Bioethics
A Coursebook

Compost Collective

https://www.openbookpublishers.com

Digital material and resources associated with this volume are available at https://doi.org/10.11647/OBP.0449#resources

Information about any revised edition of this work will be provided at https://doi.org/10.11647/OBP.0449

ISBN Paperback: 978-1-80511-510-6
ISBN Hardback: 978-1-80511-511-3
ISBN PDF: 978-1-80511-512-0
ISBN HTML: 978-1-80511-514-4
ISBN EPUB: 978-1-80511-513-7

DOI: 10.11647/OBP.0449

Cover image by Bartaku Vandeput.
Cover design by Jeevanjot Kaur Nagpal

6. Epigenetics

Introductory remarks

Why would we include an introduction to the ethics of epigenetics in an introductory bioethics textbook? Is epigenetics not a highly technical specialization of biology, hardly accessible to undergraduate students coming to bioethics from other disciplines? We hope to explain the basics of epigenetics in a simplified, understandable fashion in this chapter, because an ethical discussion of epigenetics may be illuminating for bioethics students in at least two ways:

- Epigenetics is an interesting case study to discuss the social and ethical implications of scientific progress in a domain that shows an intricate connection between our body and our environment, or our biology and our biography.
- It allows us to demonstrate that scientific research projects are never value-neutral: in the case of epigenetics, findings can be employed to bolster a wide variety of claims with regards to individual or societal responsibilities, and the priorities of the research also reveal what societies value and want to prevent.

Introduction to epigenetics

The modern term *epigenetics* has multiple related meanings. Firstly, it denotes heritable—via mitosis and/or meiosis—changes in gene function without changes in DNA sequence. Secondly, epigenetics refers to the study of those processes and mechanisms and their implications for biological functioning. To avoid misunderstandings, this introduction sometimes uses terms such as 'epigenetic mechanisms' when referring to the first sense of the word and phrases such as 'epigenetic research' and 'epigenetic knowledge' in the context of the second sense. This introduction will provide some scientific background on aspects of epigenetics that are relevant to ethical discussions.

Epigeneticists do not study changes in DNA itself but rather mechanisms that influence how and when genes—which are stretches of DNA bases—are expressed in an organism. Epigenetic mechanisms can affect the transcription and translation

 https://doi.org/10.11647/OBP.0449.06

of genes in various ways. Two important processes are histone modification and DNA methylation.

- *Histone modification*: The histone is a kind of spool made of proteins around which the genomic DNA is wrapped to save space. The complex of the DNA and the histone proteins is called chromatin. How tightly the DNA is wrapped around the histone influences how easily the DNA can be accessed and thus copied. The more tightly packed it is, the less gene expression is possible. Tightly-packed and thus less accessible parts of the chromatin are called heterochromatin. The more readable parts are called the euchromatin—genes can only be expressed when they are located here.
- *DNA methylation*: This epigenetic mechanism involves the addition of a methyl group to a DNA molecule. This does not change the DNA itself, but it does influence whether certain parts of it can be read and transcribed. We can think of DNA methylation as a process to 'silence' genes by making them inaccessible.

By regulating gene expression, epigenetic processes influence cell types and tissues phenotypes (observable characteristics), function, and developmental state. Firstly, epigenetic programming is responsible for the differentiation of stem cells into specialized cells, providing them with the 'memory' of their differentiated identity. This explains how all cells in an organism contain the same DNA while still performing a wide variety of functions. Each of the ~400 tissues of the human body, for example, has a different epigenome (i.e. a different set of epigenetic modifications), whereas all the cells share a single genome, usually.

In addition to its function in cell differentiation, epigenetics also has other functions throughout the lifetime of an organism. One way in which our epigenome changes is the 'epigenetic drift' associated with aging. In general, more epigenetic changes indicates older age, meaning that epigenetic marks can be seen as biomarkers of aging. However, our epigenome changes mostly in response to environmental stimuli, which are most relevant for ethical perspectives on epigenetics. Mechanisms such as DNA methylation can be triggered by environmental factors, both stemming from within the body and from the outside environment. Crudely put, this means that the material and psychosocial circumstances of our body—our diets, the quality of the air we breathe, and the stress we experience—can impact epigenetic mechanisms. This is why epigenetic mechanisms are often treated as missing links between our lifestyle/environment and our physical/mental health.

Metaphor: Playing the piano

Perhaps a metaphor integrating some of the process outlined above will be helpful at this point. Epigenetics can be understood by thinking of a musician such as a piano player (Raz, Pontarotti, and Weitzman 2019). The piano player interprets or decodes the musical score when they want to play a composition. The score is analogous to the encoded message of the DNA: multiple musicians might follow the same score, just like multiple nuclei contain the same DNA. How the piece is performed, however, depends on the interpretation of the piano player—and how the DNA is expressed depends on the epigenetic mechanisms at work. Even if they follow the same musical score, two pianists may perform the piece in completely different ways. They may choose to add notations to the sheet music indicating the speed and dynamics they want to use in specific sections (as violinists might add 'bow notations'), or the emphasis they want to put on some notes. Such annotations are usually made with a pencil so that the pianist can still erase or re-write them. Epigenetic methylation patterns on the DNA are also dynamic to a certain extent, which means that they can change over time. The interpretation of each musician, in turn, depends on environmental factors and is thus subject to change. A pianist may alter their playing style of the same piece depending on whether they play it for their family at home or in a big concert hall. Similarly, epigenetic signals can be triggered by environmental factors.

Epigenetic information can be regarded as another layer beyond genomic information, enriching but also challenging more traditional understandings of genetics. For example, it challenges the 'central dogma' of molecular biology which assumes that genetic information flows only in one direction, when DNA is transcribed into RNA which is in turn translated into proteins that determine the phenotype. Epigenetics shows that the interface between genes and their environment is much more complex.

