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ISCT Committee Paper

Cell and gene therapy workforce development: the role of the International Society for Cell & Gene Therapy (ISCT) in the creation of a sustainable and skilled workforce in Europe

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ABSTRACT

The development and production of cell gene and tissue (CGT)-based therapies requires a specialized workforce. Entering the CGT arena is complex because it involves different scientific and biomedical aspects (e.g., immunology, stem cell biology and transplantation), as well as knowledge of regulatory affairs and compliance with pharmaceutical quality standards. Currently, both industry and academia are facing a worldwide workforce shortage, whereas only a handful of educational and training initiatives specifically address the peculiarities of CGT product development, the procurement of substances of human origin, the manufacturing process itself and clinical monitoring and biovigilance. The training offered by traditional Master's and PhD programs is not suited for training a skilled workforce ready to enter the increasingly fast-growing CGT field. Indeed, typically these programs are of long duration and only partially cover the required competencies, whereas the demand for a specialized workforce relentlessly increases. In this paper, we (i) present and discuss our understanding of the roots of current growth acceleration of the CGT field; (ii) anticipate future workforce needs due to the expected increase of marketed CGT-based therapies and (iii) evaluate potential solutions that seek to adapt, develop and implement current educational and training initiatives. Importantly for these solutions, we call for scientific societies, such as the International Society for Cell & Gene Therapy, to play a more active role and act as catalysers for new initiatives, building bridges between academia and Industry to establish effective educational and training programs that will engage and prepare a new generation of qualified professionals for entry into the CGT field.

From Manual Processing to the Machine Revolution

A huge research and development effort in the cell and gene therapy field in recent decades has resulted in the acceleration of marketing authorizations in North America, Europe and Asia. This contrasts with apparently little progress in the actual implementation of automation and intensification of bioprocesses to produce clinical-grade cell, gene and tissue (CGT)-based therapies. Both the infrastructure and the qualified personnel capable of guaranteeing cell- and tissue-harvesting processes (e.g., apheresis or bone marrow aspirates) that isolate cells, after appropriate manipulation, for use as CGT products, have historically been the prerogative of academic centers. The increase in the demand for qualified personnel will therefore require more and more economic and educational resources from academic centers, creating talent development dynamics atypical of the way in which these entities usually operate. Moreover, the manufacture of CGT-based therapeutics is complex and remains highly dependent on

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manual production, despite the number of potential solutions commercially available, particularly in the autologous setting. Further progress in the processing of autologous and allogeneic CGT-based treatments requires the active testing and validation of bioprocess designs adapted to the characteristics of each product, coupled with continuous data acquisition and analytic tools for eventually fully-automated manufacturing [1]. Long hours spent in clean-room environments for greater bulk manufacturing is a less-appealing prospect for both scientists and research technicians, making automation even more vital. The prospect of automation and scale-up manufacturing highlights the transiency of current manual strategies and the need for professionals who understand the scientific and technical background of procedures and how to adapt these to complex logistics and strict quality standards [2,3]. The value chain in the CGT field spans from donor identification and procurement of the appropriate substance of human origin (SoHO) to patient treatment and follow-up [4]. Successful implementation of this process involves specific knowledge in basic, clinical and regulatory science, comprising scientific, technical, medical and ethical aspects of product development, manufacture and treatment, as shown in Figure 1.

Since CGT therapies will not replace but mostly add to current existing therapies, we can expect a greater and more complex workload with respect to patient care standards. In addition, all professionals involved, including the health care personnel who will administer the CGT therapies, will necessarily need to receive a regular training update. Both these issues present obstacles to the rapid growth of the sector. Important financial, time, institutional and regulatory investments will therefore need to be made before the benefits (e.g., improved health of the population and its corresponding returns) can be reaped. Focusing on the competencies and expertise needed for the procurement of SoHO, processing and thorough grounding in the regulatory and quality aspects of the development of this type of product, adequately trained professionals are hard to find amid the worldwide workforce shortage. This situation is not restricted to industry but is also present in academia, where a lack of scientists interested in becoming postdoctoral fellows has been reported in scientific forums [5,6].

