Embodied material encounters and the ambiguous promise of biomedical futures: The case of biologically derived medicines

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Therapies and prophylactics using biologically derived materials such as cells, microbes or tissues are often portrayed as key to increased future health. This article investigates the material preconditions of such visions. Building on feminist new materialist approaches, it explores the embodied material encounters between biologicals administered into living bodies and the vibrant materiality of the body. We investigate embodied material encounters through two biologicals, pandemic vaccines and stem cell therapies, focusing on vaccine-associated narcolepsy during the 2009 pandemic, and adverse reactions in an experimental stem cell therapy targeting an eye disease called AMD. We propose that the concept of embodied material encounter provides an important tool for STS by making visible the constitutive situatedness of risk and promise and the multiplicity of futures in therapeutically harnessed biological processes. We argue that ethically accountable visions of biomedical futures need to be anchored in a nuanced understanding of these embodied processes.

Keywords: age-related macular degeneration trial; biomedical future; feminist new materialism; pandemic vaccines; stem cell therapy; vaccine injury

Introduction

Technoscientific manipulation of biological material such as cells, tissues, DNA sequences or microbes is widely understood to be a precondition of emerging biomedicine, and currently underlies a range of technologies from transplantation to gene therapy (Faulkner 2012; Gottweis, Salter, and Waldby 2009; Haran et al. 2008; Salter 2013). This article explores the material dynamics on which these future visions are premised by focusing on two types of technologies amongst the growing scope of biologically derived products or biologicals: pandemic vaccines and stem cell therapies. In regulatory contexts, biologicals are a special category of medicinal products developed by growing micro-organisms and cells.
While live or inactivated vaccines can be considered traditional biologicals, cell therapies fall into the category of “advanced-therapy medicinal products” (Sheets 2017, 5–6).

It is widely acknowledged that biologicals expose patients to different risks than conventional drugs because they harness and engender cellular, molecular, immunological or neurological processes inside living bodies, and that some of these risks are difficult to predict even with inbuilt safeguards (EMA 2010; Mason and Dunnill 2009). Although traditional and experimental biologicals vary in the extent of risks involved, the underlying dilemma is the same. For example, while the general safety of routine childhood vaccines has been established through decades of use, the development of new types of vaccines faces some of the same concerns as experimental biologicals such as stem cell therapies. The differences in risks between biologicals are thus primarily a matter of scale.

In public, regulatory and bioscientific accounts, the challenge of unexpected embodied effects – especially the possibility of medical injury – is often construed as a hurdle that needs to be cleared on the path toward a realization of biomedical promise. In discussions of the ethical and political challenges of biologicals such as new cell therapies, the quality of science, funding models, governance, and public and patient engagement are usually foregrounded (Cossu et al. 2018). At the same time, the challenge of unexpected bodily outcomes is conceptualized as a matter of insufficient testing. It is understood that the safety and efficacy of biologicals need to be proven on demographically, geographically and genetically diverse populations and under long-term surveillance (Gardner et al. 2017; Plotkin 2015). In this framework, biomedical innovation is regarded as a process of overcoming technical and organizational challenges first in clinical testing and then in authorizing the novel product. Meanwhile, the very novelty of living entities as source materials for medicinal products is easily sidelined (Morrison, Hogarth, and Kewell 2013).

Science and technology studies (STS) analyses of the promise of biologicals often emphasize the tension between the realities of biotechnological innovation practices and the hype surrounding them (e.g. Faulkner et al. 2006; Gardner and Webster 2016; Sunder Rajan 2006). At the same time, STS scholars have provided nuanced analyses of the ways in which an anticipatory future-orientation structures biomedical visions of health and good life (e.g. Brown and Michael 2003; Hedgecoe and Martin 2003; Tarkkala, Helén, and Snell 2019). Yet, few STS analyses have theorized the grounding of biomedical futures on the harnessing of living material processes beyond the challenges of regulation, clinical testing, and commercial scale-up.

Our article provides such a theorization. We maintain that in order to evaluate the political and ethical implications of visions of biomedical promise built around biologicals, it is necessary to understand the embodied material dynamics involved in the possibility of unexpected bodily outcomes. Instead of conceptualizing injury as an outcome of nameable risk factors, or as a regulatory hurdle in the narrative of
scientific progress, we focus on the vibrant capacities of living bodies undergoing treatment. Through this focus, our analysis illuminates how the development and use of biologicals and the promise of healthier futures are connected on a material level.

