Introduction: Epigenetics and Responsibility

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Epigenetics: what is it, and why does it matter?

Epigenetics is a fast-growing field in molecular biology. It studies the ways in which modifications to DNA affect gene expression and cell functioning (Carlberg and Molnár, 2019), providing an interface between the genetic and the environmental. The difference between epigenetics and genetics is located in the prefix 'epi', meaning that epigenetic mechanisms are something upon, attached to, or beyond genetics.[1] Epigenetic information may be regarded as another layer beyond genomic information that not only enriches but also challenges insights from more traditional understandings of genetics. The central 'dogma' of genetics is the idea that there is a one-way progression, whereby the genetic code (DNA) is transcribed into RNA, which is translated into proteins. Epigenetics, however, calls into question the unidirectional assumption of this progression, and shows that the interface between genetics and the environment of the genes is much more complex (Hens, 2022).

By regulating gene expression, epigenetics provides a route for environmental influences, including social factors, to affect the development of phenotypes at a molecular level. Epigenome-wide analysis and similar technologies help us to discover the large-scale molecular alterations caused by environmental influences, ranging from food intake during pregnancy to particulate matter related to pollution (Fazzari and Greally, 2010; Rosen et al, 2018; Mancilla et al, 2020). Although the mechanisms described in the central dogma of genetics remain valid, epigenetics paints a far more intricate picture of human development than has often been assumed in science and the popular media alike. This raises important issues for ethicists and legal scholars. For example, it has been suggested that epigenetic changes may be passed on to future generations, extending the scope of responsibility that people may have towards current or future offspring. Moreover, although

many ethicists have reflected on the challenges related to the application of CRISPR/Cas9 (a precise gene-editing technology) in human embryos, changing gene expression may be more feasible than changing the genes themselves. As such, a full appreciation of the impact of epigenetics implies viewing it as a molecular basis for a systemic and plastic concept of human nature, situating humans firmly as dynamically altering and being altered by the systems in which they live (Canguilhem, 2008; Thompson, 2010). Which types of responsibility do people have in light of these new findings? How do such findings influence philosophical conceptions of moral responsibility in general? Questions such as these are of central concern to this volume. By looking at these recent developments in biology that reflect a 'dynamic turn' in thinking about human nature, we aim to enrich normative debates on responsibility.

To obtain a somewhat fuller picture of what epigenetics is and what it is not, some short clarifications and demarcations are necessary. Even though contemporary epigenetics as a research field has existed for no more than three decades, various study domains have already been established. The definitions of those domains may vary, and there is often considerable overlap between them. Environmental epigenetics research investigates the ways in which epigenetic alterations may mediate effects caused by environmental exposures or toxins (Jirtle and Skinner, 2007; Bollati and Baccarelli, 2010; Niewöhner, 2011). Neuroepigenetics concerns the regulation of DNA in the nervous system (Sweatt, 2013). Epigenetic epidemiology combines insights from epigenetics with those from epidemiology to improve our understanding of the mechanisms behind observations of interactions between environmental, genetic and stochastic factors and the distribution of diseases (Jablonka, 2004; Heijmans and Mill, 2012). Finally, it is important to mention epigenomics. This is a field of research that focuses on broad or even genome-wide profiles or patterns of epigenetic modifications and their effects (Kato and Natarajan, 2019). Recent research has also been investigating how epigenomics may fruitfully engage with other 'omics' domains such as genomics, which studies the whole of the genetic material in an organism (the genome), and proteomics, a field dedicated to the large-scale study of proteins (Zaghlool et al, 2020; van Mierlo and Vermeulen, 2021). In STS (Science and Technology Studies) and ELSI (Ethical, Legal and Social Implications) literature on epigenetics, the terms 'epigenetics' and 'epigenomics' are sometimes used interchangeably. Although more can be said about the relationship between the two, for our purposes we consider epigenetics to be the more general term, and epigenomics as a field within epigenetics research that focuses especially on the scale of the epigenome but that may nonetheless be regarded as part of the bigger epigenetic project.

