

PERSPECTIVE

Exploring the challenges and opportunities of public engagement with fundamental biology

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ABSTRACT

The Human Developmental Biology Initiative (HDBI) is a Wellcome-funded research consortium involving scientists based in institutions across the UK and Europe. It aims to pioneer new technologies and techniques to answer fundamental questions about human development and could, therefore, eventually improve treatments for fertility, birth defects and developmental diseases, as well as aiding regenerative medicine. HDBI research relies on human fetal and embryonic tissues donated following pregnancy terminations or fertility treatment. The situations in which these tissues are donated, their use in research and the potential healthcare impacts of this work all present complex ethical and moral questions that are of interest not only to scientists but also to the public. As such, HDBI's public engagement programme 'What makes us human?' aspires to test new ways of engaging the public with fundamental biology. In this brief Perspective, we provide an overview of this public engagement approach, exploring its challenges and opportunities, and outline our longer-term plans. We hope that by sharing our experiences we will encourage and enable others to organise similarly experimental public engagement, even if their research is very fundamental or potentially controversial.

Research with sensitive human tissue

Human tissue for Human Developmental Biology Initiative (HDBI; <https://hdbi.org>) research comes from several sources, including the Human Developmental Biology Resource (HDBR; <https://www.hdbi.org>), which is a tissue bank that collects and supplies fetal tissues from pregnancy terminations taking place 4–20 weeks post-conception, in accordance with the Human Tissue Act. Several HDBI research groups also use embryos created for fertility treatment that will not be used for family building or cannot be stored any longer, and embryos created specifically for research with donor gametes. This is regulated by the Human Fertilisation and Embryology Authority (<https://www.hfea.gov.uk/donation/donors/donating-to-research/>). The UK currently has a robust regulatory framework for research involving such human embryonic and fetal tissues. However, the International Society for Stem Cell Research (ISSCR) recently released new guidelines that recommend a relaxation to laws governing this research in the UK (Lovell-Badge et al., 2021). Consequently, the stage may be set for wider public questioning of the regulations around human tissue research as well as the research itself.

Why engage the public with fundamental research?

Although HDBI could eventually lead to improvements in many areas of medicine, its potential far-reaching implications and reliance on human embryos and fetal tissues may provoke ethical, legal and social questions. This research also relies on widespread, continuing public consent and should be carried out in accordance with societal expectations. This underscores the need to engage with the public and to approach engagement with great care, in order to reduce the risk of unintentionally provoking backlash against the research.

The importance of discussing the ethical, legal and social implications of fundamental research with the public was, in fact, recognised as early as the 1990s, amidst the backdrop of the Human Genome Project (Zwart et al., 2014). Although the practical impacts of fundamental biology research are often not clear until long after the research has taken place, it is widely acknowledged that discussing potential impacts of fundamental research with the public can benefit both the researchers (enabling them to reflect on their work and its relevance to wider society) and the public (by ensuring that the outcomes of the research are considered beneficial) (<https://sciencewise.org.uk/wp-content/uploads/2021/03/DR-7.pdf>; Wilsdon and Willis, 2004; Singh, 2008).

Supporting this idea is the concept of 'upstream engagement' (Wilsdon and Willis, 2004), more widely known today as 'Responsible Research and Innovation' or RRI. This involves discussing research with the public early on, as part of agenda-setting, and certainly before innovations leave the laboratory. RRI aims to 'align both the process and outcomes of research... with the values, needs and expectations of European society,' [European Commission, Horizon 2020: Public Engagement and Responsible Research and Innovation (<https://wayback.archive-it.org/12090/20220124160442/https://ec.europa.eu/programmes/horizon2020/en/h2020-section/public-engagement-responsible-research-and-innovation>)]. This approach to public engagement has been embraced by funders and scientists as a way of improving public acceptance of new technologies (Tait, 2017), a stance which was likely encouraged by the negative reaction of the European public to genetically modified (GM) foods in the early 2000s (Tait, 2009).

