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ORIGINAL ARTICLE

Epidemiologists' ambivalence towards the epigenetics of social adversity

François Romijn[1] · **Séverine Louvel**[2]

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Abstract This article studies how social epidemiologists get involved in research carried out on rodent models to explore the biological pathways underpinning exposure to social adversity in early life. We analyze their interdisciplinary exchanges with biologists in a social epigenetics project—i.e., in the experimental study of molecular alterations following social exposures. We argue that social epidemiologists are ambivalent regarding the use of non-human animal models on two levels: first, in terms of whether such models provide scientific evidence useful to social epidemiology, and second, regarding whether such models help promote their conception of public health. While they maintain expectations towards rodent experiments by elevating their functional value over their representational potential, they fear that their research will contribute to a public health approach that focuses on individual responsibility rather than the social causes of health inequalities. This interdisciplinary project demonstrates the difficulties encountered when research in social epigenetics engages with the complexities of laboratory experiments and social environments, as well as the conflicting sociopolitical projects stemming from such research.

Keywords Social epigenetics · Social epidemiology · Biological embodiment of health inequalities · Early adversity · Ambivalence

✉ Séverine Louvel
severine.louvel@iepg.fr

[1] LAMC – Université Libre de Bruxelles, Brussels, Belgium

[2] PACTE, Sciences Po Grenoble, 1030 Avenue Centrale, Domaine Universitaire, 38040 Grenoble Cedex 09, France

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Introduction

Since the 2000s, studies of the biological mechanisms through which material, physical and social environments 'get under the skin'—that is, become biologically embedded—have grown in number. Such research is often based on laboratory experiments conducted on non-human animals such as rodents and monkeys, which are used as models for human research. This is particularly the case in environmental epigenetics, which is the study of epigenetic changes[1] caused by material, physical and/or social environments. Social science researchers have described several features of laboratory experiments common to environmental epigenetics and other areas of research focused on interactions between genes, organisms and environments (Leonelli et al. 2014; Nelson 2018): biologists' difficulties stabilizing experimental systems (Niewöhner 2011; Chiapperino 2019; Lappé 2018); the lack of ecological validity of human social environments staged in laboratory settings (Beck and Niewöhner 2006; Chung et al. 2016); and the intertwinement of facts and values in experiments (Kenney and Müller 2017; Chiapperino 2019; Lappé 2018). While the literature provides a thorough examination of how biologists consider non-human organisms to function as technologies of translation between animal biology and human health research (Shostak 2007), little is known about their use in the latter area, in particular by epidemiologists—scientists studying the distribution and determinants of health-related states and events in populations.[2] Despite the well-acknowledged reductionist properties of lab research in environmental epigenetics (Chiapperino 2019), some epidemiologists work with research based on non-human organisms. This article questions why and how epidemiologists engage with such research. We investigate these issues in an area of environmental epigenetics where the "conceptual gulf" between laboratory experiments and human social environments has been particularly emphasized (Chung et al. 2016, p. 174), namely, in social epigenetics: the study of molecular associations between social environments (most commonly defined as psychosocial stress, socioeconomic status, living environments, and experiences of traumatic events) and health outcomes. In particular, we study what motivated epidemiologists to engage in a social epigenetics project that incorporated both human cohorts and rodent experiments to study the biological effects of adverse social experiences during early life. Conducted in a number of French universities from 2012 to 2016, the EARLY project—a designation chosen for this article—was a multi-team project integrating neurobiology, nutritional biology, social epidemiology, and research in law and ethics. The social epidemiologists involved were well aware of the difficulties of transposing findings from non-human animal models to epidemiology. Thus, we investigate the "epistemic scaffolds" (Nelson 2018) these researchers employed to facilitate circulation between experiments on rodents conducted by biologists and their own work on human cohorts.

[1] Changes to chemical markers which are either attached to a DNA sequence or which modify the chromatin structure, a complex of proteins and DNA found inside the nucleus of eukaryotic cells.

[2] Source: https://www.cdc.gov/careerpaths/k12teacherroadmap/epidemiology.html. Accessed 6 Sep 2020.

In addition, as study of the biological embedding of social inequalities is very limited in France and arouses a certain skepticism, we explore the credibility issues they encounter in French academia. Eventually this study led us to question whether interdisciplinary collaboration during the course of the project had opened up new ways of engaging with the complexity of laboratory experiments and environments, and as well, to ask which public health perspectives were associated with such collaboration.

In Sect. 1, we will introduce the social science perspective of how biologists work with non-human organisms in environmental and social epigenetics. We will describe how, in the laboratory setting, the "molecularization of environments" (i.e., the narrowing of culturally and socially embedded practices to individual exposures and behaviors; Niewöhner 2011) accompanies the cultivation of "layers of complexity" (Chiapperino 2019). In Sect. 2, we will introduce our empirical investigation of the EARLY project and the co-construction of a mouse model used to study the biological embedding of early-life adversity. We will argue that the social epidemiologists involved in the EARLY project adopted an ambivalent stance on two levels: first, regarding how rodent experiments provide scientific evidence useful to social epidemiology, and second, regarding whether the interdisciplinary project promotes a conception of public health that addresses the social causes of health inequalities.

Non-human animal models in social epigenetics: biologists engaging with "layers of complexity"[3]

A sub-domain of environmental epigenetics,[4] social epigenetics aims to uncover the molecular mechanisms that link immersion in a social environment to subsequent health states in an individual or their offspring. Environmental and social epigenetics are very small areas within epigenetics research (Larrègue et al. 2020), yet they receive steady social science and media attention.[5] These areas of research are permeated by the same controversies as epigenetics at large (Tolwinski 2013; Lloyd and Reikhel 2018; Chiapperino and Panese 2018; Müller and Samaras 2018), such as links to genetics, the reversibility of epigenetic marks, and the timeframe of epigenetic changes. These fields of study also display considerable internal heterogeneity in terms of their definitions of environments, disciplinary backgrounds and experimental apparatus. For instance, social epigenetics gathers research on monkeys and rodents subjected to experimental situations of social defeat and early-life adversity, and studies on human populations that have experienced childhood trauma, poor early-life nutrition, or adversity in early life or over the life-course (Louvel 2020). In this article, we are particularly interested in research that employs non-human

[3] Chiapperino (2019).

[4] The study of epigenetic changes associated with so-called material, physical and social environmental exposures such as toxins, air pollution, or 'lifestyle' (e.g., nutrition, physical activity, tobacco use).

[5] For a recent overview of the reasons why anthropologists, sociologists, philosophers, and political scientists are taking an interest in environmental and social epigenetics, see Niewöhner and Lock (2018).

animal models[6] to study the biological effects of nutritional and psychosocial adversity in early life, and their behavioral and cognitive consequences. Our ambition is to address "how specific propositions of epigenetics are taken up, negotiated, and interpreted in specific research contexts" (Müller and Samaras 2018) and to offer a new perspective on a research area that appears to be representative of how research in environmental and social epigenetics is conducted and communicated.[7] Like other authors (Lappé 2018; Chiapperino 2019), we also wish to highlight what this area reveals, more broadly, about ways of studying gene-environment interactions (Nelson 2018).

