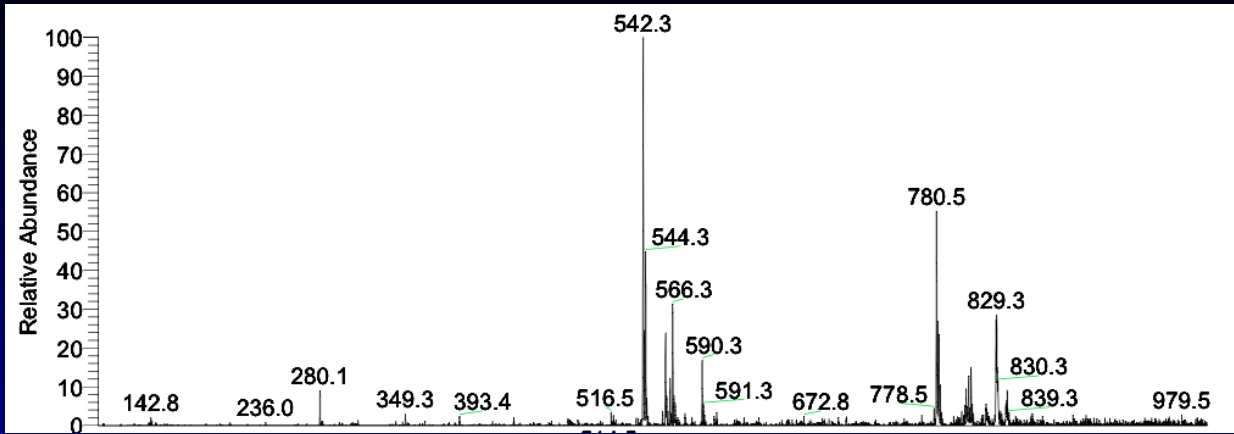
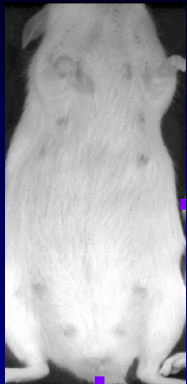
Jeff Margolis

Alan Hofmann

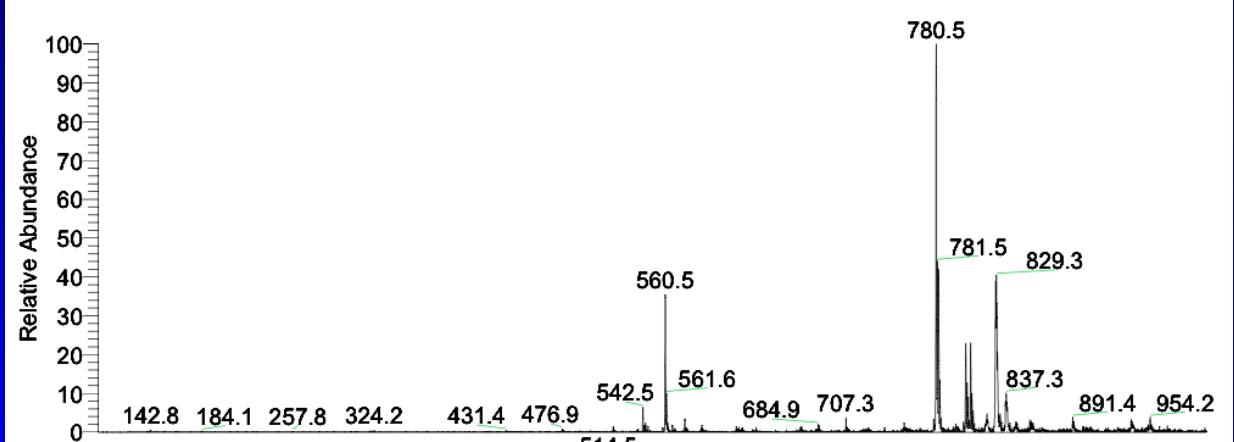
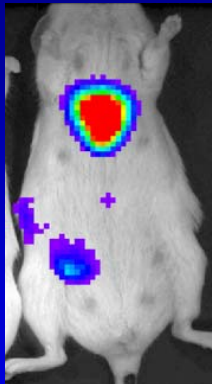




