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Epigenetic science and Indigenous health: Key issues and considerations for future research

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Résumé de l'article

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Epigenetic Science and Indigenous health: Key Issues and Considerations for Future Research

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Epigenetic Science and Indigenous health: Key Issues and Considerations for Future Research

Abstract

Environmental epigenetics is a fast-growing field of scientific research attracting interest from key stakeholders in Indigenous health internationally, including researchers, clinicians, policymakers, and advocacy organisations. It is the study of how various external factors, including food, stress, and toxins, alter genetic expression, and could be biologically passed down to children (and potentially grandchildren). This article explores the growing interest in epigenetics in Indigenous health and social policy fields in Australia and identifies the key implications and challenges for Aboriginal and Torres Strait Islander communities. The authors advocate for the urgent development of epigenetic research guidelines in Australia and beyond that centre Indigenous sovereignty.

Keywords

Epigenetics, developmental origins of health and disease, intergenerational trauma, Aboriginal and Torres Strait Islander People, health

Epigenetic Science and Indigenous Health: Key Issues and Considerations for Future Research

Environmental epigenetics is the study of how various external factors, including food, stress, and toxins, alter genetic expression. It is a growing field of scientific research that is attracting interest from key stakeholders in Indigenous health, including researchers, clinicians, policymakers, and advocacy organisations. Epigenetics is a broad umbrella term for various areas of research in environmental influence of gene expression. Particularly prominent for Indigenous health and wellbeing is the area of environmental or social epigenetics that addresses how life experiences can shape our gene expression, and through epigenetic changes, could be passed down to children (and potentially grandchildren), impacting child development and disease across the life course.

One reason why epigenetics is attracting interest in Indigenous health in Australia is because of its resonances with Aboriginal and Torres Strait Islander cultural understandings of health and disease, sitting within a holistic framework that encompasses a connection to the land, waterways, and broader environments.¹ Further, there are emphases on the ongoing health impacts of historical trauma caused by colonisation. While no direct studies of epigenetic mechanisms such as DNA methylation (one of the most commonly studied mechanisms) have been conducted with Aboriginal and Torres Strait Islander communities to date, interest in this area is growing at a fast pace. This article aims to identify the key implications and challenges of environmental epigenetics for Indigenous communities and health and policy futures at a critical time in this emerging research agenda.

We attempt here to identify implications and challenges of environmental epigenetic research *before* it is widely adopted in Indigenous health research and policy in order to minimize the risks and maximize the benefits of this emerging field. This strategy means that, at this point, the potential benefits of epigenetics for Indigenous people are not clear. In this context the word "potential" should thus be interpreted as "possible" rather than "expected." As we will discuss, these potential benefits range from the ability of epigenetics to offer a biological explanation for the effects of historical trauma; related to this, the potential use of epigenetics in advocating for additional resources and services; and the potential to inform or monitor interventions aimed at improving health or service delivery, and more particularly those focused on key windows of a child's growth and development. However, the lack of empirical evidence of these benefits means that there is a danger that this field of research will over-promise and under-deliver in terms of tangible benefits to, and defined by, Indigenous people. Among these risks associated with epigenetic research are a failure to prioritize Indigenous leadership and sovereignty in research development and translation and, at this point in time, the inadequate translation to service

¹ A note on terminology: in line with currently accepted usage, this article uses the term "Aboriginal and Torres Strait Islander" when referring to the Indigenous peoples of Australia, and "Indigenous" when referring to the Indigenous Peoples of more than one country. We acknowledge that the terms "First Nations" and "First Peoples" are increasing in their use in Australia and internationally. They are used in this article when referring to publications by organisations that use these terms in their titles.

delivery. The authors suggest the timely development of guidelines for an epigenetics research agenda in which Aboriginal and Torres Strait Islander sovereignty is fundamental.

