

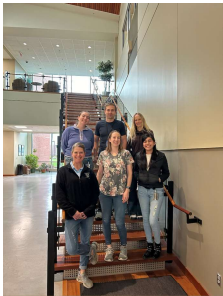
The influence of obesity on pulmonary infection with high consequence pathogens

Catharine M. Bosio, PhD Senior Investigator

Immunity to Pulmonary Pathogens Section Laboratory of Bacteriology

Horizontal lines for notes

Immunity to Pulmonary Pathogens Section Laboratory of Bacteriology

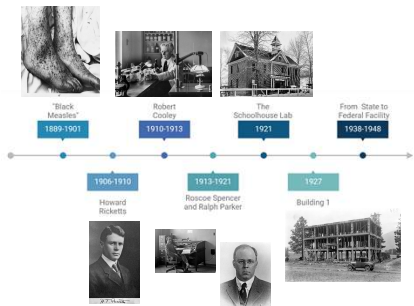


Others Emily Speranza - The Cleveland Clinic Craig Martens - NIAID/RTB Stacy Ricklefs - NIAID/RTB Animal Care Staff - RMVB

Molly Miltko Forrest Jessop, PhD Tara D. Wehrly Lydia M. Roberts, PhD Monica A. Valtierra, PhD


Horizontal lines for notes

Rocky Mountain Laboratories



Horizontal lines for notes

Rocky Mountain Laboratories

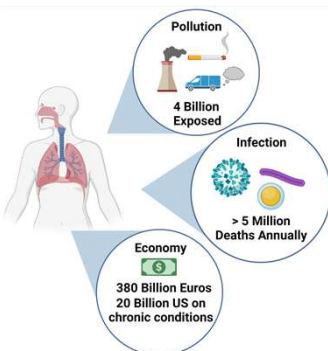


Laboratory of Virology: Ebola virus, Marburg virus, Coronavirus, CCHF, Nipah

Laboratory of Neurological Infection and Immunity: Prions, West Nile Virus, Lacrosse Virus

Laboratory of Bacteriology: Yersinia pestis, Coxiella Burnetii, Staphylococcus, Borrelia, Rickettsia, Chlamydia, Francisella tularensis

The Impact of Respiratory Diseases on Human Health



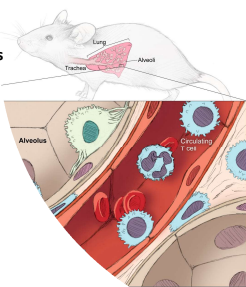
Pollution
4 Billion Exposed

Infection
> 5 Million Deaths Annually

Economy
380 Billion Euros
20 Billion US on chronic conditions

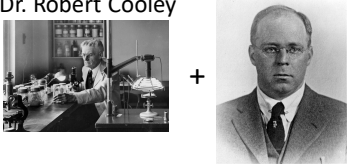
The Lung is Architecturally and Immunologically Complex

- Major Cell types/Spaces
- Airway Epithelial
- Alveolar Cells
- Pneumocytes
- Interstitial Connective Tissue
- Hematopoietic and Lymphoid Tissue
- Vascular Endothelium
- Lymphatics
- Pleura







Tularemia: History in Montana

Dr. Robert Cooley + **Dr. Ralph Parker**



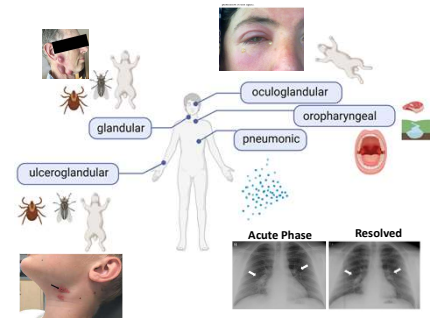
- Cooley and Parker connection through Massachusetts Agricultural College
- 1914 Cooley invites Parker to Montana to study flies and typhoid
- 1915 Parker obtains PhD and joins the Montana State Entomology Board
- 1918 Parker moves to the Bitterroot Valley to study RMSF
- Works with Dr. Roscoe Spencer at Hygienic Lab at NIH to develop RMSF vaccine
- Parker interest in ticks and Tularemia
- 1923 Parker and Dr. Edward Francis published first report the tularemia was a vectored pathogen
- 1940 Parker publishes widespread contamination of Francisella in natural streams

