U.S. ARMY COMBAT CAPABILITIES DEVELOPMENT COMMAND CHEMICAL BIOLOGICAL CENTER

Predictive Toxicology at CCDC CBC

Kyle Glover, PhD

Branch Chief, Molecular Toxicology

CCDC CBC, Toxicology and Obscurants Division

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ABOUT CCDC CHEMICAL BIOLOGICAL CENTER

Why We Exist:

To ensure operational readiness by protecting the Warfighter from chemical and biological threats

What We Do:

Combine research, development and engineering with testing, training and field operations to create new and effective chemical and biological defense solutions

Who We Are: More than 1,400 civilian, military and contractor employees who provide innovative and cost-effective chemical and biological defense technology solutions through our scientific and engineering expertise, coupled with our unique facilities and collaboration with partners.

THE HISTORY OF CB WARFARE

1899
Hague convention bans the use of "asphyxiating or deleterious gases" launched in projectiles

1915
First large-scale wartime use of chlorine gas occurs in Belgium

1917
Pres. Wilson designates Gunpowder Neck, MD as the first U.S. chemical shell filling plant

1937-1945
Japan uses various types of gases in China in over 2,000 attacks

1969
Pres. Nixon issues statement ending all U.S. offensive biological weapons programs

1980-1988
Iraq uses various gases against Iran and the Kurdish people

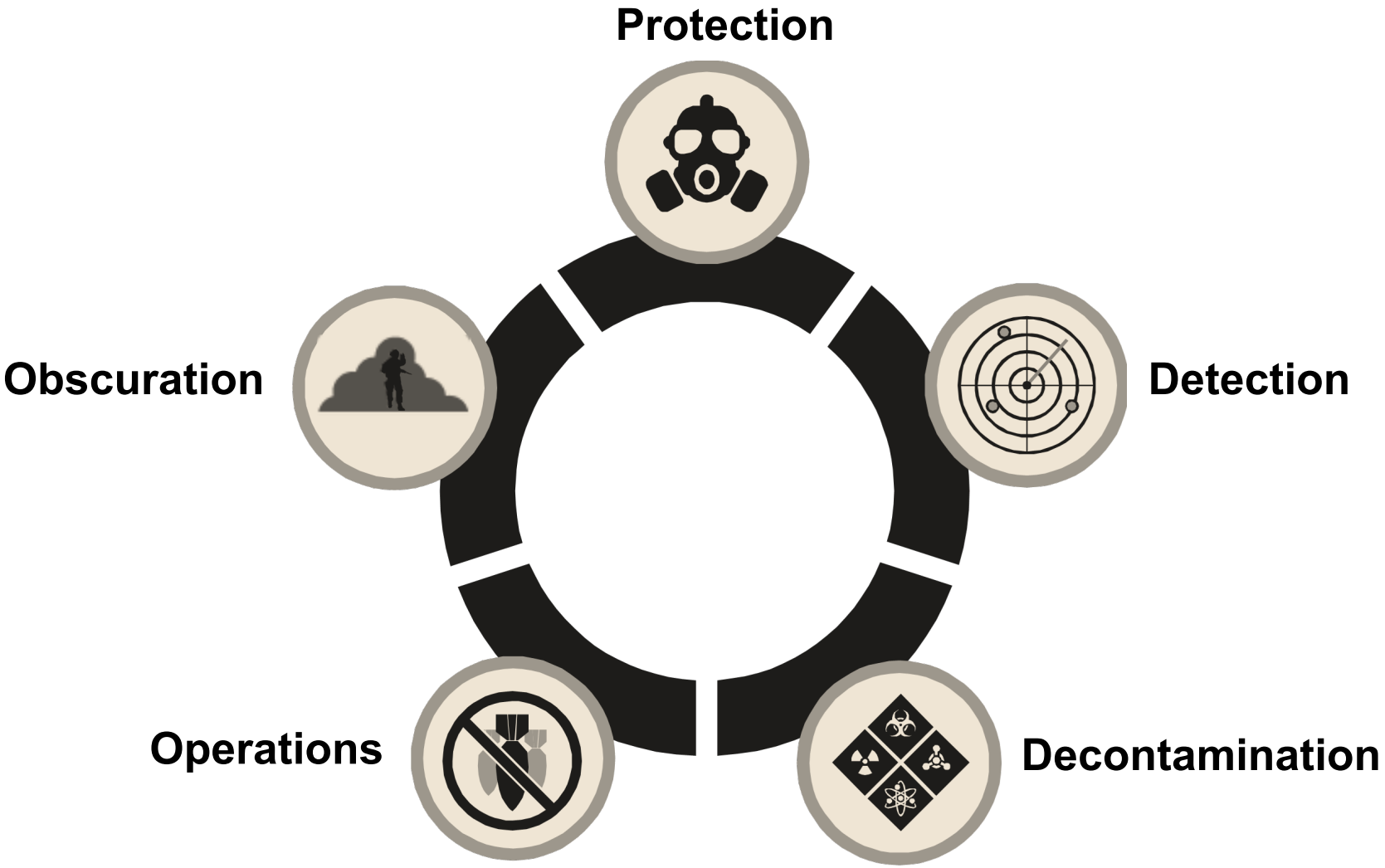
1995
Terrorists execute Sarin attack on the Tokyo subway killing 12 and injuring more than a thousand

