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Medicine

Responsible innovation in stem cell research: using responsibility as a strategy

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Responsible innovation has been introduced as an important condition for advancing the field of regenerative medicine. This is reflected in the frequent references to responsible research conduct and responsible innovation in guidelines and recommendations in academic literature. The meaning of responsibility, how responsibility could be fostered and the context in which responsibilities should be enacted, however, remain unclear. The goal of this paper is to clarify the concept of responsibility in stem cell research and to illustrate how this concept could inform strategies to deal effectively with the ethical implications of stem cell research. Responsibility can be dissected into four categories: responsibility-as-accountability, responsibility-as-liability, responsibility-as-an-obligation and responsibility-as-a-virtue. The authors focus on responsible research conduct and responsible innovation in general to move beyond the scope of research integrity and illustrate that different notions of responsibility have different implications for how stem cell research is organized.

Plain language summary: Literature and guidelines mention that responsible innovation could help the field of stem cell research to deal with ethical challenges. However, in this literature and guidelines it does not become clear how 'responsibility' should be understood, how responsibilities are recognized, how responsibilities are shared and how someone could take responsibility. In this article, different types of responsibility are discussed: responsibility-as-accountability, responsibility-as-liability, responsibility-as-an-obligation and responsibility-as-a-virtue. The types are discussed according to how they are different from one another and how they can be used to organize stem cell research. It is shown that these different types of responsibility help not only with research integrity issues but also with societal and other types of ethical challenges.

Tweetable abstract: Responsible innovation could advance the field of stem cell research. By considering different notions of responsibility, possibilities emerge to frame ethical challenges and organize stem cell research accordingly. #ResponsibleInnovation #StemCells #Bioethics

Stem cell research with adult, multipotent, hematopoietic and induced pluripotent stem cells has provided new scientific insights, opened possibilities for cell-based interventions and enabled new ways of disease modeling. It is also paired with ethical challenges in preclinical research, such as the acceptability of animal research and protection of the privacy of tissue donors. In the clinical translation of stem cell research, other ethical challenges arise, including appropriate informed consent procedures, therapeutic misconception or misestimation, the safety of interventions and the possible side effects and potential costs of an intervention [1–3]. One set of ethical challenges

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that has received ample attention in the stem cell literature is related to the responsible conduct of research, focusing on measures to counter scientific misconduct and irresponsible behavior in the field of stem cell research. Examples in stem cell research include falsely claiming the creation of stem cell lines and the cloning of human embryos [4], falsifying data [5,6] and withholding relevant risk information from trial participants [7]. There are, however, also problems for responsible conduct of research during the clinical translation phase of stem cell research and for the responsible innovation of stem cell research in general. Responsible innovation covers both the responsible conduct of research in all research phases and the ethical challenges that result from research, including the societal implications. While responsible innovation offers a helpful perspective for advancing different fields of research, it is important to consider each subfield of research on its own, as the ethical implications are context specific. In stem cell research, responsible innovation can be understood as the process in which different stakeholders, such as stem cell researchers, research institutes, research funding organizations, regulators and ethicists, collectively contribute to ensuring that the conduct and uptake of stem cell research are socially desirable and ethically acceptable [8]. Here, ethical acceptability is informed by both social and professional norms and values. As such, actions that follow from ethical deliberation and compliance with rules and regulation could contribute to responsible innovation.

One set of challenges to responsible innovation of stem cell research includes issues of clinical translation. These are ethically relevant because they may lead to harm to patients and research participants. The need to focus on these ethical issues can be illustrated by the example of stem cell clinics that provide unproven stem cell interventions and operate in areas with regulatory brokerage, thereby endangering patients physically and financially [9,10].