Francisella tularensis and Tularemia

Public Health Threat	Transmission	Target Cells	Characteristics
			
Persistent Natural Exposures Weaponized and Tested BSL-3/ABSL-3 Tier 1 Select Agent	Zoonotic with multiple vectors Readily Aerosolized < 25 CFU = Lethal	Macrophage/Dendritic Cells = Primary Permissive for other cell types	Small Gram negative Cocci/bacillus Tetraacylated LPS O-Antigen Capsule Facultative Intracellular

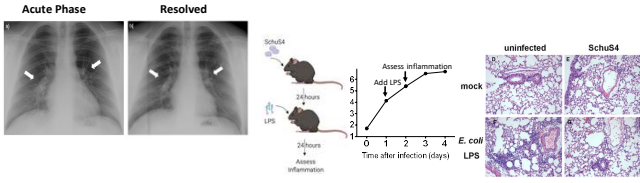
Tularemia: Forms and Presentation

- Acute Onset
- Exposure to the outdoors
 - Hiking, hunting, camping
- Agricultural Setting
- Fever
- Malaise
- Cough (end stage)



Features of Innate and Adaptive Immune Responses to Virulent Francisella

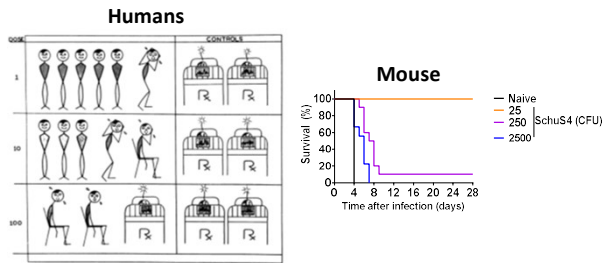
Francisella Evades and Suppress Innate Responses



Tarrnik and Berglund, 2003, Eur Respir J, 21:361
Bosio CM et al, 2007, J Immunol, 178:4538

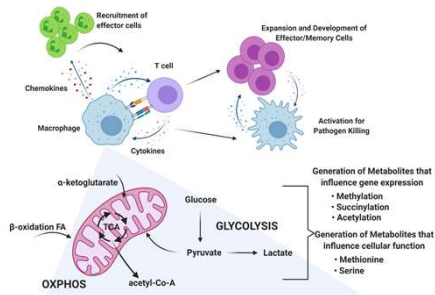
Features of Innate and Adaptive Immune Responses to Virulent Francisella

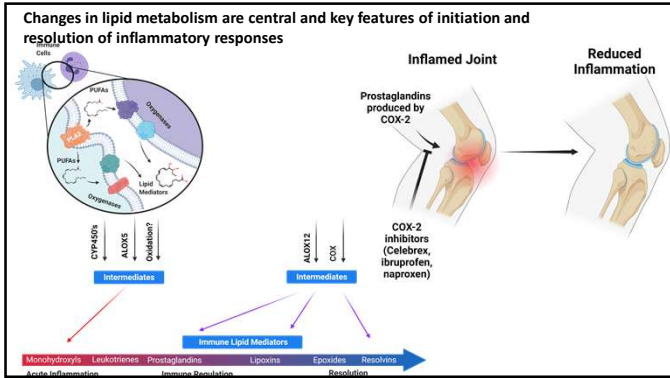
Live Vaccine Strain (LVS) Fails to Provide Durable Protection



McCumb, E. Bacterial Rev. 1961, 25:267

Changes in Metabolism are Central and Key Features of Developing Immune Responses





Metabolic Reprogramming of Host Cells by Virulent *Francisella tularensis* for Optimal Replication and Modulation of Inflammation

Elliott V. Wyatt, Karina Diaz, Amanda J. Griffin, Jed A. Rasmussen, Deborah D. Crane, Bradley D. Jones and Catharine M. Bosso

