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Creating a Competency Model for the Next Generation Workforce in Cell Manufacturing

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CONTEXT

With the FDA approval of the first cell and gene therapies in 2017, and the tremendous promise of emerging biopharmaceutical drugs, biomanufacturing - especially the transformative areas of cell and gene-therapy manufacturing - has rapidly become one of the most critical sectors of the biotech and pharma industry around the world. While early progress has been made to transition from lab-bench scale production through the first phase I and II clinical trials, to now more industrial, scaled manufacturing with 'Big Pharma' companies like Novartis, Bristol Myers Squibb, and Gilead launching commercial products, there are still large gaps that need to be addressed to move the current state of cell and gene therapy manufacturing into the future.

PURPOSE OR GOAL

The National Roadmap from the National Cell Manufacturing Consortium (NCMC) – a public-private consortium of industry, government, clinical, and academic leaders - identified the lack of a skilled cell-manufacturing workforce as a major barrier for the acceleration of promising therapies into products. The goal of this work was to develop a competency model for engineering graduate students that provides a framework to train the future biomanufacturing workforce, identify educational strategies that enable graduate students to attain the competencies and design effective processes to assess student learning.

APPROACH OR METHODOLOGY/METHODS

The competency model was developed with input from a broad range of engineering faculty with expertise in cell manufacturing technologies, including scalable cell processing, sensors and controls, and omics and modeling. Additional feedback was provided by several industry representatives to ensure the competency model aligned with their engineering workforce needs. A modified Delphi method was used to form consensus from all stakeholders. Briefly, the Delphi method is an iterative process that comprises three to four rounds before consensus is reached.

ACTUAL OR ANTICIPATED OUTCOMES

The initial model was directed at engineering graduate student education and incorporated technical competencies. Additional competencies were developed around non-technical skills including regulatory knowledge, cultural sensitivity, and ethics and public policy. Two graduate-level biomedical engineering courses have been developed to enable students to attain these competencies. Additionally, several co-curricular activities are available, including industry internships, inter-institutional research sabbaticals, and an international research experience.

CONCLUSIONS/RECOMMENDATIONS/SUMMARY

In summary, a generalized framework has been developed that articulates the competencies that engineering graduates should attain to be prepared for the biomanufacturing workforce. This framework can be broadly applied by any post-graduate program that serves stakeholders from the biomanufacturing or biopharmaceutical industry.

KEYWORDS

Biomanufacturing; Cell Therapy; Competency Model; Educational Strategies; Assessment

Introduction

Cell Therapy

Cell therapy refers to the transformative medical technologies that utilizes cells to restore, repair, or replace damaged or diseased tissues in the body. It involves the administration of live cells, either from the patient's own body (autologous) or from a donor (allogeneic), to promote tissue regeneration and restore normal cellular function. These cells can be sourced from various origins, including embryonic stem cells, induced pluripotent stem cells (iPSCs), mesenchymal stromal cells (MSCs), hematopoietic stem cells (HSCs), and immune cells (Abbaspanah et al., 2021; Bhandari et al., 2023; Cao et al., 2020; Cardoso et al., 2018; Chivu-Economescu & Rubach, 2017; Dagar et al., 2023; Maude et al., 2014; Maude et al., 2018; Song et al., 2020; Wang et al., 2023; Yang et al.). Cell therapy holds great promise for treating a wide range of diseases and conditions, including cancer (Zhao & Cao, 2019), genetic disorders (Nóbrega et al., 2020), autoimmune diseases (Mikami & Sakaguchi, 2023), neurodegenerative disorders (Sivandzade & Cucullo, 2021; Temple, 2023), cardiovascular diseases (Banerjee et al., 2018), and more. The field of cell therapy encompasses different approaches, such as stem cell transplantation, adoptive cell transfer (e.g., CAR-T cell therapy), and tissue engineering. Several cell therapies have received regulatory approval in recent years (Fala, 2018; Florko, 2017); however, a major bottleneck in the successful commercialization of these treatments is the scale at which they can be produced (Levine et al., 2017). Thus, there is a critical need to develop scalable manufacturing processes for therapeutic cells that are reproducible, safe, and affordable.