To foster responsible innovation in the field of stem cell research, prominent guidelines outline the importance of responsible research conduct and responsible clinical translation. For example, the most recent guidelines for research and clinical translation of the International Society for Stem Cell Research (ISSCR) address the need for responsible scientific research and practices and differentiate between responsibilities for researchers and for ethics committees [11]. As such, the guidelines focus on compliance with rules and regulations, patient welfare and respect for patients and participants through valid informed consent procedures. Another aim of the ISSCR is to stimulate responsible innovation of stem cell research by focusing on the researchers' to timely communicate with and disseminate their results to the public and other interested parties. In addition, the ISSCR focuses on the responsibilities of addressing and identifying the unmet needs of various social groups and ensuring the accessibility of stem cell interventions. Similarly, researchers have urged WHO to focus on the responsibilities of stem cell researchers in the context of stem cell regulation [12]. More generally, the European Research Council (ERC) states that research should adhere to ethical standards to create credible and high-quality science. Thus, the ERC focuses on the formal accountability of grant host institutions and the ethical responsibilities of individual researchers [13].

While responsibility is the common denominator of these guidelines, it remains unclear what the guidelines of the ISSCR and the recommendations of WHO and the ERC mean when referring to these responsibilities. In the academic literature, several efforts can be found that address and categorize notions of responsibilities [14–16]. Four categories of responsibility can be extracted from this more theoretical and philosophical literature: responsibility-as-accountability, responsibility-as-liability, responsibility-as-an-obligation and responsibility-as-a-virtue [14,15,17]. Differentiating between these notions of responsibility is helpful, as it highlights different ways to conceptualize and solve ethical challenges and how responsibilities are distributed among stakeholders. Moreover, the different notions of responsibility have different implications, including the restoration of trust, remedies or compensation for unwanted effects, effective dealing with ethical and societal challenges and enhanced possibilities for identifying and taking responsibility [15].

Importantly, how these notions of responsibility refer to stem cell research remains unclear. This analysis aims to contribute to how responsibility in stem cell research could be understood by discussing the different notions, how responsibility could be fostered and how individual responsibility is tied to a context in which these responsibilities should be enacted. A clear understanding of responsibilities in the field of stem cell research helps researchers understand how these responsibilities should be distributed. In addition, the analysis helps them consider how stakeholders could be equipped to take (co)responsibility through specific knowledge, skills and support and in that approach foster responsible innovation. As such, the analysis is helpful for stem cell researchers and the field of stem cell research, ranging from embryonic stem cell research and somatic cell nuclear transfer to adult, multipotent and induced pluripotent stem cells.

Responsibility-as-accountability

Responsibility-as-accountability can be used to confirm or restore the moral trustworthiness of researchers and research groups [15]. In that capacity, accountability is not primarily understood in a legal sense. It means that a person or group of persons is answerable for their actions or lack thereof [14,17]. Answerability means that researchers should provide explanations, excuses and/or justifications. In research, this could mean that researchers, groups of researchers or research institutes could be asked to answer for their actions for ethical and regulatory violations and unexpected or undesirable research outcomes, such as harmful side effects. Since having to answer for things that went wrong is not a desirable position, the possibility – or prospect – of being held accountable could be used to increase or encourage the responsible behavior of individual researchers and foster the implementation of instruments within institutes that increase responsible research conduct.

As such, responsibility-as-accountability can be applied by institutes to promote research integrity and to foster the (moral) trustworthiness of researchers and research groups [15]. Research integrity is already promoted in science in general by making researchers, among others, answerable for the reliability of their research. This is promoted by ensuring that researchers have followed accepted scientific methodologies, have reported this fully and transparently and have not falsified research findings [11,18]. For example, in the field of stem cell research reliability is promoted by the mandatory documentation of the source of the stem cells [11,19].

Similarly, accountability could be applied to restore or maintain the moral trustworthiness of researchers and research groups. As is the case when researchers and institutes do not follow protocols or rules, make mistakes or encounter unwanted outcomes, they have to account for their actions. By accounting for their actions, they are in the position to reflect upon the research process and learn lessons from what went wrong [15]. These lessons learned could be implemented to prevent similar mistakes in the future, thereby resulting in more responsible research in the future. For example, when researchers are lacking proper documentation for the traceability of stem cell lines, measures such as control mechanisms could be implemented to ensure proper documentation in the future.