Epigenetic inheritance

Can the epigenetic marks that someone accumulates due to environmental exposure and lifestyle be transmitted to subsequent generations? This question has been intensely discussed and has led to much speculation and ethical theorizing in 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 between generations, we need 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 parental germline (sex cells) to environmental stressors. This means that intergenerational inheritance is limited to the first generation of male offspring (i.e. children) and the first and second generations of female offspring. Transmission to the first generation of offspring means that epigenetic marks are passed on from one generation to the next (i.e. from parent to child). The second generation of female offspring is also included under intergenerational inheritance because oocytes (egg cells) are already present in a female foetus in the womb. This means that environmental triggers during pregnancy can directly affect not only a first, but also a second generation of offspring.

A famous example of intergenerational epigenetic inheritance occurred during the Dutch Hunger Winter famine of 1944–1945 (Heijmans et al., 2008). The children of mothers who experienced this famine during their pregnancy were found six decades later to have reduced DNA methylation of the imprinted IFG2 gene, which is associated with the risk of metabolic diseases. These and other findings lend empirical support to the hypothesis that early-life environmental conditions can cause epigenetic changes in humans that persist throughout their lives. Public discourse and research often focuses on maternal factors. However, epigenetics shows that paternal factors and postnatal exposures in later life can play a role in offspring health, in addition to influences *in utero*. We will come back to this in the final section of this chapter.

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. As was explained earlier, direct epigenetic inheritance (i.e. intergenerational inheritance) pertains to the passing on of epigenetic information to the first generation of male and female offspring and the second generation of female offspring (since her sex cells were already exposed to external influences in the womb of her grandmother). This means that we can only speak of transgenerational inheritance if the epigenetic effects of the first generation's environmental exposures are still present in the second generation of male offspring or the third generation (i.e. great-grandchildren) of female offspring. So far, most transgenerational epigenetic effects have been discovered in plants and other-than-human animals such as rats and mice. For example, researchers working with mice have found third-generation epigenetic effects of maternal diet as well as social stress levels, although others argue that multigenerational inheritance of methylation patterns in mice is an exception rather than the rule (Dunn and Bale, 2011; Kazachenka et al., 2018). A study of *C. elegans* worms by Adam Klosin and colleagues also had impressive results (Klosin et al., 2017). They genetically modified these worms to glow when exposed to a warm environment. The worms not only started to glow more when the temperature was raised, but they also retained their intense glow when researchers lowered the temperature again. Moreover, even seven generations further down the line, glowing offspring were born. If five generations of *C. elegans* worms were kept warm, this characteristic was passed on to fourteen generations.

Unfortunately, in research on human inheritance, it is virtually impossible to exclude potential confounding elements such as changes in utero and postnatal effects. It is hard to distinguish 'real' epigenetic inheritance from cultural inheritance or reconstruction of the environmental context resulting in the same experiences or health problems in offspring. Still, some studies indicate that transgenerational epigenetic inheritance is possible, albeit limited, in humans. Studying historical data of cohorts in Överkalix, researchers found correlations between grandpaternal food supply and the mortality rate of the following two generations, their children and grandchildren (Kaati et al., 2017). Because no molecular data were available, no epigenetic links could be proven. Pembrey and colleagues build on these findings to evidence sex-specific male transgenerational inheritance in humans (Pembrey et al., 2006). In a longitudinal study of men in an area around Bristol, they found transgenerational effects of smoking before puberty on the growth of future male offspring. Specifically, early paternal smoking (before puberty) was associated with a greater body mass index (BMI) in their sons. The researchers posit DNA methylation as a potential mechanism behind those links between the acquired epigenetic traits of a generation and the epigenetic marks present in the next generations.

Diseases, conditions, and cures

The following list is a selection of epigenetic research on various human diseases and conditions. It is not exhaustive, but it is intended to give you an idea of the broad scope of epigenetics research.

- Exposure to *stress* in the womb or during early childhood has been associated with epigenetically mediated adverse health effects. For example, childhood maltreatment might trigger long-lasting epigenetic marks, contributing to PTSD in adult life. Researchers have found that children of survivors of the 9/11 attack in the USA who were pregnant at the time seem more vulnerable to PTSD and behavioural issues (e.g. Jablonka, 2016). Others argue that epigenetic processes might link the antenatal mood of the mother (e.g. maternal depression) to how infants will respond to new situations (Oberlander et al., 2008).
- As is well known, *air pollution* has numerous harmful effects on health. Emerging data indicate that exposure to air pollution modulates epigenetic marks (Rider and Carlsten 2019). These changes might in turn influence inflammation risk and exacerbate the risk of developing lung diseases.
- It is well known that *lead* is a common neurotoxic pollutant that disproportionally affects the health of children. Evidence of the epigenetic basis of the effects of lead is increasing (Wang et al., 2020; Senut et al. 2012)
- The epigenetic mechanisms behind the development *of metabolic conditions* such as type 2 diabetes, diabetic kidney disease (DKD), and obesity are increasingly well-documented. Like stress, obesity has been posited not merely as a health outcome but also as a causal factor in epigenetics. Paternal prepubescent obesity has been associated with diminished lung function and asthma in adult offspring (Lønnebotn et al., 2022).

- *Neuroepigeneticists* investigate how epigenetic regulation plays a crucial role in the development and functioning of our brain. Conditions for which epigenetic regulatory mechanisms have been suggested include Parkinson's, Huntington's, schizophrenia, epilepsy, Rett syndrome, and depression. Much research seems to be particularly geared towards a better etiological understanding of neurodevelopmental conditions such as Tourette's syndrome, ADHD, and autism. However, there is still much uncertainty about the concrete causative evidence that might be implicated in the development of such conditions.

Epigenetic changes seem to be more readily reversible than genetic ones. This reversibility holds promising potential for epigenetic therapies for diseases, since epigenetic marks such as methylation patterns can be seen as targets for medical interventions and treatments.