The question of whether the epigenetic marks that a person accumulates from their environment may be transmitted to subsequent generations

has been widely discussed over the past two decades. Most epigenetic programming is rewritten or reset between generations, but there is increasing evidence that this is not always the case. When considering the transmission of epigenetic marks (such as histone modifications and DNA methylation patterns) between generations, it is important to distinguish between transgenerational and intergenerational effects. Intergenerational epigenetic inheritance refers to epigenetic marks in offspring that are the result of direct exposure of their germline to environmental stressors. This means that intergenerational inheritance is limited to the first generation of male offspring and the first and second generations of female offspring (Cavalli and Heard, 2019). The second generation of female offspring is included because environmental triggers during pregnancy may directly affect the oocytes (egg cells) that are already present in the fetus. A famous example of intergenerational epigenetic inheritance is the famine during the Dutch Hunger Winter of 1944–1945. The children of mothers who experienced this famine during their pregnancy were six decades later found to have less DNA methylation of the imprinted *IFG2* (Insulin Like Growth Factor 2) gene, which is associated with the risk of metabolic diseases (Heijmans et al, 2008). These and other findings contribute to empirical support for the hypothesis that early-life environmental conditions can cause epigenetic changes in humans that persist throughout their lives and on into the next generation(s) (Heijmans et al, 2008; Painter et al, 2008; Lillycrop, 2011). The public discourse and research are often focused on women, perhaps based on 'implicit assumptions about the "causal primacy" of maternal pregnancy effects' (Sharp et al, 2018, p 20). However, epigenetics offers an opportunity to show how not only influences *in utero*, but also paternal factors and postnatal exposures in later life, play a role in the health of offspring. Thus, in epigenetics research, attention is also paid to paternal effects such as the influence of the father's diet on spermatogenesis and offspring health (Rando, 2012; Milliken-Smith and Potter, 2021; Pascoal et al, 2022). Transgenerational epigenetic inheritance is more contested. It denotes the indirect transmission of epigenetic information that is passed on to gametes without alteration of the DNA sequence (Carlberg and Molnár, 2019). This means that we can only speak of transgenerational inheritance if the epigenetic effects of exposures of the current generation are still present in the second generation of male offspring or the third generation of female offspring (Cavalli and Heard, 2019). So far, most transgenerational epigenetic effects have been discovered in plants and non-human animals such as rats and mice. For example, researchers working with mice have found third-generation epigenetic effects of maternal diet (Dunn and Bale, 2011) as well as social stress levels (Matthews and Phillips, 2012), although others argue that multigenerational inheritance of methylation patterns in mice is an exception rather than the rule (Kazachenka et al, 2018). A study

of *Caenorhabditis elegans* worms by Klosin and colleagues also had impressive results (Klosin et al, 2017). They genetically modified these worms to glow when exposed to a warm environment. Not only did the worms start to glow more when the temperature was raised, but they also retained their intense glow when researchers lowered the temperature again. Moreover, 'their progeny inherited the glow and even seven generations further down the line, glowing worms were born. If five generations of *C. elegans* worms were kept in a warm environment, this characteristic was passed on to fourteen generations' (Hens, 2022, p 48).

Such findings in animal research sometimes lead to premature conclusions about human health and disease (Juengst et al, 2014). However, it is virtually impossible in research on human inheritance to exclude potential confounding elements such as changes *in utero* and postnatal effects (Cavalli and Heard, 2019). It is hard to distinguish between 'real' epigenetic inheritance and cases where the offspring are simply exposed to the same experiences or health problems as their parents because the context is reconstructed or culturally inherited. However, there are some studies that suggest that transgenerational epigenetic inheritance is possible, albeit limited, in humans. First, when studying historical data of cohorts in Överkalix, Sweden, researchers found associations between grandpaternal food supply and the mortality rate of their children and grandchildren (Kaati et al, 2002). However, because no molecular data were available, no epigenetic links could be proven. Pembrey and colleagues build on those findings to find evidence of sex-specific male transgenerational inheritance in humans (Pembrey et al, 2006). In a longitudinal study in an area around Bristol, UK, they found transgenerational effects of smoking before puberty on the growth of future male offspring of men. Specifically, early paternal smoking (before puberty) was associated with a greater body mass index in their sons. The researchers posit DNA methylation as a potential mechanism behind the links between acquired epigenetic traits of a generation and the epigenetic marks present in the next generations.

