Embedding a comprehensive ethical dimension to organoid-based research and resulting technologies

HYBRIDA

MISSION

Develop a comprehensive regulatory framework for organoid research and organoid-related technologies.

CHALLENGE

Address the uncertainties in organoid research and develop a conceptual and regulatory framework to overcome the "person vs thing" dualism.

UNDERLYING LEVELS OF UNCERTAINTY

Conceptual

How do people conceive entities, which are not categorized either as persons or as things? How do we know the characteristics of these entities called organoids?

Epistemological

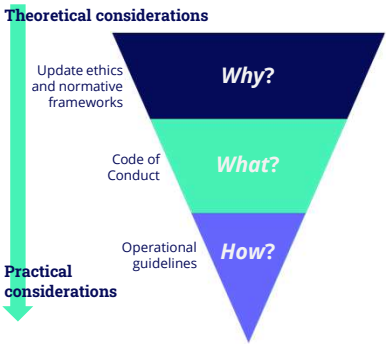
How to deal with forms of uncertainty that cannot be evaluated via statistical methods? This is particularly critical in cases where organoids are intended for personalized medicine.

Regulatory

How to regulate a recent and rapidly evolving technology with still limited use and major biological uncertainties?

HOW TO TACKLE THESE UNCERTAINTIES?

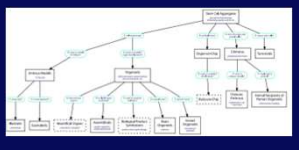
High-level description of main outcomes



- How to apply these new standards and good practices at the laboratory?
- What standards of conduct and good practices to follow to be in line with the enhanced ethics and regulatory frameworks?
- Why is there a need to enhance existing ethics and regulatory frameworks?

Fundamental concepts and definitions

HYBRIDA developed a socially robust typology of the main concepts used in organoid research. The typology identified concepts, which are briefly defined and exemplified, as well as non-definitive taxonomy that indicates directions for future study



Mapping organoids and HTA for organoids

HYBRIDA mapped and analysed how organoid technology has developed, by providing an historical overview of the key scientific advances that resulted in organoid technology, and by performing a meta-analysis on academic publications and the patent landscape over the last decade.

Amended Health Technology Assessment (HTA)

HYBRIDA develop an amended HTA methodology for evaluating organoids as emerging technologies for direct patient management in the clinic that focuses on developments to be used in personalised/precision medicine.

Map and compare normative, RE, and RI frameworks

Virtually all ethical issues pertaining to the pre-existing fields of research related to induced pluripotent stem cells & embryonic stem cell technologies, gene editing and cloning converge in organoid research.

Moral status · Consciousness · Naturalness · Biobanks

Despite the existing particularities of national or regional research environments, there are common approaches that could enable overarching regulations in organoid research with mutually respected standards.

HYBRIDA's OUTPUTS

How to assess organoid research responsibly?

An amended HTA to evaluate organoids as emerging technologies in the clinic: identifies the possible different applications of organoid technology in the clinic, delineating these applications and assessing their potentialities and limitations.

Sources & methodology

- The vision of patient-derived organoids for personalised medicine is not particularly hyped, as compared to other technological visions of the future.
- Although there is an emerging body of interventional clinical research testing, the actual use of organoids for treatment prediction cannot document clinical utility at this point. Clinical results are expected in the years to come.
- By contrast, the vision of regenerative medicine lies far away in the future.
- There seems to be no evidence on the cost-effectiveness of organoid technologies.
- There are issues of justice and economics that have implications for the responsibility of the organoid field.

How to promote responsible research?

Minimal Information about an Organoid and its Use for Researchers (MIAOU): A set of requirements to address the following: the origin of biological material (including informed consent from cell donors), efficacy/reproducibility, quality of results (size, morphogenesis, cell composition), reliability, genetic integrity, minimization of communication errors (accurate and documented description of materials and methods), compliance with safety, security and research integrity rules, prevention of research misconduct and miscommunication with the lay public.

Evaluator checklist for organoid ethical studies (EChOES): describes how to evaluate the quality of organoid descriptions in a grant application for reproducibility, replicability and rationality of the proposed organoid research. To assess the quality of an application, some elements are mandatory for scientific evaluation, while the others are contextual. It is up to the evaluators to judge whether the answers are acceptable for a given project.

Research Integrity Committee Organoid checklist (RICOCheck): intends to provide a tool for Research Ethics Committees (RECs) and Research Integrity Offices (RIOs), that will ensure transparency and anticipate ethical issues. RECs and RIOs need to consider principles, such as data confidentiality, societal impact of the research project and its anticipated results, commitment of patient associations and fair and responsible behavior of RECs involved in the evaluation of projects using organoids.

HYBRIDA recommendations (*elements*)

The recommendations for organoid research cover several critical areas including the Ethics by Design (ED) approach, the Reflexivity, Anticipation, Deliberation (RAD) process, Responsible Research and Innovation (RRI) practice, allowing the integration of ethical considerations throughout the research and development process. These approaches are aimed at ensuring that organoid research is conducted with foresight, inclusivity, and a commitment to ethical integrity, anticipating and addressing potential ethical, social, and technical challenges from the outset. The main elements are the following:

Scan here to access HYBRIDA's operational guidelines

1. Anticipate and Address Ethical Concerns Proactively
2. Incorporate Responsible Research and Innovation (RRI) Practices
3. Ensure Continuous Ethical Engagement
4. Implement Ethical Reflection
5. Foster Public deliberation and transparent regulation over Organoid Development
6. Facilitate Ethical Literacy and Education in the field of organoids:
7. Commit to respecting the informed consent process

These recommendations emphasize the need for a holistic and anticipatory approach to the ethical challenges of organoid research, integrating ethical considerations throughout the research process, and engaging with a broad range of stakeholders to ensure that organoid technologies develop in a way that is socially responsible, inclusive, and aligned with human values.

STATE OF THE ART

- Operational Guidelines for the field of organoid research and organoid-based technologies
- Code of Responsible Conduct for organoid researchers
- Supplement to the European Code of Conduct for Research Integrity
- The final conference took place on the 15th of May 2024 in Brussels
- An online workshop for researchers will take place on the 19th of June

hybrida-project.eu

Scan here to access HYBRIDA's deliverables at the project's website

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