Given the various hurdles that contribute to the current shortage of a specialized workforce (i.e., competitive wages, willingness to relocate, migration policies and millennial and Generation Z values), education and training are of key importance. The rapid growth of the CGT field in this respect contrasts with the long timescales involved in addressing the workforce shortage. There is therefore a need to direct new and creative efforts towards improving workforce development programs that focus not only on the manufacturing itself but on all aspects of product development, SoHO acquisition, manufacture and clinical use. Furthermore, continuous training to keep the workforce abreast of scientific and technical progress is needed.

Scientific Societies Are Part of the Solution

At the 2022 Annual Meeting of the International Society for Cell & Gene Therapy (ISCT), held in San Francisco (4–7 May, 2022), the theme of CGT Workforce Development was discussed, including how to address the challenges of maintaining and increasing the numbers of competent, skilled personnel in this exponentially growing field. In addition, the problems and cross-sector impact faced by the shortage of a trained workforce were explored. Neither industry nor current academic tracks seem prepared to coach a new generation of professionals in the skills and competencies needed for the design, development, production, quality control and hence wider implementation of CGT-based therapies in a tightly regulated environment [6,7]. To this end, the ISCT set out to first identify and disseminate information on the relevant training already available, then help to organize specialized training and workforce development programs currently lacking in the target value chain of the CGT field, as depicted in Figure 2.

Concerning the first initiative, at the beginning of his term as Vice President of ISCT Europe, Professor Massimiliano Gnecchi, together with the executive committee, listed the issue of workforce development among the strategic tasks to be addressed under his leadership. The first initiative in this line was to identify existing training programs, describe their characteristics and summarize all this information in a database to be made available to ISCT members. The final aim is to assist professionals looking for a specific program with which to implement their own training, helping them to enter the production chain of CGT products as experts. The initial survey on CGT-related education and training programs, focusing on Europe, identified key study areas: basic research, early discovery, non-clinical development, clinical development, regulatory review and post-market monitoring. Remarkably, the value chain from idea conception to post-market monitoring is apparently covered, but by short courses providing broad updates on specific key areas, with a rapid return of new, albeit limited set of competencies to meet at least some of the CGT chain demands (see Figure 3, supplementary File 1). This seems of use since formal educational programs (e.g., B.Sc., M. Sc., Ph.D.) offered by universities issuing official diplomas are of

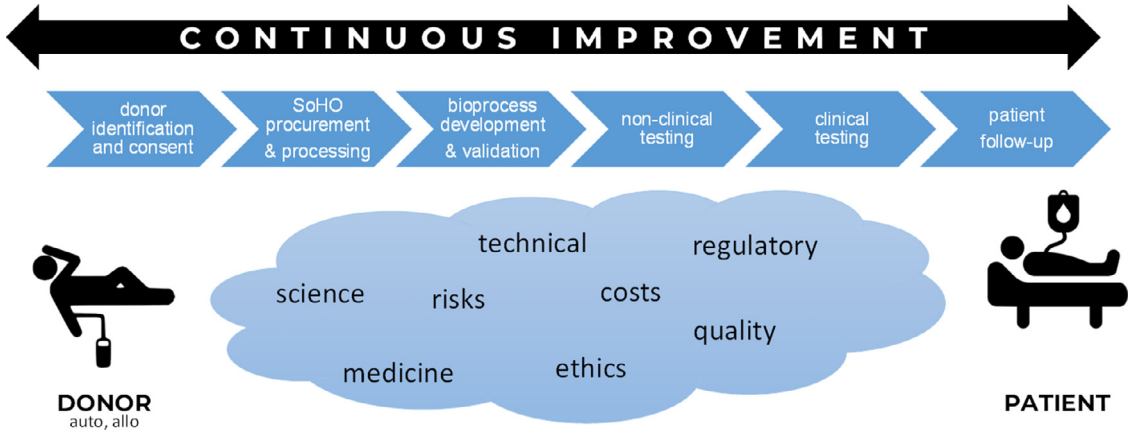

Figure 1. Phases of CGT-based medicines development and clinical use. Stages of the procurement of SoHO, product development, manufacture and treatment of patients are clearly defined, whereas transversal aspects impact at different points on the value chain. Remarkably, scientific and technical progress propels improvements in the reformulation of procedures and evidences the need for continuous training and requalification of CGT-based therapy professionals. allo, allogeneic treatment setting; auto, autologous treatment setting.