Epigenetics also relates to research into the developmental origins of health and disease, or DOHaD, which may be defined as the study of how the early-life environment affects the risk of diseases from childhood to adulthood (Bianco-Miotto et al, 2017). DOHaD also studies the mechanisms involved, which means that there are intricate connections between DOHaD and epigenetics (Vickers, 2014). A core assumption of DOHaD is humorously summarized by Maurizio Meloni as 'We are not so much what we eat, but what our parents ate' (Meloni, 2016, p 209). Thus, both fields overlap, but only partly: epigenetics has a broader focus than just prenatal and perinatal exposures, whereas DOHaD also studies other mechanisms than epigenetic alterations. Many epigeneticists, especially those working in fields such as environmental epigenetics and 'social epigenomics', also see their work as

a contribution to the body of knowledge on social determinants of health. These are conditions in people's social and physical environments that influence health outcomes throughout their life course (Mancilla et al, 2020). Such conditions may include the influence of one's family and neighbourhood and one's broader social context, as well as values, attitudes, knowledge and behaviours (Notterman and Mitchell, 2015). Mancilla and colleagues, for example, argue that epigenetics is not the only field that can shed light on social determinants of health, but one that can contribute to explanations of the ways in which socio-environmental factors influence our biology through epigenetic modifications (Mancilla et al, 2020).

The role of the epigeneticist then lies primarily in discovering more about the mechanisms that connect environmental triggers to gene expression (Milliken-Smith and Potter, 2021). A well-known example of such research is the work of McGuinness and colleagues, who investigated the relationship between socio-economic and lifestyle factors and epigenetic profiles in Glasgow, UK, a city that is known for its socio-economic and health disparities. The data were gathered in the context of a broader study on the psychological, social and biological determinants of ill health (pSoBid)[2]. They found lower levels of global DNA methylation in those with a low socio-economic status as well as participants who did manual work. Lower global DNA methylation content was in turn associated with biomarkers of cardiovascular diseases and inflammation (McGuinness et al, 2012). As Milliken-Smith and Potter note, we must be aware that the dynamic between social processes and (epi)genetic information about our health goes two ways. Authors such as McGuiness and colleagues primarily focus on providing 'an explanatory link between the social determinants of health and physiological outcomes'. However, 'a critical appraisal of how this emerging epigenetics knowledge is debated and employed' can highlight how existing biases and disparities may sometimes be reinforced in the social determinants of health framework (Milliken-Smith and Potter, 2021, p 1). We would like to add that researchers, especially those working on the ethical aspects of epigenetics, may benefit from using an intersectional approach that is sensitive to the interplay between various social and environmental conditions (Collins and Bilge, 2016).

Furthermore, epigenetics has shed some new light on our understanding of the development of diseases and disabilities. In the following paragraphs, we give some examples of conditions that are being researched by epigeneticists. It is worth noting that some of the health issues mentioned here, such as stress and obesity, have been posited as both causal contributors to disease development and the outcome of epigenetic processes.

Exposure to stress in the womb or during early childhood has been associated with epigenetically mediated adverse health effects. For example, childhood maltreatment may trigger long-lasting epigenetic marks,

contributing to post-traumatic stress disorder in adult life (Mehta et al, 2013). Epigenetic studies have also found that stress in early life can contribute to behaviour that is typical of attention-deficit hyperactivity disorder (Bock et al, 2017). Additionally, Oberlander and colleagues found that the methylation status of the human *NR3C1* (nuclear receptor subfamily 3 group C member 1) gene in newborns is sensitive to maternal depression. They argue that these findings suggest a potential epigenetic process that links the antenatal mood of the mother to the ways that infants respond to new situations, such as an increased stress response to new visual stimuli (Oberlander et al, 2008).

Pollution has numerous harmful effects on health. Emerging data indicate that exposure to air pollution brings about epigenetic changes. These changes may in turn influence inflammation risk and exacerbate the risk of developing lung diseases (Rider and Carlsten 2019). It is well known that lead is a common neurotoxic pollutant that disproportionally affects the health of children. Evidence for the epigenetic basis of the effects of lead is increasing (Senut et al, 2012; Wang et al, 2020).