The National Science Foundation (NSF) funded Engineering Research Center for Cell Manufacturing Technologies (CMaT) is an initiative aimed at advancing the field of cell manufacturing (Mardhanan et al., 2022). The center is comprised of four primary institutions: Georgia Institute of Technology, the University of Georgia, the University of Wisconsin at Madison, and the University of Puerto Rico Mayaguez. CMaT focuses on developing innovative technologies and processes for the scalable production of high-quality cells, including stem cells and immune cells, for therapeutic purposes. The center brings together a multidisciplinary team of biomedical and chemical engineers together with electrical, mechanical, industrial-manufacturing, and systems engineers (i.e., experts in cell processing, cell characterization, sensors, microfluidics, disease-on-a-chip, bioreactors, biomaterials, process engineering, manufacturing design, and supply-chain management). They work closely with cell biologists, clinicians, ethics, policy, and workforce development experts, alongside industry partners to tackle the challenges associated with cell manufacturing, such as improving cell quality, optimizing production efficiency, ensuring regulatory compliance, and developing a highly skilled workforce.

The lack of a highly skilled and interdisciplinary workforce specialized in various fields, including engineering, computational modeling, biological science, physics, chemistry, mathematics, and statistics presents the greatest threat to next-generation intelligent manufacturing around the world (Consortium, 2019; Wang, 2018). To enhance the existing and future workforce, it is crucial for the cell manufacturing community to promote effective communication between academia and industry. This collaboration will help identify the most essential skills required in the industry and align training programs with industry demands, ensuring that the workforce is well-equipped to meet industry needs and drive further advancements in cell manufacturing.

Competency Based Workforce Development

A holistic workforce should be comprised of individuals that can apply technical knowledge across engineering, data sciences, cell biology, and manufacturing sciences to solve problems

with consideration for different contexts, including societal, economic, cultural, political, and global factors. This requires students to develop intra- and interpersonal skills, workplace skills, and job-specific competencies in addition to technical competencies.

Competency-based education is built around a complex set of skills that can be characterized around knowledge, attitude and behaviour, and competence as personal ability. The notion of developing competent engineers has been around for over 30 years and was the foundation for Boeing's "Attributes of an Engineering Graduate" (Paul et al., 2015), the National Academy of Engineering "Engineer of 2020" (National Academy of Engineering, 2004) and ABET EC2000 (Volkwein et al., 2004) and has subsequently been adopted by numerous regional and national accreditors through outcomes-based assessment. In contrast to the more traditional structure-oriented and process-oriented models for curriculum design, competency models shift the focus from *what the faculty teach* to *what students learn* (Fraser & Bosanquet, 2006). Hence, the driving force for the curriculum is on students' ability to demonstrate knowledge application rather than a focus on completion of total number of credit hours passed and completion of specified credit hours in defined subject areas. The focus of assessment changes from norm-referenced, summative evaluation to criterion-referenced formative evaluation (Carraccio et al., 2002). This can be beneficial to non-traditional students and can provide greater access for adult learners and veterans, who may have acquired on-the-job skills.

The overall objective of this project is to develop a holistic (or multi-dimensional) competency model comprised of a collection of individual student learning outcomes required from each individual student to achieve the desired knowledge, skills, attitudes and behaviours deemed necessary for the biomanufacturing workforce (Straka, 2004). The initial phase of the project, and the focus of this paper, was to develop a competency model for graduate education in cell manufacturing. The model and the associated educational strategies are based on well-established principles of student learning.

Educational Strategies

The traditional, didactic classroom setting does not easily lend itself to effective training of professional outcomes and holistic competencies. Therefore, it becomes necessary to make pedagogical changes inside the classroom and look beyond the classroom at co-curricular activities that adequately prepare future graduates. Students develop their knowledge and skill over time, and it is the cumulative result of the curricular path they follow (i.e. the courses they take), the pedagogies employed by their instructors, and their co-curricular experiences (Terenzini et al., 1995), that shape their professional future, as shown in Figure 1. Co-curricular experiences may include, for example, research experiences, industry internships, involvement in student competition teams (e.g., the three-minute thesis), and international research experiences.

