Accelerate or Decelerate? Identifying Changes and Challenges with AI in Cell and Gene Therapies

Abstract
AI is accelerating research in Cell and Gene Therapies (CGTs), yet its complexity and uncertainty pose challenges to the verification and validation of biomedical knowledge. Will these challenges slow down its path to application, and how can they be addressed? This research aims to identify key changes and challenges in knowledge production, to propose targeted recommendations for different stages and stakeholders, thereby accelerating the translation of scientific knowledge into real-world use. Case studies will be conducted at the UKRI Hub for Advanced Therapeutics at Edinburgh, employing semi-structured interviews and ethnographic methods to collect data, and further promoting effective relationships among academia, industry, and funding/regulatory bodies.

Introduction
AI is accelerating research in CGTs and reshaping the CGT value chain (Bhandari et al., 2022). Existing research and practices demonstrate the significant achievements and potential of AI in this field, such as identifying new gene targets, designing novel vectors, optimising experimental conditions, predicting outcomes, and recommending optimal solutions to prevent undesirable immune responses post-gene therapy treatment (Danaeifar and Najafi, 2024). Since the first FDA approval of gene therapy in 2017 and the approval of the first CRISPR drug in the UK in 2023, these successes are largely due to improved scientific understanding and more precise control and manufacturing to meet the stringent requirements of clinical applications.

However, AI also introduces greater complexity and uncertainty, posing significant challenges to knowledge verification and validation, such as the 'chasm' between accuracy and efficacy (Kelly et al., 2019). These challenges could make it difficult to assess the risks and benefits of using AI in CGTs, particularly in cases such as oncology, cardiovascular disease, and rare diseases, where the complexity of models and biological systems is further compounded, making it difficult for regulators to determine acceptable levels of risk.

Consequently, the overall research question is: How could the use of AI in CGT research change the knowledge production process, and potentially challenge its progress towards applications? Three sub-questions are as follows:
1. How does and might AI change the construction and understanding of biomedical knowledge in CGTs?
2. What challenges do and might these changes pose to the verification and validation of biomedical knowledge in CGTs, and why?
3. How do and might these challenges affect the translation and application of CGT research, and how should they be addressed?

The questions encompass both present and future dimensions. Question 1 requires an initial understanding of the specific use and potential of AI in CGTs, observing and assessing the changes it brings to knowledge production.

Question 2 is critical in identifying the challenges brought by technological changes. Although AI can provide more accurate predictions and optimise designs, the formal verification of deep neural networks and the interpretation of causality have not yet established a general methodology (Casadio et al., 2024). The specificity of models in addressing biomedical issues, especially for therapeutic purposes, poses further challenges to validation and evaluation.

Question 3 asks whether these challenges are causing a deceleration in translation and application, how to address them, and how to accelerate without getting stuck in endless theoretical verification. This involves broad considerations in practice, including different stages of the CGT value chain, positions of various stakeholders, and dimensions such as ethics, responsibility, and sustainability.

Research Challenge

Interdisciplinary knowledge: Applicants are expected to have capabilities in qualitative research methods and interdisciplinary analysis of complex settings, as well as a theoretical background in Science and Technology Studies (STS) and Business Studies, and a good understanding of AI and Biomedicine.

Connections with external partners: This research includes both scientific and applied practices, engaging different types of stakeholders. It involves not only observation but also intervention and potential collaboration, which requires excellent networking and communication skills with diverse academic and non-academic groups.

Data & Methodology

Case studies will be conducted in the Stracquadanio Lab to investigate the impact of AI on the roles, changes, and challenges at different stages of the 'DBTL-A' pipeline:
Design (D): Generative AI for biologics design.
Build (B): Genome engineering for biologics production.
Test (T): Automated high-throughput protocols for experimental testing.
Learn (L): Deep graph neural networks to decode cancer genetics.
Apply (A): Next generation therapies for Lysosomal Storage Diseases.

Semi-structured interviews and ethnography will be employed for qualitative data collection. Interviews (years 1-2) will be conducted in the UK, primarily with scientists working on AI and CGTs, to address Questions 1 and 2, as well as with industrial partners, policymakers, and regulators in this field, to answer Question 3. Additionally, ethnographic fieldwork (year 2) will help gain an in-depth understanding of the knowledge production process in the lab.

RRI/Ethical Considerations

The outputs of the research are designed to support and guide responsible conduct of biomedical research and innovation. Research ethics considerations include the risk of de-anonymisation of participants. The research will be subject to an ethical audit and review by the Ethics Committees in both Schools of Informatics and Social and Political Science.

Expected Outcomes & Impact

The research aims to identify key changes and challenges for AI in CGTs, facilitate the translation of scientific knowledge into real-world use, and provide potential 'acceleration' recommendations. The study is expected to result in a PhD thesis, potentially accompanied by research articles, industry reports, or policy papers, generating widespread impact across academia, industry, and funding/regulatory bodies.

References

Bhandari, M., Chang, A., Devenyns, T., Devereson, A., Loche, A., & Van der Veken L. (2022). *How AI can accelerate R&D for cell and gene therapies*. McKinsey's Life Sciences Practice. https://www.mckinsey.com/industries/life-sciences/our-insights/how-ai-can-accelerate-r-and-d-for-cell-and-gene-therapies#/

Casadio, M., Dinkar, T., Komendantskaya, E., Arnaboldi, L., Isac, O., Daggitt, M. L., ... & Lemon, O. (2024). NLP Verification: Towards a General Methodology for Certifying Robustness. *arXiv preprint arXiv:2403.10144*.

Danaeifar, M., & Najafi, A. (2024). Artificial Intelligence and Computational Biology in Gene Therapy: A Review. *Biochemical Genetics*, 1-24.

Kelly, C. J., Karthikesalingam, A., Suleyman, M., Corrado, G., & King, D. (2019). Key challenges for delivering clinical impact with artificial intelligence. *BMC medicine*, *17*, 1-9.