REDUCING WASTE AND COST BY RETHINKING THE ANTIBODY MANUFACTURING PROCESS

SINGLE-USE MODULES FOR CONTINUOUS REMOVAL OF ANTIBODY FRAGMENTS

NIIMBL® The National Institute for Innovation in Manufacturing Biopharmaceuticals

North Carolina State University, Raleigh, NC

Type:
Academic Research Institution

Participating Organizations:
Ligatrap, Merck & Co., Inc., MilliporeSigma, Rensselaer Polytechnic Institute (RPI)

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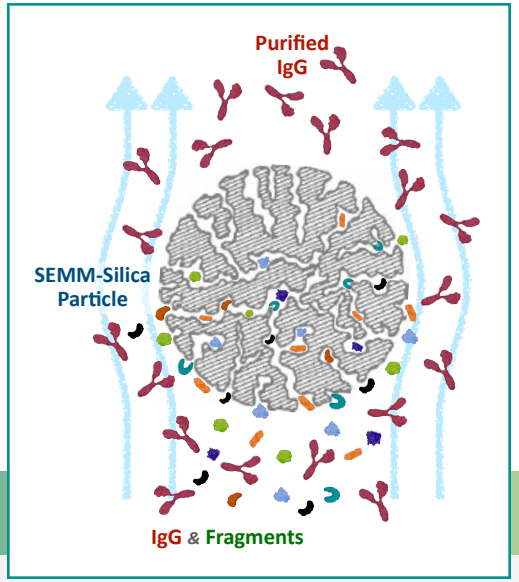

INDUSTRY NEED

In the manufacture of therapeutic antibodies, bioreactors produce the antibody product within a "soup" of spent reagents, waste products, cells, fragments of cells, and pieces of antibodies. The current approach to removing these impurities involves capturing the antibody product and washing away the impurities through a series of chromatography, filtration, and centrifugation steps, each of which requires its own set of tanks, reagents, water streams, controls, and analytics. Streamlining and simplifying the impurity removal process would have an enormous impact on reducing waste, particularly water usage, ultimately reducing manufacturing costs.

SOLUTION

Stefano Menegatti at North Carolina State University and Steven Cramer at RPI discussed flipping the impurity removal process: instead of capturing the antibody product, it might be possible to capture the impurities and let the antibody continue through the process, similar to what is done in pharmaceutical manufacturing. This "flow-through" approach would simplify the removal of impurities and reduce the number of steps and resources needed to produce a safe therapeutic antibody product.

Working with Ligatrap and Michael Phillips at MilliporeSigma, the team focused on removing antibody fragments that can cause off-target effects in patients. The team developed a porous material out of inexpensive silica and embedded chromatographic particles in the pores to bind antibody fragments. As the "soup" from the bioreactor flows through the material, smaller antibody fragments enter the pores, are captured, and remain bound, leaving the antibody product behind.

OUTCOME

To test the new technology, MilliporeSigma, Merck, and KBI Biopharma provided more than 50 bioreactor mixtures of various compositions that were fed through the porous silica prototype. With optimization, the new material was able to reduce the antibody fragments in the mixtures to between 1% and 3% of the starting concentration.

The new flow-through technology represents a radical redesign of the current approach to impurity removal in therapeutic antibody manufacturing. In addition, the technology can be applied to the manufacturing of other biological therapeutics, simply by changing the capture antigens within the pores.

> *"Flow-through methods to remove impurities during therapeutic antibody manufacturing reduce the use of natural resources and energy, lower costs, and ultimately expand access to these life-saving products."*

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