To successfully implement accountability as a strategy, it is important to determine who is responsible, who is commissioning or overseeing the responsibilities and which instrument is used to promote these responsibilities. Several examples of commissioning or establishing responsible parties as well as instruments can already be found in the field of stem cell research. For instance, to promote animal safety and research integrity, governments and regulators hold research institutes and researchers accountable through regulation and professional best practices. Moreover, funding organizations already ensure the accountability of institutes and researchers by using grant agreements, contracts and deliverables. For example, project managers are already held accountable by funding organizations and grant host institutions to make sure that important ethical challenges are identified. Ideally, they involve ethicists to identify those challenges. Furthermore, many research institutes already establish research ethics committees and animal welfare committees for oversight of, among others, animal safety and welfare. In addition, institutes could organize administrative support for researchers to ensure that research proposals are in line with legislation and animal safety. As such, research institutes implement protocols as a mechanism to hold individual researchers accountable. Another possible way to enhance responsibility-as-accountability is by leaning more on fellow researchers. For example, a buddy system could be implemented, whereby two researchers are accountable for the responsible conduct of each other's research by checking and approving each other's work. Researchers could also promote the reliability of research among their peers via thorough peer review of scientific publications. In such peer review processes, reviewers should focus more on clear descriptions of experiments and sample sizes, among others [20]. Furthermore, following the ISSCR [11], academic journals (even if not a commissioning party themselves) contribute to promoting responsible animal research by including, for example, the Animal Research: Reporting of *In Vivo* Experiments (ARRIVE) guidelines [21].

Responsibility-as-liability

Where accountability focuses through answerability and explanation, responsibility-as-liability means that a person, a group of persons or an institute should compensate its faulty behavior or be recognized and rewarded for excellent behavior [14,15]. Liability is often used to blame or punish persons for faulty behavior. Focusing primarily on this negative use could lead to an undesirable culture of blame and such use should therefore be reserved for substantial transgressions, such as cases where harm was inflicted. Simultaneously, liability could be interpreted more positively by focusing on how liability compensates actions and behavior. For instance, actions and behavior that have led to an undesirable outcome could be remedied, while actions and behavior that have led to positive outcomes could be

praised. As such, liability is not construed in a legal sense. To prevent a culture of blame and scapegoating, liability will be primarily considered positively in the following.

As such, liability can be applied to remedy or compensate for undesirable outcomes [14,15], such as scientific misconduct. For example, researchers are already criticized when they have withheld relevant risk information of a new (experimental) intervention that had led to harm, or for having falsely portrayed an experimental intervention as an actual therapy. By holding institutes and individuals liable for not following established rules and undesirable outcomes, those institutes assume the legal obligations, while individuals assume the moral obligations, to remedy any damage or harm. By doing so, liability could help remedy harm by establishing restorative justice to victims, which is new to the field of stem cell research. For instance, in so-called restorative conversations, victims could discuss with offenders in what way they have been harmed by the offenders' wrongful actions. Consequentially, it helps victims identify sanctions for the offenders, which contributes to realizing restorative justice [22]. Remedy could also involve familiar practices such as financial compensation or overt apologies to the victims.

Similarly, responsibility-as-liability also compensates for positive ethical implications of stem cell research. This means that researchers could be recognized and rewarded for their actions or behavior [15] – for example, when researchers make extra efforts to foster research integrity.

To successfully implement liability as a strategy, it is important to establish who is responsible, who is commissioning or overseeing the responsibilities and which strategy is used to promote the responsibility. For instance, judicial systems already enable the possibility to hold research institutes and specific researchers liable for inflicting harm on research participants or animals through means of prosecution, which could lead to fines, disbarment and prohibition from obtaining further funding. Funding organizations could promote positive ethical implications of research by financially rewarding exceptional research outcomes in specific categories such as societal impact and public engagement. Similarly, universities and research institutes could recognize and reward positive behavior. While this is already happening in some quarters of the world, this could be adopted more widely. In situations in which liability is used as a remedy for undesirable outcomes and behavior, funding organizations could retract funding of the grant host institution. In addition, research institutes already have the option to hold researchers liable for fraudulent behavior by submitting them to disciplinary action (e.g., suspending them). In terms of positively implementing liability, research societies (e.g., the ISSCR) could praise when research outcomes contribute to positive ethical implications by means of awards for researchers, research groups and institutes.