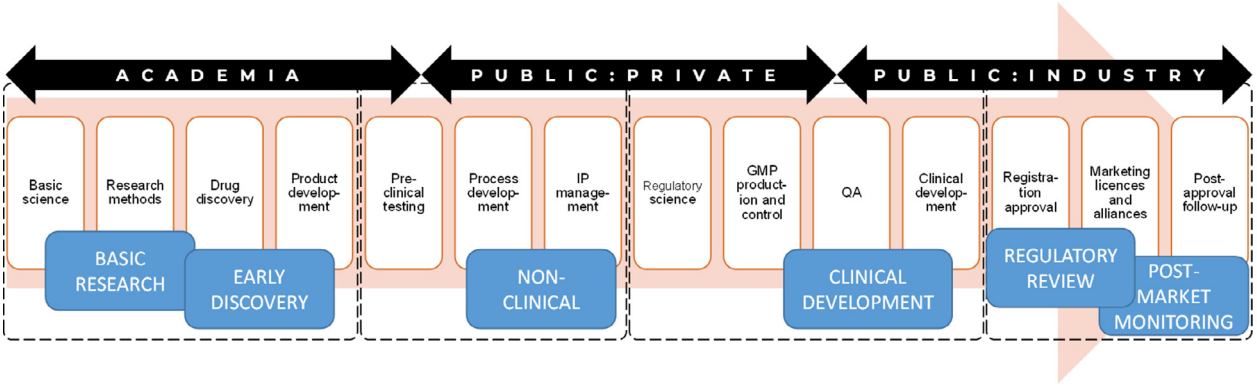

Figure 2. Target value chain in education and training in the CGT field. Identification of educational and trainings needs are represented as boxes across the value chain in CGT development, manufacture and treatment. Accountability for offering adequate training is proposed to be driven by either academia, public–private alliances or public initiatives (e.g., hospitals, academia) and industry pursuing marketing approval. IP, intellectual property; QA, quality assurance.

longer duration and require significant financial input, making this path intrinsically unable to grow quickly. We are currently optimizing the format with which the results can best be presented to the public. The platform with all the data will soon be available online via the official ISCT website, to guide potential students as well as identify the educational and training gaps that need to be addressed.

The ISCT's second initiative involves the Workforce Development in Biomanufacturing program, a global initiative in partnership with the NSF Engineering Research Center for Cell Manufacturing Technologies, which addresses key topics in CGT manufacturing and development, including stem cell and immune cell engineering and therapies; quality assurance and regulatory framework; cell bioprocessing and manufacturing; cell product characterization and the importance of standards. The ISCT is offering full tuition scholarships for members of ISCT Europe to enroll for the Master's or Specialization Degree in Manufacturing of CGT at the University of Granada/Andalusian Network for the design and translation of Advanced Therapies. This master's program was designed for professionals currently working, or intending to work, in Good Manufacturing Practice–compliant CGT manufacturing, as well as for professionals with diverse backgrounds seeking to update their knowledge [8]. Additionally, an online educational program on CGT Manufacturing is being offered free of charge for ISCT members, covering the fundamentals of regulation and the specific knowledge necessary for the development of CGT-based medicinal products, including cell and gene therapy manufacturing methods; quality assurance; product development pathways; Good Manufacturing Practice compliance; investigational medicinal product dossier writing and biosafety.

These initiatives are intended to complement those offered by other scientific and professional societies that are also aware of the situation and have explored different ways to engage scientists and technologists in CGT career paths. Some examples of these are the Spring School offered by the European Society of Gene and Cell Therapy, the Summer/Winter School offered by the Tissue Engineering and Regenerative Medicine International Society, short courses by the European Society for Animal Cell Technology, or the range of courses offered by the European Society for Blood and Marrow Transplantation [9,10].

Based on our experiences and the real need for more specialized personnel, we advocate the engagement of scientific societies, in particular as catalysers for new initiatives and promoters of collaborative efforts between regulatory bodies, academia and industry. By creating a collaborative teacher group, for instance, we might establish effective, tailor-made educational and training program to qualify a new generation of professionals for the ultimate benefit of patients. Only then will we be able to expand patient access to affordable, life-saving and life-enhancing innovative therapies.

