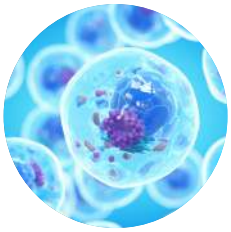
Cell Therapy – TRAcking, Circulation, and Safety (CT-TRACS)



Our Mission

The committee's mission is to facilitate the translation of cell-based therapies to the clinic by driving the development of tools, methods, and knowledge required to evaluate the safety and fate of therapeutic cells by identifying gaps/unmet needs and designing strategies to fill them, aligning "tools required" to available technology, understanding "cell fate" *in vivo*, addressing concerns regarding the potential for tumorigenicity, and developing scientific knowledge needed to help support international standards development.

Chairs

Public Chairs

Dr. Tineke van den Hoorn (Medicines Evaluation Board, The Netherlands)
Dr. Vladimir Ponomarev, Point of Administration–Biodistribution Working Group Co-Chair (Memorial Sloan Kettering Cancer Center)
Dr. Charlotte de Wolf, Tumorigenicity Working Group Co-Chair (Medicines Evaluation Board, The Netherlands)

Private Chairs

Dr. William (Bill) Shingleton (Cytiva)
Dr. Brooke Helfer (Celsense), Point of Administration–Biodistribution Working Group Co-Chair
Dr. Hiroto Bando (MEASURE Representative), Tumorigenicity Working Group Co-Chair

HESI Staff

Dr. Lucilia Mouriès (lmouries@hesiglobal.org)
Dr. Connie Chen (cchen@hesiglobal.org)

Webpage

https://hesiglobal.org/cell-therapy-tracking-circulation-safety-ct-tracs/

2021 Committee Highlights

Participating Organizations

7 government/regulatory agencies, **9** academic/research institutes, **17** industry, and **2** others

Publications

1 published

Scientific Meetings and Trainings

2 meetings and **1** workshop

- CT-TRACS Spring Business Meeting (May 2021, virtual; ~50 attendees)
- CT-TRACS Fall Business Meeting (November-December 2021, virtual; 4 individual sessions)
- EU Horizon 2021 nTRACK Invitational Workshop (March 2021, virtual; ~30 attendees)

Web Tools and Assays

1 database and 3 assays

- Cell Tracking Database: in development
- ddPCR assay: for detection of residual induced pluripotent stem cells (iPSCs) in cell therapy products derived from iPSCs (tumorigenicity assay)
- High efficiency culture (HEC) assay: for detection of residual iPSCs in cell therapy products derived from iPSCs (tumorigenicity assay)
- Induce-seq assay: for identification of double strand breaks in CRISPR edited cells (identification of off-target mutations related to CRISPR/Cas9 editing); new project launched in June 2021

Outreach

3 oral presentations and **1** webinar

- **1** oral presentation at the 20th Congress of the Japanese Society for Regenerative Medicine (JSRM) on the progress of the committee's international, experimental multi-site study (March 2021, virtual)
- **1** oral presentation at the Next Generation CAR & T-Cell Therapies Conference on "Creating a Feedback Loop Between Clinical Trials and Translational Science for Product Improvement" (June 2021, virtual)
- **1** oral presentation at the 2021 HESI Annual Meeting on "Induce-Seq for Identification of Off-Target Mutations in CRISPR Edited Cells" (June 2021, virutal)
- **1** webinar organized in collarboration with EATRIS on CT-TRACS regulatory perspectives (September 2021, virtual)

2021 Committee Highlights (continued)

Collaborations

1 internal and 3 external

- HESI Immuno-Safety Technical Committee (ITC) and HESI Genetic Toxicology Technical Committee (GTTC): formed the HESI Engineered Cell Therapies Safety Adivsory Core, with the possibility to extend collaboration to other committees in the near future
- CAR-T Consortium: ad-hoc interactions in support of project scoping
- Standards Coordinating Body (SCB): HESI staff is participating as external advisors
- EATRIS: co-organized a Regulatory Perspectives Webinar in September 2021

Geographic Representation

Germany, Japan, Netherlands, Sweden, Switzerland, United Kingdom, and United States

Working Groups

- **Point of Administration–Biodistribution (PoA/BD) Working Group (Cell Tracking).** This working group aims to identify current approaches, gaps, and needs in monitoring/evaluating the fate and activity of cells after their administration *in vivo*, to assess the safety of cell-based therapies.
- **Tumorigenicity Working Group.** This working group aims to address concerns regarding the potential for tumorigenicity of cell therapy products by assessing and/or developing methodologies and approaches that could support tumorigenicity evaluation.
  - **International Multi-Site Study.** The study is exploring *in vitro* methods to assess tumorigenicity in iPSC-derived cell therapy products.
    - ddPCR team completed step 1 of the study and is analyzing results from five sites to assess adjustments for step 2.
    - The HEC team completed the multi-site study (four sites participating) and is discussing potential follow-up studies.
  - **Advanced Sequencing.** The committee launched the first phase of a new project on advanced sequencing for identification of off-target mutations associated with genome editing. In collaboration with BrokenString, INDUCE-seq is being used to determine the level of DNA damage and genetic loci of damange of CRISPR/Cas9 edited cells.