2014
The Center successfully destroys more than 600 tons of Syria's chemical weapon stockpile aboard the U.S. ship MV Cape Ray

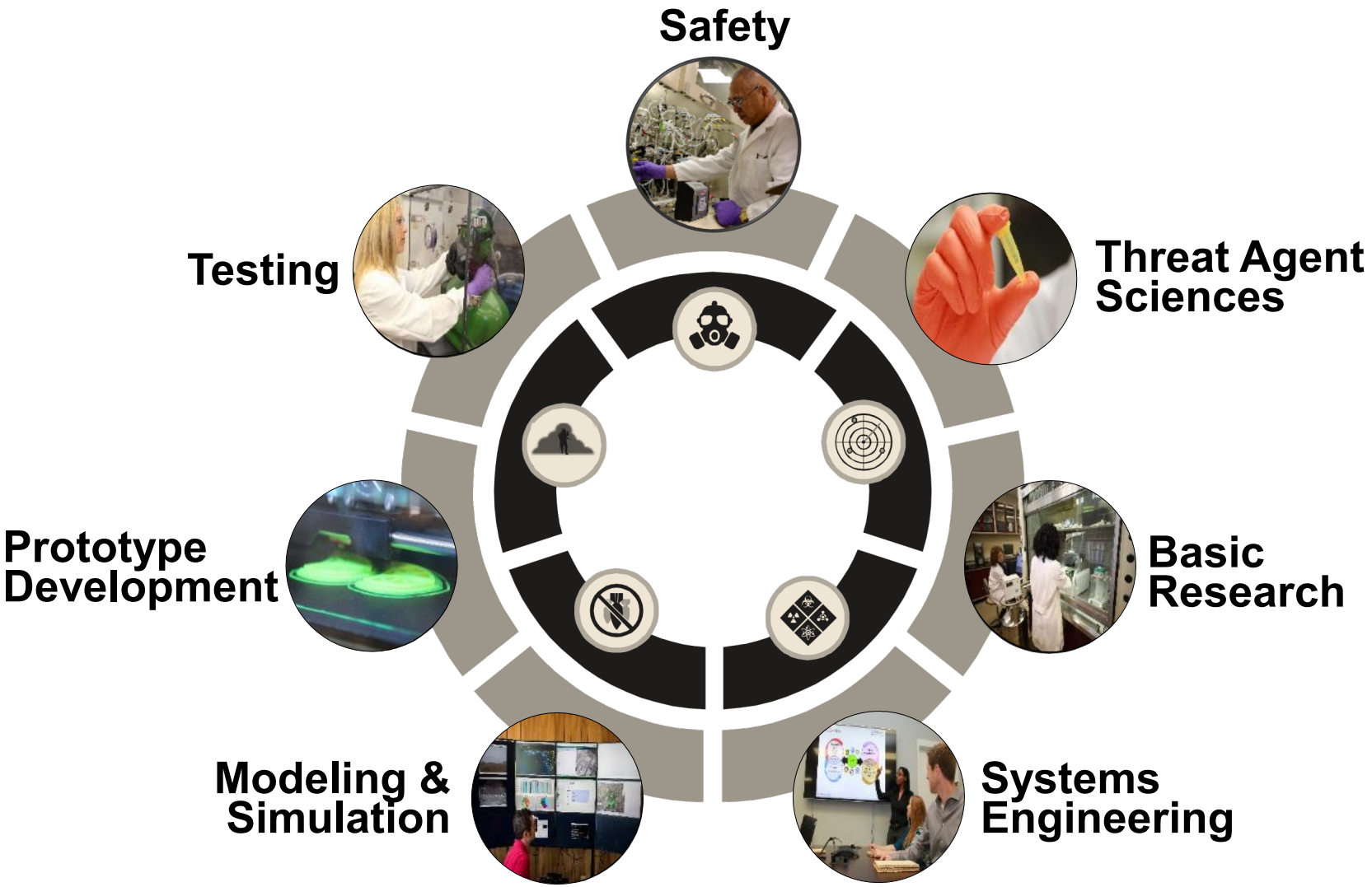
1997
Chemical Weapons Convention treaty enters into force

