Re-Purposing Drugs as Countermeasures for Chemical Weapons: Interactive Training for Undergraduate Students

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Abstract

The risk of a terrorist attack in the U.S. has created challenges on how to effectively treat toxicities that result from exposure to chemical weapons. To address this concern, the U.S. has organized a trans-agency initiative across academia, government, and industry to develop and approve drugs to treat tissue injury resulting from exposure to chemical threat agents. We sought to develop and evaluate an interactive educational session that provides hands-on instruction on how to re-purpose FDA approved drugs as therapeutics to treat toxicity from exposure to chemical weapons. Due to the COVID-19 pandemic, the Rutgers Summer Undergraduate Research Fellowship was run remotely for 6-weeks. In addition to independent virtual projects, students met twice weekly with instructors to participate in career development activities. Twenty undergraduate students participated in a two-hour session that included: 1) overview of the CounterACT program from the NIH Program Officer, 2) original research in novel methodologies to evaluate drug efficacy from a toxicology PhD student, and 3) an interactive session where teams of students were provided lists of FDA approved drugs to evaluate potential mechanisms of action and suitability as countermeasures for 4 chemical weapon case scenarios. The interactive session culminated in a competition for the best grant 'sales pitch'. Pre- and post-program self-assessments using 5-point Likert rating scales were conducted online. Each participant had a unique identifier that was blinded to instructors and used to evaluate understanding of key programmatic objectives of the activity. From this interactive training, students improved their understanding of 1) the ability of chemical weapons to cause long-term toxicities (means: pre-1.5; post-3.6, p<0.0001), 2) how to apply the mechanism of action for a drug to a new clinical indication (means: pre-1.6; post-3.6, p<0.0001), and 3) re-purposing FDA-approved drugs to treat exposure to chemical weapons (means: pre-0.8; post-3.5, p<0.0001). Taken together, use of an interactive training exercise can provide students new insights into drug development for chemical weapon toxicities.

Training Session Overview

- Overview of the NIH CounterACT Program by Dr. David Jett (Program Officer, NIH/NINDS)
- Basic Research Presentation by Alexa Murray, PhD Candidate (Rutgers University)
- Interactive Case Studies to Re-Purpose FDA-Approved Drugs as Countermeasures. Led by Dr. Joshua Gray (US Coast Guard) and Jaclynn Andres, PhD Candidate (Rutgers University)
- Grant 'Sales Pitch' Competition

Interactive Training Overview

Pre-Work: Each team was assigned a list of 10 FDA approved drugs to investigate (mechanism of action, administration, safety, etc.)

Part 1: Each team was assigned a case study scenario which included the chemical weapon exposure scenario, known pathological changes, clinical symptoms and mechanisms of toxicity.

- *Breakout room 1: Identify 5 properties desired in a therapy to treat the toxicity associated with the chemical weapon in the case study.*
- *Breakout room 2: After hearing properties from other teams, points were assigned to each property according to its importance in treating chemical weapon toxicity.*

Part 2: Moderator presents an example rubric to evaluate the utility of potential therapies researched during the pre-work.

- *Breakout room 1: Teams apply their rubric to three of the FDA-approved drugs from the pre-work in order to identify the most promising intervention.*
- *Breakout room 2: Prepare a 3-minute grant sales pitch that highlights the promise of their top candidate drug for re-purposing to treat chemical weapon toxicity.*

Part 3: In the main Zoom room, each team presented their therapeutic intervention and the audience including other participants, SURF leadership, and invited speakers voted on the best 'sales pitch'. Gift cards were provided to the top team.

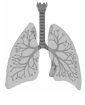
4 Chemical Weapon Case Scenarios

Phosgene Oxime Dermal Toxicity

Tetramethylenedisulfo-tetramine Neurotoxicity

Parathion Neurotoxicity

Chlorine Pulmonary Toxicity



Create your Drug Scoring Rubric

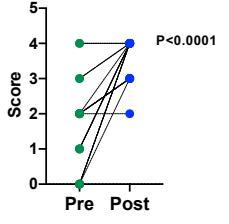
What properties should a good therapy have?

	Property	Total # of Points for This Property (1-8)
#1		
#2		
#3		
#4		
#5		
	Total Possible Points for Good Therapy: ** Note: Not all properties should be equally weighted*	**20**

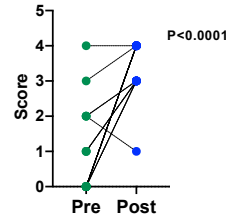
Example Template Provided to Participants

Assessment of Participant Knowledge

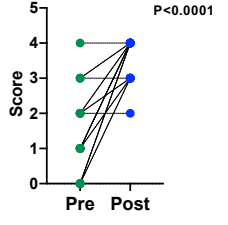
Apply the MOA of a Drug for a New Therapeutic Indication



Re-Purposing FDA-Approved Drugs to Treat Chemical Warfare



Ability of Chemical Weapons to Cause Long-Term Toxicities



Main Takeaway

An interactive training exercise can provide undergraduate students new insights into drug development for chemical weapon toxicities.

Acknowledgments

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