Epigenetics and the Intergenerational Transmission of Health and Disease

Environmental epigenetics is prominent in life-course research as it has demonstrated how external factors can shape gene expression during critical windows of development in pregnancy and prepregnancy, and early life and puberty, with potential lifelong impacts on health (Gluckman et al. 2009).² The epigenome is a set of chemical processes that modify DNA and the proteins it binds to, affecting how genes are expressed. The best known of such modifications is DNA methylation, which occurs when a methyl group attaches to certain sections of DNA and "silences" or potentiates certain genes. It is often described through the metaphor of a volume knob on a stereo: "turning down (or even off) certain genes in some cases and turning up other genes in other cases" (Sullivan, 2013, pp. 200-1). Such modifications may consequently impact development, shaping cognition, the risk of developing non-communicable diseases, or the ability of the body to cope with stress and adversity (Landecker & Panofsky, 2013).

A person's DNA sequence is generally stable throughout their life, and epigenetic processes are normal physiological processes that change with age to enable normal development and to ensure the body maintains homeostasis and healthy function. Epigenetic research has found that our gene expression can be changed through a range of environmental and lifestyle factors (Bohacek & Mansuy, 2015). These include positive factors such as a nutritious diet, stable caregiving, and a sense of belonging, as well as negative factors such as chronic stress and trauma, inadequate nutrition, unsafe or unstable caregiving, and exposure to toxins in the environment (Mehta et al., 2020). Epigenomic modifications are predominantly made in certain developmental windows when the body is more susceptible to changes from the environment (termed windows of "plasticity"). The time from conception to early infancy is a critical window of plasticity for epigenomic changes, drawing our attention to pregnancy and early life as rich time periods for enhancing health outcomes across the life course (Gluckman et al., 2009; Mulligan, 2016).

Epigenetics offers new possibilities for further understanding the disease pathways of several noncommunicable diseases, including type 2 diabetes (Gluckman & Hanson, 2012; Krishnaveni & Yajnick, 2017) and cardiovascular disease (Godfrey et al., 2011; Kuzawa & Sweet, 2009). It proposes insight into the causes of fetal growth restriction and pre-term birth, which have been shown to have lifelong developmental consequences (Kuzawa & Sweet 2009; Lewis et al. 2016; Sayers & Singh 2010). Neurodevelopmental disorders and psychological illnesses and phenomena such as post-traumatic stress

² There are many strands of scientific research on epigenetic mechanisms. The strands considered here are those of most relevance and interest to researchers and clinicians in Indigenous health: environmental epigenetics and transgenerational epigenetics (see for example Australian Medical Association, 2013; Kirmayer et al., 2014; Singh et al., 2019). These overlapping areas of inquiry focus on how external environments and negative life events (including historical events) shape gene expression.

disorder, depression, and suicide have also been linked to potential epigenetic pathways (Cecil et al., 2016; Gabriele et al. 2018; Mehta et al., 2018; Mehta et al. 2020). Researchers have correlated historical trauma events with epigenetic states in children, including those exposed to traumatic events and nutritional challenges *in utero* (Painter et al., 2008; Perroud et al., 2014; Ravelli et al., 1976; Roseboom et al., 2011; Stein et al., 1975; Stein et al., 1995; Yehuda et al., 2005; Yehuda et al., 2014; Yehuda & Lehrner, 2018). Some specific examples of traumatic events that have been studied, such as the Dutch Winter Famine and the 9/11 terrorist attacks, are discussed in the next section.

As it links both life experiences and social conditions to genome biology, epigenetics provides a potential biological mechanism for how social disadvantage, discrimination, and historical trauma impact the health of socially marginalized communities across generations. There is some speculation that epigenetic modifications can be transmitted between two generations, and up to three, in what is called "transgenerational transmission." This is well established in animal models, including the nematode *C. Elegans* (Frolows & Ashe, 2021; Woodhouse & Ashe 2020), Drosophila (Ciabrelli, 2018; Xing et al., 2007), honeybees (Remnant et al., 2016), and rodents (Gapp et al., 2014; Horsthemke, 2018; Miska & Ferguson-Smith, 2016). However, in humans, the evidence for transgenerational transmission is heavily debated by epigeneticists, many of whom argue there is, as yet, no clear evidence of mechanisms. Large cohort studies that have linked particular negative life experiences to outcomes in offspring demonstrate correlations rather than causative transgenerational pathways of epigenetic transmission (Bohacek & Mansuy, 2015, p. 650; Dubois & Guaspare, 2019, p. 159).