Many clinical research efforts in this domain are directed toward the treatment of *cancers*. Cancer cells are often characterized by epigenetic drifts, and many tumours are associated with epigenetic reprogramming. While some studies investigate the possibility of epigenetic interventions in general, others focus on specific types of cancer such as breast cancer and prostate cancer. There are many 'epidrugs' for cancers in clinical trials, but research on epidrugs for other conditions is also very prolific. Recent projects have aimed to target conditions such as Covid-19, hypercholesterolemia, neurodegenerative diseases, autoimmune diseases such as chronic kidney disease, and depression.

Ethics of epigenetics

Now that we have a basic understanding of epigenetics, we can start thinking about ethical issues concerning the research field and its findings. There are several aspects to epigenetic findings that we can take into account when thinking about the ethics of epigenetics:

1. *Influence of environment:* As we saw earlier, you can think of epigenetic mechanisms as a kind of missing link between a person's lifestyle and environmental influences on the one hand and that person's physical and mental health on the other. In other words, epigenetics makes us think about the link between our biology and our biography.
2. *Heritability:* Some epigenetic markers or changes that occur under the influence of environmental factors over a lifetime seem to be passed on to subsequent generations (e.g. the earlier example of the Dutch Hunger Winter). Another important insight is that epigenetic changes in prospective parents can affect offspring even if they occur before conception. This means that the behaviour and lifestyle of people who may not even be thinking

about having children at all yet can have an impact on the health of those future children.

3. *Reversibility:* Epigenetic changes are relatively dynamic. As we saw, this ensures that a lot of promising progress is being made in the field of epigenetic treatments for all kinds of diseases and disorders. But does this also have ethical implications? For example, if you can reverse the development of some conditions, do you have the responsibility to do so? Is it less bad to contribute to someone's ill health (e.g. by polluting a neighbourhood) if the effects may be reversible to some extent? And what about the distribution of cures or medicine—how can epigenetic treatments be distributed fairly?
4. *Uncertainty:* Finally, the actions of epigenetic mechanisms are quite unpredictable. We know that certain factors can affect those mechanisms, but we are far from knowing everything about all of them, and the question is whether that will ever be possible. After all, all kinds of environmental factors also interact. At best, it seems possible to make predictions that are accurate to some extent and to talk about 'increased odds' or a certain predisposition. Does this uncertainty make a difference in our ethical reflection, when compared to the judgements we would make if we were certain of all the mechanisms and effects involved? Can we hold people responsible for actions that may or may not have a certain effect?

Ethical issues in the literature

What, then, are some normative issues that require a closer look in light of epigenetic findings? In their literature review, Dupras, Saulnier, and Joly (2019) identify nine areas of discussion at the crossroads of epigenetics, law, and society: traditional nature-nurture dichotomy; embodiment or 'biologization' of the social; public health and other preventive strategies; reproduction, parenting and the family; political theory; legal proceedings; the risk of stigmatization, discrimination or eugenics; privacy protection; and knowledge translation. Other widely discussed issues include environmental justice, the need for bioethical approaches that integrate concern for both the environment and medicine, and ethical, legal and social issues of epigenetics research in the context of personalized medicine.

Privacy

Ensuring that the privacy of patients and research participants is respected should always be a priority for researchers. But insights from epigenetics make the safe collection and storage of health data even more urgent. For example, by gathering information about epigenetic markers (such as the DNA methylation we encountered before) it becomes very easy to identify people based on anonymous donor material.

Moreover, perhaps some agents might be interested in using these data for non-medical purposes. Information about lifestyle behaviours, whether you smoke or drink for example, might be interesting to insurance companies or employers. This is why researchers have already been calling for strict regulations and laws that forbid genetic or epigenetic discrimination. These concerns are becoming increasingly relevant with the growing availability of commercial direct-to-consumer epigenetic tests.

Exposing inequality

Epigenetics seems to provide new possibilities to map existing injustices as well as the distribution of social and environmental factors that may have a long-term, detrimental effect on people's health. It is well known that not everyone is exposed equally to external harm. Just look at recent examples in Belgium such as the 3M PFAS scandal—where local residents were found to have elevated concentrations of the toxic chemical PFAS in their bodies—and the Umicore factory in Hoboken—where lead pollution has a big impact on small children (see Case 1 below). Many people also believe that such unequal exposure is, at least in some cases, problematic or unjust. Epigenetic markers could potentially indicate who exactly is hit the most by existing inequalities. And in cases for which we already have an indication—we do not need epigenetics to tell us that people living close to highways suffer more from air pollution—epigenetics might provide new information about the impact on individuals and future generations.

Responsibility

Most normative discussions on the ethics of epigenetics are conducted in terms of distributing responsibility. For example, we can ask ourselves 'who is morally responsible for the health of current and future generations in the context of epigenetics'?

When we ask *who* can or should be responsible, we can distinguish between *individual*, *shared*, and *collective responsibility*. The idea of collective responsibility is that a group has certain characteristics that make it a moral agent that can be held responsible. This idea is not uncontested. However, most authors believe that some organizations with a clear structure—such as corporations, governmental organizations, medical organizations, or NGOs—can be said to have some kind of responsibility in the context of epigenetics.

What dimensions of responsibility do we have in mind? We often think about moral responsibility in retrospective or *backward-looking* terms. We blame people for bad outcomes, or shower them with compliments because they did something with a good outcome. But it is also interesting to think about future-oriented or *forward-looking* responsibility: how we can attribute responsibility and take responsibility with an eye on what we want to achieve or avoid in the future? When we think about our responsibility for the health of future generations, responsibility can function as a way to distribute moral labour. If we know what state of affairs we want to achieve, we can start thinking about a desirable allocation of the tasks that should be performed in order to get there.

