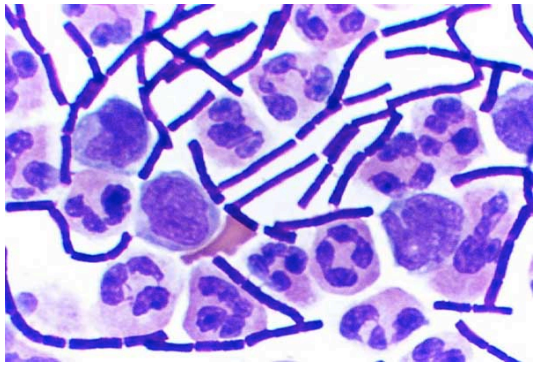
Control of Anthrax Toxin Gene Expression by the Transition State Regulator *abrB*



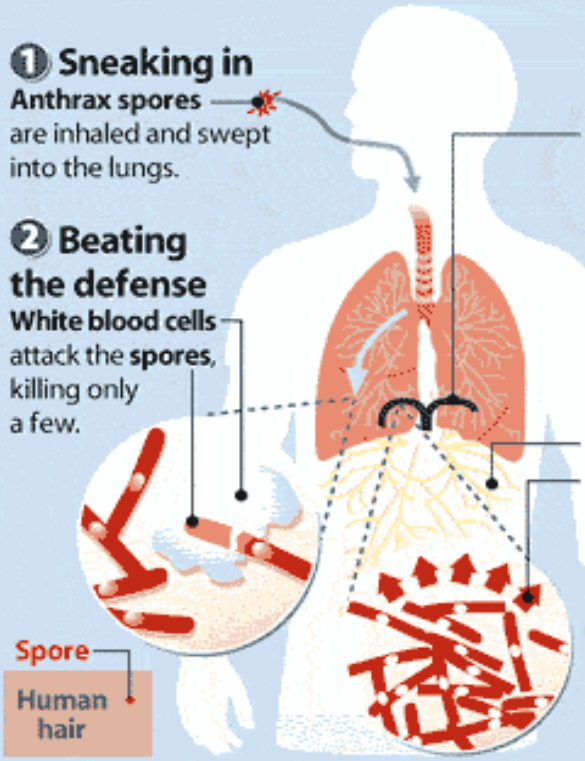
By: Elke Saile and Theresa M. Koehler

Journal of Bacteriology, Jan. 2002, p. 370-380.

Anthrax in the News

HOW ANTHRAX ATTACKS

Anthrax is a naturally occuring bacterium that plagues farm animals and, occasionally, agricultural workers. An airborne form of the disease, however, can be harnessed as a potent biological weapon.



1 Sneaking in

Anthrax spores are inhaled and swept into the lungs.

2 Beating the defense

White blood cells attack the **spores**, killing only a few.

3 Growing

Spores collect in the **lymph nodes** and develop. The immune system of vaccinated people can defeat the infection at this point.

4 Striking

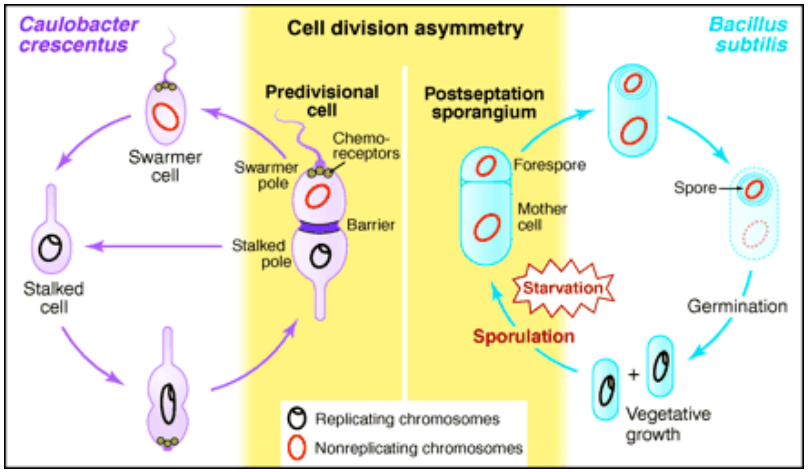
Toxins released by the bacteria spread via the **lymphatic system**. The **poison** causes internal bleeding and severe damage to the tissue of major organs. Once the poison has circulated, antibiotics will not save the victim.