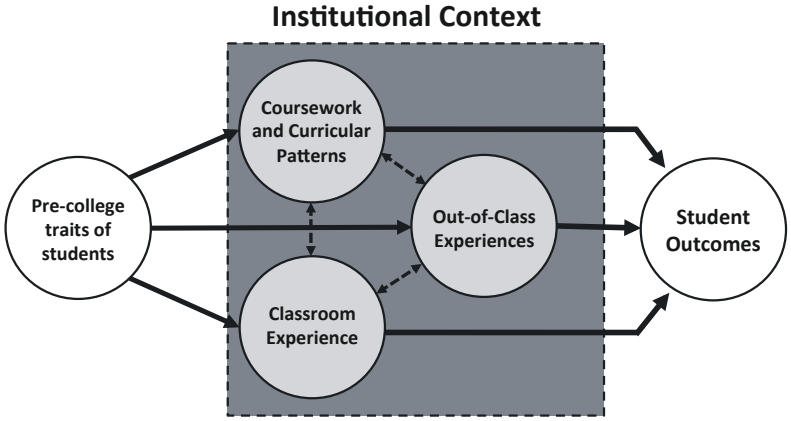

Figure 1: A general conceptual model of college influence on student learning. Adapted from Terenzini et al. (Terenzini et al., 1995).

Methods

The first stage of developing a cell manufacturing workforce-specific competency model was to identify competencies determined by our stakeholders. Our stakeholders consist of scientific and engineering domain experts from industry, academia, clinical sciences, and government organizations as well as policy experts, education experts, and experts in diversity and inclusion.

Faculty workshop

A mini workshop was scheduled with faculty from the four different institutions affiliated with CMaT who each had expertise in cell manufacturing technologies. Their technical expertise spanned three domain areas, namely (i) omics and modelling, (ii) sensors and controls, (iii) scalable cell processing and process. The goal of the mini workshop was to identify and define the competencies associated with graduate student education in cell manufacturing. During the workshop, the faculty were divided into small working groups and asked to individually brainstorm competencies associated within a specific technical area. Each competency was required to include an action verb at the appropriate level for graduate students and a specific subject for the focus of training. Following the individual brainstorming, the small sub-groups reconvened to share their ideas via a nominal group process. The output from each sub-group was collected and analysed to identify common themes.

Industry Focus groups

Following the faculty workshop, a focus group was organized with key industry partners that represent different areas of cell manufacturing. Prior to the focus group, a structured discussion guide was prepared with key questions and topics to explore during the session. It was essential that all participants in the focus group had the opportunity to share their experiences and perspectives and express their opinions related to workforce development.

After the focus group, the participant responses were analysed for key themes that emerged during the discussion. The common patterns and trends that were identified provided a comprehensive understanding of the desired competencies for the cell manufacturing workforce.

Review and Revision

An affinity process was used to condense the information from each group into a set of draft competencies. Briefly, the data were grouped into similar items and each group was labeled with a descriptive title or keyword. This helped to clarify what each group represented. The categorized information was analyzed, looking for trends, commonalities, and overarching themes. A set of competencies emerged from this process, with some being more prominent than others, although all were regarded equally, and no ranking or prioritization was performed. The draft competencies were shared with the CMaT executive committee. The executive committee was asked to comment on the competencies and provide suggestions and revisions. This collaborative approach ensures that the skills identified through the focus group and faculty workshop could be integrated into the educational curricula, training programs, and policies to support the growth and success of the cell manufacturing workforce.

Outcomes

Competencies

Based on the input received from the faculty mini workshop, the industry partners' focus group and the iterative revision process, cell manufacturing workforce competencies for bioengineering graduate students were identified in three fundamental areas. These areas were: (i) experimental design, implementation, and analysis; (ii) practical application and (iii) professional skills. The competencies identified in each of these three areas are shown in table 1. Overall, there was strong agreement on the competencies from all stakeholder groups; however, university faculty

placed a higher emphasis on technical, experimental skills, whereas industry stakeholders placed a higher emphasis on statistical analyses, project management, and regulatory affairs.

Table 1: Stakeholder informed competencies that are necessary for the future cell manufacturing workforce.

