The Anthrax Toxin

Bálint Miklós

Geometric Computations in Molecular Biology
May 16th, 2007 - ETH Zurich
Anthrax, the disease

- Infectious disease, mostly animals
- One documented case for domestic pets in the USA for the last 15 years
- First anthrax vaccine in 1881
Anthrax, the danger

- Fatal in 95% of cases even if treated
- 100 kg of anthrax sprayed on a major city could kill more than 3,000,000 people
- First-year college knowledge + minimal equipment = anthrax spores
The quarantined island

Image courtesy of www.hgstump.de
2001 anthrax attacks

Image courtesy of www.wikipedia.com
How does it work?

Bacillus anthracis produces 3 different toxins
Lethal combination

Protective antigen  Edema factor  Lethal factor
There were 3 outliers (phi, psi):

99.5% (648/651) of all residues were in allowed (>99.8%) regions.

A 350 SER (-30.8, 172.8)
A 326 SER (-174.1, -35.1)
A 324 ILE (28.1, -93.2)
A 302 PRO (-65.2, -160.0)
A 265 LEU (-58.7, 11.9)
A 258 GLU (-64.0, 20.0)
A 255 SER (-26.7, -40.6)
A 234 GLN (-2.1, -57.4)
A 233 LEU (-66.3, -85.1)
A 207 GLU (-72.2, -136.0)
A 203 VAL (3.9, -78.9)
A 174 LEU (-50.6, 4.6)
A 169 LYS (-46.2, -92.1)
A 165 GLN (56.1, -155.5)
A 159 ILE (-25.2, -80.2)
A 115 HIS (-12.2, -64.0)
A 74 TYR (-161.2, -45.7)
A 70 VAL (-49.4, 4.9)
A 55 LYS (-10.5, -57.2)
A 33 GLU (-64.6, 19.8)

98.1% (1827/1862) of all residues were in allowed (>99.8%) regions.

85.1% (1585/1862) of all residues were in favored (98%) regions.

B 460 GLY (44.1, 0.0)
B 738 SER (-88.1, -140.0)
B 294 ASP (-57.6, 84.2)

A 738 SER
A 762 THR
A 713 ASN
A 74 TYR
E 74 ARG
B 12 LEU (153.5, -4.0)
B 7 VAL (158.7, 176.0)

A 729 GLY (-55.7, 75.0)
A 671 PRO (-62.6, -73.3)
A 664 ARG (-16.6, 78.6)
A 652 GLN (-165.0, -63.7)
A 647 ASP (159.9, -76.0)
A 646 GLN (-54.9, -90.0)
A 599 ALA (4.8, -66.3)
A 572 LYS (-55.1, -90.6)
A 558 LYS (-38.8, -18.6)
A 539 GLU (47.4, -7.0)
A 516 ASN (134.1, -20.9)
A 473 LYS (-20.5, -67.3)
A 466 GLY (-37.1, -85.1)
A 460 ASN (21.8, 31.5)
A 439 GLU (168.3, 143.8)
A 382 ASP (-21.1, -25.8)
A 381 LEU (-83.4, -101.4)

A 37 LYS
A 762 THR
A 74 TYR
E 74 ARG
B 12 LEU (153.5, -4.0)
B 7 VAL (158.7, 176.0)

1jky.pdb, model 1
acc.pdb, model 1
1k93.pdb, model 1

Lethal combination

Protective antigen
Edema factor
Lethal factor
The killing machine

capsule

exotoxins

PA

LF

EF

furin

PA-heptamer

endocytosis

ATP

MAPKK

cAMP

calmodulin(CaM)

receptor (ATR)

edema

cell death
Protective antigen
Protective antigen
Intrusion
The destruction, part one
The destruction, part two
The destruction, part two
In the end

- There are open questions:
  - refolding after translocation
  - does LF target other molecules
- But it is clear, it is a very effective killing machine
Should we be afraid?

- More than 15,000 anthrax hoaxes between September 2001 and August 2002.
- The U.S. Postal Service delivers 107 billion pieces of First Class mail to 240 million adults.
- One known case of mailing 5-7 letters containing pathogenic Bacillus anthracis.
Happy end

• Statistically the odds of your next mail to contain anthrax is virtually zero.