Social scientists have documented why biologists working in environmental and social epigenetic laboratories choose certain animal models and experimental protocols, and have highlighted similarities in how the uncertainties of laboratory work are managed. In his investigation of a lab studying the transgenerational inheritance of "early-life stress" in rodents, Chiapperino (2019) observed that biologists "cultivate distinct layers of complexity" to produce knowledge that has both scientific validity and relevance for human health. The first layers of complexity relate to the modeling of stress and its biological effects. The experimental set-up (i.e., the standard stress protocols to which animals are subjected, and the targeted exploration of epigenetic modifications) leads to an "obliteration of the embodied complexities of stress" that biologists deem necessary to produce a "molecular explanation of the effects of stress" applicable to several organs, organisms and species (Chiapperino 2019). Anthropologist Niewöhner (2011), the first to conduct an ethnographic investigation in a social epigenetic laboratory, also identified the "molecularization of biography and milieu" at work in experiments on animal models. He describes researchers as "pragmatic reductionists" who use standardized animal behavioral models of early-life adversity to "reduce the messiness of environmental context in a way suitable for lab work" (op. cit., p. 289). Biologists acknowledge that their experimental models have limited representational value: "the researchers were acutely aware that human lives are much more complex than those of laboratory mice" (Lappé 2018) and even an "intrinsic normativity" (Chiapperino and Panese 2018)—they convey representations of the social world and may help reinforce them (Mansfield 2012; Richardson 2015; Kenney and Müller 2017; Sharp et al. 2018). They also acknowledge that the molecularization of research (finding the molecular pathways from environmental exposure to health outcomes) goes along with the molecularization of the human environment (Landecker 2011; Lock 2015; Niewöhner 2020). Yet biologists do not choose experimentation on animals for its simplicity. As Nelson stresses about researchers in animal behavioral genetics: "Their decision to work with animal models […] was not a rejection of complexity; it was a

[6] Hereafter, we will refer to non-human animal models as animal models.

[7] Landecker (2011) has emphasized how food gets "molecularized" (i.e., reduced to molecular events) in nutritional epigenetics. In addition, two articles—Richardson (2015) and Kenney and Müller (2017)—focus on a seminal, highly-cited study by Weaver et al. (2004) which argues that poor maternal care epigenetically predisposes rat pups to elevated levels of stress. Lastly, three ethnographic surveys—Niewöhner (2011), Lappé (2018), and Chiapperino (2019)—were carried out in labs conducting experiments on the effects of early-life stress on rodents.

different way of engaging with it" (Nelson 2018, p. 200). Likewise, biologists in environmental and social epigenetics laboratories pay constant attention to the complexity of their experiments and to the instability of experimental situations (Lappé 2018). While laboratory protocols are highly standardized, their implementation is subject to multiple variations, due in particular to interactions between the experimenters and the animals, which can modify the animals' environmental stimuli acting on the epigenetic machinery. Experimentation with animals requires a significant amount of "extra-factual work" (Nelson 2018; Chiapperino 2019) and "care of the data" (Lappé 2018, citing Fortun and Fortun 2005) which tends to remain invisible outside of lab contexts.

To summarize, biologists in environmental epigenetics demonstrate epistemic modesty (Pickersgill 2016): far from expecting their research to be directly useful in humans (for example, in finding new treatments), they carry out their experiments "in an effort to document mechanisms that may also be at play in humans" (Lappé 2018). In addition, they design experimental protocols so as to render the lab experiments tractable and to establish valid and credible results even if this "comes […] at the price of excluding a complex uptake of the embodiment of such experiences" (Chiapperino 2019). Finally, biologists are very aware that biological modifications are reactive to subtle changes in laboratory environments, but they are rarely able to modify their experimental systems accordingly (Niewöhner and Lock 2018; Niewöhner 2020). Do researchers working on human populations approach the scientific value of animal models the same way? How do they conceive of them as translation technologies between animals and humans—articulating data, technologies and practices across disciplines (Shostak 2007)? Lastly, how do they define the relevance of animal models for human health? These issues have not been thoroughly examined to date, be it in environmental and social epigenetics[8] or more broadly, in the study of gene-environment interactions.[9] This article will fill in this empirical gap with a focus on social epidemiologists' approach to using rodent models in social epigenetics. Drawing on the investigation of an interdisciplinary project studying the long-term effects of so-called cumulative stress during early-life, we analyze the "epistemic scaffolds" that social epidemiologists build to traverse from research on animals to research on humans (Nelson 2018), identifying these researchers' "assumptions of complexity" (op. cit.) about experimental

[8] However, two articles deal with the transposition of animal studies to human populations and put emphasis on the "molecularization" of human social environments taking place in this context. Lloyd and Raikhel (2018) studied how a group of psychiatrists at McGill University in Montreal built on a Weaver et al. (2004) experiment on rats to study the impacts of childhood abuse on increased suicidal risk in humans (McGowan et al. 2009). In addition, Niewöhner (2011) studied a collaboration between biologists and epidemiologists to see how changes in social positions correlate with changes in DNA methylation.

[9] There is an imbalance between the wealth of studies on animal experiments conducted in genetics, genomics and post-genomics (e.g., Shostak 2007; Lewis et al. 2013; Leonelli et al. 2014; Nelson 2018), and the still limited body of research that focuses on their use by human health researchers in general, and epidemiologists in particular. For instance, Ackerman et al. (2016) and Darling et al. (2016), who describe the work of epidemiologists in gene-environment interactions research, make only a passing mention of their use of animal models.

situations and human environments, observing how they translate these assumptions into experimental settings and how they link biological knowledge gained from these experiments with "socio-political thinking about the role of epigenetics in our societies" (Chiapperino 2019), particularly in respect to certain new perspectives on public health.

An interdisciplinary project to assess the cumulative effect of adverse experiences in humans and mice

Setting the stage: social epidemiologists meeting biologists in the French context

When first contacting the team of French social epidemiologists, our goal was to investigate whether social epigenetics brought them new insights into the study of social health inequalities. We sought to analyze how they defined and operationalized the social in social epigenetics projects, and to explore whether they saw epigenetics as a venue for new interdisciplinary collaborations between the natural and social sciences. The team was eager to contribute to sociological knowledge and wished to share their concerns about possible sociopolitical translations of social epigenetics. Their work was of particular interest to us because it claimed to be part of a social epidemiology approach (i.e., study of the biological embodiment of health) that aims to associate the biological and social sciences. The notion of biological embodiment designates "how social influences become literally embodied into physio-anatomic characteristics that influence health and become expressed in societal disparities in health" (Krieger and Davey Smith 2004, p. 92). Like social epidemiology as a whole, this approach is highly critical of the epidemiology of individual risk factors and emphasizes instead the structural determinants of health and health disparities.[10] Its specificity within social epidemiology is to examine the biological pathways that link social environments to health outcomes. The team of epidemiologists we met with were interested in epigenetic mechanisms as a preferred but not exclusive modality of the biological embodiment of social environments. They had published review and popular science articles in which they cited a wide range of well-known research in environmental and social epigenetics, to argue for the very likely association between the social environment, epigenetic modifications, and health states.[11] At that time, their own research focus was on

[10] Social epidemiology applies both the multi-causal approach (integration of cultural, economic and social factors) and the multi-level approach (population, community, and individual levels) to determinants of health in order to understand the origins of social inequalities in health (Susser and Susser 1996; Shim and Thomson 2010).