Areas of Focus for 2022

- With the publication of its review manuscript, the PoA/BD Working Group will focus on concluding and releasing the Cell Tracking Database, leveraging the data in this public resource to identify new project areas and continuing collaboration with external partners such as ISCT for outreach to the broader cell and gene therapy scientific community. Two outreach activities held this year generated possible leads for future activities, which the working group is exploring over the last quarter of 2021.
- The Tumorigenicity Working Group will continue its focus on the experimental multi-site study (a multi-year project with anticipated end date in 2022), while expanding the development of tumorigenicity battery tests applicable to other cell therapy types such as CAR-Ts and CRISPR/Cas9 edited cells:
  - From the four project proposals presented to the committee between August 2020 and January 2021, one was launched in May 2021 (INDUCE-seq project and CRISPR/Cas9) and another received funding directed to the National Institute of Health Sciences (Japan). The committee continues to explore the refinement and resourcing for the other two proposals (IL-2 proposal scoping is being updated with input from the CAR-T Consortium and the SACF assay is anticipated to be a functional assay to follow the INDUCE-seq assay).
- Continue engagement with other HESI committees as part of the newly formed HESI Advisory Core Group for Engineered T-Cell Safety.
- Continue engagement with the CAR-T Consortium and SCB.

Strategic Impact Areas

Catalysis of New Science

The development of new project proposals, public calls for participants disseminated through the website and various HESI channels, and initial seed funding from the committee budget have enabled the launch of a new pilot project in 2021 (INDUCE-seq for identification of off-target mutations in CRISPR edited cells). These developments have generated significant momentum within the committee and interest from new participants.

Increasing the Audiences for Collaborative Safety Science

New calls for participation launched in early 2021 and new topic areas (e.g., CRISPR/Cas9) created momentum and renewed interest, as demonstrated by the number of new organizations who have joined in 2021. Additionally, the committee is venturing into the CAR-T cells space and engaging with players in that field.

2021 Awards, Grants, and Recognition

- An AMED grant was awarded to the National Institute of Health Sciences (Japan) for CT-TRACS related work (advanced sequencing technologies to assess the genetic stability of hPSCs after culture).
- HESI staff selected as mentor in International Society for Cell & Gene Therapy (ISCT) 2021-2022 Mentoring Program.

Publications

Published

Helfer BM, Ponomarev V, Patrick PS, Blower PJ, Feitel A, Fruhwirth GO, Jackman S, Pereira Mouriès L, Park MVDZ, Srinivas M, Stuckey DJ, Thu MS, van den Hoorn T, Herberts CA, Shingleton WD (2021) Options for imaging cellular therapeutics in vivo: a multi-stakeholder perspective. *Cytotherapy*, 23: 757-773. doi: 10.1016/j.jcyt.2021.02.005.

Participating Organizations

Government/Regulatory Agencies

Medicines and Healthcare Products Regulatory Agency (UK)
Medicines Evaluation Board (The Netherlands)
National Institutes of Health, National Cancer Institute
National Institutes of Health, National Heart, Lung, and Blood Institute
National Institute of Health Sciences (Japan)
US Food and Drug Administration
US National Institute of Standards and Technology

Academic/Research Institutes

Imperial College London
King's College London
Leiden University
Memorial Sloan Kettering Cancer Center, Sloan Kettering Institute
Newcastle University
Stanford University, Cardiovascular Institute
University College London
University of Sheffield
Wageningen University

Industry

Astellas Pharma, Inc.
AstraZeneca
Athersys, Inc.
Bayer
Bristol-Myers Squibb
Celsense
Charles River Laboratories
Cytiva
Fujifilm Cellular Dynamics, Inc.
Janssen Pharmaceuticals
Novartis
Roche
Sanofi
Sumitomo Dainippon Pharma
Takeda Pharmaceutical Company, Ltd.
TwinStrand Biosciences
VisiCell Medical

Others

Cell and Gene Therapy Catapult (UK)
European Infrastructure for Translational Medicine (EATRIS)