Experimental design, implementation, and analysis	Practical Application	Professional Skills
- Design experiments with appropriate quality controls, statistical power, and number of replicates. - Apply univariate or multivariate statistical analysis to experimental data. - Assess differences between various culture conditions, including single cell vs. bulk/population analyses and bench scale vs. industrial scale manufacturing. - Identify assays for monitoring CQA during cell manufacturing processes. - Distinguish cell-type specific constraints on the use of various bioprocess platforms and analytical methods	- Understand project management and planning, supply chain models and their analysis. - Explain the issues pertinent to industry as they relate to regulatory affairs and GMP for cell therapies.	- Understand current and past legal, political, ethical, and social issues related to cell therapies. - Demonstrate cultural sensitivity. - Be knowledgeable of international and domestic regulatory policies and ethics. - Communicate scientific and technical information to lay audiences

Educational strategies

Graduate Courses

Two distinct graduate-level courses were developed and refined to integrate specific competencies as course learning objectives. These courses serve as core offerings, catering to graduate students from diverse academic backgrounds, such as Bioengineering, Mechanical Engineering, Chemical Engineering, Biochemistry, Industrial Engineering, among others. The primary goal was to foster a collective comprehension of the technical intricacies, as well as the broader ethical, policy, and societal dimensions associated with cell manufacturing.

The first course, titled "Therapeutic Cell Manufacturing," aims to establish a shared understanding among students from various disciplines regarding the crucial technical challenges that underpin the success of the cell therapy industry. This synchronous course is simultaneously conducted at all CMaT institutions, enabling students to engage in real-time interactions with instructors, guest presenters, and fellow participants. In addition to faculty members from each campus, industry partners deliver multiple presentations, facilitating connections between graduate students and industry representatives. These sessions provide students with insights

into the current state-of-the-art practices and existing challenges within the dynamic landscape of cell manufacturing and cell therapy.

The second course, "Regenerative Medicine, Cell Manufacturing, and Society," is specifically designed to introduce graduate students to the ethical, policy, and social considerations relevant to the field of cell manufacturing. This collaborative course was developed by content experts from the University of Wisconsin – Madison and the Georgia Institute of Technology, incorporating valuable input from leaders within CMaT with expertise in cell therapy research, innovation, technology transfer, and Diversity, Equity, and Inclusion. By exploring these interdisciplinary perspectives, the course encourages students to critically examine the ethical implications, policy frameworks, and societal impact of cell manufacturing and regenerative medicine.

Graduate Research

The objective of the graduate program is to produce graduates with research experience in various aspects of cell manufacturing and mastery of the key technical and professional skillsets necessary for engineering graduates to advance the field. To achieve these goals, graduate students conduct research aligned with the goals of CMaT, to collaborate in the creation of CMaT's center culture, and to participate in the unique educational and professional development opportunities offered by the center.

Student Exchanges

To enhance collaboration and facilitate knowledge exchange among CMaT institutions, as well as promote information sharing, protocol standardization, and an appreciation of diverse research cultures, CMaT established two short-term sabbatical programs for graduate students. These programs aim to provide valuable opportunities for students to broaden their training experiences and skillsets.

The first program is the cross-institutional training sabbatical, which enables students to engage in a 4 to 6-week training experience at a CMaT domestic partner institution or other collaborating institution. This sabbatical offers trainees the chance to acquire complementary skillsets and utilize specialized tools in cross-disciplinary settings. The primary objective of this program is to accelerate research training, ensuring standardized methods and tools across different laboratories while promoting team integration. Additionally, trainees can spend part of their sabbatical at external sites, such as regulatory agencies, government labs, patent law firms, or public policymaking institutions.

The second program is the international research experience (IRE), where students can participate in a 4 to 8-week visit to one of CMaT's international research partners. This program allows students to engage in collaborative research and experience different research cultures, fostering global perspectives and expanding their scientific networks. The IRE offers several benefits to graduate students from the United States, including firsthand research experience in Ireland, Canada, or Japan, exposing students to the research culture, socio-political background, intercultural teamwork, and research infrastructure specific at the host institution, and enabling students to experience and engage with international cultures, societies, and languages.

The expectation is that the IRE will foster future collaborations between the host laboratory and the student's home laboratory, contributing to long-term scientific partnerships and knowledge exchange.

Industry Internships

Industry internships offer graduate students an opportunity to gain practical experience in a non-academic environment. These internships enhance technical proficiency, providing exposure to industry-specific techniques and processes. Students acquire insight into regulations, quality control, and industry best practices. Internships also enable students to develop project management skills, collaboration, and problem-solving abilities. They establish professional connections, leading to future opportunities and awareness of emerging trends. By participating in internships, students acquire a comprehensive skill set, industry insights, and valuable connections, preparing them to contribute effectively to the evolving field of cell manufacturing.