Initiative (course, workshop, university prorgramme)	BASIC RESEARCH	EARLY DISCOVERY	NON-CLINICAL DEVELOPMENT	CLINICAL DEVELOPMENT	FDA/EMA REVIEW	POST-MARKET MONITORING
Stem Cells and Regenerative Medicine	3	3	3	0	0	0
Bioprocessing & Manufacturing of Gene and Cell Therapy Products Course	2	2	2	2	0	0
Cell therapy: from bench to the bedside and return	2	2	2	2	0	0
Pharmaceutical training	1	1	1	1	1	1
CAR-T cell therapies	0	0	0	3	0	0
Regulatory Science for Advanced (Gene and Cell) Therapy: Advanced Therapies - Bench to Medicine	0	0	0	2	2	2
Clinical Development	0	0	0	1	1	1
Pharmaceutical development of ATMP	0	0	1	1	1	1
Practical Application of Risk-based GMP&Quality principles to Clinical Development in ATMPs	0	0	1	1	1	1
Aseptic skills for ATMP Manufacturing Practitioners	0	0	1	1	1	1
Training courses	0	0	1	1	1	1
MSci Cellular Manufacturing and Therapy	0	0	4	4	4	0
Gene and Cell Therapy Product (ATMP) Drug Development	0	0	3	3	3	3
Genes, Drugs and Stem Cells - Novel Therapies	0	0	4	4	4	4
MSc Advanced Therapy medicinal Products	0	0	4	4	4	4
Advanced EATRIS	0	0	4	4	4	4
Stem Cell & Regenerative Therapies: From Bench to Market MSc	0	0	4	4	4	4
Master in Manufacturing of ATMP	0	0	4	4	4	4
EMTACT & Updates on TACT	0	0	4	4	4	4

Figure 3. Non-exhaustive list of educational and training initiatives in the CGT arena available in Europe. Classification of each initiative has been made based on the value chain presented in Figure 1, scoring as follows: 0 = not aligned on target subjects; 1 = superficial (often short) course on one/a limited number of target subjects; 2 = more thorough on limited number of target subjects; 3 = longer and/or higher (professional) level course combining several target subjects; 4 = academic (e.g., M.Sc.) education on more target subjects.

Outlook

Although a boost to educational and training activities sufficient to meet current CGT manufacturing requirements is urgently needed, it is likely that implementation in the use of bioreactors and automation will provide a partial solution to the shortage of a human workforce and the minimum needed to boost production without a commensurate increase in hands-on, clean room human power. However, we also anticipate a growing lack of professionals in other stages of the value chain, such as cell procurement. Indeed, these personnel will be faced with important responsibilities, such as increasing numbers of patients and real-world data management. It is therefore important that scientific societies put workforce development across the whole value chain on their agendas, and take initiatives to develop collaborative efforts between academia and industry to establish effective educational and training programs. ISCT Europe is already moving in this direction, hoping that our output may help a new generation of professionals to become key players in the CGT arena, with the ultimate goal of expanding access to affordable, life-saving and life-enhancing innovative therapies for our patients.

Author Contributions

Conception and design of the study: JV, FS-G, MG and JJZ. Acquisition of data: JV and JJZ. Analysis and interpretation of data: JV and JJZ. Drafting or revising the manuscript: JV, FS-G, MG and JJZ. All authors have approved the final article.

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Declaration of Competing Interest

JV, FS-G, MG and JJZ are members of the ISCT-EU Executive Committee. JV and JJZ are co-directors of the joint UAB & LeidenU's official inter-university Master's Degree in Transfusion Medicine and Cellular and Tissue Therapies, and the Update, both initiatives mentioned in this manuscript. JV is the co-organizer of the European Society for Animal Cell Technology's Bioprocessing and Manufacturing of Gene and Cell Therapy Products course mentioned in this manuscript. JV has contributed with teaching material to the Master's Degree in Manufacturing of Advanced Therapy Medicinal Products at the University of Granada mentioned in this manuscript.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jcyt.2023.06.006.

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