Gunnar Björnsson and Bengt Brülde (2017) created a list of factors which might help to identify moral agents and inform responsibility distribution. This could be useful for distributing responsibility for the epigenetic health of future generations. This is their list:

1. *Capacity and cost*: The individual or group that has most capacity to produce a good outcome is responsible for doing so.
2. *Retrospective and causal responsibility*: There is still some connection between what an agent did in the past and who needs to take up responsibility now, even though this is perhaps not as important as other considerations.
3. *Benefiting*: Benefiting from another's help or benefiting from harm, injustice, or danger to others can make an agent more responsible, to reciprocate for example.
4. *Promises, contracts, and agreements*: If an agent promises to deal with a problem, the agent takes on responsibility by doing so.
5. *Laws and norms*: Laws can prescribe our behaviour and can give direction to and limit our ascribed responsibility.
6. *Roles and special relationships*: We can have more responsibility towards people we have a close connection to.

Three cases

Below are three cases related to epigenetics. They all have the following features in common: (1) they link environmental influences to health outcomes, and (2) they invite us to ask ethical questions. You may use these cases to practice your ethical reflections, applying concepts, theories, and ideas.

Case 1: Hoboken

Hoboken—a district of the Belgian city of Antwerp—is home to a factory site of Umicore, one of the world's largest refiners of precious metal. The factory plant is surrounded by a residential area that was constructed over the twentieth century. Emissions of lead, cadmium, and arsenic by the factory have been contributing to widespread health problems in children from the surrounding area for decades (Pano, 2021). Despite efforts that have greatly reduced both the emissions and their impact, lead levels in the blood of children living in the neighbourhood continue to exceed the standards set by public health agencies. Epigenetic mechanisms may contribute to lead-induced health effects in children, such as behavioural issues and problems with developing gross motor skills (Senut et al., 2012; Wang et al., 2020).

Parents worry about the health of their children and often feel guilty about living in the vicinity of the polluting factory. In a documentary, Esther—a mother of two children with very high lead values in their blood—expresses her worries as follows: "I want my child to be able to be himself. If he is good at something, it should be possible to stay that way. And if he is not as good at something, that should not become worse. I do not want external factors I have no control over, such as the factory, to interfere [...] Stay away from my child, is what I think" (Pano, 2021, my translation). As the Flemish report agency Pano succinctly puts it, parents seem to be given a choice between "kuisen of verhuizen"—cleaning or moving.

Case 2: Mexico City

Since 1993, the ELEMENT (Early Life Exposure in Mexico to Environmental Toxicants) project has investigated the impact of environmental factors such as toxins and sugars on mother-child pairs in various neighbourhoods of Mexico City. Anthropologist Elizabeth Roberts collaborated with this project. First, her fellow researchers found that eating from traditional lead-glazed plates—which are said to make the food taste sweeter—was the surest predictor of high lead levels in mothers and children. The exposure to lead is both gendered—because it is women who prepare the food and inherit the plates from their (grand) mothers—and cultural, because the plates connect their users to a rural past.

Additionally, the high consumption of sweets and sugary soda is said to be an important factor in the high rates of obesity and diabetes in poorer neighbourhoods of Mexico City. Soda is almost as cheap as bottled water and is more reliably available than tap water. Inhabitants know that soda and sweets can lead to ill health, but "in Moctezuma sharing soda, liquid-food, filled with sugar, is love" (Roberts, 2015, p. 248). Because it performs important social roles, campaigns exhorting individuals (primarily mothers) to stop providing soda to their children have little effect.

Finally, there is a penetrating smell caused by "a narrow stream of dam runoff, filled with *aguas negras* (untreated sewage) and garbage" (Roberts, 2015, p. 592) in these neighbourhoods. In rainy seasons the dam often overflows, leaving the walls of the cement houses with salmonella, *E. coli*, and faecal enterococcus.

The effects of these various exposures on inhabitants of this neighbourhood are not only direct, but can also be inherited through epigenetic mechanisms.

Case 3: Farah and Alex

Farah is a postdoc researcher at a prestigious university. She loves her job and considers being an academic an important part of her identity. At the same time, various elements of her job are causing her quite some stress. When Farah gets pregnant, she makes a conscious decision to continue working her stressful job, even though she is aware of the potential influence of the accumulated stress on her offspring. Ten years later, her child Alex receives a diagnosis of ADHD after experiencing some difficulties in home and school settings. Although he sometimes continues to struggle with aspects of his ADHD, throughout his teenage years Alex starts to consider ADHD an integral part of his identity that he would not want to change.

Suppose Alex learns about studies that imply a link between stress during pregnancy and ADHD in offspring through epigenetic mechanisms (e.g. Bock et al., 2017). Maybe when Alex is in college, he talks with his mother to learn more about the decisions she made before and during her pregnancy. He may want to learn more about the decisions she made, and the circumstances that perhaps constrained them. What might his reaction be when he finds out more about her reasons for continuing her stressful work? Should he blame her, or could understanding her situation instead help to strengthen their bond?

In all three cases, epigenetics might be a part of the puzzle of biologically explaining the link between environment and health (although epigenetic links are not the *only* causal connection at play in any of these cases). A second feature these cases have in common is that they may invite us to ask ethical questions. What, if anything, should be done about the situations in Hoboken and Mexico City? Who, if anyone, is to blame for negative health outcomes in inhabitants of those places? What duties do (future) parents such as Esther or Farah have towards their offspring concerning their health? What does it mean, or what should it mean, to say that we want children to be healthy? How does that relate to wanting to protect them from the harmful effects of pollution? What is the role of scientists, policymakers, and public health institutions? Do social injustices exacerbate health disparities, and if so, what does that imply for our moral evaluation? All of these questions are, in one way or another, related to an overarching question of responsibility: who is responsible for what with regard to whom?

One finding, many ethical and political claims

For each of the ethical aspects of epigenetic research mentioned above, it is possible to formulate many different viewpoints and moral claims.

