Host Directed Therapeutics and Immunomodulators

An alternative to “one bug-one drug?”
PHEMCE Vision

• Our nation must have the nimble, flexible capacity to produce MCMs rapidly in the face of an attack or threat, known or unknown, including a novel, previously unrecognized, naturally occurring emerging infectious disease
Emerging Infectious Disease
Weaponized Infectious Disease
MCM Development Issues

- Naturally occurring or bioengineered pathogens
- Pathogen focus limits breadth and utility
- Reduced Industry R&D spend on Infectious Diseases
- Increased cost of development and reduced probability of success
- Limited shelf-life
- Pathway to licensure
To succeed, a new strategy is needed. One that

- Exploits new scientific concepts and the potential for multiple use products (including drug repositioning)
- Can rapidly procure or produce MCMs in the face of attack or threat
- Provides prophylactic or therapeutic benefit in the face of an unidentified pathogen
- Mediates the effects of multiple pathogens
- Requires decreased resources for stockpiling
Responses

- **Structural:**
  - Establishment of Working Group focused on New and Emerging Threats

- **BARDA SST BAA ; Area of Interest “3”**
  - *Therapeutics to Treat Novel and Emerging Threats*
    - Immune modulators, anti-inflammatory agents and regulators of innate immunity
    - Therapeutics with broad-spectrum mechanism of action that target a host-response

- **Scientific**
  - Focus on Host Immunity
Aspects of Host-directed Innate Immunity

- Non-specific, rapid response, may reduce likelihood of resistance mutations, interfere with host enablement of infection

- Complement, PMN’s initiate pathogenic lysis and opsonophagocytosis, chemotaxis, release of proinflammatory cytokines, activate adaptive immunity and generation of T-cell and B-cell populations

- Concerns
  - Brief duration
  - Overactivity, *i.e.* cytokine cascade
  - Genetic polymorphism (potential lack of specific dose)
  - Gender differences
  - Potential narrow therapeutic window
  - Complexity
Immune Complexity
Host-directed Mechanisms/ Classes

- IDR peptides, e.g. Defensins and mimetics
- CTLA-4 / CD28/IDO- T Cell control
- Cell surface modification
- Vaccine adjuvants
- Broad spectrum vaccines
- Toll-Like and other pattern recognition receptors
- Interferons
- Immunomodulators
Immunomodulators

- Inflammation: positive and negative aspects
  - Process required to recruit PMNs, release cytokines
  - May cause morbidity if not controlled
  - Can treatment be tailored to individuals?
Potential Host-Directed Antimicrobial Drugs

Phase of Development

- Discovery
- Phase 1
- Phase 2
- Phase 3
- Launched
SUMMARY

• Clear need for new and better treatments that can serve as MCMs

• Reduced “Big Pharma” activity

• Host-Directed innate immunity offers an opportunity

• Consider drug repositioning

• Commercial and MCM use
Partnerships

We Want to hear from you!

• This Meeting

• Medicalcountermeasures.Gov
  • https://www.medicalcountermeasures.gov/announcements/nonwopenbaa.aspx
Questions