Drawing on feminist new materialist theories, our analysis centers on what we will call embodied material encounters, the often unexpected embodied dynamics that arise from the coming-together of biologically derived products and the vitality of the living body. Embodied material encounters take place in the interiority of bodies in an environment that cannot be fully controlled through a standardized research design. Developing the concept of embodied material encounter, we propose that biomedical futures are not single but multiple. That is, depending on the outcomes of the embodied material encounters for unique individuals, different futures will emerge. Crucially, such futures are not alternative possibilities but simultaneous, unfolding realities. While all medicines interact with living bodies in unique and situated ways engendering more than one future in terms of treatment outcome, these dynamics are intensified in biologicals, which rely on harnessing vibrant and intricate material processes.

Focusing on embodied material encounters enables us to explore the dynamic relations of living matter. While genetic and epigenetic factors play a role in the embodied processes that follow from the administration of biologicals, they are entangled with molecular, hormonal, neurological and immunological processes in highly intricate ways (Gilbert 2010). The multilevel material dynamics are also temporally open, as the long-term outcomes of administering biologicals into bodies are often unknown. This implies that crucial political and ethical challenges of biologically derived medicines are inseparable from the vital effects of open-ended, embodied material processes.

The article seeks to identify patterns and tensions in how the promise of biomedical futures is premised on dynamic biological processes inside living bodies by focusing on two seemingly unrelated biologicals – pandemic vaccines and stem cell therapy. Pandemic vaccines respond to threatening viral potentialities while using that same unpredictable viral material as a source of a prophylactic. Human pluripotent stem cell-based therapies aim to deploy cells derived from patients to repair biological processes and regenerate tissue in various degenerative conditions. Through these biologicals, we can bring together two cases of biomedical injury: vaccine-associated narcolepsy following immunization with one of the 2009 H1N1 pandemic vaccines called Pandemrix, and the risk of debilitating health outcomes in an emerging stem cell therapy targeting an eye disease called age-related macular degeneration (AMD). In both cases, the material encounters inside the body take, or may take, an unexpected turn and generate serious adverse reactions.

As our focus is on theorizing the role of embodied material encounters in shaping biomedical futures, we do not produce a systematic comparison of the two biologicals or cases of injury. Instead, we use the variations and patterns between the
two to analyze how the use of biologicals renders risk and promise as materially situated and multiple. The analysis shows how the realization (in the case of Pandemrix) or potentiality (in the case of stem cell therapies) of injury may impact what counts as acceptable risk or what constitutes a potential future for situated communities such as those formed around vaccine injury or those suffering from a degenerative disease. This highlights that how the risks and promises of biologicals are managed is not only a biomedical-epistemic issue but also a political one. In particular, politics is centered on how to predict, evidence, facilitate, and justify biomedical futures in socially accountable ways when futures are multiple and cannot be fully managed.

The article is structured as follows. The first section elaborates on our methodological starting points and outlines theoretical issues important for approaching the vitality of matter. The following two sections introduce the material agents and biomedical contexts involved in our case studies. The fourth section explores the intricate embodied material encounters involved in pandemic vaccines and stem cell therapies through the occurrence or potentiality of injury. The fifth section theorizes the situatedness of risk and multiplicity of futures. Finally, in the conclusion, we reflect on the political implications of the unpredictability of materiality and the multiplicity of emerging futures.

**Theorizing embodied material encounters**

Biomedical expectations are inseparable from, and constituted by, material entities and practices. Richard Tutton proposes that a methodology of studying the future involves an “entanglement of matter and meaning” (Tutton 2017, 485). According to Tutton, we should not approach future as being only “of the mind,” as in imaginaries or visions of expected events, but also examine how futures have material forms in the present (Tutton 2017, 488). This approach encourages an investigation of biomedical futures as enacted through material-discursive practices, whether in the lab, the clinic, or everyday social contexts (Brown and Michael 2003; Hedgecoe and Martin 2003; Tutton 2017). Building on this line of work, our analysis shows that how futures unfold from pandemic vaccines and stem cell treatments is fundamentally embedded in the embodied material encounters between administered viral and cellular products and vibrant capacities of bodies.