Source: "The World's Best Anatomical Charts"; "Zoology"; Anthrax Vaccine Immunization Program; Journal of the American Medical Association

ADRIAN HOLOVATY/Missourian

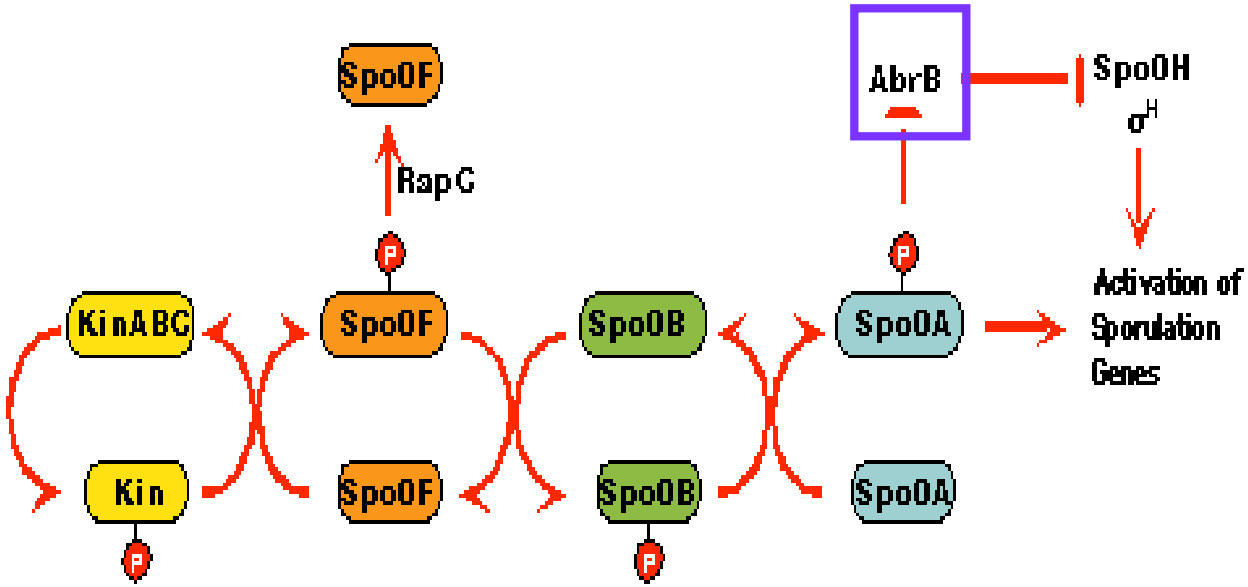
Sporulation

- Vegetative cell splits off. A layer of protein and polysaccharide is made encapsulating the chromosome. The cell lyses and the protection spore is formed.

