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

Theoretical considerations

Update ethics and normative frameworks — *Why?*

Code of Conduct — *What?*

Operational guidelines — *How?*

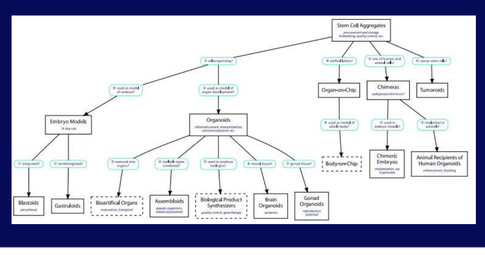
Practical considerations

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

Scientific reviews, opinion articles, news articles, and written perspective. · Published clinically relevant evidence. · Sources · 10 interviews with key actors positioned at the “epistemological hotspots.” · Registered clinically relevant trials.

Vision Assessment

1. Reconstructing the vision and its assumptions
2. Plausibility test of the vision and its assumptions
3. Vision management

- The vision of patient-derived organoids for personalised medicine, as a whole, 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): addresses 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. Some elements of EChOES are mandatory, while some are contextual (e.g. depending on the call requirements or the application domain).

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

HYBRIDA recommendations

Research:
1. Report organoid research using the Minimal Information About an Organoid and its Use for Researchers (MIAOU)
2. Evaluators should use EChOES

Ethical assessment:
3. RECs and RIOs should use RICOChejcK
4. Information should be provided to the donors about what could be done with their cells including if they want to withdraw their consent. The donor fill a Donor Organoid Wishlist when the consent form is signed.

Communication:
5. Avoid misnaming such as mini-organ, synthetic embryo.
6. Avoid exaggerated promises about the clinical applications of organoids.

Regulation:
7. Engage in a reflection to clarify the status of embryo models.
8. Engage in a reflection on sentience and consciousness of complex cerebroids.
9. Engage in a reflection on consent withdrawal.

Future up-date
10. Foresee regular update of the operational guidelines and of the Code of conduct as well as the regulatory framework of organoids and related fields according to the rapid evolution of knowledge and technology.

NEXT STEPS

- Finalize the Operational Guidelines for the field of organoid research and organoid-based technologies
- Finalize the Code of Responsible Conduct for organoid researchers
- Develop of a supplement to the European Code of Conduct for Research Integrity
- Organize a final conference, to take place in the second half of January 2024 in Brussels

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CONSORTIUM

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

This project has received funding from European Union’s HORIZON 2020 Research and Innovation programme under Grant Agreement No 101006012.