While epigenetic studies to date have particularly addressed how trauma, stress, and maternal malnutrition may have long term impacts on life trajectories, a small but vibrant area of recent research highlights how certain protective factors and methods of "environmental enrichment" may play a key role in producing resilience (Gapp et al., 2016; Chiapperino, 2021). Müller & Kenny for example, in their paper on adverse childhood experiences in the US Pacific Northwest, document how knowledge claims from the biology of early life are used to develop narratives of "collective responsibility, institutional changes, and the creation of social conditions that allow those who have experienced early life adversity to thrive" (2020, 1233). These areas of research have particular salience for epigenetic research paradigm.

Epigenetics is related to other scientific fields that explore early life exposures and the intergenerational transmission of health and disease. The most prominent of these is the Developmental Origins of Health and Disease (often called DOHaD), a multidisciplinary field that explores how parental (more often maternal) and environmental factors from pre-conception onwards affect a child's development and future health outcomes. Epigenetics is considered a component of the DOHaD umbrella as a plausible mechanism of intergenerational transmission (Singh et al., 2019). The field of DOHaD research has informed a growing focus internationally on the "first thousand days" of a child's life, from conception to age two, as a critical window for establishing lifelong health. This international focus is reflected by

World Health Organisation campaigns and priorities focused on improving nutrition in pregnancy and early life in developing countries (World Health Organization, 2014).

Alongside DOHaD, epigenetics has been explored in psychiatry and psychology research investigating the transmission of psychiatric conditions such as post-traumatic stress disorder, post-natal depression, and schizophrenia (Tsankova et al., 2007). Epigenetic mechanisms have emerged as an important paradigm for understanding the potential causes of psychopathology and pathways of transmission. The relationship between trauma and epigenetic transmission explored in these fields also has particular salience for efforts to apply an epigenetic lens to the inheritance of impacts from historical trauma, including colonisation.

Epigenetics, together with DOHaD, is attracting increasing attention among policymakers and health researchers in Australia (Australian Medical Association [AMA], 2013; NSW Health, 2019). There are a growing number of research programs and policy papers pointing to the important role of early life in establishing lifelong and even intergenerational health outcomes and calling for increased government investment in this area (Moore et al., 2017; PriceWaterhouseCoopers, 2019). Epigenetics is attracting growing attention from a range of different audiences, and now features in popular media reporting on intergenerational disadvantage and the health outcomes of communities impacted by marginalization (Dubois & Guaspare, 2020, pp. 161-70; Dubois et al., 2019). In some instances, the engagement with epigenetics beyond the scientific community is being generated by Aboriginal and Torres Strait Islander people themselves. For example, prominent Indigenous commentator and singer-songwriter Mitch Tambo, a Gamilaraay and Birra Gubba man, recently discussed genetic inheritance of trauma on a program on the national broadcaster, saying, "this transgenerational trauma stuff, it is scientifically proven it can be passed on through the DNA—it is real" (ABC Q&A, 2021). When the National Centre for Indigenous Genomics (NCIG) was launched, the Chair of the Indigenous-majority Governance Board, former Aboriginal and Torres Strait Islander Social Justice Commissioner Mick Gooda, stated that "looking at how our genes are influenced by the environment can answer some important questions for Indigenous health, like how trauma can affect health across generations" (Australian Indigenous Health Info Net, 2014), emphasis added). Indigenous communities are among those expressing interest in epigenetics research, and who stand to benefit from this fast-developing field, provided that research and clinical translation take place in ways that are culturally aware and centre Indigenous leadership and voices.