[11] They cite human studies on the epigenetic modifications caused by early-life nutrition (Heijmans et al. 2008) and the association between socioeconomic position during childhood and DNA methylation in adulthood (McGuinness et al. 2012; Borghol et al. 2012); they also refer to animal studies on the epigenetic changes associated with early exposure to psychosocial stress (Weaver et al. 2004) and to pesticides (Anway et al. 2005).

early-life social environments and endorsed the Developmental Origins of Health and Disease, or DOHaD, perspective in epidemiology.[12] According to these epidemiologists, epigenetic mechanisms triggered by experiences during the early years of life may underlie the formation of health inequalities that later in life become difficult to reduce. During our first exchanges at the end of 2018, they reported that an essential part of their work in recent years had been the development and realization of a large interdisciplinary project. They described this project, which started in 2013 and ended in 2017, as "unique" and "unprecedented". On their initiative, the EARLY research project[13] brought together teams in social epidemiology, developmental biology, neurobiology and nutritional biology, as well as a researcher in law and bioethics, and a sociologist, to examine the relationship between exposure to an adverse environment in early life and the emergence of pathologies in adulthood (such as cancers and metabolic diseases). EARLY had been an attempt, rare in the French context, to combine animal experiments and epidemiological research, and to build bridges between biology, epidemiology and the social sciences. Intrigued by this presumably unusual project, we conducted an in-depth study of its implementation and development, based on extensive material: semi-directive interviews with participants from all teams, attendance of scientific meetings and workshops,[14] and extended reading of the projects' publications. This rich empirical data allowed us to uncover expectations and doubts about social epigenetics that would remain elusive if we were to rely solely on what these researchers write in their papers. In the next section, we will present the EARLY project and explain why it stands out as unique in the French context.

The EARLY research project

A team of social epidemiologists initiated the EARLY project to explore the biological mechanisms underlying social inequalities in health, with the aim of

[12] The DOHaD perspective started with the hypothesis of a fetal origin of adult diseases (Barker 1990). Initially focused on fetal undernutrition, it was extended in the 2000s to postnatal nutrition, early psychosocial adversity and early exposure to environmental toxicants (Gluckman et al. 2005). Currently, the DOHaD perspective brings together researchers from epidemiology and the biomedical sciences who study how experiences in the early years of life impact health in adulthood. It is not a unified theory but rather a loose conceptual framework which supports a variety of scientific claims: some DOHaD researchers argue, for instance, that health is 'programmed' early in life, others give more consideration to biological plasticity throughout life (Samaras and Müller 2018). In addition, DOHaD-inspired policy measures vary substantially across space and time. For instance, while Barker's hypothesis emphasized geographical and socioeconomic constraints on the health of mothers and children, the reproductive medicine literature that followed showed a "*narrow understanding that locates the reproduction of obesity in the interiors of women's bodies*" (Warin et al. 2011, p. 458).

[13] In order to preserve the anonymity of the researchers involved, we refer to this project by this invented name which insists on the temporality of the adverse events studied. All data have been de-identified and the names of the participants changed.

[14] We attended conferences where several of the scientists involved in EARLY presented their research. We also organized two meetings with the team of social epidemiologists to discuss their research and to present our preliminary analysis. Lastly, we invited members of the team to present their work during one of our lab seminars.

strengthening social epidemiology against the epidemiology of individual risk (Galéa and Link 2013). This is a major undertaking in France (Goldberg et al. 2002): most French epidemiology researchers are clinical epidemiologists trained in medical schools, and there are few public health schools, while most social epidemiology training is located in countries such as England, Canada, or the United States. The two senior epidemiologists of the EARLY project (Ada and Alexis), received part of their research training abroad, in university centers where clinical epidemiology does not dominate public health research and where research in social epidemiology is carried out in close dialogue between social science and public health researchers. In France, they have genuine difficulties making their colleagues, who come from the "very clinical, very biomedical" French tradition in epidemiology, understand that "social inequalities in health are not only a question of behavior […] and individual responsibility" (Ada, senior researcher in epidemiology, project leader). These difficulties culminated in the social epidemiologists being described, rather unflatteringly, as "sociologists": "In the view of many of my colleagues, [if] we are interested in social factors, we are sociologists" (Ada). The team wishes to gain credibility by demonstrating that social environments leave biological marks: "If you show an epidemiologist who has always used a biomedical model that there are epigenetic changes in relation to social exposures, it is serious, it's solid. It's real proof" (Ada). In addition to initiating the EARLY project, there is a desire to increase competence in biological research, for example by obtaining authorization to use biological databases or by recruiting researchers trained in molecular biology and epidemiology. This quest for credibility bore fruit in a previous project, where the team's researchers co-authored an article in the prestigious journal Nature on how social factors shape health through underlying biological mechanisms.

EARLY is a rather unusual project, not only in France, in that it combines analysis of data from epidemiological cohorts[15] with laboratory experiments conducted on rodents. Due in particular to the difficulties of adjusting temporalities between research protocols and the high cost of laboratory experiments, EARLY's social epidemiologists tend to rely on published studies on animal models that suggest a link between social environments, epigenetic modifications and health states.[16] The epidemiologists of the EARLY project seized the opportunity of a national call for projects on the social determinants of health that would fund large interdisciplinary projects. They proposed setting up the EARLY project to biologists they knew informally, and also invited a researcher in law and bioethics and a sociologist to focus on the "ethical and societal challenges" posed by the possible biological incorporation of social inequalities. Thus, the social epidemiologists describe the EARLY project as having a "momentum of openness" (Callard and Fitzgerald 2015, p. 22) towards

[15] To study the biological incorporation of social human environments, epidemiologists use the biological material collected in the cohort (e.g., blood samples).

[16] For example, a series of articles tested the hypothesis of a correlation between socioeconomic levels and methylation of genes involved in the inflammatory system (Miller et al. 2009; Borghol et al. 2012; Stringhini et al. 2015). The authors selected these genes from studies conducted on rodents or monkeys subjected to various situations of social adversity (e.g., prenatal stress, lack of maternal care, or dominated position in the group).

interdisciplinary collaborations that came to an end with the closure of the call for tenders, and the failures of subsequent attempts to fund the continuation of the EARLY project: "we were told [N.B. by the funding agency] that we should submit two projects, one purely biological and one epidemiological" (Ada, project leader).