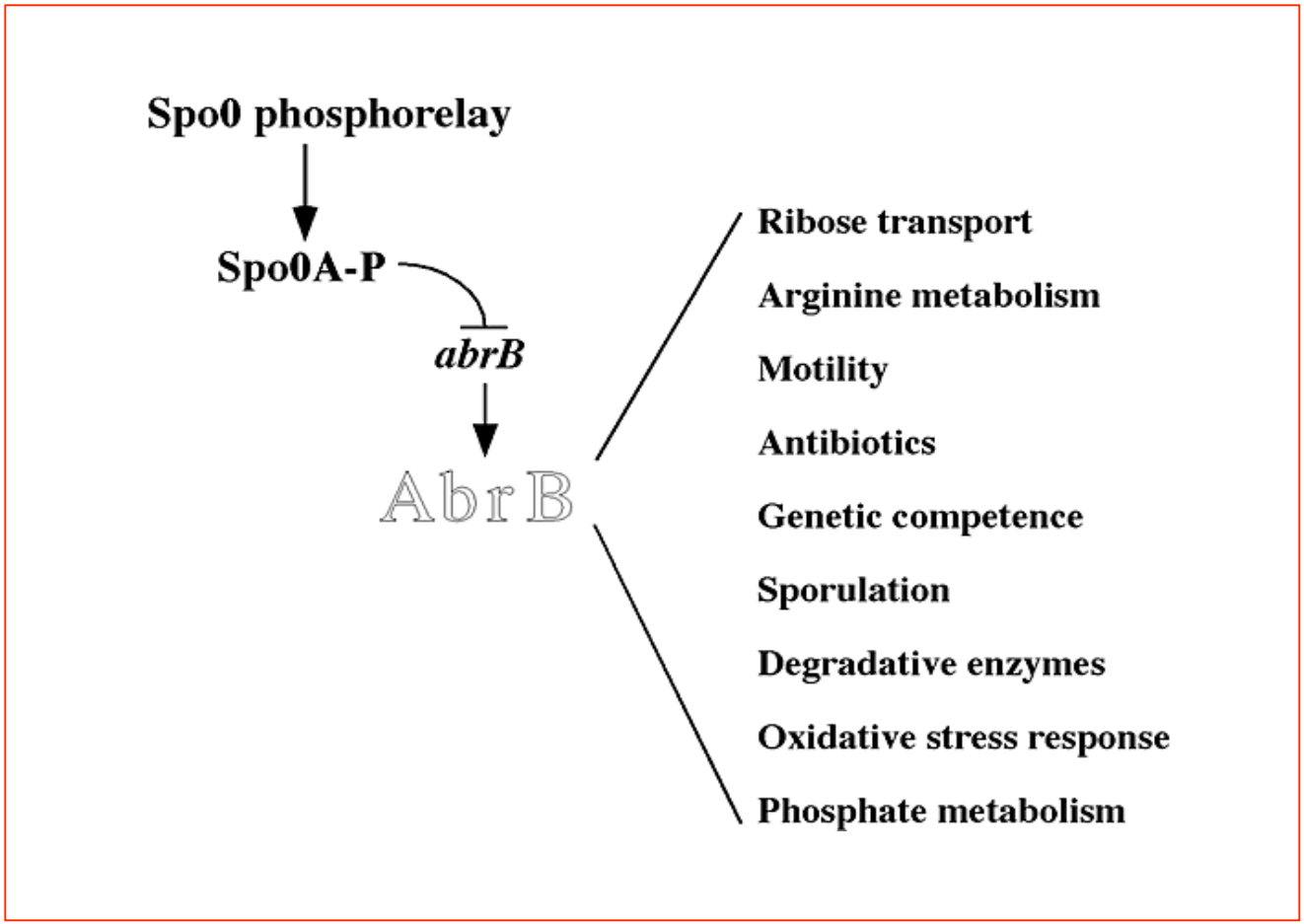


•Environmental stressors include: Starvation, Temperature, pH, cell crowding, antibiotic exposure

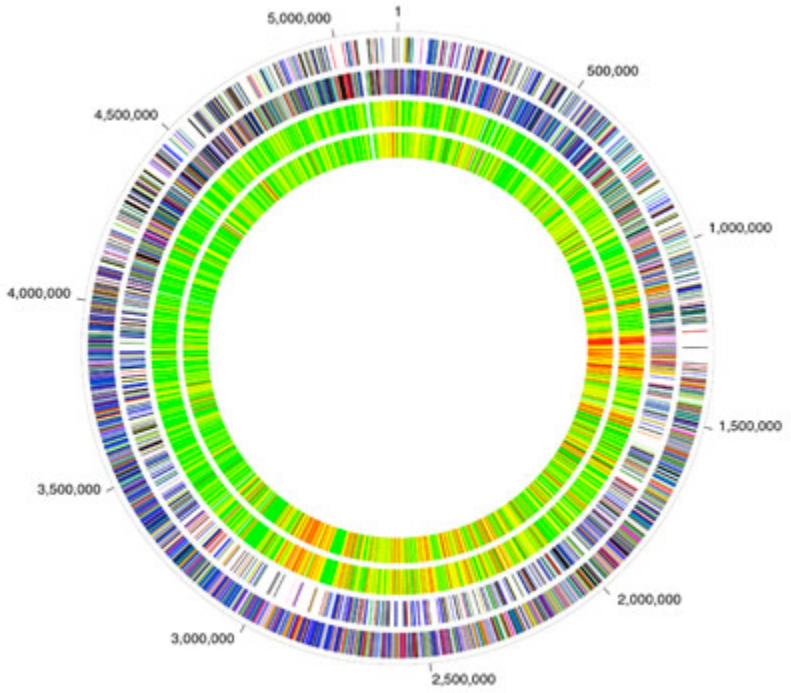
Cell Signaling in *B.subtilis*



AbrB


Spo0 phosphorelay
Spo0A-P
abrB
AbrB
Ribose transport
Arginine metabolism
Motility
Antibiotics
Genetic competence
Sporulation
Degradative enzymes
Oxidative stress response
Phosphate metabolism