Pandemic vaccines and stem cell therapy are based on their biomedically proven ability to generate wanted biological reactions and processes, such as immune responses or regeneration of healthy tissue. Yet, these material processes are challenging to render fully under control. In exploring this uncontrollability of matter, we draw on feminist new materialisms that encourage thinking about what nonhuman material entities can do (Roy 2018; see also e.g. Alaimo and Hekman 2008; Åsberg and Braidotti 2018). In the case of biologicals, paying attention to embodied material processes reveals how nonhuman and human biological materials are co-constituted as they are harnessed for therapeutic purposes. Our analysis
aligns with the idea of lively powers of material formations developed by scholars such as Jane Bennett (2010), who uses examples from omega-3 fatty acids and food to metals and embryonic stem cells to argue for analytical sensitivity toward the active participation of matter in everyday practices and political work. For Bennett, the vitality and vibrancy of matter often emerges as the capacity of nonhuman entities to “impede the will and designs of humans” (Bennett 2010, viii). In this article we trace how the two biologicals challenge the intentions of their human designers, and how their promises are entangled with the inherent possibility of unexpected bodily outcomes for some groups or individuals.

Focusing on the vitality of matter is important because it renders visible how the hoped-for biomedical futures are uncertain on a material level. But how should we conceptualize this grounding of biomedical futures in lively material formations? Feminist research has illustrated how the dynamics of technoscientific practices arise from the fundamental relationality of human and nonhuman entities. Addressing posthumanism and multispecies worlds, Donna Haraway conceptualizes the involvement of the non-living and the non-human in human world-making as “constitutive relationalities” (Haraway in Gane 2006, 141) and “encounters” between species (Haraway 2008, 46). Meanwhile, Karen Barad explores the concept of “intra-action” (Barad 2007) to theorize the ontological inseparability of entities, concepts and technologies. Following this line of thinking, we focus on biophysiological intra-actions that are constitutive relations in preventive and therapeutic practice conducted through biologically derived medicines and aimed to yield better biomedical futures. In order to specify our target of analysis conceptually and underscore our site of exploration, the human body, we propose and develop the notion of embodied material encounter. This notion allows us to describe the vibrant material processes that take place inside living bodies and engender diverse material effects over time. Embodied material encounters are both the starting point and the end result in the development and use of biologicals. Biologicals aim at generating particular kinds of reactions (i.e. material encounters) in the body. At the same time, the effectiveness of biologicals such as novel vaccines and cell therapies is also an outcome of induced material processes. Embodied material encounters are thus central from initial clinical experimenting and testing to final administration of the biologically derived medicine in the patient body.

Furthermore, embodied material encounters structure how biologicals engender diverse and often unforeseen material effects over time in treated bodies. In this sense, embodied material encounters are constitutive of multiple unfolding futures. Such multiplicity is ontological: the futures that unfold from the use of biologicals exist as simultaneous, materially engendered realities. Our analysis is inspired by STS theorization of multiple ontologies underlying seemingly coherent objects such as diseases (Law and Singleton 2005; Mol 2002) and of indeterminate ontologies in which entities are co-constituted through their changing relations and contexts (Schrader 2010). We contribute to these debates by exploring the
multiplicity of futures as an outcome of a material process – the embodied material encounter.

Developing a theorization of embodied material encounters requires acknowledging the crucial material differences between the two types of biologicals we examine. Viruses are considered non-living, or not quite living, biological entities (Chen 2012), whereas stem cells are living material (Meskus 2018). Likewise, pandemic vaccines and stem cell technologies arise from different technoscientific temporalities: while pandemic vaccines are produced with speed, the development of stem cell therapy is characterized by extreme slowness and caution. The two biologicals also differ in their orientation toward health and illness: one is a prophylactic administered to presumably healthy bodies, the other is aimed to treat seriously ill patients. These differences are, however, precisely what makes the comparison illuminating for an exploration of biomedical futures beyond a single technology.

Our analysis of embodied material encounters builds on data collected in our respective research projects. The data on pandemic vaccines and vaccine injury is part of an ongoing project on the affective politics of H1N1, HPV and MMR vaccines in Europe (Oikkonen 2020). The data on age-related macular degeneration and induced pluripotent stem (iPS) cell-based therapy originate from an ethnographic study on the making of the iPS cell technology, conducted between 2011 and 2017 (Meskus 2018). We have cross-analyzed the data focusing on selected examples of embodied material encounters to illustrate the risks, promises and temporalities that emerge through the comparison of the two cases. We draw especially on international and national epidemiological reports, immunological research articles, and media stories about the emergence and effects of vaccine-associated narcolepsy during the 2009 H1N1 pandemic, and stem cell research articles, news items on the AMD clinical trial using iPS cells, and supranational regulatory texts on stem cell-based clinical translation.