Challenges with engaging early

The practical outcomes of fundamental science are often unknown even to the researchers themselves. This can make it difficult to discuss societal implications of fundamental research with members of the public (Tait, 2009), and may even encourage ideology-based reactions, leading to polarisation and conflict (Tait, 2017). In addition, fundamental research often revolves around topics that are relatively distant from people's everyday lives, for example cell lineage decisions in normal development. Informed and meaningful discussions therefore require substantial groundwork to develop shared language and understanding. For members of the public, this involves understanding the research environment and process, and

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the science itself. For researchers, this involves understanding public contributors' existing knowledge and experiences, and finding effective ways to communicate, including explaining concepts and asking the right questions.

One example of RRI is the UK public consultation around mitochondrial transfer, so-called 'three parent babies'. Through this consultation, which took place in 2012, the public were able to discuss whether this treatment option should be made available, as well as scrutinize and provide input on the use of different mitochondrial replacement techniques. Furthermore, the engagement began taking place well before the law allowing mitochondrial donation came into effect in the UK (Craven et al., 2018; Trevelyan, 2013).

However, this example differs from HDBI in at least one important aspect: the potential application to clinical practice was clear at the time of the mitochondrial replacement dialogue. By contrast, it is not yet clear precisely how HDBI research might be translated into clinical applications. In addition, the donation of embryonic and fetal tissue and gametes often takes place in contexts that are emotionally and ethically complex [e.g. during pregnancy terminations and *in vitro* fertilisation (IVF) treatment]. Together, this presents us with a paradox: while we can aim to engage the public with a highly intimate and emotive topic, the outcomes of the research are temporally distant and not always fully known at the time of engagement.

There are also several questions of societal concern that are frequently unasked and unanswered in many areas of fundamental research. These include: 'Should this new information be used, and if so, how and by whom?'; 'Who will own the outcomes of this new information?'; 'Will the benefits of these discoveries be distributed equitably?'; 'Who is in charge and can we (the public) trust them?' (Wilsdon and Willis, 2004; Singh, 2008; Bruce and Bruce, 2019; Morrison and de Saille, 2019). Although Tait (2017) cautioned against engaging with the public too early in the research cycle, examples like the UK controversy around GM crops demonstrate that asking these questions too late, when there is no real opportunity for public input to be meaningfully included in decision-making, can lead to adverse public reactions, including polarisation and scepticism (Rowe et al., 2005; Singh, 2008; Marris, 2015; Morrison and de Saille, 2019; de Saille and Martin, 2018).

Public scepticism about new technologies is also often attributed to lack of trust between the public and scientists, regulators of research and technology (de Saille and Martin, 2018), or concern about profit-making big pharma companies. Transparency is cited as a way in which to bolster trust between the two groups (McLeod, 2018). However, as recent public engagement programmes about animal research in the UK and Switzerland indicate, in order to be truly transparent and build trust, we must be open to more than just 'provision of information' – we must also engage in mutually beneficial discussion about the research process (de Saille and Martin, 2018; McLeod, 2018).

In addition to large societal questions about the potential impacts of HDBI research, we must be sensitive to, and transparent about, ethical issues that can arise when discussing research with this particular type of human tissue. Questions like 'when does personhood begin?', 'what counts as killing?', 'what is unnatural' and 'should we be able to create life at will?' often feature in discussions about research that uses human tissue from terminations and IVF. The unease often associated with this research is commonly referred to as 'the yuck factor', a term which suggests this reaction is emotion-based, and not based on logic or higher-order thinking (Morrison and de Saille, 2019). However, the 'yuck'

response to this type of research can be more than just a gut-level reaction or one that arises because of religious beliefs – it can also be an intellectual response resulting from cultural habituation and arising from a sense that things have shifted away from what is 'natural'. Scientists are less likely to experience this 'yuck factor' themselves because they have years of training that normalises laboratory techniques (Morrison and de Saille, 2019).

Exploring these intersections between science and society in an open, safe and accessible environment will help researchers ensure their work remains relevant to society and empower them to transparently discuss their work with the public. The continuation of human developmental biology research and the application of any potential outcomes relies not just on ongoing tissue donations but also on general public consent, trust and shared decision-making. Missteps could result in dramatic consequences, such as changes in legislation that make it difficult or impossible to continue conducting such research. We hope to begin tackling some of these issues with an experimental approach to public engagement with fundamental biology.

