

## Singapore's SMART researchers develop novel tool to detect microbial contamination in cell cultures

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**The UV and machine learning-aided rapid, label-free method can be used as a preliminary step in cell therapy products (CTPs) manufacturing to detect contamination in advance**



A collaborative innovation from Singapore has led to the development of a novel method that can quickly and automatically detect and monitor microbial contamination in cell therapy products (CTPs) early on during the manufacturing process.

Researchers from the Critical Analytics for Manufacturing Personalized-Medicine (CAMP), interdisciplinary research group (IRG) of Singapore-MIT Alliance for Research and Technology (SMART), MIT's research enterprise in Singapore, in collaboration with Massachusetts Institute of Technology (MIT), A\*STAR Skin Research Labs (A\*SRL), and National University of Singapore (NUS), have successfully developed the method.

By measuring ultraviolet (UV) light absorbance of cell culture fluids and utilising machine learning to recognise light absorption patterns associated with microbial contamination, this preliminary testing method aims to reduce the overall time taken for sterility testing and, subsequently, the time patients need to wait for CTP doses. This is especially crucial where timely administration of treatments can be life-saving for terminally ill patients.

A major challenge in CTP manufacturing is quickly and effectively ensuring that cells are free from contamination before being administered to patients. Existing sterility testing methods, based on microbiological methods, are labour-intensive and require up to fourteen days to detect contamination, which could adversely affect critically ill patients who need immediate treatment. While advanced techniques such as rapid microbiological methods (RMMs) can reduce the testing period to seven days, they still require complex processes such as cell extraction and growth enrichment mediums, and they are highly dependent on skilled manpower for procedures such as sample extraction, measurement, and analysis. This creates an urgent need for new methods that offer quicker outcomes without compromising the quality of CTPs, that meet the patient-use timeline, and with a simple workflow that does not require additional preparation.

SMART CAMP researchers described how they combined UV absorbance spectroscopy to develop a machine learning-aided method for label-free, non-invasive, and real-time detection of cell contamination during the early stages of manufacturing.

This method offers significant advantages over both traditional sterility tests and RMMs as it eliminates the need for staining of cells to identify labelled organisms, making it label-free, avoids the invasive process of cell extraction and delivers results in under half an hour. It provides an intuitive, rapid "yes/no" contamination assessment, facilitating automation of cell culture sampling, with a simple workflow that requires no additional incubation period, growth enrichment mediums, and manpower. Furthermore, the developed method does not require specialised equipment, resulting in lower costs.

"This rapid, label-free method is designed to be a preliminary step in the CTP manufacturing process as a form of continuous safety testing, which allows users to detect contamination early and implement timely corrective actions, including the use of RMMs only when possible contamination is detected. This approach saves costs, optimises resource allocation and ultimately, accelerates the overall manufacturing timeline," said Shruthi Pandi Chelvam, Senior Research Engineer at SMART CAMP and first author of the paper.

Moving forward, future research will focus on broadening the application of the method to encompass a wider range of microbial contaminants, specifically those representative of Current Good Manufacturing Practices (cGMP) environments and previously identified CTP contaminants. Additionally, the model's robustness can be tested across more cell types apart from MSCs. Beyond cell therapy manufacturing, this method can also be applied to the food & beverage industry as part of microbial quality control testing to ensure food products meet safety standards.

The research is conducted by SMART and supported by the National Research Foundation (NRF) Singapore under its Campus for Research Excellence and Technological Enterprise (CREATE) programme.

*Photo Credit: SMART CAMP Senior Research Engineer Shruthi Pandi Chelvam*