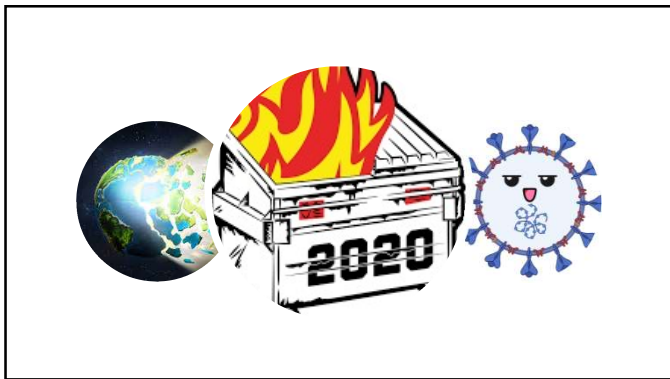
J Immunol 2016; 196:4227-4236; Prepublished online 30 March 2016; doi: 10.4049/jimmunol.1502456 <http://www.jimmunol.org/content/196/10/4227>

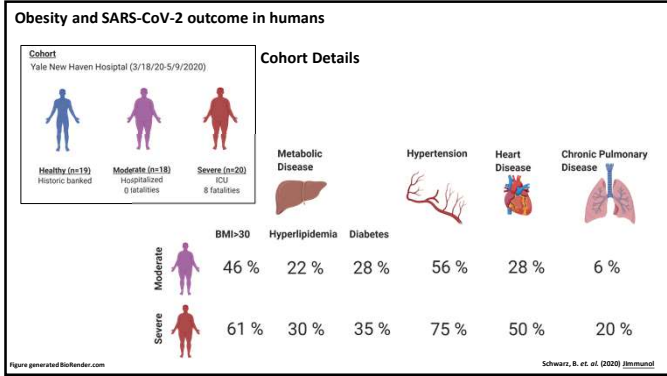
Temporal Manipulation of Mitochondrial Function by Virulent *Francisella tularensis* To Limit Inflammation and Control Cell Death

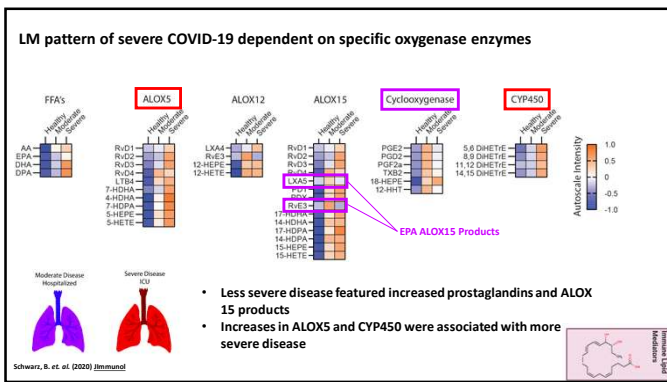
Francois Jacquot, Benjamin Schwart, Emily Nettleton, Robert Baugty, Tara Whaley, Catharine M. Bosso

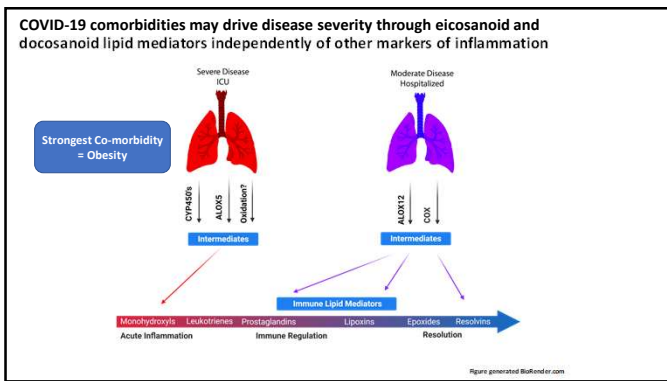
Interferon Gamma Reprograms Host Mitochondrial Metabolism through Inhibition of Complex II To Control Intracellular Bacterial Replication