'Zero adversity', 'one adversity', 'two adversities' and '+adversities': exposure to social adversity in the EARLY project

EARLY had three main components: the definition in humans of early psychosocial exposures likely to have an impact on long-term health status; the study in rodents of the biological effects, and particularly the epigenetic effects, of early-life stress; and finally, using results from the first two components, the study in epidemiological cohorts of the links between early social environment, biological functioning and adult health status. The researchers spent several months discussing how to operationalize exposure to an adverse environment during early life in both humans and mice. The epidemiologists were interested in exposure to psychosocial adversity during childhood and in "chronic stressful conditions that harm child development" (Alexis, senior investigator in epidemiology). The literature on childhood adversity lists a large number of adverse events of varying intensity and duration: the team favored those related to the child's family environment because of "the chronic and stressful aspect of having complicated relationships at home" (op. cit.). The focus on the accumulation of stressors is part of the life course epidemiology approach, which "contains the idea that there is an accumulation of risks, a kind of mechanism over the course of life, which can be positive or negative, or neutral. That is, you can accumulate risk, and you see a snowball effect in social terms that is very clearly demonstrated" (op. cit.). Also, while the epidemiologists were aware that other stressors were in play such as stress related to the school environment or neighborhood, they chose not to mobilize these variables because they were not of the same quality in their database. Finally, the EARLY's social epidemiologists wished to select events and situations that previous epidemiological research, including their own work, had associated with changes in allostatic load. Allostatic load has been conceptualized as "the physiological burden imposed by stress" (Geronimus et al. 2006). It is quantified by a score based on assessment of the state of several physiological systems such as the brain, the cardiovascular and metabolic systems, and the immune system. The team was particularly interested in allostatic load because it has been shown to be socially patterned (Dowd et al. 2009), and thus may provide evidence for the biological underpinning of social inequalities in health. At the same time, they were well aware of methodological limitations since the calculated scores for allostatic load depend, among other things, on the available biomarkers for the different regulatory systems. The epidemiology team had previously studied the relationship between allostatic load and socio-economic position early in life. They wished to gain a more precise understanding of social adversity through the accumulation of adverse events. In addition, they wished to further examine the biological pathways linking social circumstances and health states: "We show that adversity has an effect on allostatic load and that allostatic load has an effect on mortality.

So that's it, we find our biological mediator. And then the question becomes, how is the allostatic charge actually incorporated?" (Gilles, doctoral student in epidemiology). Epigenetic mechanisms seem likely to play a role, as studies have shown that epigenetic changes mediated by the neuroendocrine system impact allostatic load and health states (McEwen and McEwen 2017).

In the EARLY project, the epidemiologists defined exposure to social adversity during childhood as a combination of adverse events (such as abuse, death of a parent, growing up in a foster home, having a parent in prison, or psychosis of a parent). They distinguished between groups of individuals with "zero adversity", "one adversity", "two adversities" and "+ adversities" (Ada). Their first discussions with the biologists aimed to define a protocol of cumulative stress to conduct experiments on mice: "We've put people around the table, saying, we're going to look at what happens in terms of adversity in humans, and pathologies in adulthood, including cancers and metabolic problems. Could you do the same in animals and see if the results are consistent?" (Ada). How did they make the case that putting mice under chronic stress may be useful for studying the biological effects of stress in humans? And how did they select the combination of stresses inflicted on mice? Epidemiologists and biologists built an "epistemic scaffold" between research on human cohorts and experiments on rodents (Nelson 2018) that relied on two particular arguments: the "neuroendocrine argument", which claims that in several animal species, similar biological mechanisms may be at play and responsible for the deleterious effects of a lack of early maternal care—in particular, that induced by maternal separation—on stress responses, cognitive development and inflammatory responses (Meaney et al. 1991); and the "gut-brain axis argument", which claims that gut microbiota and nutrition impact stress-related behaviors and mental health, and that nutrition and exposure to stress may interact (Valles-Colomer et al. 2019). The neuroendocrine argument is crucial in the choice of a mouse strain: "The C3H mouse was chosen because its maternal behavior makes the impact of maternal separation greater. The mother takes sawdust, everything in the cage, to make a nest. She lies on the nest, she nurses her cubs, she protects them, she wraps them" (Viviane, biologist). The selection of the cumulative stresses was justified by both neuroendocrinology and the literature on the gut-brain axis, as well as the expertise of biologists participating in certain experimental protocols of the project. The biologists assigned to different groups of mice the application of either a single stress model (nutritional stress applied to the pregnant female via an excessively rich diet or maternal separation stress), a two-stresses model (nutritional stress + maternal separation stress), or a three-stresses model (nutritional stress [pregnant female] + maternal separation stress + nutritional stress [pup]). The objective of the mice model was to "really model chronic stress applied to the mother and the child in the lactation period, a period of breastfeeding for the woman" (Viviane). The model was not set up to establish whether the effects of stress are similar to the effects of adverse events on humans. Rather, it was a matter of inflicting chronic and lasting stressors to mice, observing their physiological effects and studying the underlying biological mechanisms. The biologists planned to analyze epigenetic, metabolic and inflammatory profiles of several tissues (the brain, liver, hypothalamus, and epididymis) and of blood cells.

We have suggested that in France, epidemiological research on the biological embodiment of social environments is motivated by scientific expectations and by the desire to gain the level of credibility afforded to clinical epidemiology. In this context, the social epidemiologists who initiated the EARLY project chose to collaborate with biologists, in order to investigate epigenetic changes following exposure to early life adversity, which they operationalized as an accumulation of stressful situations. We now turn to the ambivalence of epidemiologists regarding the experimental mouse model's usefulness in social epidemiology, and explore how they nevertheless managed to maintain their expectations.

Ambivalent epidemiologists

Reassessing scientific expectations for animal models

For the epidemiologists of the EARLY project, experimentation on animals is more relevant than cohort epidemiology when studying the biological effects of exposure to an environment. First of all, this is because biologists are able to stabilize cumulative stress and its effects as the main variables of interest (Lappé 2018), in a way that is not accessible to epidemiological research (Bauer 2008). Biologists have a certain degree of control over the environments in which the animals evolve: "Biologists are a little more familiar with environmental conditions. […] They have a way of isolating the stress. They control everything else: the food is the same, the air is the same, mice don't smoke, they don't drink" (Ada, project leader). Biologists claim to establish direct links between the occurrence of stressful experiences and the biological effects that will ultimately lead to a health outcome. In contrast, depending on the variables available in a given cohort, epidemiologists are not always able to control for confounding variables (other environmental events or genetic conditions) or to identify mediating variables. This limits their ability to assert that the exposure being studied is causally related to the outcome being studied. Just as lab environments for mice must be as standardized as possible, likewise their genetic makeup be standardized to control for possible genetic factors. Epidemiologists are aware that mice of different strains do not respond in the same ways to stress, which is why they chose the C3H strain. They accept this limitation of experimental work because it guarantees a certain degree of quality (Chiapperino 2019; Lappé 2018; Nelson 2018). Secondly, animal biology is viewed as ahead of epidemiology in terms of identifying biological markers of material and social environments, due to both the availability of biological data and relaxation of experimental constraints. In particular, few cohort surveys include biological data obtained from the tissues of interest to epidemiologists: "We may not find anything in blood because we should have looked in another tissue. But in humans, it's going to be difficult to find any tissue other than blood" (Karen, a senior researcher in molecular biology and epidemiology). In addition, the biological markers commonly used in epidemiology are not necessarily those that are the most relevant, as explained by Marieke, a Ph.D. student in molecular biology: "epidemiologists often look for interleukin 6 in people with plasma disease. But it's a marker that is unstable and not relevant at all. Still,

epidemiologists keep looking at this marker". Animal experimentation, therefore, seems indispensable for identification of epigenetic biomarkers that may be present in humans. Lastly, animal experimentation is intended to establish and test hypotheses on the biological mechanisms at work in humans, and provide explanations for correlations established in human cohorts. Viviane, a biologist, recalled that "Barker's hypothesis worked and was popularized because animal models immediately proved that it had a basis experimentally. And then, based on these animal models, we went back to epidemiology."[17] Karen justified the use of animal experimentation with the fact that certain biological systems function similarly across several species: "We can assume that the inflammation mechanism is preserved across the species barrier. When I started working on inflammation, I took a database that lists all the genes potentially involved in inflammation. I took them all without looking at all to see if they were found in animals, in this, in that".