Responsibility-as-an-obligation

Responsibility-as-an-obligation involves the attribution of duties to specific persons or groups to ensure that those duties are fulfilled. This can be understood as the allocation of a responsibility to an individual or a group to ensure that an ethical challenge is dealt with [23]. The notion of responsibility-as-an-obligation helps researchers strategize in dealing with ethical challenges that are not directly caused by persons or groups, as well as with challenges that are (relatively) new and have not (yet) been dealt with as an issue of accountability or liability.

Thus, research institutes and funding institutes can apply responsibility-as-an-obligation to increase the effectiveness of promoting positive research outcomes at the individual and societal levels [15]. By doing so, responsibility-as-an-obligation could be used to deal effectively with ethical challenges due to current societal expectations or a change in such expectations. For example, when society funds science, it is argued that science should serve society: science should fill knowledge gaps that are relevant for society [24]. To fulfill this obligation, responsibility-as-an-obligation could be used to ensure that insights into the needs and wishes of society are gathered by engaging with the general public and relevant stakeholders. Research goals also need to be formulated in alignment with those needs and wishes.

Moreover, like other fields of research, stem cell research has obligations to future generations [25]. While future generations cannot represent themselves, they could be negatively affected due to the consequences of contemporary research. An example can be found in exhausting (natural) resources or pollution of the environment. In stem cell and other biomedical research, this can be found in, among others, the use of disposable plastic items [26] and the energy that laboratories consume [27]. Thus, responsibility-as-an-obligation here helps to arrange that the use of plastic is reduced or plastic is replaced with more sustainable materials for conducting stem cell research – for instance, by implementing programs that aim to prevent waste and minimize the use of resources [28–30]. Responsibility-as-an-obligation also helps establish a reduction of energy use and promotion of renewable energy in the laboratory.

Similarly, responsibility-as-an-obligation could be used to deal effectively with ethical implications that result from technological and scientific innovations. For example, when a person donates blood or skin cells for the creation of induced pluripotent stem cells, that person shares his or her own genetic data as well. These genetic data could be reinterpreted when new research findings link a gene – carried by the donor – to a disease. In turn, this leads to a responsibility for communicating new findings to donors [31]. Thus, responsibility-as-an-obligation could ensure that by appointing researchers or other stakeholders to ensure that conditions for recontacting donors are identified for informed consent and that donors are recontacted about new genetic findings accordingly.

To successfully implement responsibility-as-an-obligation as a strategy, it is important to establish who is responsible, who is commissioning or overseeing the responsibilities and which strategy is used to promote these responsibilities. Funding organizations can, and at times already do, require research institutes to consider the soft impacts of technology and research, such as behavioral and psychological effects and changes in moral values and societal structures [3,32,33]. This could be ensured by means of deliverables. Moreover, funding organizations could contractually oblige research institutes to ensure that the needs and wishes of different groups in society are included. Subsequently, research institutes could appoint stem cell researchers or other stakeholders, such as patients or members of the public, to ensure that those needs and wishes are gathered in a fair and inclusive manner – for example, by organizing public engagement possibilities. Furthermore, it should be strategized how these needs and wishes can be aligned with the goals of the research project.

Responsibility-as-a-virtue

Responsibility-as-a-virtue refers to specific character traits and (self-)development that contribute to dealing with ethical challenges. As such, responsibility-as-a-virtue helps researchers consider which competencies contribute to fostering positive implications and mitigating negative implications of stem cell research, as well as which competencies help researchers recognize responsibilities and act on them. Examples of such virtues include perseverance, curiosity, intellectual honesty and openness to the ideas of others [34,35]. Since virtues develop through knowledge, practice, education and good examples [34,36], and therefore take time to develop, there should be attention to teaching virtues that are relevant to research, to the practicing and cultivation of virtues and for the fact that becoming virtuous is a (lifelong) process. Responsibility-as-a-virtue also involves the idea that researchers are continuously learning and thus are attentive to their missing virtues [36,37]. By means of reflection, education and dialogue, researchers could get insights into which virtues they miss and what they still need to learn. While responsibility-as-a-virtue might have similar goals as responsibility-as-an-obligation, responsibility-as-a-virtue focuses on how individuals can be equipped in terms of attitude, skills and knowledge, rather than on realizing organizational arrangements and changes in research processes.