Our approach: the 'Insights Group'

The foundations of our RRI approach to public engagement rest on a panel of nine public stakeholders. This panel, called the 'Insights Group', will be trialled for 18 months in the first instance, aiming to provide an ongoing opportunity for researchers to discuss their work and its ethical, legal and social implications with members of the public in a truly inclusive and safe environment. This will give researchers the opportunity to reflect on societal concerns about their research, as well as provide members of the public with an opportunity to influence how this research is conducted and communicated.

As the implications of HDBI research might affect many people in ways that we cannot currently anticipate, and as the donation process provides a direct link to HDBI work, we recruited panellists who have had experiences that could be associated with HDBI tissue donation, primarily terminations or fertility treatment. However, panellists do not need to have agreed to donate tissue to research to be involved in this Group. We also aimed to recruit panellists who did not have a specialist background in biology (as biologists' viewpoints can be well-represented by HDBI researchers).

Panel members were recruited through charities that support people who experience termination and fertility treatment and through the NIHR People in Research website (<https://www.peopleinresearch.org/>), which advertises a wide range of public involvement opportunities. We received a total of 16 initial inquiries in response to our advertisements. Twelve responded after being sent more information and scheduled informal online screening chats. Nine actually attended the screening chats. All nine were deemed suitable and invited to participate in the Group.

For budgetary reasons, the Group can only include a maximum of 10 people, so we cannot expect the members to represent all possible views of the wider public. For example, there is limited gender diversity, with six members identifying as female, two as non-binary and only one as male. However, there is some diversity in the Group in terms of age (ranging from 29 to 60, with an average age of 44) and ethnicity: five are White British or White (other), two Black or Black British (African), one Mixed (other), and one who preferred not to identify their ethnicity. In addition, four group members have stated that they are neurodiverse. If Group members drop out during the initial 18 months, we will aim to recruit to replace them.

We firmly believe that anyone can provide useful insight on research, and we thus strove to recruit people from all walks of life. We made this explicit in the recruitment material and stated that we would provide support to ensure anyone who is interested would be able to participate in the Group to the best of their ability. However, we recognise that the topic area itself could be a barrier to engagement and might be likely to attract people with a high level of confidence in discussing intellectually demanding content. All of the panellists so far have received some form of post-secondary education (three have post-graduate degrees, five have undergraduate degrees and one has a Higher National Diploma).

Group members are paid £20/h for participating in bi-monthly online meetings and compensated for expenses incurred as a result of their participation (for example, childcare). They are also remunerated for time spent on tasks outside of meetings. They provide written reflections about their experiences of participating in the panel after each meeting and are sometimes asked to review and comment on digital content.

Benefits and risks

The benefits of the Group are clear for HDBI researchers, who will have the opportunity to explore and better understand societal concerns about their research in an informal environment, to reflect on their work and to develop their skills in responding to public questioning. However, beyond their remuneration, benefits to the public members are less obvious. Group members told us that they had a range of reasons for getting involved, including to learn more about human development, to understand more about research ethics and to influence research communication to the wider public.

This is in contrast to typical Patient and Public Involvement (PPI), which tends to happen within clinical research with immediate medical application. Here, many people get involved because they ‘want to help others and contribute to a better healthcare system’ (Marjanovic et al., 2019; A. Stranks, personal communication; A. Taylor-Gee, personal communication) and they want to feel like their input makes a difference (A. Stranks, personal communication; S. Williams, personal communication). However, HDBI research is unlikely to directly impact healthcare in the short term and, although small changes to research questions could be possible, the overarching agenda for HDBI has already been set.