B. anthracis genome



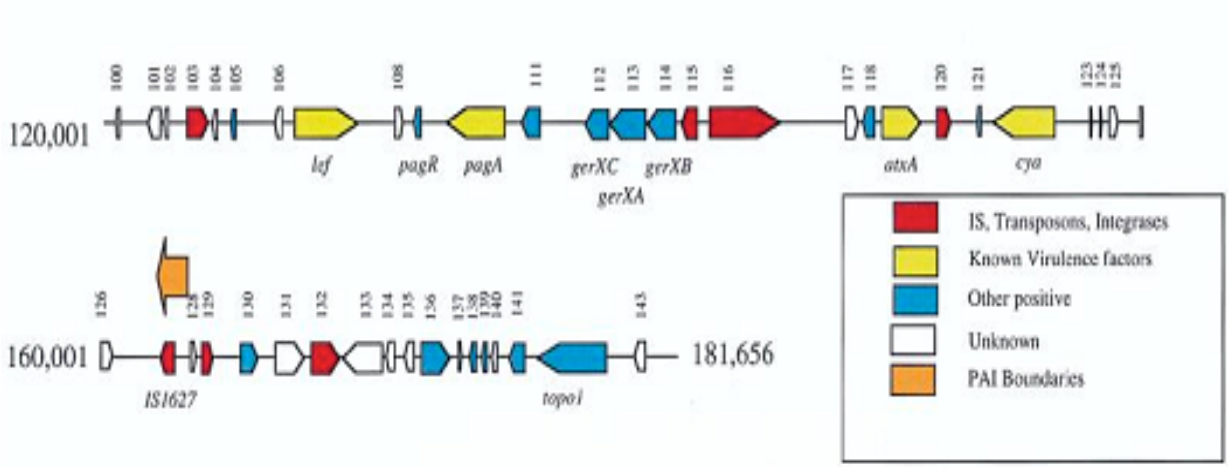
Chromosome

pXO1
182kb

pXO2
95kb

Virulence plasmids

Anthrax Toxins on pXO1

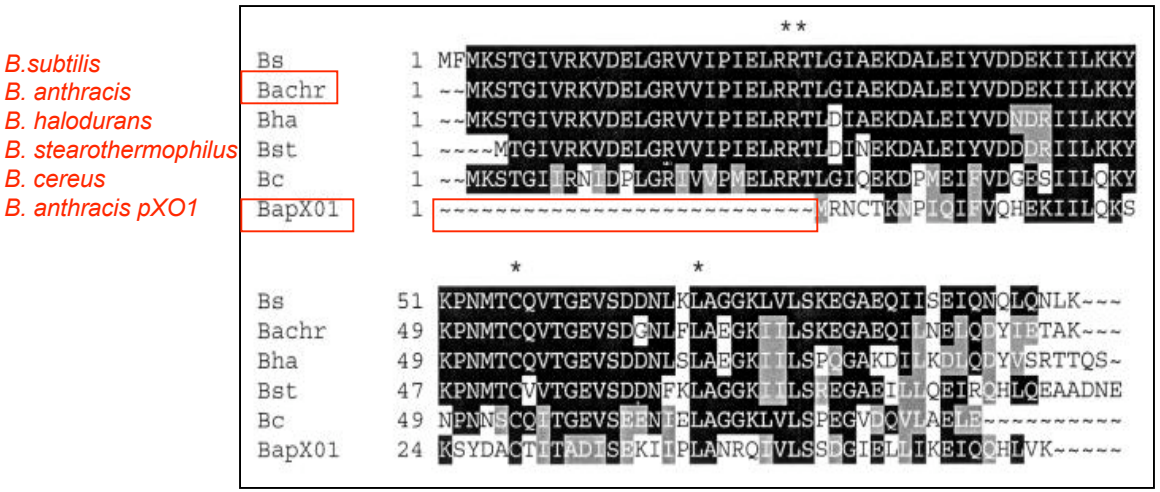


lef: lethal factor: LF
pagA: protective antigen: PA
atxA: anthrax toxin activator
cya: edema factor: EF