To sum up, experimentation on mice allows epidemiologists to conduct experiments that are impossible in humans for ethical reasons (e.g., in testing separation stress between mother and child), and to avoid experimental constraints (e.g., availability of biological data) or temporal limits (e.g., observing intergenerational effects). They expect that the biological markers identified will provide reliable proof, established in a controlled environment, of the existence of a biological pathway between the exposure of interest (i.e., social adversity) and a health outcome. They define the purpose of mouse stress protocols as to elucidate how stress acts biologically, not to investigate its actual effects in humans: "Mice eat the same, behave the same, sleep the same. […] In humans, there's always a cocktail effect. Humans eat pesticides, food additives, they breathe polluted air, they smoke/do not smoke, they drink alcohol. They eat fatty, rich, sweet, salty products. They smile, they are happy, they are unhappy. And that—all of that—it interacts" (Ada, project leader).

At the same time, EARLY's social epidemiologists are ambivalent about the scientific utility of the mouse model for their own work. Their concerns reveal their commitment to the complexity of the experimental settings in the lab, and of the social environments studied (Nelson 2018, p. 142). First of all, they question the extent to which laboratory protocols stabilize experimental situations, as environmental conditions are less controllable and standardizable than expected. In particular, a minor change in the handling of the mice can alter their behavior: "We used to house mice in a small room and we moved them to a larger room. And we can't quite reproduce the same results. Because of the large room and because more people come and go, all the animals are stressed all the time. So our model doesn't work anymore, because even the control group is stressed" (Marieke, Ph.D. student in molecular biology). While biologists working on stress are very aware of the problem, especially when they have extensive training in the behavioral sciences, epidemiologists discover its prominence during the course of the project: "We realized

[17] David Barker mentions parallel findings between epidemiological surveys, clinical and animal research on the long-term effects of prenatal nutrition, pointing "to the importance of long term programming in early life" (Barker 1990, p. 1111).

that they had sources of variability much more frequent than they thought. They don't control everything" (Ada, project leader). The epidemiologists' response to the complexity and variability of the experiments is quite similar to that of biologists (Lappé 2018; Chiapperino 2019; Nelson 2018; Niewöhner 2020): they see it as further evidence of the relevance of studying the effects of the environment on gene function, particularly through epigenetics: "For us it's great because it shows that even in situations we think [are] under control, tiny differences in the environment can alter the experimental results, underlining how not everything is genetic" (Ada). At the same time, they deplore biologists' attempts to eliminate sources of variability rather than to integrate them into their analyses: the "extra-factual work" (Nelson 2018), especially the care work (Lappé 2018), and its effects on the experimental situation remain invisible.

Epidemiologists also question the ability of the experimental protocol to model social environments in a manner suitable to social epidemiology. It is not a matter of comparing the environments of rodents and humans, let alone rendering them equivalent. Instead, assessing the validity of the experimental model "involves an evaluation of both the biological features of the experimental organism being used and of […] the environment in which the organism develops" (Leonelli et al. 2014, p. 4). In other words, epidemiologists seek to achieve balance between the functional value of animal experiments (i.e., their capacity to identify biological mechanisms that may be at play in humans) and their representational potential (i.e., the reproduction of human behaviors or pathologies; Lewis et al. 2013). At the time of our interviews, the research conducted on mice had provided preliminary results: in mice exposed to maternal separation stress, the genes involved in motivation showed different methylation profiles in the brain. In mice exposed to maternal separation stress and nutritional stress this difference disappeared; however, the mice become obese. The epidemiologists had not yet investigated in their human cohort whether exposure to the selected social adversities resulted in the same epigenetic marks. However, these results looked promising for the purposes of identifying certain biological effects of social adversity, thus demonstrating the functional value of the animal models: "We can imagine that there's a biological mechanism behind this. When we see that the two stresses that mice are exposed to interact or compensate for each other, it may suggest things in humans" (Ada, project leader). At the same time, epidemiologists credit animal experimentation with a certain representational potential. Even if the social adversity inflicted on mice was not representative of how adversity manifests itself in humans, the accumulation of stressful situations provides, in the epidemiologists' view, a more accurate model of human environments than a single type of stress taken in isolation. Epidemiologists' appreciation that EARLY does not fully grasp the complexity of social environments extends to the animal experiment and the human cohort study alike, as both components of the project only deal with environmental exposures with measurable physiological consequences. In the experiments on mice, this criterion precludes the study of protective or restorative social environments: the biologists consider it too difficult to adapt their protocol so as to

include "environment enrichment".[18] In the cohort study, the epidemiologists primarily focus on forms of social adversity that produce physiological stress—which they measured in previous projects by scores of allostatic load—even though they had fine knowledge of the various and disputed meanings of social adversity: "When it comes to psychosocial stress, the first two questions an epidemiologist asks are: How do you measure it? And is what you measured really what you wanted to measure? So we wanted to study an adversity that is commonly accepted as producing stress. For us, the gold standard for measuring stress is its physiological measures" (Alexis, senior researcher in epidemiology). Eventually, in communication with the biologists, the epidemiologists used social adversity interchangeably with chronic stressors or cumulative stress. Terminological indeterminacy facilitated navigation between experiments on mice and epidemiological research, and social adversity became a loosely defined "boundary concept" with strong cohesive power facilitating collaboration across disciplinary boundaries (Löwy 1992).[19] At the same time, the EARLY project set aside forms of social adversity that might not have strong physiological manifestations and did not account for possible resilience to stressors. This operationalization of social adversity in EARLY impeded collaboration with the sociologist involved in the project. This sociologist understood very well the experimental constraints of the experiments on mice, and agreed that the animal model had a high functional value. However, he expected social epidemiologists to have more flexibility in defining experimental protocols and was dismissive of how the validity of the experimental context was defined in EARLY (Leonelli et al. 2014). Its low representational potential made it of no interest, in his opinion, to social epidemiology: "the attempt to reproduce social phenomena in the laboratory seems absurd. The problem is that you model these notions of stress, adversity, in the non-human animal model, as to whether one licks the little one enough or not. Where is the social? It's a bit of a stretch to reduce maternal care to licking" (Pierre, senior sociologist).