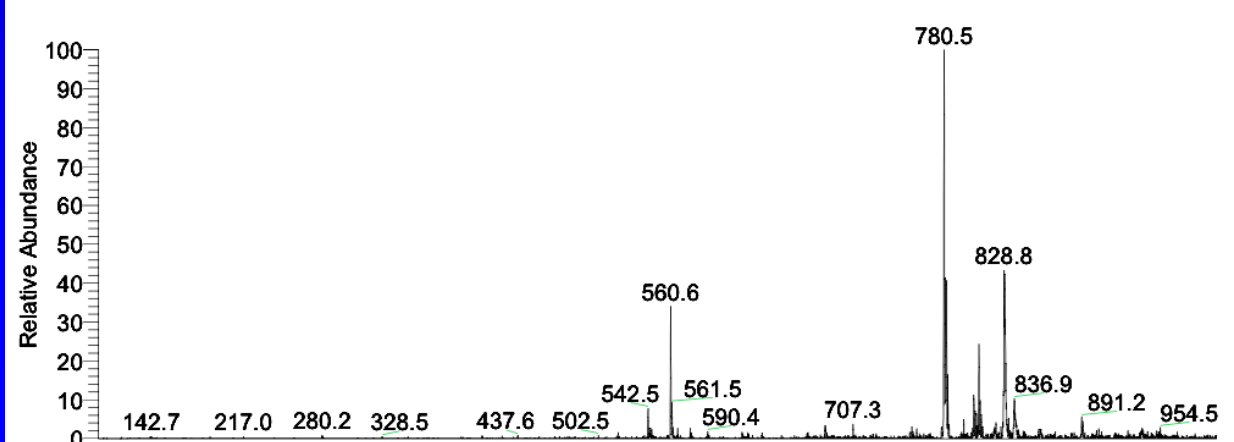
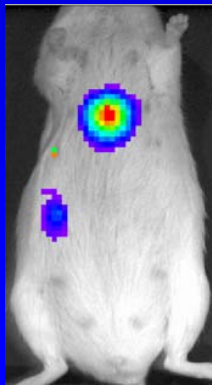
A