Pandemic vaccines and the 2009 H1N1 pandemic

Pandemic vaccines are tools of pandemic preparedness (Caduff 2015). They are imagined across public health policy and cultural discourses as means of securing communal, national and individual futures. Pandemic vaccines are developed promptly as a response to a potentially life-threatening novel virus that spreads to immunologically unprotected populations. This conjoiner of future orientation of pandemic preparedness, the necessary speed of vaccine development, and unpredictably mutating viruses renders pandemics illustrative of tensions in using biologicals to seek biomedical futures. In terms of embodied material encounters, pandemic vaccines seek to produce a robust immune reaction against a novel virus through manipulation of that same viral material in the lab and administering it into presumably uninfected bodies. The biomedical effects of pandemic vaccines are generated through the interplay of viral entities, materials used to boost the immune reaction, and the immunological responses of the bodies-to-be-protected.
When a novel H1N1 (“swine flu”) outbreak emerged in Mexico in the spring 2009, the World Health Organization (WHO) declared a pandemic, and pharmaceutical companies started developing and manufacturing vaccines, often based on their previous vaccine candidates for other influenza viruses (Abeyesinghe 2015, 102–132). By the end of the summer, multiple vaccines were available and licensed by regulatory bodies; in Europe alone, eight H1N1 vaccines were marketed for pandemic use (ECDC 2012). By the end of the year, vaccination campaigns were well under way in many countries, although vaccination policies and vaccine uptake differed from country to country. Compared to the years-long processes through which routine childhood vaccines are developed, tested and approved, this speed was remarkable. Since the vaccine was needed before the pandemic peak, clinical trials were reduced to the accepted minimum, and the licensing processes were expedited. This meant that turning the disease-causing viral material into a biologically derived prophylactic could not be based on long-term follow-up studies.

This speed raised several concerns. One centered on the unpredictability of viral mutations, which had always been a challenge in influenza vaccines (Dehner 2012). The stability of the novel H1N1 virus was unknown, and viral mutation could reduce the effect of vaccination efforts (MacPhail 2014, 132–151). Another unknown concerned the immunological reactions in vaccinated bodies, as the temporal constrains of the pandemic made large-scale testing unfeasible. Some critics pointed out that some of the new pandemic vaccines included an adjuvant (Stafford 2009). Adjuvants are agents that boost the immune reaction, thereby manipulating immunological responses inside the genetically and materially unique bodies. While adjuvants allowed the use of smaller amounts of viral material and thus the production of larger amounts of vaccine, they were relatively new in licensed vaccines. The public concern about the adjuvants makes visible the underlying logic of immunization: the effectiveness of vaccines is premised on the embodied material encounters between technologically altered, biologically alien pathogenic material and individual embodied immunological responses to that material.

The case of vaccine-associated narcolepsy discussed in the following sections concerned one of the adjuvanted vaccines, GlaxoSmithKlein’s (GSK) Pandemrix, which was the most widely used vaccine in Europe (ECDC 2012). None of the other pandemic vaccines, or any other vaccine, has been connected to narcolepsy. While research suggests that the adjuvant is likely to have played a role in the emergence of vaccine-associated narcolepsy, the biological mechanisms and unpredictable processes inside the body turned out to be much more complex, ambiguous and situated than in the initial concerns over the adjuvant. Thus, our analysis will show, multi-level, unpredictable material encounters within vaccinated bodies emerge as a site where risk and promise of pandemic vaccines becomes pinned.
Next-generation stem cells and age-related macular degeneration

The embodied material encounters we focus on in stem cell therapy involve the relatively recent technology of reprogramming adult cells into iPS cell lines. These cell lines can be differentiated into wanted tissue type to be used in research but also, in the expected future, applied for therapeutic purposes. This form of biologically derived product development is at its early, experimental phase with much discussion on the riskiness of the source material (Meskus 2018). IPS cell lines are usually derived from a patient’s skin biopsy or blood sample. They are created by inserting into the somatic cells copies of three or four genes known to be important for reprogramming the cell back into the state of pluripotency. According to the Japanese research group who first published this method, the importance of the iPS cell line is that it allows the creation of pluripotent stem cells directly from patients (Takahashi and Yamanaka 2006).

Although current preclinical research uses iPS cells widely, only one clinical trial has involved transplantation of such cells in patients (Cossu et al. 2018). In 2013, seven years after the publication of the iPS cell technology, the first in-human clinical study using iPS cells was launched in Japan. The study is led by Masayo Takahashi, the leader of the Laboratory for Retinal Regeneration at Riken Research Centre in Kobe, in collaboration with the Institute for Biomedical Research and Innovation at Kobe (Riken 2019). The study concerns AMD, an incurable condition where the progressive deterioration of light-sensing photoreceptor cells and their supportive retinal pigment epithelium (RPE) causes blindness. Approximately 170 million individuals are said to be affected with AMD globally, making it the leading cause of visual disability in the industrialized world and the third leading cause globally (Wong et al. 2014). As the pathogenesis of AMD has become the topic of genetic, epidemiological and molecular study aiming to unravel the mechanisms that underlie this complex disease, AMD has also raised the interest of stem cell research, and those experimenting on applying the iPS cell technology to clinical translation (Reardon and Cyranoski 2014).