Epidemiologists manage their ambivalence towards the scientific value of experiments on mice for social epidemiology in two ways: they accept that the stabilization of experimental situations comes at the price of rendering its variability invisible; and they prioritize the search for biological mechanisms over the representativeness of social environments modeled in the laboratory. We will now explore how epidemiologists are uncertain whether their interdisciplinary project will serve a

[18] Environmental enrichment designates changes in the environments of animals held in captivity that aim to improve their general well-being. Marieke, a Ph.D. student in molecular biology in charge of conducting the experiments on mice, said she would have liked to integrate "small toys for mice so they don't get bored". However, her Ph.D. supervisor declined this request, arguing that adding these elements might render the results non-cumulative with previous work: "If we now place a small tunnel in their cage, we can no longer say that they have suffered the same stress as those of two years ago" (Marieke). Chiapperino (2019) has studied one of the few labs in environmental epigenetics that set up "enriched" environments so as to consider a more complex vision of social environments.

[19] I. Löwy defines "boundary concepts" as a class of "boundary objects" (Star and Griesemer 1989) that "facilitate the constitution and the maintenance of heterogeneous interactions between distinct professional 'groups'" (Löwy 1992, p. 375).

conception of public health policy that addresses the social determinants of health inequalities.

Sending the right message: credibility tactics against potential misuses of their research

At the time of our interviews, the social epidemiologists were still a long way from producing public health recommendations based on EARLY; however, they emphasized their goal of identifying the social determinants of health inequalities and of providing population-based public health recommendations. Their previous research on allostatic load as well as their references to the concept of biological embodiment position them among social epidemiologists who promote a 'critical physiology'—that is, who argue that physiological measures reflect socio-historical contexts (Arminjon 2016) and that public action should target the socioeconomic conditions that produce individual pathologies. While established in social epidemiology, this approach remains marginal compared to the biomedical perspective that aims to correct individual deviations from health norms. Epidemiologists were concerned that their work in social epigenetics could give credence to this biomedical perspective, coupled with an individualistic vision of health risks and inequalities, especially since it claims to provide molecular evidence of the biological embodiment of stress and its intergenerational effects.

The epidemiologists believe, however, that the EARLY project should not support such policies, as the cumulative stress model focuses on adverse environments rather than on single adverse events or individual behaviors. In addition, they do not view the experiments on mice as placing emphasis on the responsibility of mothers, even though the experimental protocol for psychosocial stress aims to study the behaviors of mouse mothers and how their relationships with their pups affect their health. Yet, in the epidemiologists' discourse, it is as though the cumulative stress model escapes a "politics of experimental design" (Kenney and Müller 2017; Sharp et al. 2018) targeting mothers, which operates by associating their centrality in the experimental situation with social stereotypes about maternal roles and responsibilities (Chiapperino and Panese 2018).[20] But at the same time, EARLY's social epidemiologists know that the experiments on mice can be interpreted differently, as they contribute to the DOHaD perspective in behavioral and developmental biology, which in their view conveys a radically different public health message than their own—pointing to individual responsibility, especially that of mothers; emphasizing early-life determinism rather than biological plasticity over the life-course (Müller and Samaras 2018), and employing different credibility tactics, such as outright animal-to-human extrapolations. At the end of 2018, we joined the epidemiologists in attending the annual congress of the DOHaD French society. We observed how they strongly disapproved of certain ways biologists presented their results.[21] In

[20] As emphasized below, this is a major source of disagreement with the sociologist involved in EARLY.

[21] DOHaD biologists are much more nuanced in other circumstances, for instance when they reflect on their practices during sociological interviews (Chiapperino and Panese 2018). The biologists of the EARLY project also stress the importance of the broader context for putting mothers under stress. Vivi-

particular, a post-doctoral researcher presented how he had used a rodent model to study the effect of weight change in a pregnant female mouse on the health of her newborn pups. At the end of his presentation, a senior researcher from the audience asked him about public health recommendations to be implemented. The post-doctoral researcher answered that the French High Authority of Health already recommended that doctors warn obese women of the risks associated with a possible pregnancy. The senior researcher then argued that much stricter measures should be taken—without specifying what these measures should be. In short, she used the results of an animal experiment on about 30 mice to suggest broad public health measures that could potentially restrict individual freedoms. The social epidemiologists involved in EARLY did not deny that weight gain or loss during pregnancy can have an effect on health, but pointed out that animal models do not allow quantification of this impact in humans: "The real question is […] does it explain 10%, 50% or 1/1000 of the phenomenon?" (Alexis, senior epidemiologist). They criticized the tendency of some biologists contributing to the DOHaD perspective to oversell their research by emphasizing its relevance for public health: "It's ridiculous to make a conceptual leap from the non-human animal model to "there's now enough evidence to say that an obese pregnant woman is going to create problems for her child." And on that basis, telling women to lose weight before they get pregnant? And there are people in France who are very much in favor of these actions. […] As a researcher and as a woman, I've always found it really disturbing" (Ada, project leader).

EARLY's epidemiologists are also concerned about how the mainstream press reports on environmental and social epigenetics and fear that their aim of intervening in the social milieu may be misinterpreted as an assertion that each individual bears the responsibility for their health. Their opinions are very similar to the conclusions drawn by social science researchers (Pentecoste and Meloni 2020; Richardson et al. 2014; Chiapperino and Testa 2016; Lappé 2016), some of whom they have met at conferences or whose papers they have read. By pointing to the biological effects of individual behavior, social epigenetics could be used in the future to promote repressive public health measures focused on individuals, especially in cultural, legal and political contexts that promote individual responsibility in healthcare over social responsibility[22]:

> Epigenetics [...] raises, for example, the question of the responsibility of one generation towards the next or the value of health in relation to that of other

Footnote 21 (continued)
ane, for example, told us: "Thanks to the stress model of maternal postnatal separation, we can draw attention to the fact that this is a critical period. And that women who become single may be more at risk of transmitting chronic stress to their child, which would be harmful in adulthood".

[22] In their view, social epigenetics could be used to establish new surveillance modalities for pregnant mothers and newborns and justify the need for preconception care. The EARLY's social epidemiologists point to an example in the United States: in the state of Tennessee, mothers have been sentenced to prison terms for having consumed illegal drugs during their pregnancy, if it caused their child to become disabled (Tennessee Senate Bill SB 1391, passed by the House on April 9, 2014). The bill does not rely on scientific evidence provided by epigenetics, however the social epidemiologists believe that social epigenetics could lend more credence to such policy measures.