Hypothesis

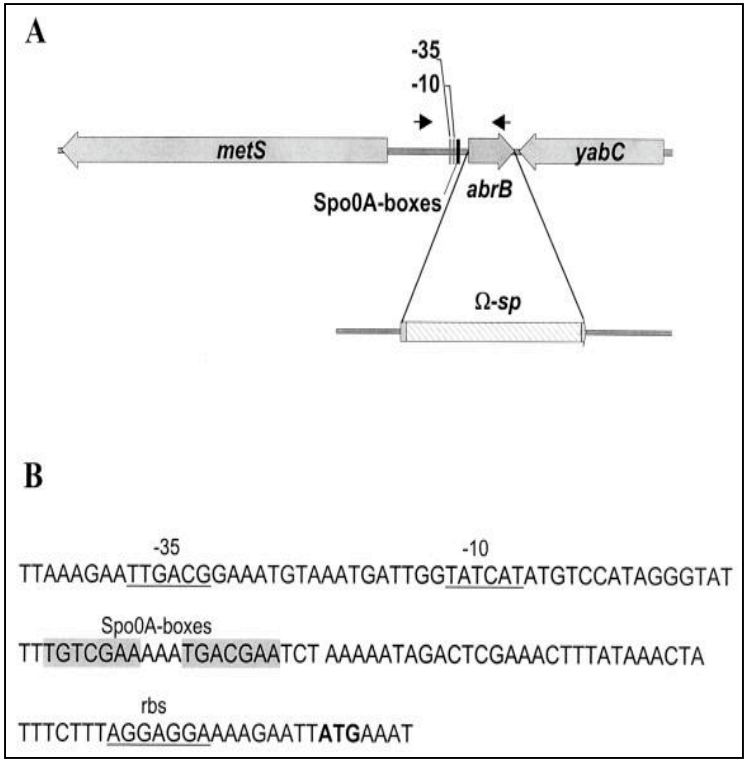
- Timing of the toxin gene expression by *B. anthracis* is controlled by a transition state regulator, such as *AbrB* of *B. subtilis*.

Figure 1: Protein sequence alignment of *AbrB*

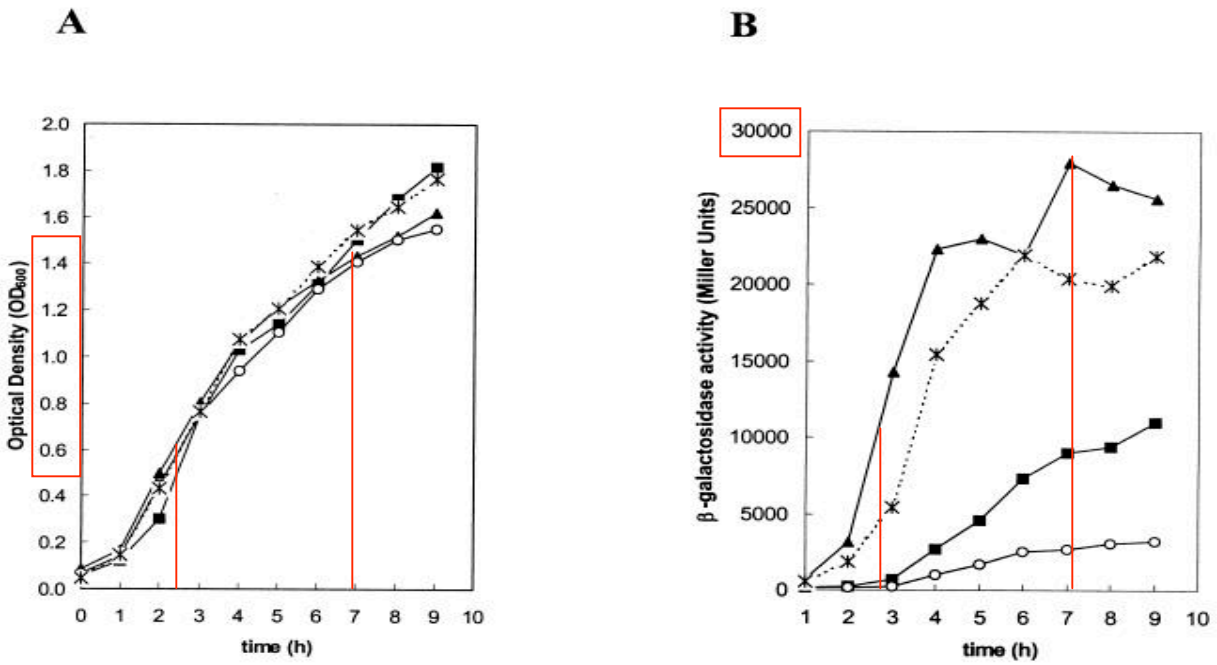


* Denote essential amino acids in mutational studies.