B

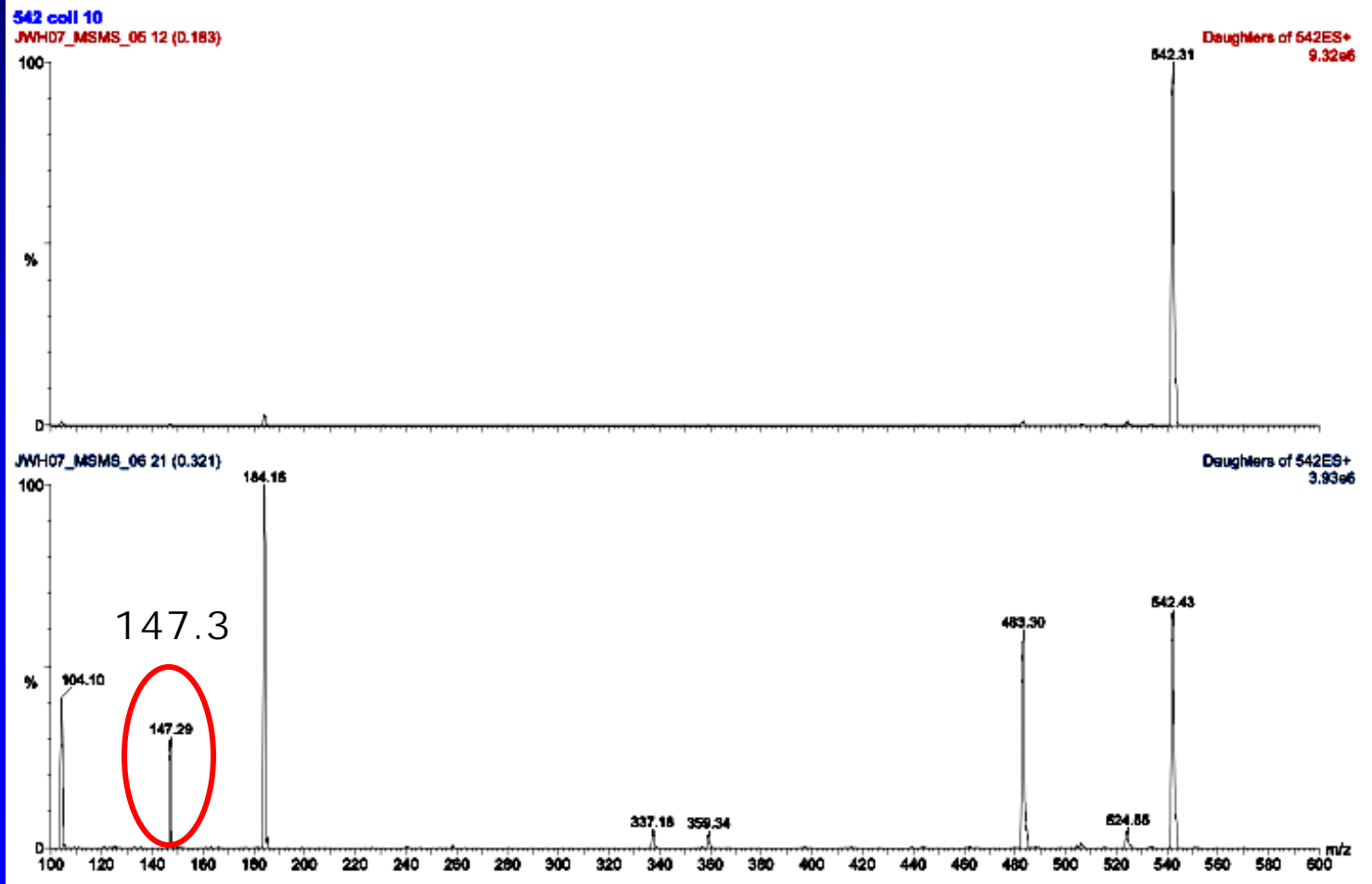


C

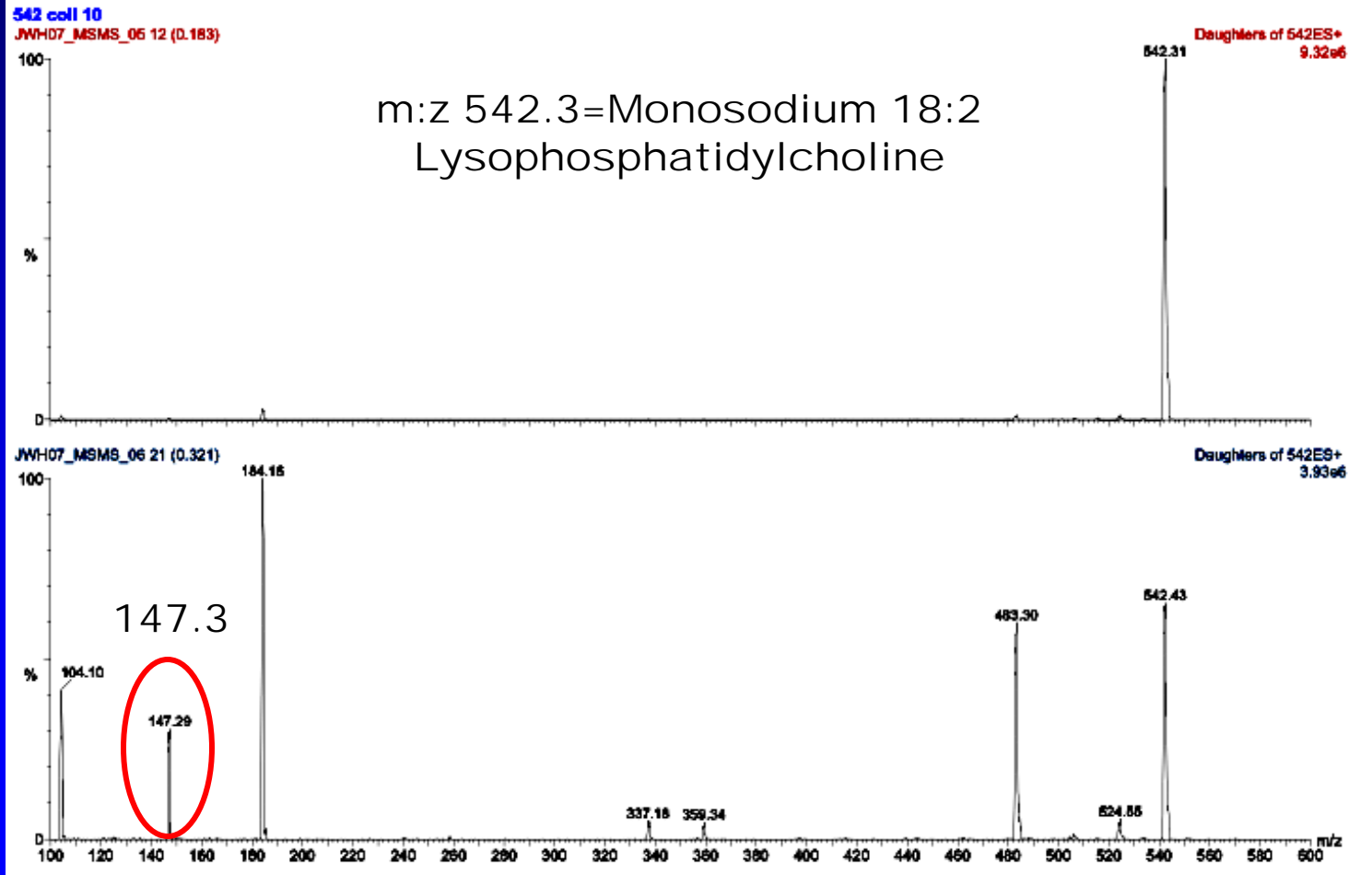


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