> freedoms. It also raises questions about the implementation of policies that focus on the individual versus those that focus on the social and collective conditions. (Ada, senior researcher in epidemiology)

The social epidemiologists adopted several credibility tactics to avoid possible misinterpretation of their research. They concluded some of their oral presentations (e.g., during training courses for health professionals, seminars with social scientists, and talks during the annual congress of the French DOHaD society) with slides in which they criticized sensationalist journalistic discourse about social epigenetics. In addition, they were cautious in presenting the potential impacts of their research. On the scientific level, they insisted on the importance of positioning epigenetic changes linked with social adversity in the complex causal chains through which everyday experiences impact cells, organs and physiological functioning. They also reminded their audiences that these social experiences are diverse, and that they occur in distinct temporalities. With regard to public health outcomes, they recalled that the vocation of epidemiology is, on one hand, to produce population level predictions of a probabilistic nature, and not to establish individual diagnoses; and on the other hand, to produce recommendations for categories of populations, and not to prescribe behaviors or actions:

> I have quite recently added precautionary slides on how our work can be used. Because I've been told, "You've been working on adversity and motherhood, you're saying that if a child has gone through this when he was little, he's going to die sooner"—with the aim of making a diagnosis based on our definition of adversity, which is a tool for epidemiological work, and of being able to say, "If this child has three adversities, he's at risk and we have to take him out of his environment." That worries me a lot. (Alexis, senior researcher in epidemiology)

In contrast to biologists who cite research on rodent models as evidence in itself for human populations (Lloyd and Raikhel 2018), and to epidemiologists who mention epigenetics for the purpose of giving "molecular credibility" to observational studies in human cohorts (Kenney and Müller 2017, p. 38), these social epidemiologists seem to take particular care to never say or write that experiments on mice prove that similar biological responses are at work in humans. Their communication is remarkably subtle, as they only refer to laboratory experimentation to hypothesize that the phenotypic changes observed in humans following environmental exposures may be underpinned by a biological mechanism. Furthermore, epidemiologists are careful to point out that this needs to be confirmed by further experimental research and that this would not infer anything about the actual impact of such environmental factors in real life:

> If the changes observed in the brains of mice can also be observed in the blood (which remains to be analyzed), and if these same changes are observed in the blood of people subjected to adversities during childhood, we can imagine that these adverse exposures are likely to be associated with epigenetic changes in the reward circuit in humans, which can then be asso-

> ciated with behaviors such as smoking, alcohol, or even pathologies such as obesity found in greater proportion in people exposed to adversities. (Ada)

Lastly, their credibility tactics seem to have limited success with their French colleagues in the social sciences, as already illustrated by the critical stance of the sociologist involved in EARLY. While the social epidemiologists would like to get closer to the social sciences, they fear being accused of 'biologizing' the social. We attended a talk given by Ada in an auditorium packed with social science students and researchers at a French University, during which she took a defensive stance even before being asked how she studies the biological embedding of social environments: "We talk about a social biology, not about sociobiology.[23] I don't explain the social with biology. I'm trying to explain biology with the social. That's different, it's a total reversal. That's important!" (Ada, project leader). She then backed up her argument by emphasizing that sociologists promote the same shift in perspective: "That's what Meloni says in his book—that we have the possibility with epigenetics that the biological opens up completely to environmental influences. And so, we have the impression that the social has a causal role in biological functioning. That too is new."[24] In their view, French social science researchers are either suspicious or don't grasp the novelty of their approach: "For someone in the social sciences, explaining that social organization is likely to influence the health status of populations is nothing new" (Ada). On the contrary, these social epidemiologists find interdisciplinary dialogue with anthropologists and sociologists to be smoother, more widespread and recognized in countries such as the United States and the United Kingdom, for two reasons: the disciplinary boundary between health sociology and social epidemiology is much less defined, with the two specialties frequently collaborating in epidemiological cohort studies; and there are more sociological studies that explore the interpenetration of biological (genetic and epigenetic) and environmental factors in the constitution of social inequalities (Shostak and Freese 2009; McEwen and McEwen 2017).

Conclusion

The scientific literature as well as the general media tend to present social epigenetics as a promising area of research for discovering the mechanisms of the biological embodiment of social environments and providing evidence of their physiological effects during the life of an individual and their offspring. Much of this research is done on animals, which are used by biologists to model human behaviors and environments. In-depth laboratory studies have shown that biologists engage with "distinct layers of complexity" (Chiapperino 2019), in considering experimental settings and human social environments modelled in the lab. Biologists have also

[23] In the mid-1970s, the term 'sociobiology' was introduced to designate the study of the biological basis of human and non-human animal social behavior (Wilson 1975).

[24] During her talk, Ada referred to Meloni (2016).

been described as "pragmatic reductionists" (Niewöhner 2011) who are very aware that their experimental systems imply oversimplifications, but see this as the price to pay for producing knowledge that may have both scientific validity and relevance for human health. While this body of work provides very rich descriptions of the "complexity talk" (Nelson 2018) of biologists working on gene-environment interactions, as well as the "epistemic scaffolds" (op. cit.) they establish between experimental models and humans, there has been little inquiry into how epidemiologists make use of animal models to study the effects of environments on human health, and whether they engage in the same kind of complexity talk.

In this paper, we have addressed these issues by investigating a project focused on the epigenetics of social adversity during early life that involved close collaboration between social epidemiologists and biologists as well as occasional exchanges with social scientists, in the French context. Both the epidemiological and biological components of the project aimed to study the physiological effects of cumulative stresses—either multiple adverse events during childhood or a combination of psychosocial and nutritional stressors applied to mouse mothers and pups—and their underlying biological mechanisms. The scientific arguments supporting the "epistemic scaffolds" (Nelson 2018) between rodent experimentation and epidemiological research were borrowed from biomedical research in neuroendocrinology and research on the gut-brain axis. We have argued that the EARLY's social epidemiologists were ambivalent towards the scientific utility of laboratory experiments on rodents for studying the biological embedding of human social environments, as well as in regard to the capacity of this interdisciplinary project to advance their agenda for public health. We have emphasized that this research was conducted in France, where social epidemiology is less developed than it is in other countries, where analyses of the biological incorporation of social environments remain infrequent, and finally, where clinical epidemiology dominates, with the primary objective of uncovering individual risk factors. The EARLY project was initiated by two senior social epidemiologists eager to strengthen their specialty and develop an interdisciplinary dialogue in public health research that they thought would be too limited in France. For these social epidemiologists, close collaboration with biologists represents an unprecedented opportunity for gaining scientific credibility, whereas the prospect of uncovering the biological mechanisms that perpetuate social inequalities in health stands as a source of scientific enthusiasm and a "hopeful vision" (Nelson 2018, p. 72). We studied a project "in the making" and at a time when epidemiologists had not yet explored whether the epigenetic marks that biologists observe in animals under stress were also found in humans subjected to one or more situations of social adversity. This may explain why expectations, hopes and doubts are so prominent in their discourse. In a way, when observing this particular stage of the project we witnessed project participants expressing the kind of scientific uncertainty that tends to be overlooked once research is completed and published.