Figure 2: Knockout of *abrB* in *B. anthracis*



Growth Curve and _-galactosidase activity *pagA::lacZ*



Early-exp: 0.08-0.2

Mid-exp: 0.5-0.7

Stationary: 1.3-1.5

■ parent strain

▲ *abrB* mutant

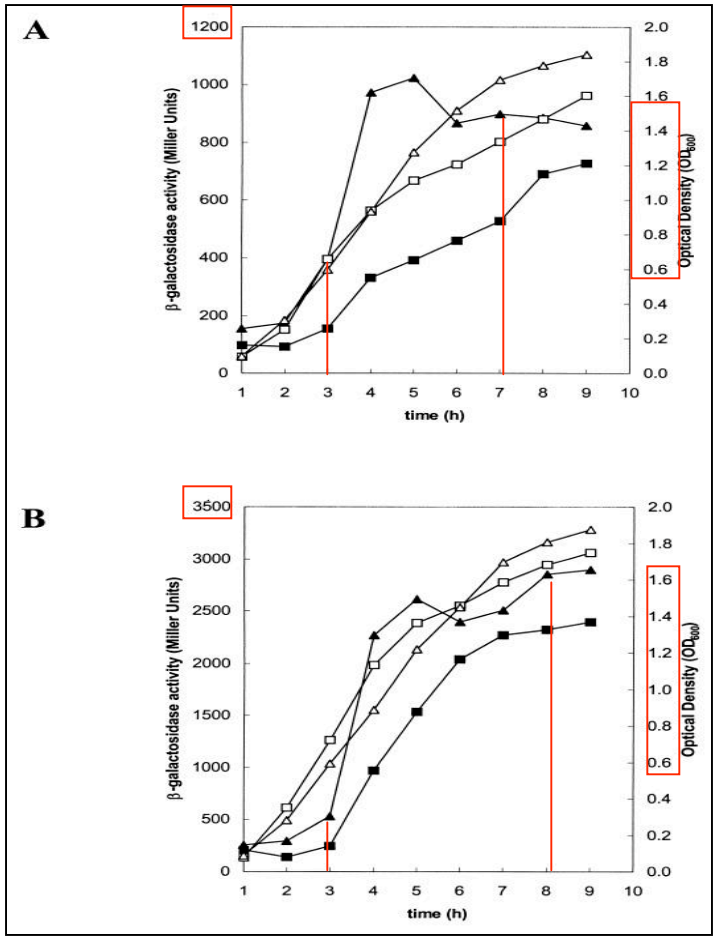
○ abrB complement

*control

Growth Curve and _-galactosidase activity *lef::lacZ and cya::lacZ*

lef::lacZ

cya::lacZ



■ Parent strain

▲ *abrB* mutant

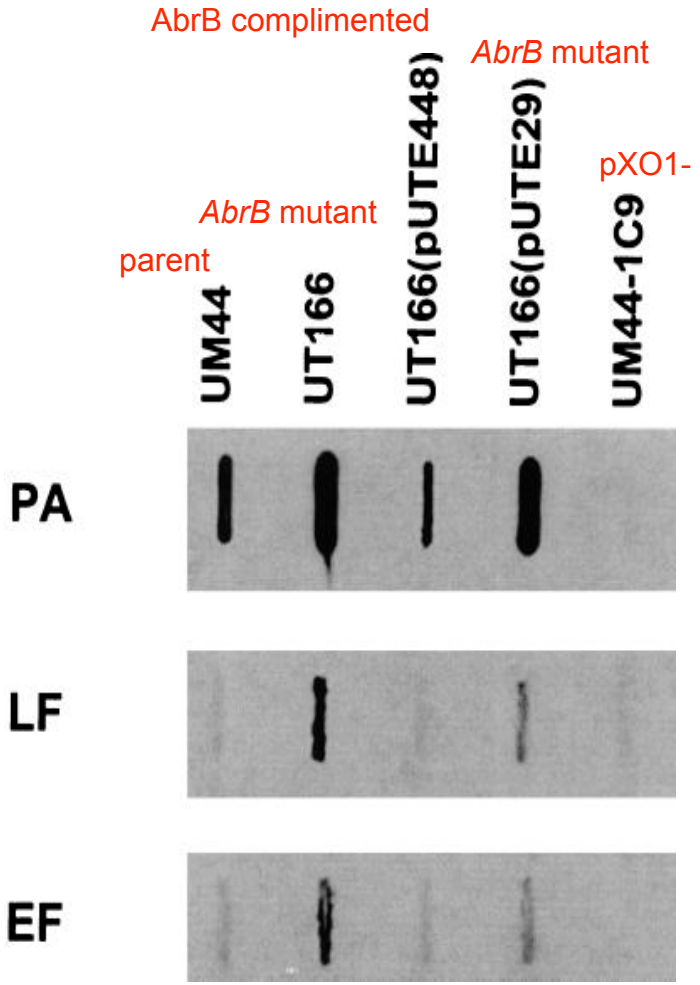
□ Parent strain

△ *abrB* mutant

Open symbols: growth curves