WWI
WWII
Korean War
Vietnam War
Cold War
Gulf War
2001
9/11
War in Iraq
War in Afghanistan

DELIVERING INNOVATIVE SOLUTIONS



ENABLING FACTORS

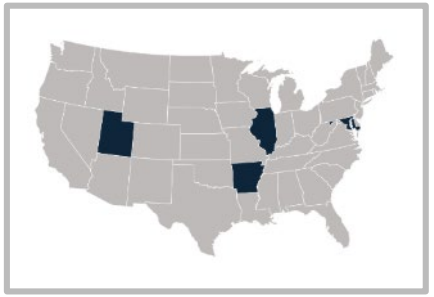


UNIQUE INFRASTRUCTURE

1.22 million square feet of laboratory and chamber space spanning 200 buildings worth $2 billion. This infrastructure, along with our unique workforce and engineering controls, creates a one-of-a-kind scientific and engineering environment. Key features of our infrastructure include:

- The majority of the nation's chemical surety hoods
- BSL-2 and BSL-3 laboratories
- Chambers capable of handling explosive/toxic material

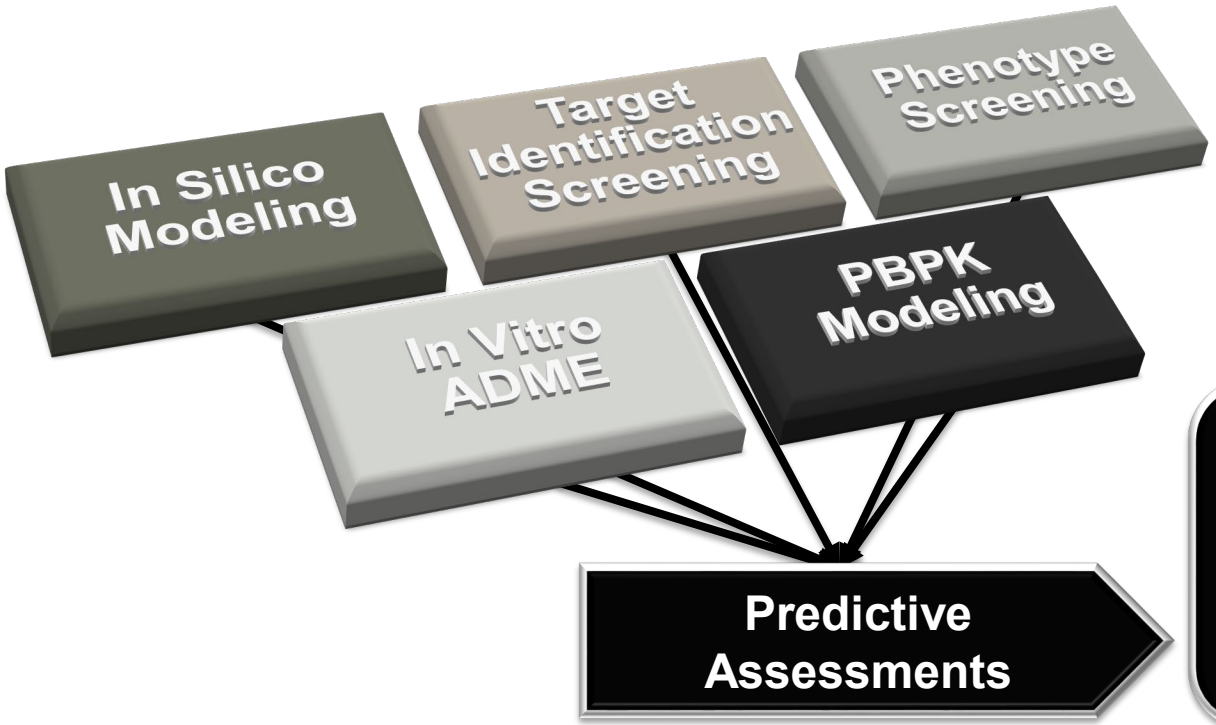
Did you know?



Our major campus is located in the Edgewood Area of the Aberdeen Proving Ground, Maryland. We also have employees and facilities located at Rock Island Arsenal, Illinois; Pine Bluff Arsenal, Arkansas and Dugway Proving Ground, Utah.

BUILDING FOR FUTURE CB NEEDS

Primary Thrust Areas for Molecular Toxicology



- Potency
- Molecular Target(s)
- Mechanism of Toxicity
- Similarity Assessment
- Species Differences
- Human Risk Assessment

IN SILICO MODELING

Predict what?

