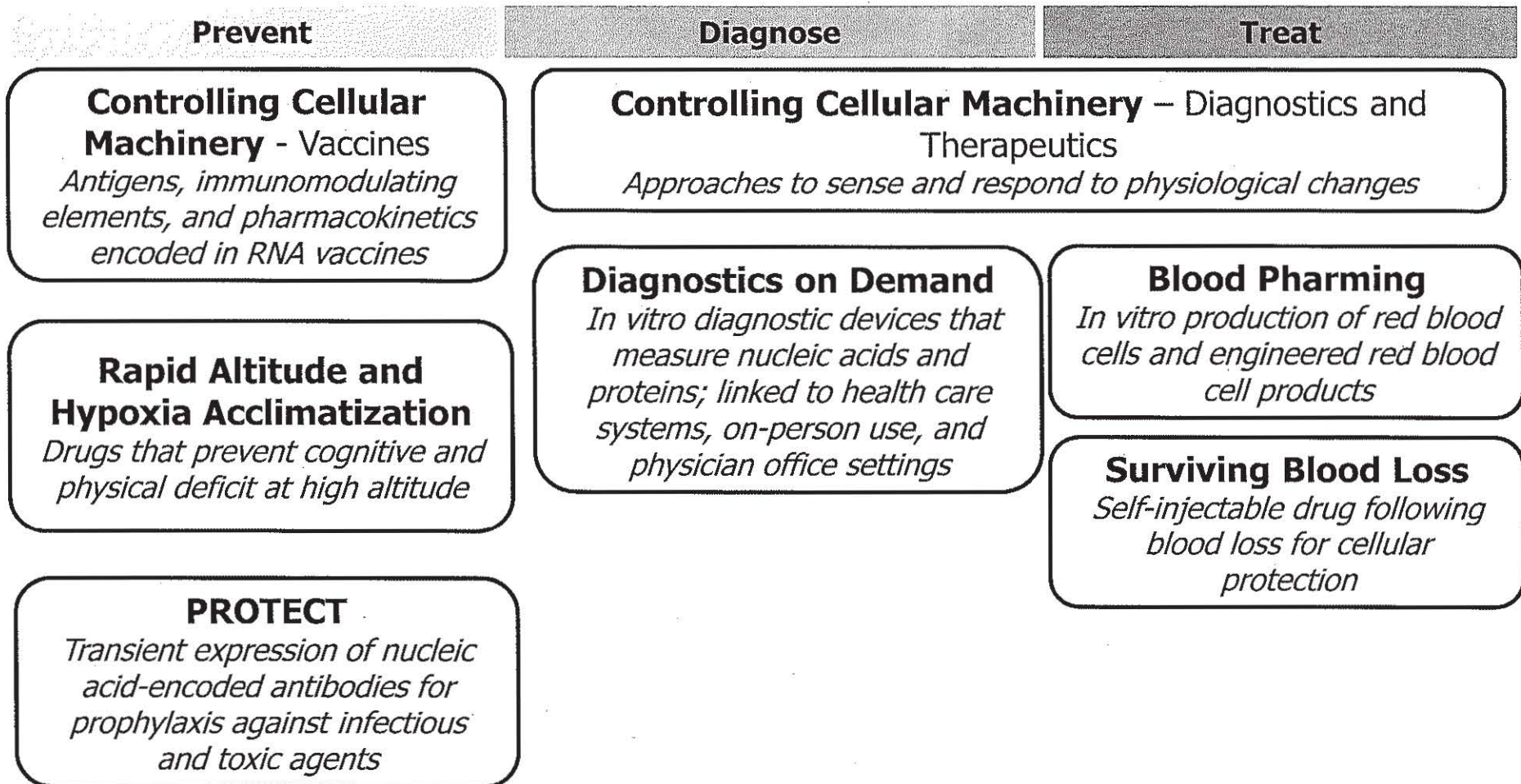




Autonomous Diagnostics to Enable Prevention and Treatment (ADEPT)

Rapid, distributed diagnostics, vaccines, and therapeutics brought to the warfighter.