For us, the case opens up a unique view into the complexities of embodied material encounters involved when human bodies are treated with living biological material. The first clinical stem cell transplant experiment used iPS cells from a 77-year-old Japanese female patient suffering from advanced neovascular or “wet-type” AMD, where abnormal growth of blood vessels behind the retina of the eye damage the overlying retinal pigment epithelium needed for vision. Genetically matched iPS cells were derived from the patient’s skin cells and then “coaxed” in the laboratory to differentiate into RPE cells. These were then further cultured to generate a small monolayered sheet that was transplanted in a hospital surgery operation behind the retina of the same patient (Mandai et al. 2017; Riken 2014).

This type of technoscientific manipulation of biological material increasingly grounds future visions of biomedical treatment. Like the production and
development of new vaccines, regenerative medicine through stem cell therapy is conditioned by safety and efficacy requirements which reflect the scientific difficulty of knowing and controlling the biophysiological processes – material encounters – the administered cell transplants engender in the human body. Given this challenge, it is not by accident that the eye has become the first site for iPS cell-based therapy. Compared to many other tissue types, it is relatively easy to differentiate iPS cells into RPE cells even though the process is labor-intensive and requires extensive monitoring and testing. The eye also provides an isolated environment. It can be closely monitored for targeted effects as well as side effects and pathologic changes. It is walled off, protecting the transplanted cell sheet from damaging inflammatory responses from outside the eye. The eye thus facilitates the biomedical experimentation of embodied material encounters between degenerative and regenerative tissue. As such, it has become a testing ground for the realization of hoped-for biomedical futures.

**Embodied material encounters and the unpredictability of injury**

This section will take a closer look at the embodied material encounters taking place in the two cases. An important part of these encounters is the characteristics of the cellular and viral material employed in each biological. Vaccine development seeks to manipulate viral material in ways that make the material noncontagious while rendering it capable of producing a robust immune reaction. Stem cell transplants are crafted with the view of creating a process of cell and tissue regeneration in the body while averting cancerous tissue growth and preventing the travel of the implanted material to wrong locations in the body. Focusing on these material entities and processes, we illustrate how the prospect of disease-free futures achieved through biologicals is often precarious.

The material entanglement of promise and risk in pandemic vaccines became visible in the summer 2010 when doctors in Finland and Sweden started reporting cases of suspected adverse events among children and adolescents vaccinated with Pandemrix (ECDC 2012). The adverse events involved the sudden onset of narcolepsy, a currently incurable neurological disease characterized by excessive and uncontrollable daytime sleepiness and often accompanied by sudden loss of muscle control (cataplexy), frequent nightmares, and sleep paralysis. Narcolepsy can range from a manageable condition to a highly debilitating illness that severely interferes with a person’s everyday life. An increase in narcolepsy cases following Pandemrix was subsequently reported and analyzed in other countries including France, Ireland, Norway and the United Kingdom (Dauvilliers et al. 2013; Heier et al. 2013; Miller et al. 2013; O’Flanagan et al. 2014).

Once the realness of Pandemrix-associated narcolepsy was established through epidemiological studies, research focused on the invisible material processes inside the living body (Oikkonen 2020). What had happened in the material encounters between the novel vaccine and the living body that had resulted in
the onset of narcolepsy in some previously healthy young people? Not surprisingly, first concerns focused on the adjuvant, AS03, which had engendered critical comments before the vaccination campaigns started (Hall and Wolf 2019); there was also some evidence that similar adjuvants had been linked to adverse reactions in other species (Nohynek et al. 2012). However, the association with narcolepsy appeared to be absent in GSK’s Arepanrix, which had the same adjuvant as Pandemrix (Vaarala et al. 2014).

This turned researchers’ attention to differences in the production processes of the vaccines, and to the fact that Pandemrix included considerably higher levels of viral nucleoprotein than Arepanrix (Vaarala et al. 2014). Narcolepsy is an autoimmune disease in which the body attacks neurons linked to the production of hypocretin (orexin), which regulates sleep. It was suggested that the close structural resemblance between the viral nucleoprotein and the hypocretin-receptors had allowed antibodies engendered by the vaccine to cross-react with the hypocretin-receptors resulting in permanent damage (Ahmed et al. 2015; Vaarala et al. 2014).