Epigenetic Frameworks that are Potentially Relevant to Understanding Aboriginal and Torres Strait Islander Health

Embodied Legacies of Colonial Violence

Epigenetics offers an additional layer to understandings of embodied legacies of colonisation by linking the intergenerational effects of colonial violence to a biological mechanism (Conching & Thayer, 2019). In addition, in studies on the transmission of epigenetic modifications from parents to offspring through

exposures *in utero* and in early life, there is some indication that epigenetic marks may be inherited by multiple generations, through what is known as *trans*generational inheritance (Francisco Perez & Lehner, 2019). It is important to note that these findings are still in their infancy and are as yet confined to animal models. To date there have been no studies measuring the epigenetic signatures associated with historical trauma among Aboriginal and Torres Strait Islander communities. However, key epigenetic studies on historical trauma, in particular those focused on descendants of Holocaust survivors, and those young adults who were *in utero* in New York at the time of the September 11, 2001 World Trade Centre attacks, have identified correlations between these collective trauma events and adverse developmental and stress responses in offspring (Yehuda & Lehrner, 2018). The possibility of intergenerational and transgenerational epigenetic inheritance is a rapidly evolving area of scientific research with significant ongoing implications conceptualizing Aboriginal and Torres Strait Islander experiences of historical trauma.

There is strong evidence assembled over several decades that historical trauma associated with colonisation has ongoing impacts on Aboriginal and Torres Strait Islander health today (see in particular Australian Institute of Health and Welfare [AIHW], 2019; De Maio et al., 2005; Hunter et al., 2011; Ketheesan et al., 2020; Kulunga Research Network 2008; Silburn et al., 2006; Zubrick et al., 2005). Scientists have linked the trauma of colonisation to disproportionately high rates of mental illness, posttraumatic stress disorder and suicidality (Gone & Kirmayer, 2020; Kirmayer et al., 2014; Yehuda & Lehrner, 2018), as well as disparate rates of chronic disease and premature birth in a range of communities, including Indigenous Australians, Indigenous Peoples in North America, and the African diaspora in the United States (Geronimus, 1992; Singh et al., 2019). These health disparities have long been discussed in Indigenous and First Nations communities through various frameworks, for example as a feeling of collective "loss" among Indigenous communities in North America (Whitbeck et al., 2004), and the inheritance of "communal wounds" and "trauma trails" (Atkinson, 2002) among Aboriginal and Torres Strait Islander peoples. There is also an extremely robust evidence base established in fields using social and emotional wellbeing paradigms for the effects of intergenerational trauma on Aboriginal and Torres Strait Islander people, and the positive impact of community-led health interventions and connecting to culture (see Atkinson, Nelson, Brooks, et al., 2010; Department of Social Services, 2020; Jones et al., 2018).

For many stakeholders, epigenetics presents a useful framework that might complement the wealth of pre-existing research on Indigenous wellbeing and healing. Epigenetics is seen as potentially useful for both explaining in genetic terms how health challenges in Indigenous communities are transmitted intergenerationally, and providing a potential mechanism for addressing these challenges and promoting healing (see in particular AMA, 2013; Arabena et al., 2016; Arabena et al., 2021; Boulton & Taylor, 2018; Brown, 2020; Kowal, 2016; Singh et al., 2019). For example, in their 2012-13 "Report Card" on Aboriginal and Torres Strait Islander Health, the Australian Medical Association (2013, p. 1) identified the period from conception to the age of five as a "time of both risk and opportunity" for lifelong health. The report identifies epigenetics as a primary mechanism for the transmission of intergenerational health

outcomes among Indigenous people, explaining how early life experiences of deprivation, adversity, and toxic stress can impact the health of not only individuals but their descendants (p. 3-4). As the report stresses, epigenetics research identifies the early years as a window of opportunity for establishing health, and for addressing intergenerational cycles of trauma and disease through supportive and culturally enriching strategies. While negative experiences such as trauma can alter the epigenetic profile of an individual for future ill health, interventions that focus on positive experiences can modify an individual's epigenome in a way that creates opportunities for, or aids, healing. Strengths-based interventions are strongly prioritized by Aboriginal and Torres Strait Islander people and hold the potential for a positive impact on health outcomes and broader social trajectories.