PROTECT – method for immediate transient immunity

PROTECT provides prophylactic protection against disease by treating people with nucleic acid constructs that encode protective monoclonal antibodies.

- **Immediate:** eliminates the need for an evolved immune response or can be used in combination with a vaccine
- **Transient:**
 1. Absence of integration
 2. Antibodies expressed temporarily and/or eliminated from /circulation
- **Universal:**
 1. Effective in healthy people (adult, child, and senior)
 2. Broad disease specificity (e.g., most or all influenza strains)
- **Scalable:** can be produced and distributed to millions (versus one person per donor)
- **Oligoclonal:** antibody diversity consistent with efficacious immunity
- **Uncomplicated delivery:** few doses, non-infusion delivery
- **Platform technology:** rapid development accommodates emerging diseases
- **Storage:** no cold-chain requirements
- **Manufacture:** significantly decreases cost and time requirements for design/manufacture compared to conventional vaccination

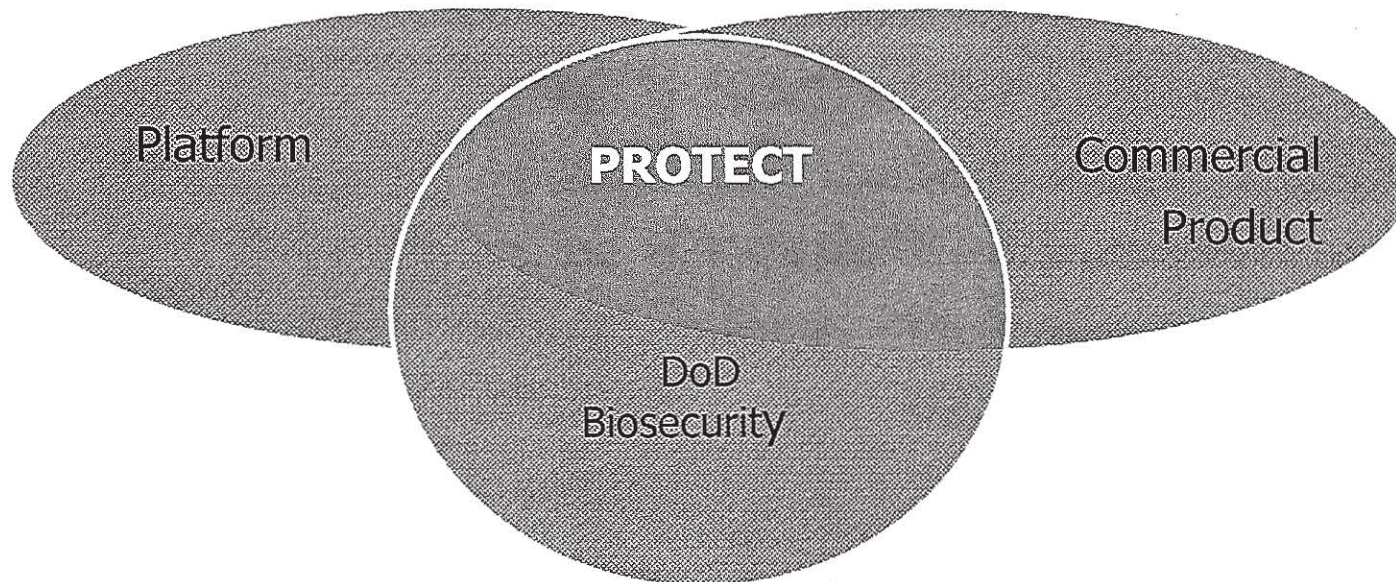


Keep in mind....