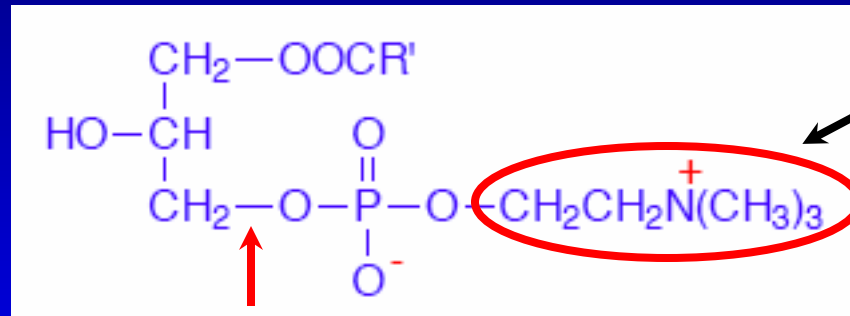
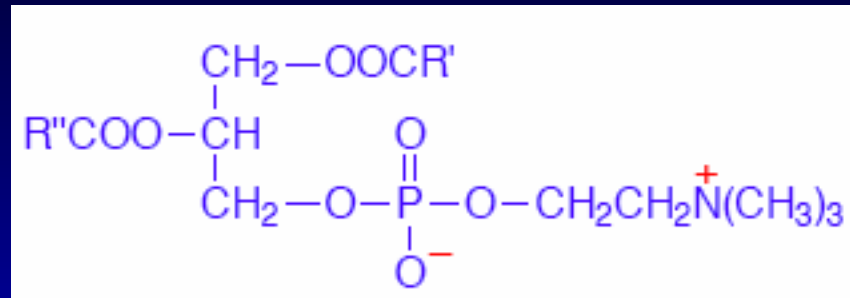
# Daughters of 542.3