How then, can we ensure that involvement in the Insights Group is more meaningful to participants? Firstly, in recruiting the members, we used a detailed information sheet that clearly outlined the scope of the Group and the fundamental nature of HDBI research. Secondly, the Public Engagement Manager provides regular feedback to members on how their input has been incorporated into plans for engagement projects, including researcher training. Researchers who interact with the Group will also be asked to reflect on how their interaction has changed their thinking about their work, how it is communicated and its relevance to society. These researcher reflections will be shared with the Group when appropriate. Additionally, if Group members determine that something else might be beneficial to them as part of their involvement, the Public Engagement Manager will make a reasonable effort to respond to that request.

We are also keenly aware of our duty of care to the Group, particularly if members are selected based on having had a potentially traumatic experience, such as a termination or IVF. Members may refer to these experiences as they express their thoughts and feelings in discussions. We do not wish to inadvertently harm participants psychologically or socially by asking them to refer to these very personal and potentially emotional

experiences, or by exposing them to information or images that show the ways in which embryonic and fetal tissues are used in research. Although we know that some women who donate see this as a positive outcome of a difficult or traumatic situation (A. Farnworth, personal communication), we are also aware that this subject can be distressing and may be especially difficult for anyone who has donated tissue to research. For example, one study found that women’s positivity toward fetal tissue in research decreased as they considered more fully what the research might involve. The women in this study were particularly troubled by the idea that the research might in some way extend the fetus’s existence beyond the termination, which was the opposite of their intention in having the termination (Pfeffer, 2008).

Therefore, recruitment materials for the group were explicit in the content to be discussed and members were screened through informal chats with the Public Engagement Manager to check for interest in the science as well as openness to others’ viewpoints. Group members are also regularly reminded that they can withdraw from any meeting or the Group overall at any time without needing to explain. Contact details for various pastoral support services were also provided to all participants on recruitment. Finally, all panellists were asked to sign confidentiality documents in which they agreed to keep their discussions anonymous. Researchers wishing to interact with the Group are also required to sign confidentiality forms and to share details of what they would like to discuss with the Public Engagement Manager for approval and review beforehand.

Progress so far

At the first meeting in March 2022, the Group were introduced to HDBI research and its public engagement plans. Even this introduction to the research provoked some unanticipated responses from panellists, which are already contributing to researchers’ thinking about their work and how it is shared with the public. For example, in response to a researcher saying that some of the research could eventually lead to better treatments for neurodevelopmental disorders, one group member said ‘this frightens me because of eugenics’ and questioned the overarching aim of the initiative. The researchers acknowledged the worrying possibility of their work being misused and welcomed discussion and comments from the Group on this issue. In reflecting on the meeting, the researcher said: ‘I felt that the group valued and were very supportive of the research that we are aiming to do... but I need to think more carefully about some of the ways that I describe aspects of the project – words that are innocuous to me can have emotive responses in others and so the meeting was extremely useful in helping me to understand this better.’ This exchange and reflection highlights the need to develop a common language with which to discuss our research, as well as the Group’s capacity to draw attention to researchers’ underlying assumptions. We are looking forward to more interaction, learning and reflection on all sides.

Perspectives

We have yet to find evidence of other attempts to involve public stakeholders in fundamental biology in similar ways to our Insights Group. The challenges described above provide ample reason for this; however, we hope to overcome them and realise some of the potential benefits of an RRI- and PPI-based approach to public engagement with fundamental biology. Similar to the HDBI science grant being a stepping stone for fundamental human developmental biology, we hope that our public engagement programme will be a stepping stone to further public discussion about how this fundamental research should be conducted and communicated.

In this article, we aimed to highlight the importance of, and possible difficulties associated with, public involvement in fundamental research. Although it may be challenging, public involvement is essential because it ensures both the underlying assumptions and ultimate outcomes of research are considered mutually beneficial by society. We hope that by sharing our experiences and methodology, we can empower and inspire others to involve public stakeholders in their fundamental or potentially controversial research. We would be happy to share materials and help others develop their own methods for longer-term public engagement and involvement in fundamental research.

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Competing interests

The authors declare no competing or financial interests.