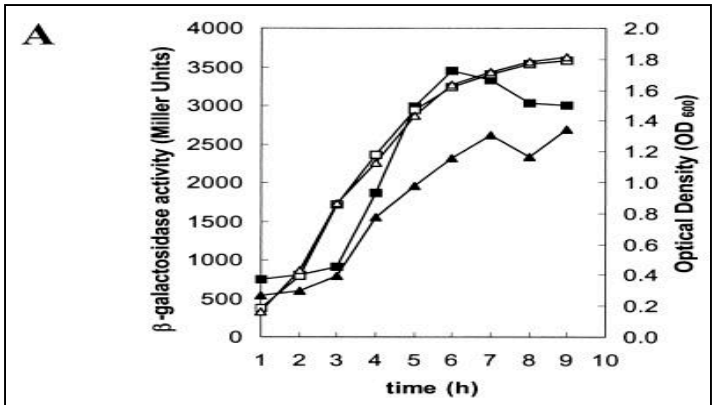
Closed symbols: _-galactosidase

Western blot looking at *abrB* control of toxin production



Growth Curve and _-galactosidase activity *abrB::lacZ* and *atxA::lacZ*

abrB::lacZ



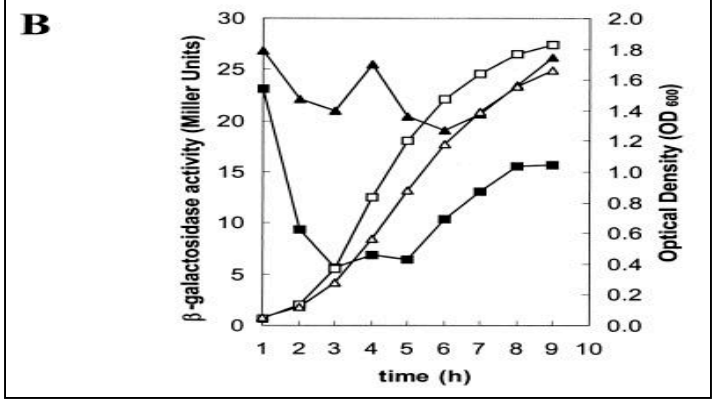
■ parent strain

▲ atxA mutant

□ parent strain

△ *atxA* mutant

atxA::lacZ



■ parent strain

▲ *abrB* mutant

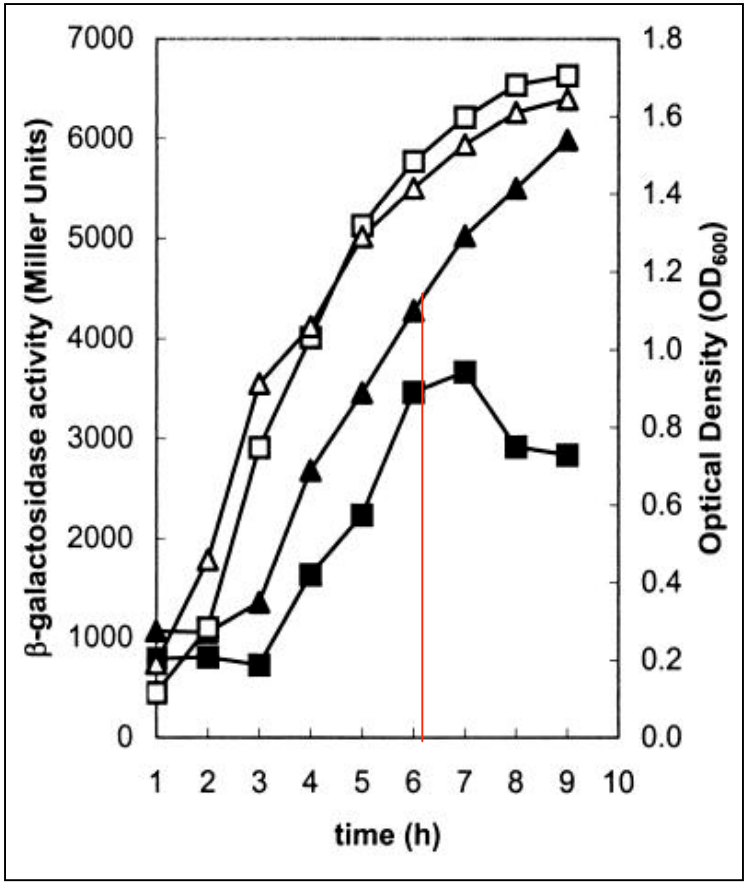
□ parent strain

△ *abrB* mutant

Open symbols: growth curves

Closed symbols: _-galactosidase

