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CREATING YOUR TALKING POINTS

The following questions are designed to help you develop a concise, lay friendly explanation of your scientific research. You can use this as a worksheet to develop your key talking points. Remember to avoid science jargon and use familiar language or descriptions to explain complex ideas. You can contact Shawn Rhea at srhea@gc.cuny.edu if you'd like help with this process.

Question	Response
What exact research question did you set out to answer/What are the most important findings of your paper?	
Who might eventually benefit from the findings of this study/Why should they care?	
What would need to be done before we could achieve these benefits?	
What background information would someone who is completely unfamiliar with your field need to know to understand the findings in your paper?	
Are there any partnered organization or funders that should be acknowledged?	

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Use the responses above to develop your talking points/message map. The following example (taken from a recently published study from GC researchers) shows how these answers can be adapted and shortened to create lay friendly soundbytes or ascending themes for use during interviews:

EXAMPLE:

Questions

1. **What exact research question did you set out to answer/What are the most important findings of your paper?**

C. difficile infection (CDI) is a binary toxin, meaning it requires two components to function. The enzymatic component CDTa needs to enter healthy cells to damage them. This is achieved by a pore-forming component CDTb, which bind to our cells, forming a channel on the membrane and delivers CDTa inside the cell. There was a hypothesis that seven CDTb subunits need to join together to form the channel similar to anthrax toxin, but the DNA sequence of this toxin also had parts that were very different from the anthrax DNA sequence. The structure therefore had to have different components and a different mechanism of action. We therefore aimed to visualize the CDTb channel at the molecular level to understand how different it is from Anthrax and how it works. By learning how it works, we could find a way to jam it, to block it from getting the cell-killing CDTa into the cell. The 3D image of the CDTb channel would show us where every atom of that killing machine is and will greatly enhance our understanding of its mode of action. It will be a great starting point for discovering therapeutic strategies for this prevalent disease.

We were able to visualize with cryo-electron microscopy the toxin in 3D at a resolution high enough to see the position of every atom of that channel-forming machine. This information is critical for designing pharmacological drugs against it.

We observed two similar but distinct forms of the toxin, one where we see the channel and one where it is invisible, probably unfolded. This can give us clues as to how to prevent the formation of the channel stop CDTa from entering the cell.

We visualized what domains of this toxin are different from anthrax, including a domain that help shield the channel before it attacks the cell, a little bit like concealing your weapon until the last moment before striking. Additionally, we identified a novel Calcium

binding site on one of the CDTb domains, which is not found in any other similar toxins, suggesting the importance of Calcium in regulating the formation and transitions of these novel structures.
Although the structures were solved primarily by an increasing popular technique in the structural biology field, cryogenic electron microscopy (cryo-EM), many aspects of this research would not be possible without combining multiple biophysical and structural tools, including X-ray crystallography, nuclear magnetic resonance (NMR), and small-angle X-ray scattering (SAXS). We believe this work is an excellent demonstration of how scientific research can benefit from a syngenetic approach by integrating multiple techniques.

2. **Who might eventually benefit from the findings of this study/Why should they care?**

This research will guide the design of drugs targeting *Clostridium difficile* infections, and specifically, the more severe CDT releasing strains. If an effective therapeutic strategy is discovered, millions of people who are under the risk of, or currently suffering from CDI will benefit.

3. **What background information would someone who is completely unfamiliar with your field need to know to understand the findings in your paper?**

Clostridium difficile infection (CDI) is a prevalent concern in many health care facilities here in the United States, primarily due to the overuse of antimicrobial therapies. When a patient is under long-term antibiotic treatment, the microbiome of his/her digestive system will be disrupted, resulting in an overgrowth of this harmful bacteria species, causing severe diarrhea, nausea, internal bleeding, and even death. Around half a million Americans are suffering from CDI, resulting in nearly 13,000 death every year. The health cost related to CDI is suggested to be over 5 billion dollars in the United States alone, with more than 11 million people included in the CDI surveillance program, according to the center for disease control (CDC). CDI is difficult to treat with typical antibiotic treatments, with high chance of recurrence and risk of acquired antibiotic resistance. Other treatments include fecal transplant, and recombinant antibodies, but each with its own limitations. More recently, a new type of toxin released by some strains of *C. difficile*, the *C. difficile* binary toxin (CDT) has been discovered, which is the culprit to some of the most severe outbreaks of drug resistant CDI in recent years and has no FDA approved treatments against it. Understanding the mode of action of this toxin and finding a cure to it is both urgent and of great importance to the healthcare community. Using a combination of biophysical tools, we have discovered

the structure and molecular details of this toxin, which will help us to rationally design pharmacological drugs blocking the action of this toxin. The direct therapeutic potential of this study is a reason why this work has been done as a direct collaboration with Merck.

4. **What would need to be done before we could achieve these benefits?**

The next step will be for researchers to figure out how to block the C. difficile toxin from creating an entry point into the cell.

5. **Are there any partnered organization or funders that should be acknowledged?**

This is a three-lab collaboration, corresponding authors listed below:

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Resulting Talking Points/Message Map