# Daughters of 542.3



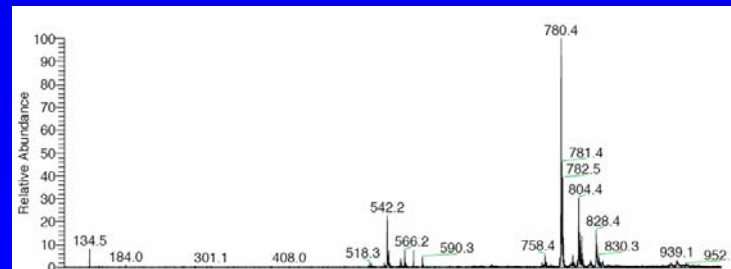
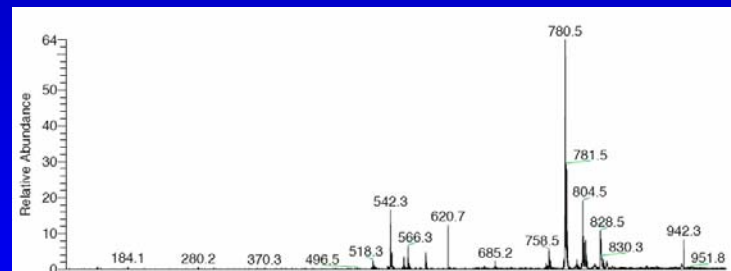
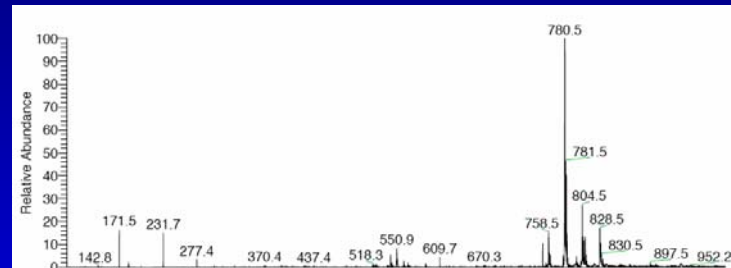
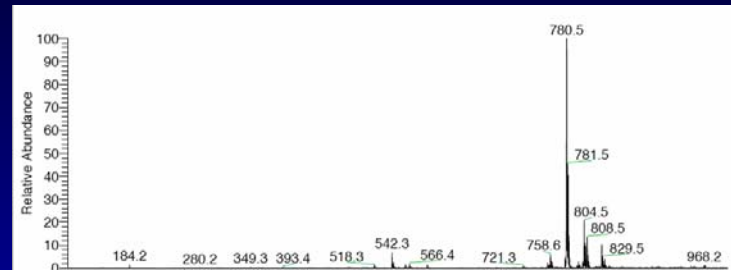
# 18:2 Lysophosphatidylcholine



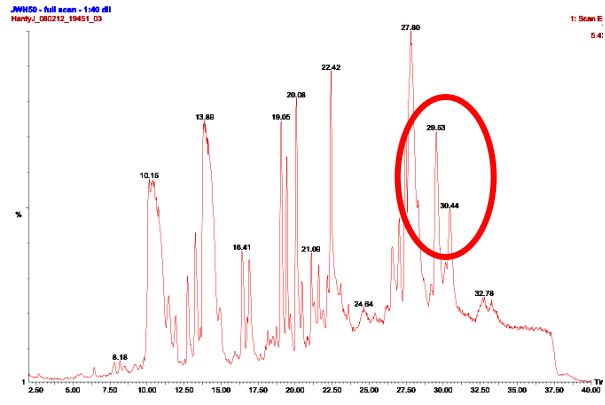
Choline group

R' = 18-Carbon chain  
with two double bonds

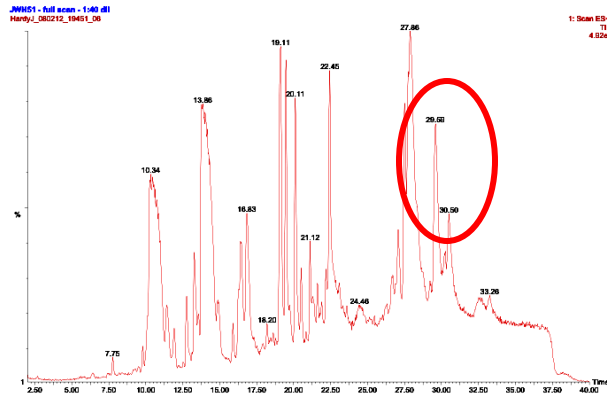
# Uninfected Animals



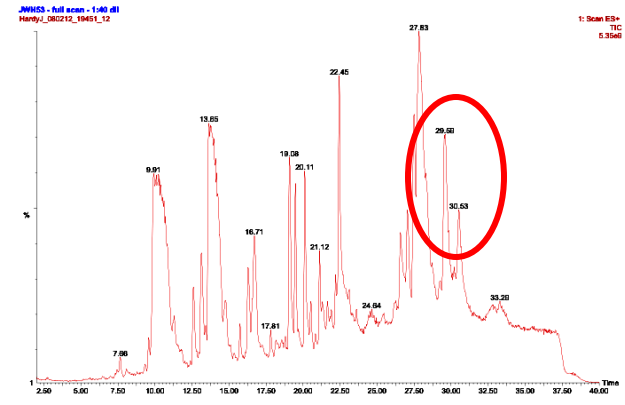
JWH 50 - positive mode ESI - chromatogram