However, the process could not be pinned down to the vaccine alone. As the theory of cross-reacting antibodies suggested, the material processes inside the living body played a key role. For example, vaccine-associated narcolepsy appeared primarily among children and adolescents, suggesting that there was something materially vulnerable about how young bodies functioned and developed. Also, practically everyone with Pandemrix-associated narcolepsy carries a particular common haplotype (HLA-DQB1*0602) associated with narcolepsy in previous research. Yet only a small percentage of young people, or of those with the risk allele, developed narcolepsy after Pandemrix. This suggested that risk was located in the unique, situated material processes that took place when the vaccine interacted with the living materiality of the body (Ahmed et al. 2015). What happened inside the living body after vaccination was likely to be highly complex, involving interactions among adjuvants, nucleoprotein, antibodies, neurons controlling hypocretin, and the HLA-DQB1*0602 risk allele. In this, Pandemrix-associated narcolepsy shows how causal relations are often obscure and material entities may embody unexpected vitality. The tensions between risk and promise were heightened further by the retrospective nature of biomedical knowledge: in the case of Pandemrix, risks arising from complex and vital materiality were knowable only through the emerging injuries.

IPS cell therapy is only at the stage of first clinical safety-study involving a handful of patients (Riken 2017a, 2019), and thus the case is not directly comparable to pandemic vaccines with their wide, population level application. Also, while vaccine-associated narcolepsy provides a retrospective account of embodied material encounters, the pilot study of iPS cell-based intervention in AMD offers a prospective one. However, the AMD case is important for our theorization of embodied material encounters because, unlike vaccines, stem cell therapies harness laboratory-grown, genetically modified living cellular material to engender therapeutic reactions in a specific location in the patient body.
With iPS cell-derived transplants, two feared biomedical outcomes of embodied material encounters stand out. The body’s immune system could attack the transplanted cell sheets. The sheets might also contain some cells that are still in the pluripotent state, and those cells could turn into cancerous tissue. In the AMD study, the risks of immune reactions and cancerous tissue growth were reported to be closely monitored (Riken 2019). This involved the identification and control of multiple biological functions (such as morphology and gene expression) throughout the processing of the biological material. The laboratory-created RPE cells were checked to be as “pure” as possible (not containing residual iPS cells that could result in the formation of teratomas). The produced cell grafts had to show structural rigidity needed to withstand the physical stresses associated with the transplant procedure. Finally, before transplantation, the RPE grafts had to be tested with animal models for immunogenicity to pre-empt immune system reactions (Kamao et al. 2014; Mandai et al. 2017).

The embodied material encounters on which stem cell therapy relies involve unpredictability at several phases of the treatment process from the sourced original cell material and the achieved new cell type such as RPE cells to generated bodily reactions. Significantly, in the first iPS cell-based AMD clinical experiment, a planned second patient, a 68-year-old Japanese man, was not treated because his cells prepared in the same way as with the female patient were found to contain genetic abnormalities, or DNA deletions, both in the iPS cells and iPS cell-derived RPE cells (Mandai et al. 2017). The embodied material encounter involved in the planned treatment was thus seen as too risky.

Takahashi’s research group has reported that one year after the transplant surgery, the transplanted sheet remained intact in the female patient’s eye and there was no sign of graft rejection (Mandai et al. 2017). As the primary aim of this study was to demonstrate a proof-of-concept (i.e. safety) for this particular form of stem cell therapy, the research group reported they had indeed achieved this proof, bringing the future of clinical use of iPS cells one step closer to realization (Riken 2017b). In their study report, Takahashi’s team “advice caution” in extrapolating the results to other types of iPSC-based transplantation, acknowledging that findings from treating a single patient are insufficient to address the scope of risks associated with the transplant procedure (Mandai et al. 2017). Nevertheless, the promise of the therapeutic material encounters engendered by this type of stem cell treatment is that, in sufficiently controlled circumstances, it can become a successful path towards curing presently incurable disease. The Riken Research Centre announced in early 2017 that its researchers had showed that iPS cell-derived retinal tissue transplanted into “end-stage retinal degeneration model mice” had not only halted the disease progression but caused “improved vision” in the test animals (Riken 2017c).

