Nanotechnology and microbiology: basic science and applications that can impact cell biology

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1st Annual Symposium Integrating Nanotechnology With Cell Biology and Neuroscience
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Focus of research is on host-pathogen interactions to understand and combat disease.
Illnesses spread by insects represent a significant portion of emergent and reemergent diseases

Plague (Drug resistance)
Tularemia
Lyme disease
Relapsing fever
Typhus
West Nile virus
Rocky Mountain Spotted Fever
Dengue
Yellow fever
Malaria (Drug resistant)

Temporal-geographical spread of WNV in the US through mosquitoes
*Y. pestis* is a bacterial pathogen of significant historical and current interest

- Justinian Plague (541-544)
- Black Death (1347-1351)
- Oriental Plague (1855-1900)

- Multiple recent smaller epidemics
- Classified as a reemergent pathogen
- Classified as a biowarfare/bioterrorism agent
*Y. pestis* is maintained in nature by flea-rodent enzootic cycles.

**Diagram:**
- **Sylvatic Cycle**
  - Wild Rodent → Infective Flea → Contaminated Soil → Wild Rodent
  - Winter Dormancy
  - Hibernation

- **Bubonic Plague**
  - Direct Contact: Wild Rodent → Infective Flea → Human
  - Lethality: 40-60%

- **Pneumonic Plague**
  - Person to Person
  - Secondary Plague Pneumonia
  - Lethality: 99%

- **Urban Cycle**
  - Direct Contact: Infective Flea → Domestic Rodent

**Pathways Table**:
- Usual
- Occasional
- Rare or theoretical
Both the virulence and geographical distribution of *Y. pestis* are linked to the flea vector.

- **Bloodstream:** bacteria/ml?
  - ID$_{50} = 1 \times 10^8$ bacteria/ml

- **Various organ systems:** liver, spleen, lung

- **Temperatures:**
  - 21 °C
  - 37 °C
*Y. pestis* virulence factors: anti-phagocytic and anti-inflammatory

F1 pseudocapsule

V-antigen

Cornelis et al., 2002
Atomic force microscopy can help to visualize bacterial nanostructures

*Yersinia pestis* 21 ºC

*Yersinia pestis* 37 ºC

Jonas et al. (2007)
Novel microscopy techniques like HSI-MVCR help to visualize true host-pathogen interactions

E. coli pAsRed2

Y. pestis pAsRed2
Y. pestis pathogenesis is dependent on both modified lipid A and YOPS

Rebeil et al., 2004
TIRF microscopy permits the study of receptor-ligand interactions on the cell surface at the nanoscale level

= fluorescently labeled LPS

RAW 264.7 mouse macrophage
*Y. pestis* transmission by fleas is by a unique mechanism.
Novel application of X-ray photoelectron spectroscopy (XPS)

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K.E. = hν - E_L

X-ray photons

Vacuum

X-ray Photoelectrons

1s

2s

2p

3s

3p

4d

Element 1s 2p 2s O 1s N 1s Si 2p P 2s Fe 2p Na 1s Si 2p O 2s C 1s P 2s Si 2s Fe 2p N Auger Na 1s O Auger
XPS shows that significant changes occur to the flea-bloodmeal after digestion.
Time of Flight- Secondary Ion Beam spectroscopy will provide additional information
Free Iron plays a crucial role in *Y. pestis* gene regulation: XPS can help determine the state of iron in the flea.

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XPS analysis reveals different Iron species in *Y. pestis* clumps depending on growth conditions.
Applications to cell biology and pathogenesis: host-pathogen, cell-cell, neuron-synapse.

Note: Great technology requires great biology
Aknowledgements

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