Developmental Effects

Epigenetics may provide a model to understand how developmental programming *in utero* and early life can lead to development of chronic diseases that Aboriginal and Torres Strait Islanders face at a disproportionately high rate. These include cardiovascular and metabolic diseases, which are the primary causes of the 10-11-year gap in life expectancy between Indigenous and non-Indigenous Australians (Titmuss, 2019). One example of a key metabolic disease for which epigenetics could provide a useful framework is type 2 diabetes. Recent evidence suggests that Aboriginal and Torres Strait Islander children are eight times more likely to develop Type 2 diabetes than their non-Indigenous peers, and Aboriginal and Torres Strait Islanders of all ages are four times more likely to be hospitalized for diabetes complications (AIHW, 2014; Burrow & Ride, 2020, 3). Further, exposure to type 2 diabetes during pregnancy increases the likelihood of developing the disease before the age of 30 years (Jabar et al., 2019; Maple-Brown & Hampton, 2020). The high incidence of type 2 diabetes in Aboriginal and Torres Strait Islander children cannot be fully explained by genetic mechanisms (Titmuss, 2019), nor can it be explained by popular stereotypes around unhealthy diets and risky lifestyles that are often used to stigmatize many families and communities. Rather, emerging evidence from epigenetics and DOHaD highlights that increased rates of type 2 diabetes in Aboriginal and Torres Strait Islander communities may be intimately connected to experiences of socio-economic disadvantage, chronic stress, depression, and the disproportionate exposure to adverse childhood experiences that Indigenous people face, including during pregnancy (Diehm et al., 2018). These factors are a consequence of deep-seated systemic racism and the enduring trauma of colonisation (for a discussion of this causal relation and evidence base, see Brown, 2020).

Pregnancy complications such as foetal growth restriction and preterm birth may also be better understood using epigenetic frameworks (McEwan et al., 2019). Indigenous communities face both of these conditions disproportionately: in 2016-18, preterm birth rates for Aboriginal mothers were 13.8% as compared to 8.4% for non-Aboriginal mothers, and the low birthweight rate was 11.9% among Indigenous mothers as compared to 6.4% among non-Indigenous counterparts (AIHW, 2021, pp. 21, 25). Australian studies with Aboriginal and Torres Strait Islander cohorts have demonstrated that such complications are connected to experiences of chronic stress, racism, and material disadvantage, and have highlighted the link between these conditions and the development of chronic diseases in offspring, as well as greater risk of child mortality (Mah et al., 2019; Kildea et al., 2019).

The Global Context: Black and Indigenous Engagements with Epigenetics Outside Australia

There is growing engagement with epigenetics as an explanatory framework for the health disparities faced by Indigenous communities in South Africa and across North America. These communities also experience a disproportionate burden of disease, as well as historical trauma which has been associated with subsequently high rates of substance abuse, depression, post-traumatic stress and suicide, and high rates of adverse childhood experiences (ACEs) (Brockie et al., 2013; Bombay et al., 2011, 2014; Kim, 2020; Pentecost et al., 2018; Phillips-Beck et al., 2018). Many communities have signalled interest in epigenetics as a framework for understanding the intergenerational transmission of these health challenges as it is culturally relevant and resonates with Indigenous understandings of historical trauma and ancestral memory (Brockie et al., 2013; Bombay et al., 2014; Thunderbird Partnership Foundation, 2019; Warin et al., 2020).³ Epigenetics offers a potential mechanism for demonstrating how historical and contemporary experiences of trauma are intimately connected, and showing how the atrocities of colonisation have an ongoing and cumulative impact at a biogenetic level (Bombay et al., 2014; Walters et al., 2011).

In Canada, particular attention is being paid to the Indian Residential School (IRS) system. Although no direct studies of epigenetic mechanisms have been conducted with this community to date, researchers are suggesting the putative effects of epigenetic modifications as an explanatory mechanism for how the trauma of IRS attendance continues to shape the health outcomes of descendants (Bombay et al., 2014; Brockie et al., 180-82; Walters et al., 2011). Survivors of the IRS system continue to experience high rates of mental and physical health challenges, and the descendants of First Nations people who were forced to attend IRSs also suffer higher rates of depression, suicidal ideation, and poor educational outcomes (Assembly of First Nations, 2007, 37; Bombay et al., 2011). Epigenetic studies may contribute important knowledge on how the embodied experiences of violence of those who attended IRSs are being felt across generations.