The epigenetic mechanisms behind the development of metabolic conditions are becoming well-documented. Molecular links between environmental factors and type 2 diabetes have been discovered (Ling and Groop, 2009; Slomko et al, 2012; Rosen et al, 2018), as well as mechanisms that regulate the expression of genes associated with diabetic kidney disease (Kato and Natarajan, 2019). Various studies have also looked into the epigenetics behind obesity, both as a contributory factor and as a health outcome (Lillycrop, 2011; Slomko et al, 2012; Rosen et al, 2018). As type 2 diabetes patients are often more likely to suffer from cardiovascular disease, the influence of environmental factors and the diet of ancestors on the epigenome has also been investigated (Kaati et al, 2002; Lillycrop, 2011). Like stress, obesity has been posited not merely as a health outcome but also as a causal factor that induces other epigenetically mediated conditions. For example, there seems to be an association between overweight in prepubescent boys and diminished lung function and asthma in those boys' adult offspring (Lønnebotn et al, 2022).

Neuroepigeneticists investigate the crucial role that epigenetic regulation plays in the development and functioning of the brain. Conditions for which epigenetic regulatory mechanisms have been suggested include Parkinson's disease, Huntington's disease, schizophrenia, epilepsy, Rett syndrome and depression (Tsankova et al, 2007; Carlberg and Molnár, 2019). Much research is geared towards a better aetiological understanding of neurodevelopmental conditions such as Tourette's syndrome (Müller-Vahl et al, 2017), attention-deficit hyperactivity disorder (Bock et al, 2017; Pineda-Cirera et al, 2019; Wang and Jiang, 2022) and autism (Schanen, 2006; Eshraghi et al, 2018; Waye and Cheng,2018; Gowda and Srinivasan, 2022; Wang and Jiang, 2022). However, there is still much uncertainty about the concrete causal

evidence that may be implicated in the development of such conditions (Wang and Jiang, 2022).

In addition to offering new understandings into the ways in which specific diseases arise, epigenetics may also suggest new routes for therapy. Epigenetic changes appear to be more readily reversible than genetic ones (Hens, 2022). This reversibility holds potential for epigenetic therapy, as epigenetic marks such as methylation patterns may be seen as targets for medical interventions and treatments (Heerboth et al, 2014; Carlberg and Molnár, 2019; Nakamura et al, 2021). Many of the clinical research efforts in this domain are directed toward treatments of cancers (Falahi et al, 2014; Lu et al, 2020). Cancer cells are often characterized by epigenetic drifts: the divergence of the epigenome as a function of age due to stochastic changes in methylation (Shah et al, 2014). Many tumours are associated with epigenetic reprogramming (Carlberg and Molnár, 2019). While some studies have investigated the possibility of epigenetic interventions in general, others focused on specific types of cancer such as breast cancer (Falahi et al, 2014) and prostate cancer (Pacheco et al, 2021). Lu and colleagues list so-called 'epidrugs' in clinical trial, with targets also including melanoma, lymphoma, ovarian cancer, bladder cancer and brain tumours (Lu et al, 2020). Research on epidrugs for other conditions is also prolific. Recent projects have aimed at targeting conditions such as COVID-19 (Zannella et al, 2021), hypercholesterolaemia (Paez et al, 2020), neurodegenerative diseases (Janowski et al, 2021), autoimmune diseases such as chronic kidney disease (Tejedor-Santamaria et al, 2022), and depression (Tsankova et al, 2007).

Epigenetics: old wine in new bottles?

Do all these advances in epigenetic knowledge suggest that there is something scientifically or ethically unique about epigenetics to such a degree that we should dedicate an entire volume to it? After all, thousands of books and papers have already been written about genetics and its ethical implications. Is epigenetic exceptionalism – a term coined by Mark Rothstein in line with Thomas Murray's 'genetic exceptionalism' – warranted (Murray, 2019; Rothstein, 2013)? In other words, are new findings in epigenetics so 'extraordinary in kind or degree' that they necessitate new analytical frameworks or novel approaches to deal with their unique character (Rothstein, 2013, p 733)? Before discussing answers to this question, a distinction must be drawn between the potential revolutionary scientific character of findings in epigenetics on the one hand, and the potential unique ethical and social implications of such findings, including those with regard to responsibility, on the other. Rothstein argues that the label of scientific epigenetic exceptionalism is warranted on at least five grounds. First, he contends that epigenetic changes occur much more frequently than mutations

in DNA sequences. Moreover, 'an individual's susceptibility to epigenetic change is highly dependent on the dose of the environmental agent and the stage of development at which exposure occurs' (Rothstein, 2013, p 734). Furthermore, he notes that epigenetic changes are intrinsically reversible and tissue- and species-specific. He concludes: 'From a scientific standpoint, epigenetic discoveries are extraordinarily exciting because they represent a new way of understanding the processes by which various harmful exposures cause disease in humans and, in some cases, their offspring. Furthermore, epigenetics could point the way to new methods of preventing and treating numerous disorders' (Rothstein, 2013, p 734).