As these two cases demonstrate, the goal of biologically derived medicinal products is to deploy material processes so that wanted therapeutic reactions outweigh possible unwanted side-effects. Both the risks and promises surrounding
biologicals, that is, are rooted in the vitality of material processes inside the body. Following Bennett’s (2010) notion of vibrant matter, the lively powers involved in these biotechnologies are enrolled and constituted in laboratory and clinical practice. Yet, as the cases show, harnessing lively matter for medicinal purpose requires accepting uncontrollability arising from material complexity. Our analysis in the next section suggests that this is why biomedical futures in the use of biologicals are inherently multiple.

Situated risks, multiple futures

To begin with, vaccination campaigns are premised on a tension between population-level and individual-level risk and protection. Vaccines derive their legitimacy from their promise to protect people on the population level. While vaccination campaigns often target particularly vulnerable bodies – those of infants, pregnant women, elderly and people with chronic diseases – the population-level goal is to prevent disease from spreading across communities through herd immunity. However, as the unexpected occurrence of narcolepsy shows, risk and promise may occur differently for different people or communities, with the result that multiple embodied futures emerge. While Pandemrix-associated narcolepsy appears as a slight rise in population-level statistics (e.g. ECDC 2012), it shaped some individual lives dramatically through the unexpected material encounters inside living bodies after vaccination (Lundgren 2017; Oikkonen 2020).

The fact that vaccines are administered to healthy people, and that pre-existing conditions did not increase the likelihood of narcolepsy, raised the political stakes around vaccine-associated narcolepsy, especially since those affected were primarily children. This tension between individual and population is a common theme in the media coverage of vaccine-associated narcolepsy. Many critical media stories not only questioned the way individual children suffered to protect the population; they also sought to establish those affected by vaccine-associated narcolepsy as a population (i.e. a significant demographic group). For example, a 2014 article in the International Business Times combines an emotionally appealing case of an 8-year-old boy in the UK with numerical statements such as: “Across Europe, more than 800 children are so far known to have been made ill by the vaccine” and “many more are expected to come forward with the symptoms” (Porter 2014).

The tension between individual-level and population-level risk and promise operates somewhat differently in stem cell therapies, which have focused primarily on individual-level embodied material encounters. In contrast to vaccines, stem cell therapies operate on radically smaller scale, with strong aspirations to offer “personalized” medicine and individually matched treatment (EMA/CAT 2009). The first AMD clinical experiment with iPS cells was built around the idea of deriving stem cell-based transplantable tissue from the patient herself in “autologous” treatment, to avoid tissue rejection and the need for immunosuppression. In autologous
treatment, the same patient is also the sole recipient of the created cell transplant (Foley and Whitaker 2012). However, the Japanese research team at Riken encountered the concern that cells from macular degeneration patients, who tend to be elderly, might have accumulated genetic defects (Cyranoski 2017). Indeed, autologous cell lines prepared for the second patient in the clinical study were found to contain genetic abnormalities and were never implanted. As a result, the Takahashi team announced it would use other type of source material, procured from a Japanese iPS cell bank, thereby moving from individualized strategy to population-based sourcing of stem cells. A new clinical study was initiated that aimed to recruit five patients to be transplanted with cell suspensions of RPE cells made from iPS cells generated from other donors (Riken 2017d). The cells were procured from Kyoto University’s Center for iPS Cell Research and Application (CiRA), which had been building a collection of cells from healthy donors to create an “iPS cell stock for regenerative medicine” that would cover the HLA haplotypes of most of the Japanese population by 2022 (CiRA 2019).

As with pandemic vaccines, the multiple futures emerging in a stem cell therapy are embedded in the tension between individual and population. For instance, individual risks in immunological rejection grow with the use of donated iPS cell lines from other genotypes. With scale-up in cell production, and resulting increase in in vitro replication, the risks of genetic and chromosomal abnormalities also increase in the generated material. However, in many current assessments, these and other risks are estimated as subordinate to the promises of using donated, ready-made cell lines from population-level matched haplobanks, which are expected to speed up the production of transplantable tissue. These so-called allogeneic cellular therapies are based on the premise of one donor and many recipients. They fit with the existing biopharmaceutical model better than autologous treatments, as they involve manufacturing therapeutic cellular material at a large scale (Foley and Whitaker 2012; Mason and Dunnill 2009; Morrison 2017).