Take ‘reproduction, parenting, and the family’ as an example. We know that epigenetics deepens and extends our knowledge about the impact of parental behaviour as well as environmental factors on the development of foetuses and young children alike. However, there are a myriad of ways in which this knowledge might be translated into moral or political claims. Especially in popular science communication, perinatal influences are often cited to inflate the individual responsibility of parents (and mothers in particular). However, as philosopher Daniela Cutas points out, epigenetic knowledge might also help us to see that the category of biological parenthood may need to be broadened. It seems safe to assume that everyone who is closely involved in raising a child influences their environment and experiences and also modulates their molecular biology in doing so. She suggests that those people may not have parental or procreative responsibilities, but based on their epigenetic contributions they might have a biological 'responsibility for shaping'. Seen from that perspective, epigenetic knowledge production "brings closer together or altogether blurs the margins between parental, non-parental, primary, secondary, individual and collective responsibilities for children" (Cutas, 2024, p. 107). The final section of this chapter will delve deeper into this theme.

Consider responsibility for environmental pollution as another example. As was explained in the introduction to epigenetics, epigeneticists can point out with increasing accuracy which environmental stimuli trigger epigenetic mechanisms that contribute to adverse health outcomes. But how can we translate this into moral claims or political action? This is a contentious matter. Who bears responsibility for certain kinds of pollution, or for the impact on public health? How do we distribute responsibility among many actors in a complex network of interactions? Big factories may be clear culprits in some cases, but governmental organizations allowing them to operate in harmful ways may also have responsibilities here. What about the health of animals and whole ecosystems? And how do we qualify 'adverse health effects' or 'epigenetic harm'? In the case of Farah and Alex, for example, it becomes clear that Alex does not think of his ADHD as something harmful, but rather as a valuable part of his identity. Although neurodiversity theory is currently spreading awareness about the problems with a deficit approach to conditions such as ADHD and autism, much epigenetic research unfortunately still defines those conditions only in terms of deficits.

We may want to ascribe responsibilities to involved individuals and collectives on a variety of grounds and moral principles. As we already saw more generally in earlier chapters, no moral theory can provide a clear-cut answer that points in just one direction here. In short, epigenetic research never holds straightforward implications for healthcare and society. One reason for this is that epigenetic mechanisms in and of themselves are often not sufficient for a disadvantageous outcome. Instead, they always interact with largely pre-existing social, economic, and environmental factors and (dis) advantages. Epigenetic findings alone cannot tell us when a situation is unjust, nor do they provide specific ways to combat situations we do characterize as unjust.

In addition, we need to keep in mind that knowledge production in science is never a morally or politically neutral process either, and epigenetics is no exception. Scientists, research institutions, and funding agencies all have their own moral, political, and scientific values that impact their research, and choices made in the process of knowledge creation are always context-dependent. This is not unique to epigenetics; but as a science that has quickly gained a lot of broader public attention, it does make a very good example. This is also not a problem that needs to be avoided or mitigated. Rather, it is important that everyone involved is explicit about their values and considers how those influence their work.

Epigenetic knowledge itself thus cannot simply be regarded as either a burden or a blessing, but at best as a "double-edged sword" (Meloni, 2016). Epigenetic knowledge can be applied to morality and politics in a variety of ways depending on the values, commitments, priorities, and biases of the person applying it. Thus, it is important that researchers explicitly state which values underlie their research claims wherever possible. One way to start thinking about this may be to distinguish between (1) the normative lens, (2) moral theories, and (3) considerations of various practical and normative aspects that might play a role. A *normative lens* is an overarching perspective or paradigm that characterizes the commitments of a researcher, such as a commitment to egalitarianism, or an intersectional feminist approach. *Moral theories*, such as those discussed in earlier chapters, can also guide one's judgement in certain directions, although they usually leave it open to various conclusions. Which *practical and normative aspects* of a situation you find relevant for the ethical judgement of a particular case depends on your normative lens(es) and the ethical theory you are working with. Your moral and political views may also influence the relative weight or importance you attach to each aspect.

Parental responsibility in epigenetics

The final section of this chapter zooms in on a specific ethical debate in the context of epigenetics: the responsibility of (prospective) parents for the health of their offspring. As we saw earlier, findings in intergenerational epigenetics give rise to a 'temporal expansion' of normative discussions about parental responsibility. This section is intended to show how ethicists working on epigenetics can take very different approaches based on the same research findings and societal context of their research. Broadly, we can distinguish between *cautionary* and *emancipatory* approaches.

Cautionary approaches

The lifestyles, behaviours, circumstances, and exposures of people who are planning to have a child, or are already pregnant, are indeed subject to intense normative scrutiny in both scientific and popular discourse, but is this fair or just?

Most of the literature on the potential ethical and social implications of epigenetic discoveries for procreation and parenthood takes a cautionary approach (Dupras, Saulnier, and Joly, 2019). Articles can generally be categorized as criticizing one or both of two tendencies they observe in the scientific and popular discourse on epigenetics:

(1) increased responsibilization of individual (prospective) parents, which does not take the wider social context into account; and (2) disproportionate focus on maternal (as opposed to paternal) behaviour before and during pregnancy.

Individual and collective responsibilities

Most scholars and philosophers working on the ethics of epigenetics have seen it as their task to criticize, either explicitly or implicitly, a scientific and societal discourse that excessively attributes responsibility to individual people—particularly mothers—for epigenetic alterations in offspring. They point out that expecting individual (prospective) parents to prevent disease or suboptimal epigenetic transmission in their offspring by minimizing every possible risk factor seems to ignore the extent to which exposures, diets, and stressors are shaped by social, economic, and political forces. In this context, scholars often emphasize the importance of collective responsibility. As we saw before, Daniela Cutas argues that the environmental aspect of epigenetic mechanisms implies that all agents who causally contribute to a child's environment being a certain way might together bear some collective responsibility for the child's wellbeing.

Another concern is the personal and private nature of individual and familial decisions about childbearing and raising children. Although dealing with the inequities that shape the lives of individuals and their children requires societal change, it is far from clear to what extent the state should be allowed to interfere.