Laura Benítez-Cojulún discusses the use of various terms used by researchers in describing the significance of epigenetics. Some researchers talk of epigenetics as evoking 'a substantial transformation' (Benítez-Cojulún, 2018, p 135), others use the terms 'epigenetics revolution' (Meloni, 2015, p 141), 'epigenetic turn' (Nicolosi and Ruivenkamp, 2012, p 309) or 'epigenetic shift' (Willer, 2010, p 13). Some use the less favourable term 'epigenetics hype' (Maderspacher, 2010; Deichmann, 2016) to describe 'the far-reaching, revolutionary claims of having discovered entirely new mechanisms of heredity and evolution which are supposed to replace older concepts' (Deichmann, 2016, p 252). Juengst and colleagues appear to consider that exceptionalist language itself is what makes epigenetics exceptional, noting that 'scientific hyperbole rarely generates the level of professional and personal prescriptions for health behaviour that we are now seeing in epigenetics' (Juengst et al, 2014, p 427). Based on a series of in-depth interviews, Kasia Tolwinski has shown that scientists working on epigenetics hold a variety of views with regard to the impact and future of their field. She notes that some epigeneticists are 'champions' of epigenetics as a promising new field. In contrast, others hold a more moderate position, and still others may be considered 'sceptics' regarding the novelty or autonomy of epigenetics as a discipline (Tolwinski, 2013).

The ethical and social implications of epigenetics findings depend partly on their perceived scientific status. However, arguing for some kind of scientific exceptionalism does not necessarily commit one to the view that ethical implications are equally exceptional. Rothstein, for example, does not think that the scientifically distinctive features of epigenetics warrant an ethical exceptionalist approach, stating that 'there is nothing inherently unique about the science of epigenetics that it demands an entirely new ethical paradigm and legal regime' (Rothstein, 2013, p 734). Researchers interviewed by Martyn Pickersgill generally hold similar positions. They 'expressed various kinds of unease about the notion that epigenetic research held straightforward implications for healthcare and society' (Pickersgill, 2021, p 609). Moreover, the respondents 'did not generally conclude that there were immediate ethical ramifications distinct to epigenetics' (p 610).

Jonathan Huang and Nicholas King agree. They do not wish to 'shy away from the potential of epigenetic research' (Meloni and Testa, 2014, p 129). They believe it 'holds promise in identifying and clarifying the different ways in which environments, broadly construed, directly interact with human biology, both within and across generations' (Huang and King, 2018, p 77). However, they have a few concerns. First, they note that 'there is already copious evidence for the impact of social, economic and environmental factors on the health of current and future generations' (p 75). Additionally, they point out that 'epigenetic mechanisms do not in themselves necessarily produce disadvantage; they always work in concert with extant social and economic disadvantages. As such, the injustice of a particular epigenetic variation is always perfectly circumscribed by an existing mechanism of disadvantage, which includes both a prior recognition of a disadvantaged group and an undesirable outcome' (p 74). With regards to responsibility theories in particular, they believe that commentators should refrain from the impossible enterprise of ascribing responsibility and remedy based on epigenetic findings alone, because such findings 'never imply who should be held responsible for any particular causal mechanism' (p 73). They conclude that, in many instances, 'the role of epigenetics is to recapitulate existing claims rather than generate new ones' (p 78). Moreover, they warn against straightforwardly 'using epigenetics to bolster existing ethical claims' (p 73) because of the difficulties involved in characterizing epigenetic changes as harmful and in 'separating unjust epigenetic variations from the social or environmental processes that produced them' (p 73).

