Anti-**V**irulence **A**pproaches to **T**reat **A**lgal **C**rops (AVATAC)
Submitted by New Mexico State University

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Predatory bacteria infect a variety of algal strains in cultivation systems globally. These bacteria negatively influence biomass productivity, and if conditions are right, can quickly decimate an algal crop. Despite the ability of bacterial pests to destroy algal crops, the current SOT in bacterial pest monitoring and management remains rudimentary. In most cases, the SOT in bacterial detection relies on microscopy or molecular tools to confirm infection. Each of these technologies has severe limitations for detection at scale. Management of predatory bacteria typically consists of applying chemical agents like oxidizers and antibiotics, which through time can lead to treatment resistance. To effectively maintain algal cultures in open ponds in the field, an integrated pest management (IPM) strategy must be implemented. As part of this strategy, industries require multiple tools in their crop protection toolbox, including the ability to rapidly disarm bacterial pathogens. One approach that has been proposed to treat pathogens (and simultaneously reduce treatment resistance) is the use of antivirulence strategies. Rather than killing pathogen populations, antivirulence strategies *disarm* pathogens by affecting or blocking virulence. Hundreds of antivirulence compounds have been validated against pathogenic bacteria; however, to our knowledge, there has not been an attempt to catalog and apply antivirulence strategies to pathogenic bacteria in algal cultivation ponds.

In this project, we will advance the development of antivirulence strategies based on the life cycles and predatory modes of our model bacteria. First, we will develop a database of antivirulence compounds that can be tested against pathogenic bacteria and annotate this for compounds that can feasibly be deployed at commercial scale levels. Then, relying on pest models as well as mixed bacterial assemblages from field cultures, we will test compounds, combinations of compounds, and combinations of approaches (if necessary) in iterative lab-field experiments to refine treatment strategies. The outputs and outcomes of our project include: (1) the development of deployable antivirulence treatment strategies (i.e., dose amounts, frequency) that disarm bacterial pathogens across multiple DOE-relevant and SOT algal strains; (2) the development of a singular, publicly available database of antivirulence compounds with cost estimates for deployment at scale; and (3) pre-pilot demonstration of antivirulence strategies showing increases in mean time to failure to generate at least two-fold increases in mean time to failure (MTTF), with no losses to productivity. Our project approach is innovative because antivirulence strategies can be broadly applied (1) to multiple algal crops and (2) against an array of bacterial pests without knowing the identity of tracking individual pests through time. Antivirulence strategies also reduce the risk for treatment resistance and support probiotic microbiomes.