Finally, even if we attribute collective responsibility for the epigenetics of future generations rather than holding individual parents solely responsible, it is unclear what should be done about this. Excessive blaming of individuals is a potential downside of accounts which heighten individual responsibility. On the other hand, increased social pressure and state interference might be a downside of an approach that puts too much emphasis on collective responsibility. For example, the line between preventing harm and optimizing or enhancing an outcome is not at all easy to draw, especially in the context of parental responsibility. Epigenetic findings might be employed to intensify societal pressure on individual parents (and especially women) to have healthy children, thereby "maximizing human capital and productivity" (Wastell and White, 2017, p. 178). Some commentators even worry about the risk of 'epi-eugenics' through "increased social pressure on prospective parents to undergo preconception and prenatal testing for epigenetic alterations" (Juengst et al., 2014, p. 428).

Maternal and paternal influences and responsibilities

Pregnancies, and thus women's bodies and behaviours, seem to have become the main target of intervention suggested in epigenetic literature. While epigenetics expands the temporal window of potential influence, this overemphasis on maternal influence itself on the health of a foetus, baby, or child is nothing new.

There seems to be a growing consensus among commentators that the overemphasis on maternal influences in epigenetic risk messaging is unfair because it risks ascribing excessive blame to women. In an influential paper, Richardson and colleagues compellingly demonstrate that narratives about epigenetic findings risk perpetuating "a long history of society blaming mothers for the ill health of their children" (Richardson et al., 2014, p. 131). They give examples from the media such as panic around Fetal Alcohol Spectrum Disorder (FASD) and 'crack babies' in the USA, and the popularity of theories about 'refrigerator mothers' whose 'cold' parenting style supposedly caused autism in their children. They warn us that although the scientific findings underpinning these societal blaming practices are often rather moot or proven to be plain wrong, women still experience the blame to this day.

Thus, researchers should be aware of existing biases and moralizing tendencies in society when they share their findings, in order to minimize the risk that their findings inspire unfair blaming practices. However, the problem seems to be situated on a more fundamental level than the biased language in science communication. The disproportionate attention and resources science has been directing toward maternal influences, specifically in the perinatal period, should also be critically questioned. As we saw earlier in this chapter, ethical considerations also play a role in the construction of epigenetic knowledge itself.

The focus on maternal influences seems to be a continuation of the centuries-old "bewitching idea that the environment in which you are gestated leaves a permanent imprint on you and your future descendants" (Richardson, 2021, p. 1). However, epigenetics offers an opportunity to strike a new balance in parental responsibility between contributors, because it shows that other influences besides *in utero* influences also play a role in offspring health.

In recent years, epigenetics researchers seem to have heeded calls to research paternal influences as well—e.g. by creating a POHaD paradigm (paternal originals of health and disease) that researches the impact of paternal lifestyle and exposure and their impact on, for example, sperm quality (Mayes et al., 2022). However, venturing into this area requires some caution. These new findings could reduce the burden of responsibility currently placed on mothers, but researchers should also be careful not to reconstruct the stigmatizing and blaming tendencies of discourse about maternal influences in the discourse about paternal influences.

Emancipatory approaches

We can conclude that most existing work on the ethics of epigenetics points out the dangers of employing this knowledge in such a way that overburdens (prospective) parents or blames them unfairly or disproportionally. Although such warnings are important and necessary, there might also be more positive or emancipatory ways of thinking about new developments in epigenetics.

We will now look at the examples of empowerment, procreative autonomy, and benefits to the parent-child relationship.

Empowerment and procreative autonomy

A first possible way to think positively about epigenetic knowledge in an unequal society is to see it as a tool in striving toward the *empowerment* of individual citizens and communities. There is no consensus about the definition of empowerment. It is usually understood as the process of enhancing people's capacities to control the determinants of their own quality of life ('empowering people'), and/or as the state that results from this process ('empowered people').

The use of 'empowerment' in health care is a good example of how a concept can be used to serve various ethical or political goals. For example, Luca Chiapperino and Giuseppe Testa are critical of how the concept of empowerment is often used (Chiapperino and Testa, 2016). They observe that epigenetic knowledge is frequently employed as the basis for a neoliberal project of individualizing responsibility for health. Language of empowerment can be used to serve this project that seeks to transfer responsibility for health from the state to individual citizens and expects this move to make the healthcare system more economically sustainable or even profitable.

However, Chiapperino and Testa do not rule out the potential use of empowerment in emancipatory discourse. They refer to a more radical history of the concept, for example in the tradition of liberatory pedagogy. They argue that epigenetic knowledge can be empowering in that it shows people how social factors and environmental exposures can affect their health and that of their offspring. What an empowerment discourse should be mindful of, then, is that people also need to be sufficiently free from financial, social, and material constraints to act on this knowledge.

Such an emancipatory project could be served by a sufficiently refined concept of *procreative autonomy*. That is the right of people to decide whether, when, and under which circumstances to procreate. A related concept is parental autonomy, which involves the rights of people to parent their children as they see fit. How autonomous an agent is depends not only on their capacity for self-governance but also on the extent to which they are socially and politically free to make decisions that impact their own life. Epigenetics is relevant to both parental and procreative autonomy. Perhaps epigenetic knowledge can empower vulnerable (potential) parents-to-be to make informed decisions.

Note that although procreative autonomy can benefit a (future) child, this is not necessarily the case. When we emphasize the right of future parents to make choices about procreation and pregnancy, we need to acknowledge that those choices need not always be good for the foetus' or future child's health. With limited state intervention or nudging, the actions of parents may well lead to worse health outcomes for future children or go against their interests more broadly. However, some room for making bad choices may need to be allowed in order to protect people from far-reaching public involvement in the private sphere, which could be even more harmful.