Therefore, responsibility-as-a-virtue could help researchers deal with existing ethical challenges related to research integrity. For example, by embodying the virtue of intellectual honesty, research integrity could be promoted. Intellectual honesty involves being honest about the different facets of research, including the conduct, the analysis and the dissemination. This way, intellectual honesty contributes to the trustworthiness of research. A possible result of trustworthy research is that it could lead or contribute to social value. Thus, virtues that promote research integrity could also be relevant to ethical implications on a societal level. Other relevant virtues that could promote research integrity (and animal safety) include reliability, transparency and respect [36].

Similarly, responsibility-as-a-virtue could help researchers deal with changing and new (unforeseen) ethical challenges. For stem cell research, this means that researchers need to develop virtues through training and practice to be (ethically) reflective and attentive to the socio-ethical impacts of new innovations and the needs and wishes of patients and society. This means, for example, that researchers should have knowledge about what types of ethical implications innovations could have and how these could affect the existing practice of stem cell research [3]. In turn, this affects the possible role that researchers themselves could play in preventing and mitigating side effects and undesirable ethical implications.

With respect to the interaction among patients, society and researchers, responsibility-as-a-virtue could play a role in finding instruments for improving communication. For example, competencies to partake in meaningful discussions, such as a dialogue between researchers and the public, could be helpful in deducing the needs and wishes of patients and society [38]. In addition, understanding the nuances and uncertainties of science and communicating with patients or the public is also an important competency for improving the relation between researchers and patients and the public. This requires researchers to be transparent about research processes, clinical trials and

Table 1. Overview of strategies for responsible innovation.				
Type of responsibility	Area of effect	Commissioning party and oversight	Responsible party	Instrument to fulfil responsibilities
Accountability	• Research integrity • Animal safety	• Governments • Professional societies (e.g., International Society for Stem Cell Research) • Funding organizations • Research institutes • Regulators	• Scientific community • Research institutes (e.g., putting protocols in place) • Research groups • Administrative support • Research ethics committees • Individual researchers	• Legislation • Regulation • Protocols • Guidelines • Contracts • Peer review
Liability	• Societal impacts • Inclusive research (e.g., patient or public involvement) • Animal safety • Research integrity	• Legal systems • Professional societies • Funding organizations • Research institutes	• Research institutes • Research groups • Individual researchers	• Withdrawing funding • Financial reward • Awards/prizes • Disciplinary action • Positive publicity • Restorative conversations
Obligation	• Societal impacts • Public engagement • Future generations • Research integrity	• Society/public discussions (as input) • Government • Research institutes	• Research institutes • Individual researchers • Other stakeholders (members of public, patients etc.)	• Funding strategies • Structural changes in research environments • Fair assessment procedures
Virtue	• Societal impacts • Inclusive research • Patients • Research integrity • Animal safety	• Funding organizations • Research institutes • Ethics councils • Ethicists and philosophers • Researchers	• Research institutes • Individual researchers	• Education • Training • Workshops • Supervision • Time and financial resources

descriptions of time frames to clinical implementation [39], as well as being aware of uncertainties in datasets and being transparent about how these uncertainties in datasets should be interpreted [37].

To successfully implement responsibility-as-a-virtue as a strategy, the focus should be on how virtues could be cultivated and who should support this. First, ethicists are in a good position to educate both early-career and experienced researchers regarding the skills and knowledge to foster responsibility-as-a-virtue and to reflect upon possible missing or underdeveloped virtues. This could be offered as (part of) a course in which is discussed how virtues relate to the nature of science and how virtues could contribute to realizing the scientific, societal and ethical goals of research [34]. Hence, a basic understanding of virtues and practical wisdom should be established by offering some theory on virtues, while the focus should be on the practical effects of virtues on the conduct of research, how virtues relate to being a good researcher and how virtues could be developed and acquired. Second, experienced researchers could function as role models for young researchers. They could supervise young researchers in their training, make them attentive to their missing virtues, reflect with them on their behavior and engage in discussions about what kind of attitude, skills, knowledge and virtues researchers need. Since this is a career-long process, senior researchers should engage in such discussions with peers as well. Arguably, researchers themselves are responsible for considering in which areas they need to develop themselves, as they themselves should be attentive to their missing virtues. Third, since the cultivation of virtues takes time and effort, research institutes should invest time and financial means for researchers to receive education, training, workshops and career-long possibilities to ethically reflect upon their work. Funding organizations could play a role in ensuring that research institutes and researchers take time for ethical reflection.