- Relative potency within a chemical class
- Route of exposure
- Potential physical hazards
- Potential molecular target
- Potential target affinity

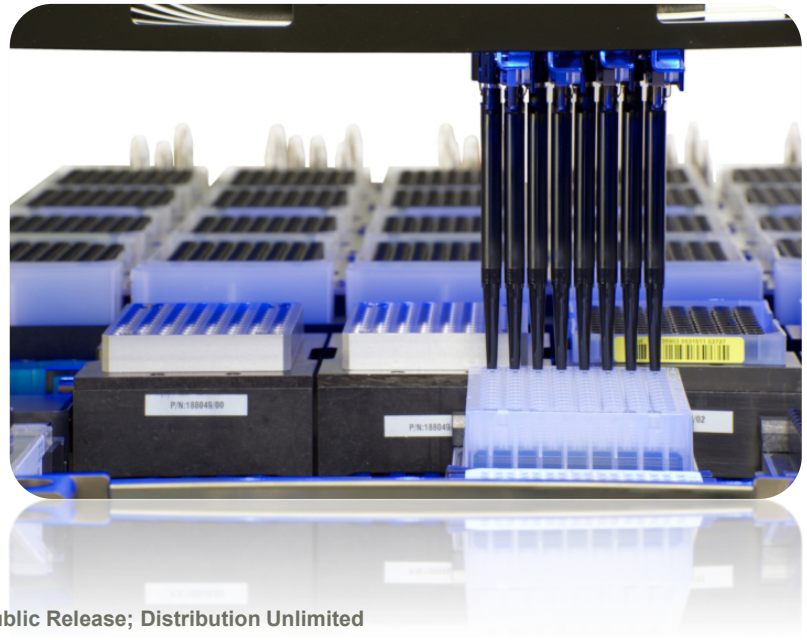
Using what?

- Decades of publically available acute toxicity data
- Internal data sources
- Open-source databases

TARGET IDENTIFICATION

Models in use or under development:

- Reporter assays using human receptor engineered cells
- G-protein coupled receptor screening platform (PRESTO-TANGO)
- Automated electrophysiology (e.g. patch clamp)
- Numerous cell based assays (e.g. AChE inhibition)



PHENOTYPIC SCREENING

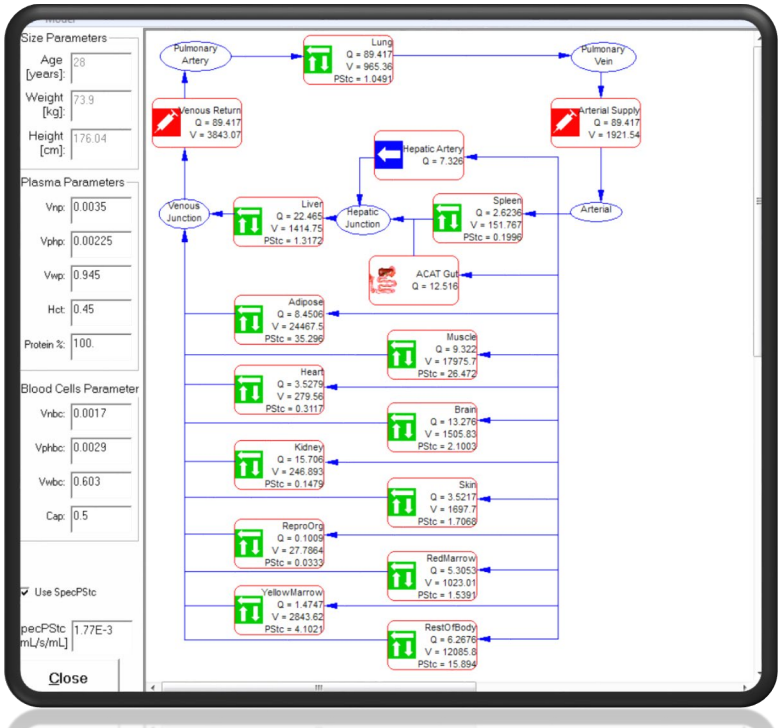
Focus on target agnostic, functional readouts

- Cardiotoxicity: 2D/3D iPSC-derived cardiomyocytes
- Hepatoxicity: 2D/3D liver spheroids and liverchips
- Neurotoxicity: iPSC-derived neurons
- Behavioral: zebrafish embryo at 6 days post fertilization

PBPK MODELING

Running both high-throughput and compound specific PBPK models to aid in:

- Route to route extrapolation
- Species extrapolation
- Reverse dosimetry



IN VITRO ADME

Assays to better characterize human relevant ADME

- Species specific microsomal clearance
- Blood brain barrier penetration
- Blood partitioning
- Plasma protein binding

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