Other authors, such as Maria Hedlund, a contributor to this volume, lean more towards the idea that at least there should be a 'change in degree' (Hedlund, 2012) in the ethical response to new findings in epigenetics. She argues that certain ethical concepts or themes, such as collective responsibility, should be used more. Luca Chiapperino, also a contributor to this volume, holds that 'epigenetics poses no new ethical issue over and above those discussed in relation to genetics' (Chiapperino, 2018, p 49). However, he does believe that epigenetics may have important implications for pre-existing ethical issues, arguing that 'epigenetics encourages … "thickening" moral exercises of privacy, responsibility, justice and equity with a complex biosocial description of situations, of persons or actions, in order to afford their significantly balanced evaluation' (p 59). Findings in epigenetics urge us to 'adjust and refine, in a situated manner, the problem frames and categories that inform our ethical and political questions as well as judgements' (p 59).

Similarly, Charles Dupras and Vardit Ravitsky argue that 'the normative accounts of epigenetics do require a heightened degree of bioethical attention, especially considering its potential impact on the political theory of the family and its relation to social as well as intergenerational justice' (Dupras and Ravitsky, 2016, p 2). Rothstein and colleagues argue that

most ethical issues related to epigenetics are similar to those already raised by genetics. However, they hold that 'the role of environmental exposures in producing epigenetic effects adds new concerns' such as those about individual and societal responsibilities to prevent hazardous exposures and the multigenerational impact of such exposures (Rothstein et al, 2009, p 2).

Responsibility: a complex relationship

When considering fairness and justice issues in public health, the concept of responsibility has often proven to be an indispensable tool. Epigenetics scholarship is no exception. It seems safe to say that issues related to responsibility are the most-discussed ones in the context of the ethics of epigenetics. A growing body of literature exists on responsibility for actions, such as causing or avoiding epigenetic harm or health and damaging or protecting one's epigenome. The current volume builds on this literature. To do this, let us first investigate what is meant by the concept of 'responsibility'. 'Responsibility' has a wide variety of meanings that are often highly context-dependent. Philosophers of action, ethicists and legal scholars alike have developed competing but often overlapping taxonomies of kinds of responsibility. Here, we introduce the reader to a few general distinctions that will return in other chapters of this volume.

Questions regarding normative responsibility typically involve an analysis of three aspects: who (1) is responsible for what (2) concerning whom (3)? Additionally, we may ask based on which normative standard (4) we wish to hold an agent responsible (Neuhäuser 2014).

Who

The subject of responsibility may be an individual agent, a group of individuals, or a collective agent. The idea that it makes sense to ascribe responsibility to individuals goes relatively unchallenged (a notable exception being Waller, 2011). Although debates about the requirements for and limitations to individual responsibility ascriptions are central to the philosophy of action, the individual agent is often seen as the 'basic bearer of responsibility' (Narveson, 2002). Also not very controversial is the idea of shared responsibility, which is a distributable responsibility that falls on multiple individual agents without them necessarily having any connection or means of communication between them. With collective responsibility, however, matters are more complex. According to proponents of collective responsibility, the collectivity of the subject lies in some qualities of the actions and capacities of the agent that make it appropriate to ascribe responsibility to this collective agent rather than to the individual agents that constitute it. This claim is contested. Methodological individualists do not believe that

genuinely collective agents exist. Normative individualists argue that, even if they do, it would be wrong to ascribe responsibilities to them rather than their individual members (Smiley, 2022). Most of the contributions in this volume, however, consider that collective responsibility is a philosophically sound and ethically fruitful concept in the context of epigenetics.

What

Agents may be held responsible for a variety of situations, outcomes, tasks or actions. These are the objects of responsibility. As many authors in this volume point out, responsibility claims are either forward- or backward-looking. Backward-looking approaches, often focusing on whether an agent deserves praise or blame for a specific state of affairs, are the most common in philosophical work on responsibility. Conversely, what is specific about the lesser-discussed forward-looking responsibilities is that they are 'ascribed for the purpose of ensuring the success of a particular moral project rather than for the purpose of gauging the moral agency of a particular group' (Smiley, 2014, p 6). A particularly salient aspect of epigenetics in this regard seems to be the potential reversibility of epigenetic changes (Falahi et al, 2014). Does such reversibility relieve people or collectives of part of their forward-looking responsibility? Do we invest in restorative strategies rather than preventive strategies, or do we invest in both? Most authors in this volume consider both kinds of responsibility relevant to epigenetic responsibility debates. Chapter 2 draws upon work by Linda Radzik (2014) to introduce an additional distinction between the orientation and justification of responsibility ascriptions.