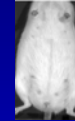
JWH 51 - positive mode ESI - chromatogram



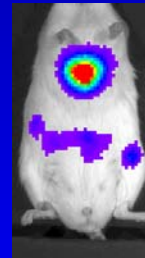
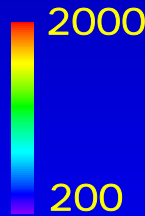
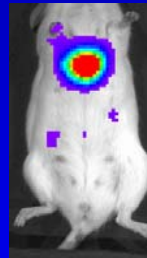
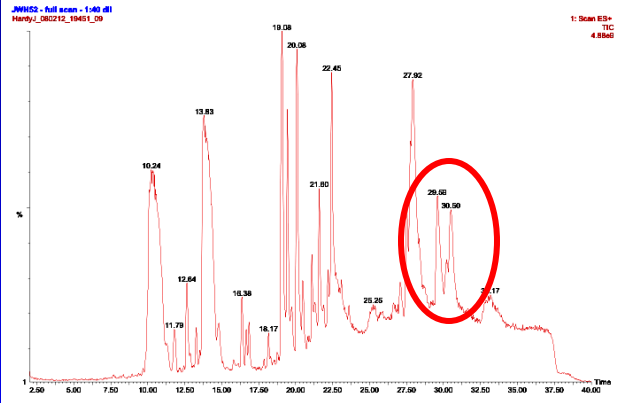
JWH 53 - positive mode ESI - chromatogram