Growth Curve and _-galactosidase activity *abrB::lacZ* in *Spo0A* null mutant



■ parent strain

▲ Spo0A mutant

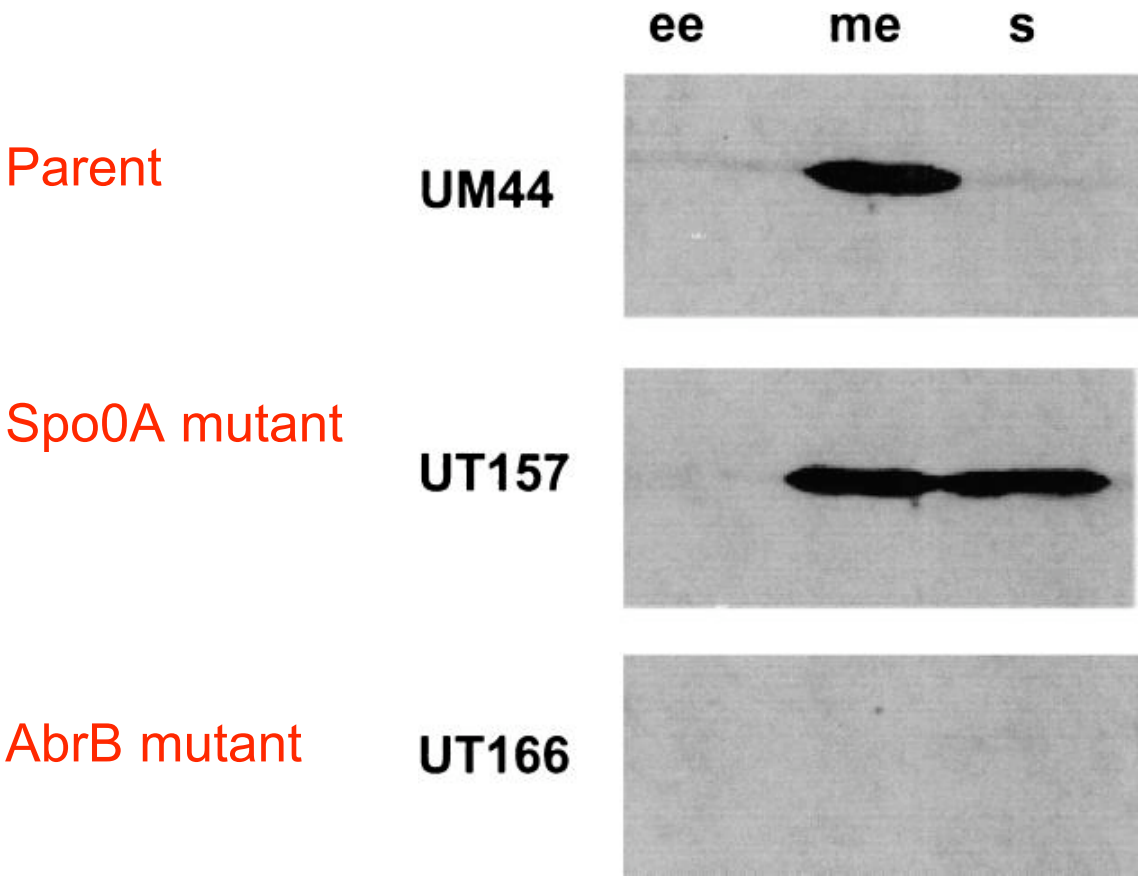
□ parent strain

△ *Spo0A* mutant

Open symbols: growth curves

Closed symbols: _-galactosidase

Detection of AbrB in *B. anthracis* cell extracts from different growth stages



Discussion/Conclusions

- AbrB negatively regulates expression of toxin genes in *B. anthracis?*
- AbrB is negatively regulated by Spo0A in *B. anthracis*