Discussion

As the authors have shown, considering different notions of responsibility could help implement the ethical principles of the ISSCR guidelines and the WHO recommendations that aim to promote responsible conduct and responsible innovation in stem cell research. To stimulate responsible innovation in stem cell research, it is important to identify the ethical challenge or range of ethical challenges that should be addressed, who is responsible for attending to them, who is commissioning or overseeing and which instrument is used to promote the responsibility (Table 1). This paper adds to the academic debate of responsible research and innovation in several ways. First, the analysis enabled the authors to differentiate among the implicit notions of responsibility in the existing professional guidelines. For example, the WHO recommendations [12] focus primarily on scientific misconduct and unproven interventions, which could be tackled by adopting strategies that are linked to the notions of accountability and liability (Table 1). The ISSCR, however, has a broader conception of responsible research conduct. Its implicit assumptions of responsible research conduct and innovation can be found in the ethical

principles underpinning its guidelines (research integrity, transparency, participant welfare, respect for patients and research participants and social as well as distributive justice). Second, this analysis advances responsible research conduct innovation by identifying different and possibly more effective strategies for realizing responsible research conduct and innovation.

An implicit assumption of responsible research conduct can be found in the ISSCR's principle of research integrity. This principle involves ensuring trustworthy, reliable and accessible research data, which is responsive to "*scientific uncertainties and priority health needs*" [11]. Here, the ISSCR sees a role for oversight and accountability. However, it is questionable whether these strategies alone would lead to compliance and research integrity, since externally enforcing rules and regulation could be perceived as a burden that inhibits research. As such, researchers are less inclined to comply with rules and regulation [34]. Another, more effective strategy to increase research integrity is following responsibility-as-a-virtue. As such, targeted training and education that aims at internalizing relevant values by researchers improves intrinsic motivation and results in better compliance with rules and regulation [36,40]. Within the context of technological and scientific innovations, research integrity could also be improved by identifying more effective instruments to be responsive to scientific uncertainties and priority health needs. Innovative technologies are a common and well-known challenge for slowly evolving law and regulation [41], leaving researchers with no or little guidance for responsible innovation. Here, responsibility-as-a-virtue could offer instruments that enable researchers to consider the ethical implications of such innovations for their research, by considering   how innovations affect research integrity and subsequently how these innovations could be integrated into research in a desirable manner. Moreover, the strategy of responsibility-as-an-obligation could offer other instruments that improve research integrity by eliminating or mitigating academic pressure and competition. Academic pressure and competition are often the result of a high workload, a necessity to publish in high-ranking journals and the need to produce positive, publishable results. Such pressure could be eliminated or mitigated through different assessment procedures that focus on assessing researchers through peer judgment, public engagement activities and educational ventures. In addition, administrative support for ethical and regulatory applications help unburden researchers [42–44].

Third, this analysis contributes to several aims that are mentioned in the academic literature about responsible research and innovation (RRI). For instance, mechanisms of responsibility-as-a-virtue help identify the relevant knowledge gaps, needs and wishes of society and contribute to RRI's aim of science for society [45]. In addition, implementing instruments related to responsibility-as-a-virtue benefits the continuous reflection upon research processes, which aligns with RRI's aim of institutionalizing responsiveness [45]. Furthermore, by focusing on how responsibility could be used as a strategy that contributes to the (re)division of moral labor by explicating oversight, commissioning parties and responsible parties and the type of moral labor [46], this analysis aligns with RRI's aim of reframing responsibility [45]. Consequentially, this analysis contributes to explicating roles, responsibilities and arrangements, which could advance the prevention of possible gaps in responsibility [47].