Parent-child relationship

Take another look at the case of Farah and Alex earlier in this chapter. Might there be any value for the child or the parent-child relationship in having shared knowledge of the lives of parents before they conceived? Or before they were even thinking of conceiving, when their experiences may have impacted the child's biological make-up nonetheless? If we answer 'yes' to this question, we can consider whether epigenetic knowledge has a role to play here. Epigenetic knowledge can perhaps play a contextualizing role, affirming that aspects of the child's health or personality are not isolated from the actions, behaviours, or exposures of their parents in the past. Consider an example related to environmental pollution:

> *Jenn and her parents*: Two people who intend to have children together have both grown up in a poor neighbourhood close to a polluting factory. They are aware of this pollution and its potential health effects on themselves and their future offspring. Although this is far from easy, they manage to move to another part of their city with relatively clean air. There, they conceive, and their daughter Jenn is born. However, their epigenetic marks from having lived in the polluted neighbourhood may have been inherited by Jenn to some extent.

Would it be valuable for Jenn to know this? And if so, how might she react?

Jenn might be thankful that her parents decided to move away from a place that they were very attached to for her sake. She might gain a better sense of appreciation for their considerations (although it is not unthinkable that she might also feel guilty for being the reason they made such a drastic and costly change). Moreover, knowledge about epigenetic mechanisms might help Jenn understand why she is more prone than others to certain conditions such as asthma. Conversations about the ways in which social determinants of health—conditions in the social and physical environments of people that influence health outcomes throughout their life course—have affected both Jenn and her parents may lead them to a sense of mutual understanding.

In short, the power of epigenetic knowledge might lie in helping people to integrate their biography and their biology. Another way to put this is that parent-child conversations on such topics help the child to create their own narrative identity: it can help parents, children, and families to tell stories about why they are who they are.

Moreover, epigenetic research can help to value the contributions different individuals make towards the upbringing of children. Lesbian mothers who gestate a child conceived with their partner's oocyte and donor sperm (Bower-Brown et al., 2024) and surrogates (Pande, 2009) often use epigenetic research as biological proof of their meaningful contribution to a child's being. In queer families, epigenetic effects are used to argue that kinship can be based on other biological connections than mere genetics.

Kinship is then seen as connections between people who care for each other every day, whatever the genetic bond between them. In the same way, epigenetic findings allow for a broader understanding of 'mothering' as a practice by multiple people: parents and other caretakers, for example day care staff or grandparents. Thus, epigenetic research not only enables multiple people (or the community at large) to be perceived as responsible for a child's well-being, but also enlarges the web of connections between them. By involving groups of people in kinship in a meaningful way, epigenetic knowledge has the emancipatory potential to queer existing kinship schemes.

Conclusion

In this chapter, we showed various ways in which researchers and students can engage in ethical discussions of developments in epigenetics. After a brief introduction to the scientific background of epigenetics, we formulated several ethically relevant aspects to epigenetic findings that we can take into account when we are considering the moral impact of such findings: the influence of the environment, heritability, unpredictability, and reversibility. We outlined ethical issues which are being discussed recurrently in bioethical literature on epigenetics, and presented readers with a few cases that invited them to ask ethical questions and practice moral reflections, applying concepts and theories. Finally, we discussed two particular issues in more detail: (1) how the case study of epigenetics demonstrates that scientific research projects are never value-neutral, and (2) how research findings can be employed in multiple ethical discourses in the specific debate on the responsibility of (prospective) parents for the health of their offspring.

Bibliography

Björnsson, Gunnar, and Bengt Brülde. 2017. "Normative Responsibilities: Structure and Sources". In *Parental Responsibility in the Context of Neuroscience and Genetics*, edited by Kristien Hens, Daniela Cutas, and Dorothee Horstkötter, 69, pp. 13–33. Cham: Springer International Publishing. https://doi.org/10.1007/978-3-319-42834-5_2

Bock, Joerg, S. Breuer, Gerd Poeggel, and Katharina Braun. 2017. "Early Life Stress Induces Attention-Deficit Hyperactivity Disorder (ADHD)-like Behavioral and Brain Metabolic Dysfunctions: Functional Imaging of Methylphenidate Treatment in a Novel Rodent Model". *Brain Structure and Function* 222 (2): 765–80. https://doi.org/10.1007/s00429-016-1244-7

Bower-Brown, Susie, Kate Shaw, Anja McConnachie, Vasanti Jadva, Kamal Ahuja, and Susan Golombok. 2024. "Biogenetic kinship in families formed via reciprocal IVF: 'It was [my partner]'s egg... but my blood flowed through her'". *Sociology* 58 (3): 735–752. https://doi.org/10.1177/00380385231212398

Chiapperino, Luca, and Giuseppe Testa. 2016. "The Epigenomic Self in Personalized Medicine: Between Responsibility and Empowerment". *The Sociological Review* 64 (1): 203–20. https://doi.org/10.1111/2059-7932.12021

Cutas, Daniela. 2024. "Epigenetics, Parenthood and Responsibility for Children". In *Epigenetics and Responsibility*, edited by Emma Moormann, Anna Smajdor, and Daniela Cutas, pp. 98–109. Bristol: Bristol University Press. https://doi.org/10.56687/9781529225440-007

Dunn, Gregory A., and Tracy L. Bale. 2011. "Maternal High-Fat Diet Effects on Third-Generation Female Body Size via the Paternal Lineage". *Endocrinology* 152 (6): 2228–36. https://doi.org/10.1210/en.2010-1461

Dupras, Charles, Katie Michelle Saulnier, and Yann Joly. 2019. "Epigenetics, Ethics, Law and Society: A Multidisciplinary Review of Descriptive, Instrumental, Dialectical and Reflexive Analyses". *Social Studies of Science* 49 (5): 785–810. https://doi.org/10.1177/0306312719866007

Heijmans, Bastiaan T., Elmar W. Tobi, Aryeh D. Stein, Hein Putter, Gerard J. Blauw, Ezra S. Susser, P. Eline Slagboom, and L. H. Lumey. 2008. "Persistent Epigenetic Differences Associated with Prenatal Exposure to Famine in Humans". *Proceedings of the National Academy of Sciences of the United States of America* 105 (44): 17046–49. https://doi.org/10.1073/pnas.0806560105

Hens, Kristien, Christina Stadlbauer, and Bart H. M. Vandeput. 2022. *Chance Encounters: A Bioethics for a Damaged Planet*. Cambridge: Open Book Publishers. https://doi.org/10.11647/obp.0320