Whom

Generally, when agents have specific responsibilities, these responsibilities are focused on another agent or group of agents. For example, a corporation may be responsible for limiting its environmental impact because the inhabitants of the neighbourhood close to the factory grounds have suffered from its activities. In the context of epigenetics, scholars often urge us all to consider the epigenetic responsibilities we may have towards our offspring and future generations in general (Chiapperino, 2018). Environmental influences on gene expression may affect future children during pregnancy and before people even consider having children. Does knowledge of epigenetic heritability increase individual responsibility, or is there a heightened collective responsibility to ensure a healthy environment for procreation over a lifetime? The potential heritability over generations of epigenetic changes complicates the issue further. Should people change their behaviour if their activities may affect the health of their grandchildren or great-grandchildren?

Should this fact be part of policy decisions? Does it even make sense to say that people who do not yet exist, or who might never come into existence, are the indirect object of a responsibility relationship? Various philosophers have pointed out that, when the people who are impacted by our choices do not yet exist, this may seriously complicate our moral reasoning about those choices. It perhaps comes as no surprise that Derek Parfit's famous 'non-identity problem', which arises from the tension between those complications and our intuitions (Parfit, 1984), has been the focus of various authors working on the ethics of epigenetics (for example Räsänen and Smajdor, 2022; Chapter 4 of this volume).

Basis

Responsibility may have a variety of normative standards, such as moral, causal, legal or political ones. Although it is sometimes very hard to draw the line between those kinds of responsibility in practice, this volume engages primarily with debates about moral responsibility in the context of epigenetics.

Epigenetic responsibility

Whether we conceive of human biology as something static and separate from environmental influence or as dynamic, in constant interaction with, influencing and influenced by the environment, has implications for our understanding of responsibility. For example, concepts of human nature play a role in the debate on what to do about environmental change and who should do it. It has been suggested that humans could be genetically engineered to mitigate or adapt to harmful environmental changes and reduce carbon emissions (Liao et al, 2012). Thus, changing ourselves could be a response to the problems we face concerning the environment. Such suggestions look to genetics to solve global problems in ways that may seem unjustifiably optimistic. At the same time, appeals to human nature are sometimes used as arguments against the acceptability of specific technologies. For example, Fukuyama has argued that human nature, as 'the sum of the behaviour and characteristics that are typical of the human species, arising from genetic rather than environmental factors', is a guiding principle and that any genetic technologies would unacceptably change human nature (Fukuyama, 2003, p 130) – as such, using or subsidizing these technologies is regarded as irresponsible. Interestingly, it appears that both those who argue in favour of modifying humans to adapt to the environment or to increase their health and those who are against modification of human nature take one aspect of human nature for granted: that it is genetically determined.

However, geneticists and biologists have always been aware that the unidirectional central dogma of genetics cannot explain certain phenomena. Philosophers of biology have reflected extensively on how plasticity, the ability of organisms to adapt flexibly to environmental change, affects the nature–nurture distinction (West-Eberhard, 1989; Bateson and Gluckman, 2011; Nicoglou, 2011; Baedke, 2019). Findings in epigenetics, as well as other observations in biology, appear to challenge the idea that human norms can be understood apart from an individual's environmental context (Oyama, 2000; Keller, 2010). For example, Griffiths has suggested that human nature results from the whole organism–environment system that supports human development. As such, he challenges the assumption that human nature is something 'from within' (as in a genetic blueprint) or that human nature is universal (Griffiths, 2011). Moreover, as Hens points out in Chapter 1, the concept of nature as distinct from culture or as static may, in itself, be one that is prevalent only in a specific geographically and temporally defined area.

How does a more dynamic view of human nature influence conceptions of moral responsibility? This is the overarching question that concerns the editors and contributors of this volume. By looking at the recent developments in biology that reflect this 'dynamic turn', namely epigenetics and microbiome research, we aim to enrich normative debates on responsibility for health. There has been a particularly lively debate with regard to which kind of responsibility concepts to use when discussing the ethically salient characteristics of epigenetics. This volume builds on such debates and offers new contributions to them.