In the United States, researchers have also drawn on epigenetics to explore the health impacts of chattel slavery and enduring racism experienced among Black communities. For example, Kuzawa and Sweet (2009) argued that epigenetics provides a more compelling model than genetics to understand the racially patterned nature of cardiovascular disease in the United States. African Americans experience higher rates of both cardiovascular disease and one of its common correlates, low birth weight. More than half of all African Americans over 20 years old suffer from cardiovascular disease (Tsao et al., 2022), and they are 1.3 times more likely to die from this disease than white Americans (Mensah et al., 2005). Linking the experiences of stress, trauma, and material disadvantage associated with racism experienced by Black people as a socially defined racial group to disproportionately high cardiovascular disease rates,

³ For a related discussion in the context of planetary health, see Redvers et al., 2020.

Kuzawa and Sweet (2009, 10-11) proposed epigenetics and early life experiences as important developmental pathways through which social experiences of racism result in biological harms for marginalized groups.

A number of Black and Indigenous researchers, organisations, and collectives are embracing scientific findings of epigenetics to agitate for changes to social policy, including increased support for culturally relevant medical and mental health services, particularly during pregnancy and early life. Epigenetics was centred in a 2018 resolution ratified by the Californian State Legislative Assembly (ACR 177). Authored by African American legislator Reginald Byron Jones-Sawyer, this resolution sought to draw attention to the impacts of historical trauma on some citizens of California (Californian Legislative Assembly, 2018). Black and Indigenous community members are also increasingly deploying the concept of epigenetics to understand their own individual and familial biographies, and to advocate for reparations (Grossi, 2020, p. 93-5). Many researchers point to the potential of further scientific research in this area to improve the evidence base regarding the effects of colonization, racism, and cultural trauma on the epigenome of Indigenous or Black populations (Bombay et al., 2014;). There is also some reticence from these communities about the processes of collecting biological samples, research translation, and an overemphasis on the experience of trauma in contrast to healing, issues that will be discussed in the section below. In addition, many other communities in the global South are engaging epigenetic knowledge in harmony with non-Western knowledges and holistic traditions of medicine, such as Ayurveda in India (see Rooney, 2020).

Implications of Epigenetics for Aboriginal and Torres Strait Islander Healthcare

A Powerful Explanatory Framework

As described in the previous section, the explanatory power of epigenetics is one of its most impactful aspects. In a settler-colonial state such as Australia, empirical scientific knowledge is often seen to hold greater truth value and political leverage than anecdotal accounts and knowledge grounded in Indigenous ontologies (Warin et al., 2022; Watson-Verran & Turnbull, 1995). In this context, epigenetic science could be strategically employed to bolster the concern that past (and continuing) social harms and injustices have lasting impacts on the bodies and lives of Aboriginal and Torres Strait Islander People. The biological effects of colonization seen across generations challenges the racist and widely held notion that Indigenous communities and individuals are solely responsible for the "poor" health outcomes that they experience. For example, recent reports from both the Healing Foundation (2014) and AIHW (2019) point to the significant impacts of forced child removal on the health and wellbeing of children of Stolen Generation survivors. By making visible the intergenerational links between policies in Australia such as forced child removal and current experiences of poor health and wellbeing, the onus is placed on policy makers and service providers to acknowledge that social environments are directly linked to health outcomes, and that to "break the cycle" of this intergenerational harm and the effects of ongoing racism, more resources are required to support Aboriginal and Torres Strait Islander communities to improve these environments.