Jablonka, Eva. 2016. "Cultural Epigenetics". *The Sociological Review* 64 (1): 42–60. https://doi.org/10.1111/2059-7932.12012

Juengst, Eric T., Jennifer R. Fishman, Michelle L. McGowan, and Richard A. Settersten. 2014. "Serving Epigenetics before Its Time". *Trends in Genetics* 30 (10): 427–29. https://doi.org/10.1016/j.tig.2014.08.001

Kaati, G, Lo Bygren, and S Edvinsson. 2002. "Cardiovascular and Diabetes Mortality Determined by Nutrition during Parents' and Grandparents' Slow Growth Period". *European Journal of Human Genetics* 10 (11): 682–88. https://doi.org/10.1038/sj.ejhg.5200859

Kazachenka, Anastasiya, Tessa M Bertozzi, Marcela K Sjoberg-Herrera, Nic Walker, Joseph Gardner, Richard Gunning, Elena Pahita, Sarah Adams, David Adams, and Anne C Ferguson-Smith. 2018. "Identification, Characterization, and Heritability of Murine Metastable Epialleles: Implications for Non-Genetic Inheritance". *Cell* 175 (5): 1259–71. https://doi.org/10.1016/j.cell.2018.11.017

Klosin, Adam, Eduard Casas, Cristina Hidalgo-Carcedo, Tanya Vavouri, and Ben Lehner. 2017. "Transgenerational Transmission of Environmental Information in C. Elegans". *Science* 356 (6335): 320–23. https://doi.org/10.1126/science.aah6412

Lønnebotn, Marianne, Lucia Calciano, Ane Johannessen, Deborah L. Jarvis, Michael J. Abramson, Bryndís Benediktsdóttir, Lennart Bråbäck, Karl A. Franklin, Raúl Godoy, Mathias Holm, Christer Janson, Nils O. Jõgi, Jorunn Kirkeleit, Andrei Malinovschi, Antonio Pereira-Vega, Vivi Schlünssen, Shyamali C. Dharmage, Simone Accordini, Francisco Gómez Real, and Cecilie Svanes. 2022. "Parental Prepuberty Overweight and Offspring Lung Function". *Nutrients* 14 (7): 1506. https://doi.org/10.3390/nu14071506

Mayes, Christopher, Elsher Lawson-Boyd, and Maurizio Meloni. 2022. "Situating the Father: Strengthening Interdisciplinary Collaborations between Sociology, History and the Emerging POHaD Paradigm". *Nutrients* 14 (19): 3884. https://doi.org/10.3390/nu14193884

Meloni, Maurizio. 2016. *Political Biology*. London: Palgrave Macmillan. https://doi.org/10.1057/9781137377722

Oberlander, Tim F., Joanne Weinberg, Michael Papsdorf, Ruth Grunau, Shaila Misri, and Angela M. Devlin. 2008. “Prenatal Exposure to Maternal Depression, Neonatal Methylation of Human Glucocorticoid Receptor Gene (NR3C1) and Infant Cortisol Stress Responses”. *Epigenetics* 3 (2): 97–106. https://doi.org/10.4161/epi.3.2.6034.

Pande, A. 2009. “‘It may be her eggs but it’s my blood’: Surrogates and everyday forms of kinship in India”. *Qualitative Sociology* 32: 379–297. https://doi.org/10.1007/s11133-009-9138-0

Pembrey, Marcus E., Lars Olov Bygren, Gunnar Kaati, Sören Edvinsson, Kate Northstone, Michael Sjöström, Jean Golding, and ALSPAC Study Team. 2006. “Sex-Specific, Male-Line Transgenerational Responses in Humans”. *European Journal of Human Genetics* 14 (2): 159–66. https://doi.org/10.1038/sj.ejhg.5201538.

Raz, Aviad, Gaëlle Pontarotti, and Jonathan B. Weitzman. 2019. “Epigenetic Metaphors: An Interdisciplinary Translation of Encoding and Decoding”. *New Genetics and Society* 38 (3): 264–88. https://doi.org/10.1080/14636778.2019.1601009.

Richardson, Sarah S. 2021. *The Maternal Imprint: The Contested Science of Maternal-Fetal Effects*. Chicago: University of Chicago Press. https://doi.org/10.7208/chicago/9780226807072.

Richardson, Sarah S., Cynthia R. Daniels, Matthew W. Gillman, Janet Golden, Rebecca Kukla, Christopher Kuzawa, and Janet Rich-Edwards. 2014. “Society: Don’t Blame the Mothers”. *Nature* 512 (7513): 131–32. https://doi.org/10.1038/512131a

Rider, Christopher F, and Chris Carlsten. 2019. “Air Pollution and DNA Methylation: Effects of Exposure in Humans”. *Clinical Epigenetics* 11 (1): 1–15. https://doi.org/10.1186/s13148-019-0713-2

Roberts, Elizabeth F. S. 2015. “Food Is Love: And so, What Then?” *BioSocieties* 10 (2): 247–52. https://doi.org/10.1057/biosoc.2015.18

Senut, Marie-Claude, Pablo Cingolani, Arko Sen, Adele Kruger, Asra Shaik, Helmut Hirsch, Steven T Suhr, and Douglas Ruden. 2012. “Epigenetics of Early-Life Lead Exposure and Effects on Brain Development”. *Epigenomics* 4 (6): 665–74. https://doi.org/10.2217/epi.12.58

Wang, Tian, Jie Zhang, and Yi Xu. 2020. “Epigenetic Basis of Lead-Induced Neurological Disorders”. *International Journal of Environmental Research and Public Health* 17 (13): 4878. https://doi.org/10.3390/ijerph17134878

Wastell, David, and Susan White. 2017. *Blinded by Science: The Social Implications of Epigenetics and Neuroscience*. Bristol/Chicago: Policy Press. https://doi.org/10.56687/9781447322368