Overview of the chapters

In Chapter 1, Kristien Hens reflects on the different meanings of epigenetics. She argues that a developmental view of life, as championed by Waddington and others (Waddington, 2012; Jablonka and Lamb, 2014), can help shed light on the role that bioethicists can play in research projects. She draws on the example of autism research to illustrate how bioethicists can work with scientists to challenge reductionist views of life that consider human beings and their challenges as merely the result of either genetic or environmental factors. In such a context, acknowledging the importance of integrating experiences of stakeholders in the research is extremely important.

In Chapter 2, Emma Moormann discusses the concept of 'forward-looking collective responsibility' in ethical debates involving epigenetics. After reviewing previous uses of the concept in an epigenetics context, she goes on to formulate suggestions for the integration of forward-looking collective responsibility in a framework of responsibility for epigenetic justice. Starting from an intersectional feminist, egalitarian perspective, she uses the case of a Mexico City neighbourhood to show how those concerned about

epigenetic responsibility can resist calls for 'epigenetic eliminativism', the idea that we should not and perhaps cannot make responsibility claims in light of epigenetic findings.

Luca Chiapperino and Martin Sand also delve into the issue of collective epigenetic responsibilities in Chapter 3. They build on previous work on (moral) luck that questions the causality condition of epigenetic responsibility claims for both individuals and collective agents. They argue that collective agents are subject to the complexities and uncertainties of epigenetic mechanisms that limit their epigenetic knowledge as well as their capacity to act on it. However, they consider it important to identify normative reasons to let collective agents play a role in an effective societal scenario of epigenetic knowledge. Thus, they argue that residual epigenetic responsibilities may be ascribed to collective agents on alternative grounds. Drawing on notions of 'aretaic blame', the authors propose a model for collective commitments to the protection of our epigenomes that is based on evaluation of the worth of these collective agents.

In Chapter 4, Anna Smajdor explores the question of whether epigenetic alterations to sperm, eggs or embryos may be viewed as harmful to resulting offspring. In particular, she addresses the 'non-identity problem', which has been instrumental in shaping the debate in reproductive ethics. She notes that the concept of genetic identity is deeply problematic. Focusing on epigenetics may resolve some of these problems, but in turn raises others.

In Chapter 5, Daniela Cutas analyses the implications of findings in epigenetics for determination of responsibility for children, particularly for parental responsibility. She reviews various accounts of responsibility for children, and shows how these have been based on widely shared assumptions about children being, ultimately, 'made' by their biological (genetic) parents. By blurring the boundary between social and biological contributions to children's lives, epigenetics extends the reach of responsibility for children, and thereby calls into question the proportion of responsibility that should fall on the shoulders of the 'biological' parents. As many of the forces that shape children's lives are systemic rather than individual, remedial action must also be systemic.

In Chapter 6, Maria Hedlund broadens the discussion about epigenetic responsibility to investigate the ways in which developments in artificial intelligence (AI) further complicate questions of epigenetic responsibility. She elucidates some of the complexities in the responsibility equation that arise when AI technology in general, and machine learning in particular, are employed to analyse epigenetic data. She concludes with a call for interdisciplinary collaboration and the need to focus attention on the ethical dimensions of precision medicine.

Chapter 7, by Kristien Hens and Eman Ahmed, goes beyond epigenetics to discuss the microbiome. As with epigenetics, recent findings

regarding the microbiome–gut–brain axis challenge atomistic and static conceptions of organisms. The authors investigate how the questions raised by epigenetics are also relevant for ethical questions surrounding the microbiome. They describe the idea of the 'holobiont', and how it matters for responsibility. This raises questions about privacy: what kind of private information can we get from stool samples? Is this different from genetic information? How does the link between the microbiome and mental health affect our self-understanding? They end by suggesting that, even more than epigenetics, microbiome research posits human beings and other organisms as firmly entangled with, and partially defined by, the environment.

Notes

[1] Although we follow many authors who explain the term in this way, we acknowledge that it cannot serve as a proper aetiology of the term. Stotz and Griffiths note that Waddington introduced the term as a fusion of 'epigenesis' and 'genetics', rather than as 'genetics' with the prefix 'epi' (Stotz and Griffiths, 2016).

[2] See: https://www.gcph.co.uk/publications/421_psychological_social_and_biological_determinants_of_ill_health_psobid

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