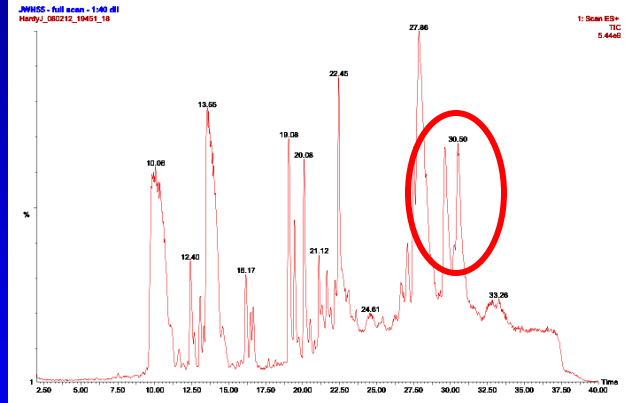
Uninfected



JWH 52 - positive mode ESI - chromatogram



JWH 55 - positive mode ESI - chromatogram



Infected

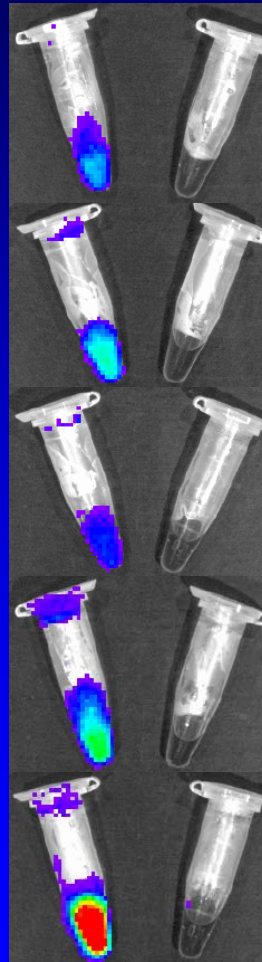
Infected



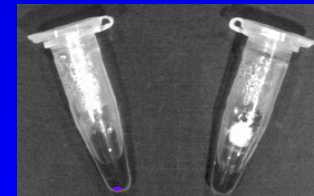
# *L. monocytogenes* Grows in Pure Bile

Human Bile  
1:3 in H<sub>2</sub>O  
+10<sup>6</sup> CFU of  
Listeria

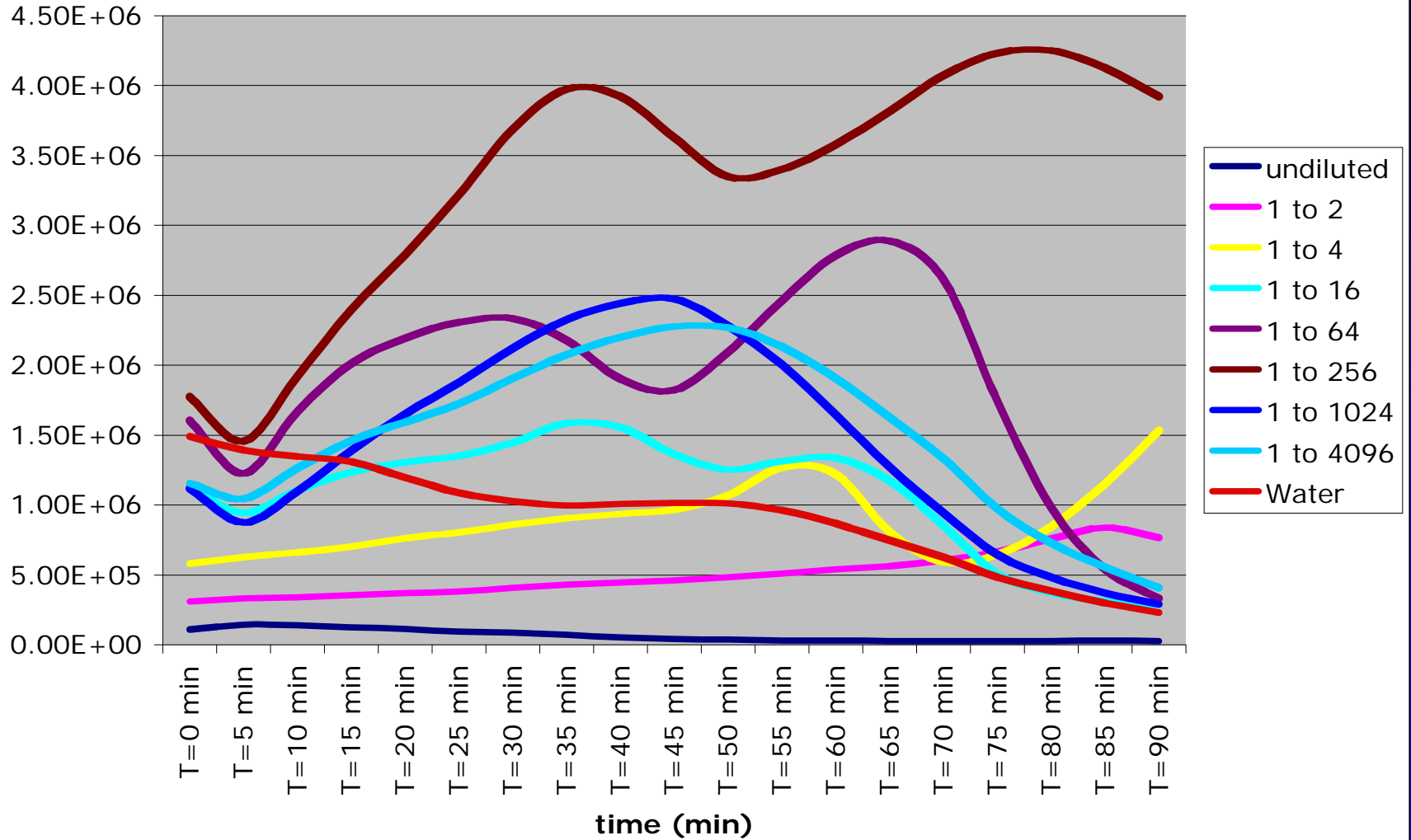
T=0  
30 min  
60 min  
90 min  
120 min