Moreover, this analysis could be considered as a precursor for researchers in other disciplines and fields of study within regenerative medicine. The typology that is provided in this article helps researchers think about responsibility as a set of different strategies to deal with ethical implications of stem cell research. In addition, this article presents several types of responsibility but may not provide an exhaustive list for the field. Rather, the authors aimed to provide a starting point to further the debate on responsibility and responsible innovation in stem cell research.

Conclusion & future perspective

Responsibility comes in different forms. Distinguishing among the different forms is helpful for the field of stem cell researc, as it helps frame ethical challenges and highlight how responsibility is distributed among several stakeholders. Thus, the different forms of responsibilities offer several insights into strategies and actions to improve responsible research conduct and innovation. These forms highlight possibilities that move beyond guidelines for realizing the ERC's desire for trustworthy and excellent research, the guidelines of the ISSCR and the WHO recommendations.

Whether responsible research and innovation can be successfully conducted in the field of stem cell research depends on the effective implementation of strategies that address individual researchers, research institutes and other stakeholders alike. Research institutes might adopt different strategies due to differences in organizational structures, financial means, the number of researchers and other personnel working at the institute and personal or institutional preferences.Therefore, it is important for research institutes to identify and prioritize responsibilities in

order of importance, highlight which responsibilities are resource heavy to comply with but still are worthy to foster. Finally, research institutes should address which responsibilities are not appropriate to be shared with stakeholders beyond the researcher community, and thus need to be allocated to the researchers themselves.

Executive summary

Introduction
- Responsible innovation receives increasing attention, but it remains unclear how it relates to stem cell research.
- Differentiating among the different notions of responsibility is helpful, as it highlights different ways to conceptualize and solve ethical challenges and how responsibilities are distributed among several stakeholders.
- The different notions of responsibility help researchers consider how stakeholders could be equipped to take (co)responsibility through specific knowledge, skills and support and in that approach foster responsible innovation.

Responsibility-as-accountability
- Responsibility-as-accountability promotes the answerability of persons or a group of persons for their actions or lack thereof.
- Responsibility-as-accountability can be applied by institutes to promote research integrity and to foster the (moral) trustworthiness of researchers and research groups.

Responsibility-as-liability
- Responsibility-as-liability focuses on how a person, a group of persons or an institute should compensate for faulty behavior or be recognized and rewarded for excellent behavior.
- Responsibility-as-liability can be applied to remedy or compensate for undesirable outcomes and to promote positive ethical implications of stem cell research.

Responsibility-as-an-obligation
- Responsbility-as-an-obligation involves the attribution of duties to specific persons or groups to ensure that those duties are fulfilled.
- Responsbility-as-an-obligation can be implemented to increase the effectiveness of promoting positive research outcomes at the individual and societal levels and of dealing with ethical implications that result from technological and scientific innovations.

Responsibility-as-a-virtue
- Responsibility-as-a-virtue refers to specific character traits and (self-)development that contribute to dealing with ethical challenges.
- Responsibility-as-a-virtue focuses on equipping individual researchers to be responsive to ethical challenges.

Discussion
- Considering different notions of responsibility could help promote responsible conduct and responsible innovation in stem cell research.
- To stimulate responsible innovation in stem cell research, it is important to identify the ethical challenge or range of ethical challenges that should be addressed, who is responsible for attending to them, who is commissioning or overseeing and which instrument is used to promote the responsibility.
- This analysis is a precursor for researchers in other disciplines and fields of study within regenerative medicine. The typology that is provided in this article helps researchers think about responsibility as a set of different strategies to deal with the ethical implications of stem cell research.

Conclusion & future perspective
- Distinguishing among the different concepts of responsibility is helpful for the field of stem cell research, as it helps frame ethical challenges and highlight how responsibility is distributed among several stakeholders.
- It is important for research institutes to identify and prioritize responsibilities in order of importance andhighlight which responsibilities are resource heavy to comply with but still are worthy to foster.

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