- Contracts are divided into base and option periods
- The minimum is not the goal
- The cadre of teams selected for PROTECT have diverse strengths that together could be combined into strong and mutually beneficial programs. Get to know the other teams and determine if complimentary areas can be leveraged to achieve a stronger approach
- This is a dynamic program that is likely to morph as progress is made



Competing goals will all be used to evaluate progress



Platform goals:

- Reusable
- Ease of production
- Improved duration compared to mAb therapy
- Transient
- Rapid onset (hours to days)
- Oligoclonal
- Safety

Biosecurity goals:

- DoD and HHS priority targets
- Transmission prevention
- Easily deployable
- Rapidly adaptable

Commercialization goals:

- Relevant commercial target
 - Preclinical and IND-enabling studies possible
 - Known path to licensure
- Ease of use
- Safety
- GMP manufacture
- Cost



Priority pathogens - NIAID and federal partners

Viruses

- Influenza^{C2}
- Variola major (smallpox) and minor^{A1}
- Monkey pox²
- Arenavirus^{A2} (LCM, Junin, Machupo, Guanarito, Sabia, Lassa, Lujo)
- Bunyavirus—Hanta^{A2}, Rift Valley Fever^{A2+}, Crimean-Congo^C
- Flavivirus^{A2} (Dengue)
- Filovirus^{A1} (Ebola, Marburg)
- Alphavirus—EEE^{B2}, VEE^{B2+}
- Severe acute respiratory syndrome (SARS) associated coronavirus^{2C}
- Paramyxoviridae^{C2+} (Hendra and Nipah)
- Chikungunya^C
- Rabies^C

PROTECT indications do not include cancer or HIV.

Bacteria

- Bacillus anthracis*^{A1}
- Coxiella burnetii* (Q-fever)^B
- Yersinia pestis*^{A1} and *enterocolitica*^B
- Francisella tularensis*^{A1}
- Rickettsia prowazekii*^{B2} (typhus fever)
- Brucella* spp.^{B2+}
- Burkholderia mallei* and *pseudomallei*^{B2+}
- Diarrheagenic *Escherichia coli*^B
- Pathogenic *Vibrio* spp.^B
- Shigella* spp.^B
- Salmonella* spp.^B
- Listeria monocytogenes*^B
- Campylobacter jejuni*^B
- Borrelia burgdorferi* (Lyme disease - CDC nationally notifiable disease)
- Mycobacterium tuberculosis*^B

Toxins

- Clostridium botulinum* toxin^{A1} (botulism)
- Ricin^{B2}
- Saxitoxin²
- Staphylococcal enterotoxins²—A, B^B, C, D, E

Other

- Nerve agents²
- Cyanide²
- Protozoa^B (*Cryptosporidium parvum*, *Cyclospora cayatenensis*, *Giardia lamblia*, *Entamoeba histolytica*, *Toxoplasma gondii*)
- Fungi—*Microsporidia*^B
- Prions^C
- Ticks (anti-vector)

^A NIAID category A, ^B NIAID category B, ^C NIAID category C, ¹ Tier 1 HHS, ² HHS (non-Tier 1), + HHS & USDA (overlapping priority)



ADEPT: Other possible CBRN Application

Biologics other than antibodies can be used to protect against CBRN threats.

Chemical

- Catalytic enzymes as prophylactic scavengers
 - Catalysis enables a lower concentration of single antibody to bind and neutralize chemical nerve agents such as Sarin and blood agents such as cyanide
- Non-essential amino acids as chemoprotectants
 - High expression of mucolytic and antioxidant N-acetyl-L-cysteine (NAC) reduces toxicity associated with blistering agents such as mustard gas

Biological

- Therapeutic/protective enzymes
- Applications for MDR bacteria
 - Anti-toxin
 - Treatment specific to MDR bacteria, not commensal

Radiation/Nuclear

- Antibody against radiation damage-induced biological intermediate
 - Anti-ceramide antibody protects against gastrointestinal ionizing radiation
- Overexpression of DNA repair enzymes to reverse ionizing radiation damage