AI-ENABLED BIOMANUFACTURING

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Despite their immense promise and transformative potential, access to cell therapies is limited to a small number of patients and only at leading clinical centers – primarily due to manufacturing complexities and limitations. The six approved CAR-T cell-based therapies are also some of the most expensive medicines in human history, with overall cost often reaching from $500K to $1M per patient. This is unsustainable for industry, government, and patients alike. COVID-19 has further exposed the tremendous inadequacy of our largely-manual, empirically-driven biomanufacturing processes for advanced therapies. In order to generate highly effective products while remaining scalable, low cost, lower-risk, and Quality by Design (QbD)-driven, the future biomanufacturing of therapeutic cells and biologic products must undergo a transformative shift. This means moving away from the current empirical and manual processing paradigm to Artificial Intelligence (AI)-enabled biomanufacturing with integrated AI and real-time process modulation.

As an advanced therapy, manufacturing cells as a product poses complex challenges, different from those historically experienced by the pharmaceutical and protein therapeutics industry. First, the product (cells) is a “living” entity whose properties and function can change with every manipulation, requiring a whole new paradigm for large-scale manufacturing and quality control. Second, for most cell-based therapies, even with promising pre-clinical and clinical data, little is known about Critical Quality Attributes (CQA) and how to control them, i.e., the set of multivariate cell properties that render them safe and effective for specific disease indications. Thus, QbD, a fundamental premise of current industrial-scale manufacturing practice, has not been implemented in cell manufacturing. QbD, as defined by the FDA, is a systematic approach to drug development where manufacturers must design and develop cells and processes such that there is exquisite control on the product phenotype and a pre-defined “quality” can be achieved consistently. Without the ability to implement such principles, large-scale, reproducible, low-cost production of high-quality, safe cells and cell-products cannot be achieved, and the promise of cell therapies will remain elusive to society overall.

Georgia Tech has a robust program that is addressing the critically needed fundamental and applied research into in-line or at-line process analytical technology integrated with control-centric models to enable feedback controlled closed-system automation along with innovative data analytical and cyberinfrastructure tools – especially at the TRL3-7 levels. This effort combines both biological, i.e., Systems Biology driven AI, and mechanoelectrical AI, i.e., Flexible Automation, Real-time sensing, and Internet of Things (IoT) driven AI across the cell-manufacturing pipeline to create the first comprehensive fully-controlled integrated data-driven manufacturing system. This system is able to both act as a discovery platform for novel CQAs as well as a production platform with the potential to minimize process variability. This will mitigate manufacturing risks and batch failures which will eventually enable these life saving medicines to reach more patients faster and at lower cost.

This talk will highlight these efforts and applications to both hollow fiber bioreactor development for Mesenchymal Stromal Cell (MSC) and vertical wheel bioreactor development for T-Cell production. An overview of our novel sensing and control techniques will be presented along with initial results from laboratory studies.