What does a donor need to know? A critical look at informed consent documents for brain organoid research

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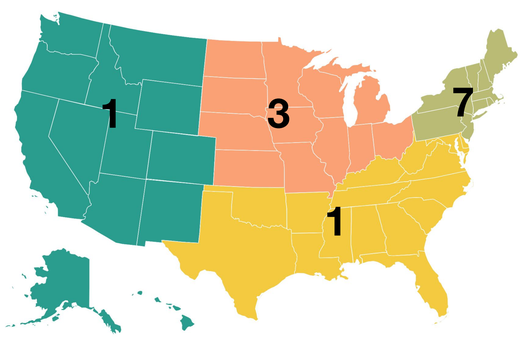
Introduction

- Brain organoids (BOs) are 3D assemblies of neural tissue grown from induced pluripotent stem cells (IPSCs), derived from donor biospecimens (Trujillo & Muotri 2018)
- Ethically sensitive
  - Donors may not understand what BOs are, how their cells are used, and implications of this research (MacDuffie et. al 2023)
- Functions-based approaches to informed consent emphasize transparency, promotion of welfare, concordance with values, and respect (Dickert et. al 2017; Wilfond & Kraft 2017)
- **Guiding question:** What information is shared in informed consent documents for brain organoid research? Does provided information fulfill the function of transparency?

Methods

- Brain organoid research teams were identified through PubMed and NIH RePORTER database searches
  - 630 teams identified
- Consent documents were collected from brain organoid research teams via REDCap survey
  - 118 completed responses; 35 eligible participants (US-based, working with BOs derived from donor biospecimens); 12 documents uploaded from 7 institutions
- Coded using ATLAS.ti software to identify educational and future use statements, and explanations of study procedures
  - Exemplary quotations were transparent, richly informative, and written in (mostly) accessible language
  - Standard quotations did not provide further transparency beyond boilerplate or vague statements



Number of consent forms collected from each region


Brain organoids in the laboratory. The BOs are the small white dots in the dish. A pen and finger are provided for size reference.

Results

- 0 uses of the term 'brain organoid'
- Future use statements present in 9/12 consent forms
- Quantity and quality of educational statements and explanations of study procedures highly variable
- Wide variety of biospecimens collected from donors, with blood and skin biopsies being the most common

Exemplary Future Use Statement

Your cells might be used in projects involving genetic alteration of the cells. Your cells might be mixed with other human cells, mixed with animal cells or grown in lab animals like mice. Your cells might also be used to reproduce tissue and cells, including for the purpose of human cloning. [Document 3]

Standard Future Use Statement

All data and each of the samples will be banked and stored and to be used for future studies. All the information obtained is kept in a secure research database and coded biological samples are kept in a secure storage space. [Document 12]

Exemplary Educational Statement

This project is based on the recent discovery of techniques that allow pluripotent stem cells to be created from subject skin and blood cells. These stem cells can then be used to study the cell biology of nerves derived from subjects with inherited neurological disorders [...]. These cells will be studied for their ability to survive, to change into different cell types, and for features that distinguish them from healthy cells in a laboratory setting. [Document 9]

Standard Educational Statement

Stem cells are cells that can change into many different types of specialized cells (like brain cells). These "stem cells" allow us to study how changes in genes in developmental brain disorders affect how cells function. [Document 10]

Exemplary Explanation of Study Procedures Statement

This skin biopsy or blood draw will be used to make human stem cells through a reprogramming process in a laboratory. […] We will model disease progression using these cells and test new therapeutics as well. [Document 8]

Standard Explanation of Study Procedures Statement

If you agree to participate in this study, you will undergo a one-time procedure to obtain either a skin biopsy or blood sample, dependent on the researcher's purposes. [Document 9]

Conclusions

- We do not believe all of these forms fulfill the crucial transparency function of informed consent outlined by Dickert et. al (2017), and thus do not demonstrate respect, a related function emphasized by Wilfond & Kraft (2017)
- Most documents fulfill other functions, such as adherence to regulatory requirements, and promoting integrity of research and researchers
- Variability of information presented in informed consent documents creates a barrier within consent process
  - Lack of transparency compromises donors' ability to assess ethical considerations of participation
  - Few documents provided specific options for values-based decision making regarding biospecimen use
- Short document length and high frequency of exemplary transparent statements greatly improve comprehensibility
- Need for balance in how much information is presented

Limitations

- Small sample size unlikely to be representative of the field at large
- Quotations coded as 'exemplary' often included in-depth explanations using higher level scientific concepts, which may present a comprehension barrier for some readers

Future Directions

- Careful consideration is warranted when writing consent forms to provide clear, comprehensive, digestible information for prospective biospecimen donors
  - Writing should place respect at the forefront for a target participant pool with diverse racial/ethnic, educational, and religious/spiritual backgrounds

References & Supplementary Materials

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