These tensions between individual and population show that biologicals do not engender either health or harm, but simultaneously both – just for different people. The range of material encounters inside the body constitute a site from where mutually contradictory futures emerge for different individuals and communities. How the future was enacted in the case of a person receiving the Pandemrix vaccine depended on how the encounters between material entities such as genes, autoimmune reactions, nuclear protein structures, infections, and hypocretin levels unfolded in the body over time. These potential futures differed from the futures imagined on the level of immunologically protected populations. In the case of human pluripotent stem cell therapies, the material encounters inside the patient’s body are expected to lead to brighter futures for some patients suffering from presently incurable, often degenerative diseases. At the same time, futures remain unknown as it is impossible to know which emerging forms of stem cell therapy – autologous or allogeneic treatments – will deliver the promises of
actual cures and what kinds of possible harms, and to whom, need to be managed before licensing their use.

Regarding the future of biomedicine, our two cases illustrate that enactments of the future are dependent on the alignment of various materialities in the present (Hedgecoe and Martin 2003; Tutton 2017). We have argued that these materialities are vibrant, entangled, and ambiguous (Bennett 2010; Roy 2018), and often knowable only after risk has already actualized as injury. The point we want to make here is that biomedical futures with biologicals are never singular and binary – progress or failure of science. Despite stringent standardization and risk-control measures, these biomedical futures are multiple in the sense that different dynamics of risk and promise unfold differently for different people, while the processes of unfolding are simultaneous. The roots of these multiply unfolding futures, in turn, are in the vibrant embodied material encounters that constitute the organizing rationale of biologicals and their potentially groundbreaking medicinal effects.

Conclusions

Risk and promise are complicated matters in future-oriented biotechnologies that rely on harnessing embodied material encounters in targeted individuals and populations. Guided by Haraway’s notion of constitutive relations (Gane 2006) between human interventions and biological processes, and feminist new materialist approaches that underscore the vitality of matter, our analysis has demonstrated that with biologically derived products, promises and risks are mutually entangled due to the constitutive variability of the material encounters generated in the body. While clinical research in biologically derived medicines attempts to isolate and curtail unwanted embodied reactions first on the individual level and then in large scale, we maintain that – with the rising promise of biologicals – it is increasingly important to develop STS tools to theorize how risk and promise are situated. Through the concept of embodied material encounters, we have shown that risk and promise may be flipped around unexpectedly through unforeseen reactions, and that they may be realized differently for different individuals and communities. Thus, what is progress for one person or community may turn out to be a curtailed or complicated future for those suffering serious adverse effects.

In the case of swiftly developed pandemic vaccines, the promise of futurity – the absence of death and serious illness caused by the pandemic virus – is premised on the acceptance of some degree of risk, and the difficulty of fully predicting who will be harmed and who will benefit. While a new vaccine is recommended only if there is evidence that it will save lives on the population level, vaccine-associated narcolepsy demonstrates inherent tensions in this model. Although the 2009 pandemic vaccines prevented infections and reduced hospitalization (Lansbury et al. 2017), one of the vaccines, Pandemrix, also engendered unforeseen injuries in certain bodies. With stem cell therapies, the future promises of new cures to presently incurable diseases are likewise premised on the acceptance of certain levels of
risk, ranging from variabilities in the original cell sources to impurities in the biological material applied. While stem cell-based regenerative treatments receive marketing authorization only if they are assessed safe and effective enough, political and ethical issues remain as to which individuals and population groups can benefit from them and with what health and economic costs.

Deriving medicinal products from living entities challenges STS scholars to theorize biomedical futures as enacted through the vibrant, constitutive materialities of the present. Our analysis of the two cases contributes to the STS understanding of biomedical futures by demonstrating that there seldom is a single biomedical future that will unveil from the present moment of biotechnological innovation. Rather, such futures are multiple and mutually contradictory because they unfold simultaneously from material encounters between situated living bodies and complex prophylactic and therapeutic products. While it can be argued that this is the case with any medicines, the stakes are higher in biologicals because the vitality of matter constitutes the precondition and rationale of these technologies.

Our analysis of pandemic vaccines and stem cell therapies suggest that the management of biomedical futures involves strategically highlighting some futures over others. On the basis of our analysis, we argue that in an evaluation of risks and promises it is not enough to engage with the economically and politically attractive population-level gains of biologically derived medicinal products. While population-level gains are an important consideration especially in the public health management of infectious diseases, critical investigations should also unpack the societal implications of biologicals by focusing on unique, incoherent, materially situated vibrant bodies marked by age, genetic and epigenetic constitution, and immunological histories. Crucially, the material encounters inside unique, living, differently constituted bodies may or may not deliver the promises of healthier futures, or they may deliver them in the case of some biologicals but not others. The ways in which visions of healthy futures are premised on the vibrant material processes inside living bodies is thus of considerable significance for STS analyses of biomedical futures.

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