Potential for Healing

If epigenetics can help to explain intergenerational trauma in ways that appeal to policy makers, it can also help to advocate for Aboriginal and Torres Strait Islander health policy that foregrounds environments and social determinants as additional factors that contribute to ill-health. This may then allow for a recognition that healing and recovery for Aboriginal and Torres Strait Islander peoples is intimately connected to investment in culturally competent services, including perinatal and early childhood care, as well as nutrition, education, mental health services, secure housing, and the avoidance of youth incarceration. As we described at the beginning of this article, epigenetics is often characterized as a volume knob that can be turned up or down. If epigenetic science demonstrates that "poor" environments can have lasting negative impacts on health, it may also highlight that strengths-based approaches are needed to improve environments, health, and wellbeing. This potential for healing, growth, and positive change is an important consideration for the development of evidentiary support for the mediating role of epigenetic modifications in Aboriginal and Torres Strait Islander health and illness, where narratives of healing and strengths-based approaches to support and recovery are so urgently sought.

Challenges and Risks

Perpetuating a Deficit-Based Discourse

Despite the potential for a narrative of healing, one of the most concerning aspects of epigenetics literature to date is its propensity to focus on "damage" or "suffering," and to ascribe these negative factors to certain groups of people. Moreover, the tendency to look at ethnic groups as biologically homogenous not so much because of shared genes or ancestry but common exposure to traumatic events may further reinforce stigmatization (see Meloni et al., 2022). By focusing on trauma, damage, and suffering, and overlooking inter-individual variations and stochastic factors in development, epigenetic research can continue to perpetuate a deficit-based discourse that has become commonplace in Indigenous health settings and research.

The Lowitja Institute defines deficit discourse as a 'discourse that represents people or groups in terms of deficiency—absence, lack or failure' (Fogarty et al., 2018, p. vi). Given that epigenetics is often used to point to the ways in which "negative" environments or experiences reveal themselves in the biological body through negative health outcomes, studies risk being inherently oriented towards deficit. If epigenetics is used to describe ways in which Aboriginal and Torres Strait Islander Peoples are "marked" or lacking at a molecular level, this could perpetuate racist stereotypes rather than challenge them. As sociologist Lisa Blackman (2016, p. 269) writes, even though epigenetics holds the "promise to qualify the relations between biology, psyche, and trauma . . . it is also at risk of erasing the nuances of lived, embodied experience in its attempt to discursively molecularise the environment" (Blackman, 2016, p. 269). In other words, epigenetics has the potential to be deployed as just another form of deficit-based,

reductionist discourse that drags colonial shadows of eugenics into the present to reinstate narratives of a molecularly "damaged" Indigenous population.

To reduce the harm that would be perpetuated by narratives of epigenetics oriented around deficit, it is necessary to consider whether there are ways of discussing epigenetics that balance both the benefits and risks of this research paradigm—while focusing on resilience and the potential for positive interventions and reversal of epigenetic changes. It is also important to critically examine to what extent epigenetics can be used to tell a "strengths-based" story about intergenerational health. It is important to attend to how governments and policy-makers can be held accountable for the intergenerational effects of colonization on Aboriginal and Torres Strait Islander communities: keeping the focus on the violent implications of a long history of damaging and deficit-oriented Indigenous policy, and the need for community-led policy and healthcare reform that focuses on self-determination and improving collective conditions, rather than focusing on individual epigenomes.

Research Translation and Intervention

Aboriginal and Torres Strait Islander communities in Australia, and those who work in Indigenous health more broadly, are very familiar with undelivered promises when it comes to scientific and medical interventions that claim to be able to address or "close" the gap in Indigenous health and wellbeing. There is a risk that, if not adequately governed, research on epigenetics in Indigenous contexts could be another example of a research agenda which over-promises and under-delivers. More specifically, without considered and critical discussion on what sorts of interventions might be made possible through epigenetic research, there is a risk that epigenetic knowledge produced by scientific researchers will not be adequately translated. This means translation into effective strengths-based healthcare interventions and service delivery models that support health and cultural needs in safe spaces. Much work is already being done in Australia by Indigenous-led research teams and service providers with regards to breaking cycles of trauma and supporting Aboriginal and Torres Strait Islander families and children in early life (see for example We-Al-li, Healing the Past by Nurturing the Future, First 1000 Days Australia [Arabena et al., 2016]). The question becomes: can epigenetics offer anything new in terms of service delivery and health care initiatives? While epigenetic science may offer a novel explanatory framework for understanding the transmission of intergenerational trauma and ill-health, we should be cautious in positioning it as a new form of knowledge with the capacity to inform new interventions to improve Aboriginal and Torres Strait Islander lives and livelihoods. There is a long history of (non-epigenetic) research and healing strategies responding to intergenerational trauma among Aboriginal and Torres Strait Islander communities that should be foregrounded in epigeneticinformed research in this area going forward. Further, the hope inherent in the current embrace of epigenetics may not actually eventuate, and there is potential harm in promoting or popularizing a hopeful epigenetics without certainty that it can be delivered. What epigenetics may do, however, is be strategically employed to advocate for increased funding and recognition of current services and