Mapping Competencies and Educational Strategies

To ensure that our education strategies fully supported the attainment of the student competencies, we mapped each activity to the different proficiencies. The mapping is shown in Figure 2 below.

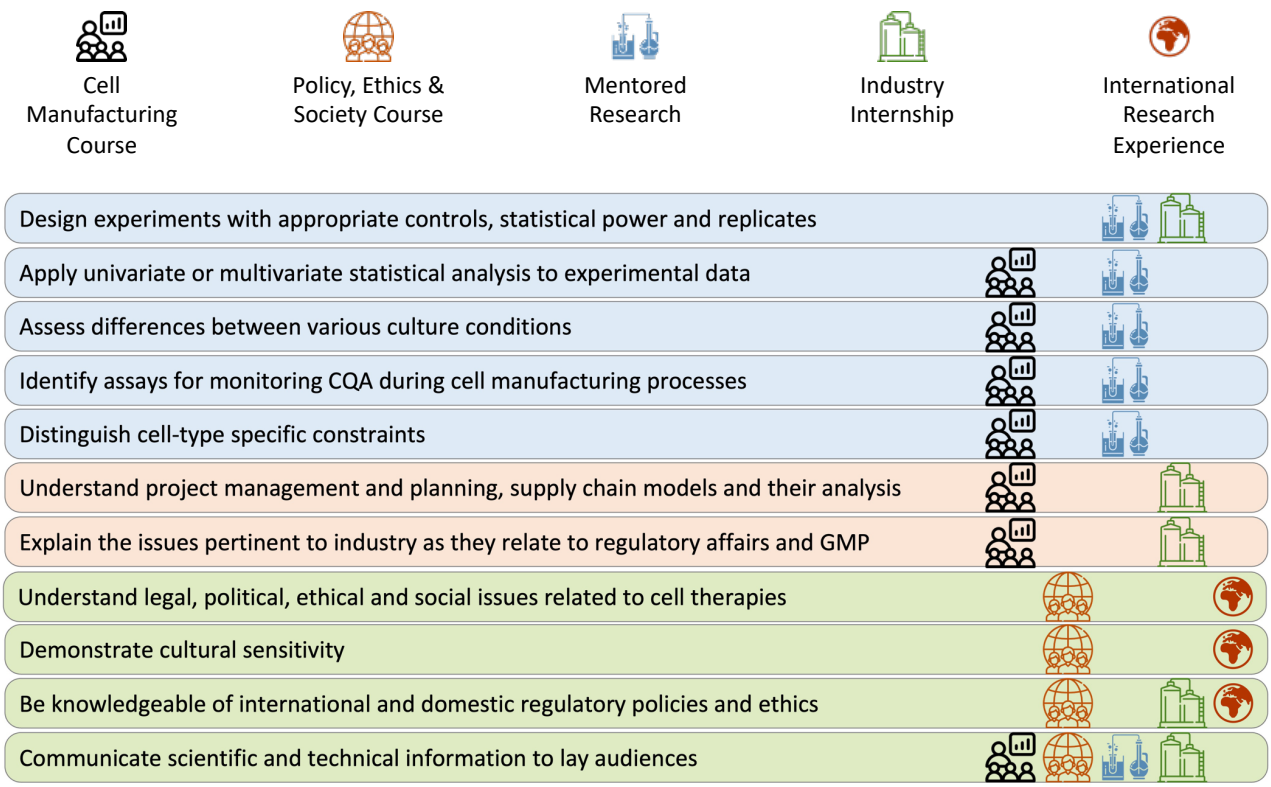

Figure 2: Mapping to show how the educational strategies, including the *Cell Manufacturing* course, the *Policy, Ethics and Society* course, mentored research (including domestic student exchanges), industry internships and international research exchanges contribute to the development of the cell manufacturing competencies for graduate students.

Conclusions

In summary, a generalized framework has been developed that articulates the competencies that engineering graduates should attain to be prepared for the cell manufacturing workforce. This framework can be broadly applied by any post-graduate program that serves stakeholders from the biomanufacturing or biopharmaceutical industry.

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