20 hours



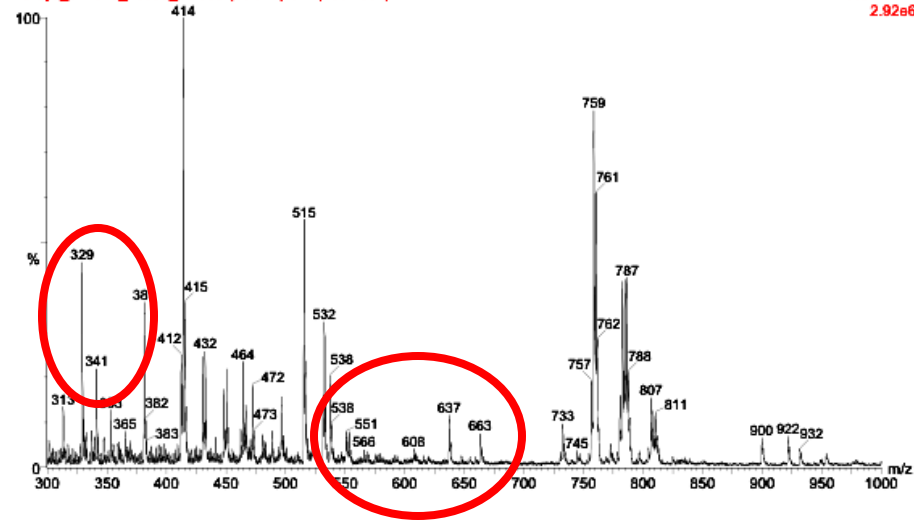
# Bile Culture Dilutions



**JWH47 - full scan**

HardyJ\_071015\_18853\_08 953 (30.924) Cm (265:1087)

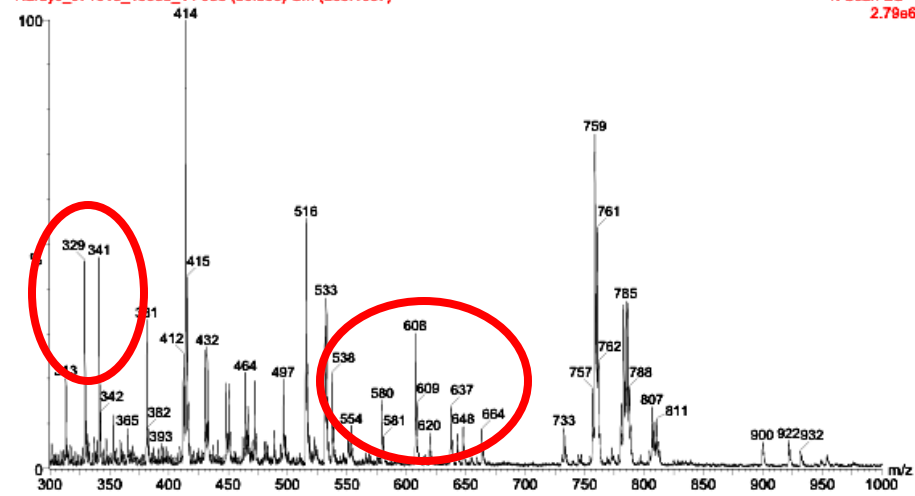
1: Scan ES+  
2.92e6



**JWH49 - full scan**

HardyJ\_071015\_18853\_14 950 (30.833) Cm (265:1087)

1: Scan ES+  
2.79e6



# Proteins in Mouse Bile

- Pancreatic amylase
- Immunoglobulins (antibodies)
  - Pancreatic lipases
  - Sterol esterases
- Carboxypeptidases
  - Collagen
- $\alpha$  Andrenergic receptor?
- Transcription initiation factor TFIID?

# The Future

- More *in vitro* cultures with mouse bile, which is cleaner and has less variation
- More mice with the attenuated strain which grows for a long time without making the mice sick
- More protein data from both *in vitro* and mouse samples to look for *Listeria* proteins (!)
- Use pure substances and look for changes upon culture, which will be tricky
- Use bacterial mutants such as phospholipase mutants

# People to Thank

Jeff Margolis

Pauline Chu

Alan Hofmann

Lee Hagey

Janet Bueno

Cormac Gahan

Allis Chien

Karolina Krasinska

Theresa McLaughlin

Lindsay Comeaux

Chris Adams

Christopher H. Contag