programs which support intergenerational healing across the life-course, and which explicitly acknowledge the impacts of colonisation and ongoing trauma on ill-health.

Next Steps: An Indigenous-Controlled Epigenetics Research Agenda

Indigenous Direction and Control

If epigenetic research is to take place with Aboriginal and Torres Strait Islander communities in Australia, it must be unequivocally Indigenous-led and controlled. We are not advocating here for "inclusion" in epigenetic research programs—rather, we advocate for Aboriginal and Torres Strait Islander researchers, communities, and participants having control and agency at every step of how and why research happens, including having a say in what sorts of questions epigenetics may help to answer, which if any cohorts will be involved in studies, and for what reasons. It is vital to prioritize the aspirations of Aboriginal and Torres Strait Islander peoples throughout research design (see for example Beaton et al., 2015; Kowal et al., 2011; Kowal & Anderson, 2012; Taniguchi et al., 2012). "Indigenous data sovereignty," a concept and global movement that emphasizes Indigenous Peoples' governance over their data, should be a guiding principle for epigenetic research going forward (Kukutai & Taylor, 2016; Tsosie et al. 2021; Walter & Russo Carroll, 2020). It will also be vital to centre the wealth of culturally specific knowledge about intergenerational trauma, wellbeing, and embodiment that has been established by scholars, clinicians, and community leaders working in non-genetic and non-academic paradigms.

Key to future directions in an Indigenous-controlled epigenetics research agenda is the strategic development of an Indigenous workforce in this field. International workshops such as the Summer Internship for Indigenous Peoples in Genomics (SING) are an excellent example of developing an Indigenous-led workforce in technical and laboratory-based skills in genomics, including attention to epigenetics and its social, legal, and ethical implications. Beginning in the United States in 2011, this workshop and mentoring program has inspired a global network of similar programs in Australia, Canada, and Aotearoa New Zealand, making clear cases for how Indigenous knowledges and cultures "can and should impact on genomic research" (Sing Australia, n.d.). Importantly, these workshops seek to elevate Indigenous voices, leadership, and representation in all areas of policy, government, and research, highlighting best practices of community and scientific engagement in epigenetics (and genomics more broadly). Sustained investment in an Aboriginal and Torres Strait Islander-led workforce across a range of sectors (community, community controlled, government, universities, notfor-profit, policy, and health) will further enhance opportunities to develop conversations, skills, and knowledge in the delivery, implementation, translation, and trajectory of epigenetic research (see also Arabena et al., 2020).

Epigenetic research with Aboriginal and Torres Strait Islander communities could lead to positive policy and health outcomes, but only if this research is designed, implemented, and communicated in ways that centre Indigenous sovereignty, knowledge, and ownership of data. First Nations scholar Eve Tuck (2009) presents "desire-based research" as a counter to deficit-based research methods. Desire-based research supports the desires and agency of researched peoples, rather than falling back on deficit models to try to enact change. The authors of this article advocate that epigenetic research with Indigenous participants should align with elements articulated in desire-based, strengths-based research, and oriented around Indigenous data sovereignty. This involves fostering meaningful leadership and participation of communities and placing epigenetic models in dialogue with the many robust and non-epigenetic models of healing intergenerational trauma developed by Aboriginal and Torres Strait Islander scholars and community workers (e.g. Atkinson, Nelson, & Atkinson, 2010; Atkinson, Nelson, Brooks, et al., 2010). Only when placed in this context can epigenetics offer real benefits to Aboriginal and Torres Strait Islander communities.

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