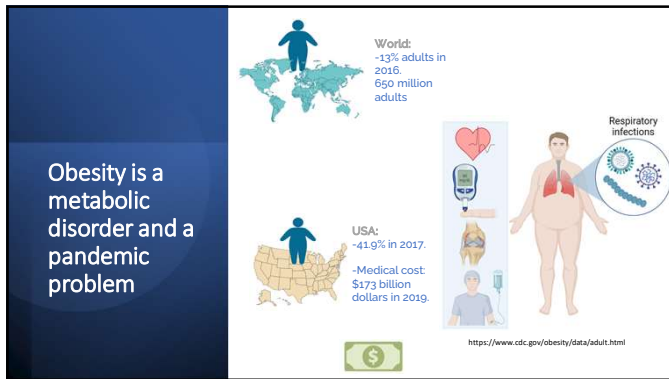
Francois Jacquot, Robert Baugty, Benjamin Schwart, Tara Whaley, Drew Scott, Catharine M. Bosso

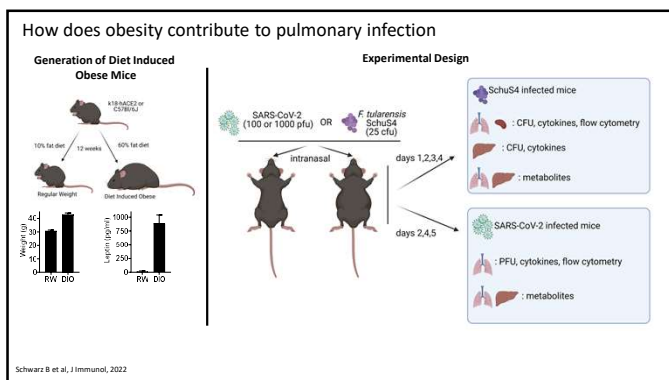


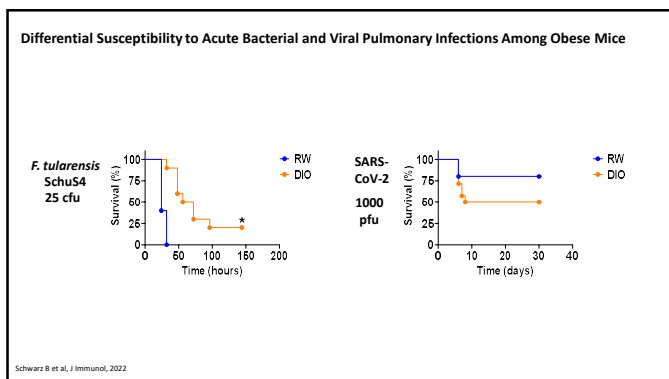


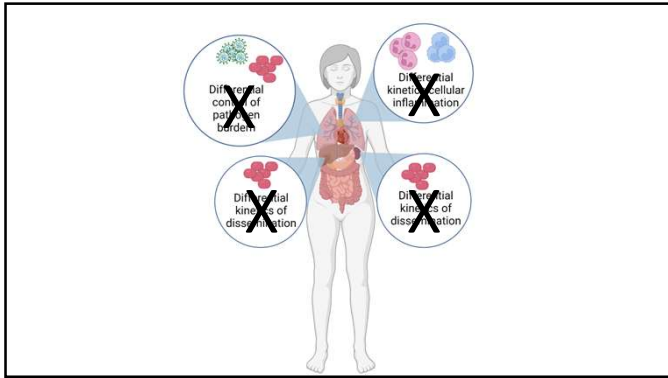


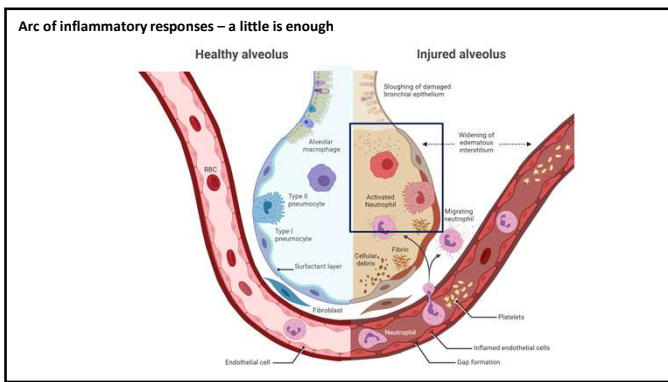


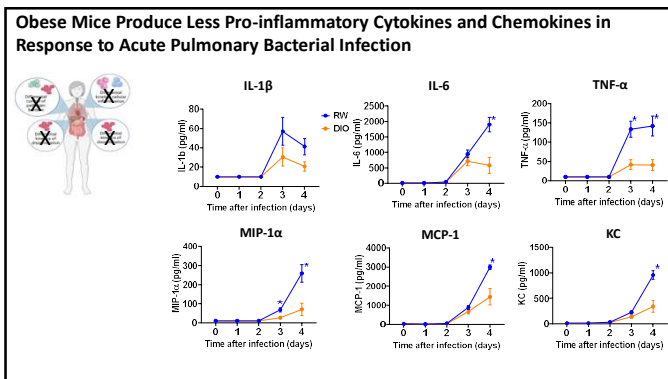




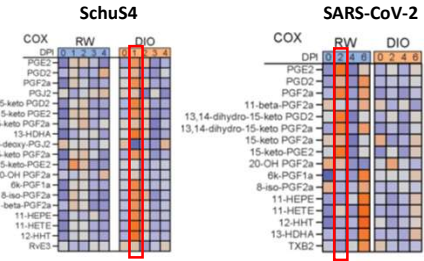






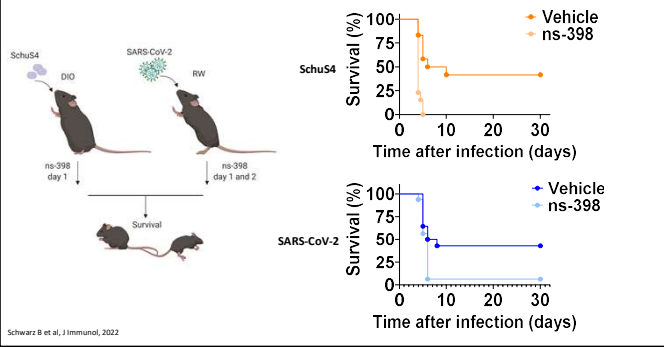


Increased survival associated with early production of COX products (prostaglandins)



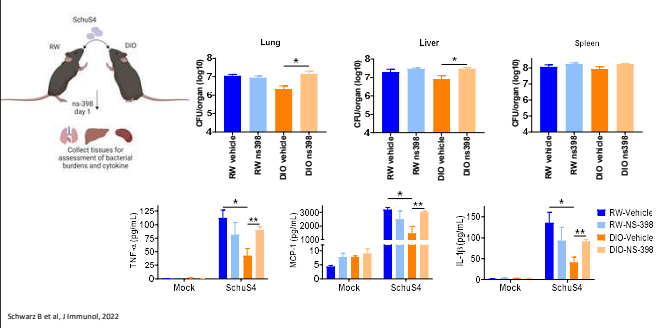
Schwarz B et al, J Immunol, 2022

Early inhibition of Cox-2 reverses protective phenotype during SchuS4 and SARS-CoV-2 infection



Schwarz B et al, J Immunol, 2022

Early inhibition of Cox-2 in DIO mice increases bacterial load and reverses dampened cytokine response



Schwarz B et al, J Immunol, 2022

Does the obesity advantage extend to other bacterial infection?

Bordetella pertussis: Whooping cough

Bordetella pertussis

Characteristics

- Gram (-) Cocci bacillus
- Strictly aerobic
- Pertussis toxin
- Adenylate cyclase toxin
- Tracheal toxin

Target cells

Ciliated epithelial cells

Transmission

Highly contagious.
Person to person.
Affect all age groups

Public Health

Life threatening in newborns and young children
24 million cases
161 000 death/year

*<https://www.cdc.gov/vaccines/pubs/pinkbook/pert.html>. *Frenkel LD. Allergy Asthma Proc. 2021