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References

- Bruce, A. and Bruce, D.** (2019). Genome editing and responsible innovation, can they be reconciled? *J. Agric. Environ. Ethics* **32**, 769-788. doi:10.1007/s10806-019-09789-w
- Craven, L., Murphy, J., Turnbull, D. M., Taylor, R. W., Gorman, G. S. and McFarland, R.** (2018). Social and ethical issues in mitochondrial donation. *New Bioethics A Multidiscipl. J. Biotechnol. Body* **24**, 57-73. doi:10.1080/20502877.2018.1440725
- de Saille, S. and Martin, P.** (2018). Monstrous regiment versus Monsters Inc.: Competing imaginaries of science and social order in responsible (research and) innovation. In *Science and the Politics of Openness: Here be Monsters* (ed. B. Nerlich, S. Harley, S. Raman and A. Smith), pp. 148-166. Manchester: Manchester University Press. <https://library.oapen.org/handle/20.500.12657/30733> [accessed 11 August 2021].
- Lovell-Badge, R., Anthony, E., Barker, R. A., Bubela, T., Brivanlou, A. H., Carpenter, M., Charo, R. A., Clark, A., Clayton, E., Cong, Y., et al.** (2021). ISSCR guidelines for stem cell research and clinical translation: The 2021 update. *Stem Cell Rep.* **16**, 1398-1408. doi:10.1016/j.stemcr.2021.05.012
- Marjanovic, S., Harshfield, A., Carpenter, A., Bertscher, A., Punch, D. and Ball, S.** (2019). *Involving Patients and the Public in Research*. The Healthcare Improvement Studies Institute, University of Cambridge and RAND Europe.
- Marris, C.** (2015). The construction of imaginaries of the public as a threat to synthetic biology. *Sci. Culture* **24**, 83-98. doi:10.1080/09505431.2014.986320
- McLeod, C. M.** (2018). Assuaging fears of monstrosity: UK and Swiss initiatives to open up animal laboratory research. In *Science and the Politics of Openness: Here be Monsters* (ed. B. Nerlich, S. Harley, S. Raman and A. Smith), pp. 55-74. Manchester, Manchester University Press. <https://library.oapen.org/handle/20.500.12657/30733> [accessed 11 August 2021].
- Morrison, M. and de Saille, S.** (2019). CRISPR in context: towards a socially responsible debate on embryo editing. *Palgrave Communications* **5**, 110. doi:10.1057/s41599-019-0319-5
- Pfeffer, N.** (2008). What British women say matters to them about donating an aborted fetus to stem cell research: a focus group study. *Social Sci. Med.* **66**, 2544-2554. doi:10.1016/j.socscimed.2008.01.050
- Rowe, G., Horlick-Jones, T., Walls, J. and Pidgeon, N.** (2005). Difficulties in evaluating public engagement initiatives: reflections on an evaluation of the UK GM Nation? Public debate about transgenic crops. *Public Underst. Sci.* **14**, 331-352. doi:10.1177/0963662505056611
- Singh, J.** (2008). The UK Nanojury as 'upstream' public engagement. *Participatory Learn. Action* **58**, 27-32. <https://www.participatorymethods.org/resource/uk-nanojury-upstream-public-engagement>. [accessed 29 June 2021].
- Tait, J.** (2009). Upstream engagement and the governance of science: The shadow of genetically modified crops experience in Europe. *Eur. Mol. Biol. Org. Rep.* **10**, S18-S22. doi:10.1038/embor.2009.138
- Tait, J.** (2017). From responsible research to responsible innovation: challenges in implementation. *Engineering Biol.* **1**, 7-11. doi:10.1049/enb.2017.0010
- Trevelyan, G.** (2013). *Medical Frontiers: Debating Mitochondria Replacement: Open Consultation Meetings: London and Manchester*. Office for Public Management. Report to Human Fertilisation and Embryology Authority.
- Wilsdon, J. and Willis, R.** (2004). *See-through Science: Why Public Engagement Needs to Move Upstream*. London: Demos. doi:10.13140/RG.2.1.3844.3681
- Zwart, H., Landeweerd, L. and Van Rooij, A.** (2014). Adapt or perish? Assessing the recent shift in the European research funding arena from 'ELSA' to 'RRI'. *Life Sci. Soc. Policy* **10**, 11. doi:10.1186/s40504-014-0011-x