We have described how EARLY's social epidemiologists managed their ambivalence about experiments on mice and thus maintained their scientific expectations: in particular, by prioritizing study of the forms of social adversity that produce physiological stress, and by giving predominance to the functional value of animal experiments (their ability to provide a reliable measure of the biological manifestations of

social experiments) over their representational potential (their suitability for accurately representing human behaviors and environments). We have also depicted the credibility tactics they deployed to convince researchers outside of their scientific community and a wider audience that their research could point to the social causes of health inequalities. In particular, they differentiated their research from that of biologists from the DOHaD perspective, who in their view have the tendency to overestimate the representational potential of animal models, and to extrapolate animal-based research to human populations. In addition, they multiplied cautionary statements about how to interpret laboratory findings regarding the biological mechanisms induced by exposure to adverse social environments. Lastly, we emphasized the mixed success of their credibility strategies. These social epidemiologists run the perpetual risk that the potential public health benefits of their research will be dismissed outright by clinical epidemiologists who remain skeptical of the validity of the physiological measures of exposure to social adversity. Their results may also be misinterpreted by public health policy-makers as predictive of the health outcomes of individuals, whereas the ultimate goal of these epidemiologists is to improve the accuracy of population-level predictions. Finally, the use of animal models in social epigenetics proved to be a double-edged sword for these social epidemiologists. On one hand, it could provide evidence that social adversity is biologically embedded and intergenerationally transmitted through epigenetics, giving social epidemiologists a much-needed institutional legitimacy and respectability in the French context; on the other hand, it has the potential to legitimize health policies focused on individual responsibility rather than on the social causes of health inequalities.

More broadly, our study of a project involving biology and social epidemiology offers new perspectives on research practices in the post-genomic sciences, i.e., those research areas which criticize simple assumptions about genetic causality (Landecker 2016, p. 80) and emphasize "complexity, indeterminacy and gene-environment interactions" (Richardson and Stevens 2015, p. 3). Throughout this article, we have addressed how EARLY's social epidemiologists contribute to the "complexity talk" characteristic of the post-genomic sciences (Nelson 2018), and we have related their "assumptions of complexity" to their epistemological commitments (op. cit., p. 23). We found significant similarities between their commitment to the complexity of experimental situations and that of biologists. After having experienced a moment of "complexity crisis" due to the unexpected variability of rodent experiments ("where they began to doubt that anything could firmly be said about genes and behavior at all"; Nelson 2018, p. 19), the social epidemiologists began to engage with ideas of "situated biologies" (Niewöhner and Lock 2018). It was through dialogue with the biologists that the epidemiologists acknowledged that even subtle environmental changes result in biological responses, but that they are rendered invisible to stabilize the experimental laboratory settings. We also found commonality in the way EARLY's social epidemiologists and biologists approached the complexity of human social environments to be represented in the lab. On this subject, epidemiologists do not draw a sharp distinction between the reductionism at work in epidemiological research and that found in laboratory experiments: they are aware of being "pragmatic reductionists" (Niewöhner 2011) when choosing exposure variables in their cohort, just as biologists are when designing their

stress models. At stake in interdisciplinary dialogue is ensuring that epidemiological and biological research protocols convey a similar, albeit limited, representation of the complexity of social environments, which was conceptualized in EARLY as an accumulation of adverse or stressful situations.

This article also addresses how interdisciplinary exchange with the social sciences may contribute to dialogues on complexity in the post-genomic sciences. Sociological or anthropological investigation may aim to elucidate which visions of the social are embedded in the experimental settings of environmental and social epigenetics (this was also our original intention) and to guide researchers in clarifying the assumptions embedded in their work as well as the social issues involved in its potential uses. Chiapperino and Panese (2018) describe the reflexivity of the scientists interviewed for their study as "thin and under-theorized" (p. 11). On the contrary, in the project we studied, social epidemiologists were highly reflexive, deeply concerned with how they defined and operationalized the social in their research, and relied on social science research to question the normativity of the experimental settings in social epigenetics as well as the public health messages their research could give credence to. While their reflexivity and their commitment towards interdisciplinarity are partly due to their personal research experiences, these qualities more broadly reflect the development of research perspectives in social epidemiology which advocate for more dialogue between and integration of epidemiology and social theory (Wemrell et al. 2016), in particular the life course approach to chronic disease (Ben-Shlomo and Kuh 2002), and the theory of the biological embodiment of health inequalities (Krieger and Davey-Smith 2004). While they may remain unmet in other research fields, ongoing calls to develop "sociological-cum-biological research programs" in environmental and social epigenetics (Meloni 2013) find a particularly strong echo within these two research agendas in social epidemiology. In this context, our study provided a space where epidemiologists could explain their scientific objectives and freely express their ambivalence, as well as the tensions and contradictions inherent in their approaches. Having expressed from the outset our interest in studying whether social epigenetics may renew the interdisciplinary dialogue between the biological sciences and the social sciences, epidemiologists did not consider us a priori suspicious of the study of the biological incorporation of social environments, an attitude they had previously observed among French social scientists. While they needed to be more assertive in other communication arenas, they freely expressed their difficulties and reflected on the limitations of interdisciplinary dialogue with biologists. Our study was also an opportunity to evoke the relative failure of their previous exchanges with sociologists who criticized the implicit visions of the social embedded in the experimental settings with mice, or even disagreed with the importance of discovering biological mechanisms.

Social scientists have argued that tensions "between collective and molecular/individual interventions [are] at the core of epigenetics' biopolitics" (Chiapperino and Testa 2016, cited by Chiapperino 2019), and that environmental and social epigenetics may sustain several social and political imaginaries (Chiapperino and Panese 2018; Lamoreaux 2016). Our study of the EARLY project contributes to this discussion, as this interdisciplinary project navigates between three conflicting imaginaries. The first is put forward by social epidemiologists working on the

biological embodiment of social conditions: it is oriented towards identifying the social causes of health and illness by demonstrating that exposures to environments harmful to health (e.g., exposure to toxicants, lack of social support, reduced access to medical care etc.) are socially patterned, defining social interventions at different levels (neighborhoods, households, low-income populations, etc.) and ultimately reducing social inequalities in health. Projects such as EARLY offer hope of providing biological evidence of how deprived social environments, where people experience an accumulation of stresses, leave their marks on bodies. However, this imaginary struggles to find any support among French social scientists, who are either not convinced of the need to demonstrate biological proof of the influence of the social, or are alert to the risk of biologizing social adversity. A second imaginary was developed by clinical epidemiologists aiming to identify risk factors (e.g., age, blood pressure, diet, physical activity) for certain diseases, with the goal of designing prevention measures for at-risk populations. Central to risk-factor epidemiology are the measurement and statistical control of potential confounding variables, such as geographic location, genetic predisposition, diet, tobacco smoking, level of education and occupation. Social epidemiologists initiated the EARLY project with the desire to gain some of the credibility afforded to clinical epidemiology, and with the hopes of demonstrating that social environments are not just possible confounders in epidemiology, and that cumulative exposure to social adversity has measurable biological effects. However, they are concerned that their research might be taken up to identify risky behaviors (e.g., having a high-fat diet) and to provide a rationale for both "the micro-management of the individual body" and "the macro-surveillance of the body politics" (Saldaña-Tejeda 2018). A third and last socio-political imaginary is shared by biomedical researchers, among others: it aims to find, based on experiments on non-human animals, actionable biological targets for pharmacological or behavioral interventions. The reversibility of certain epigenetic marks linked with environmental exposures gives credence to this imaginary, as well as experimental results suggesting that by combining several exposures, researchers can cancel out the deleterious effect of a given exposure on the epigenetic machinery. Highly visible in the biological component of the EARLY project, this third imaginary strengthens that of clinical epidemiology by specifying the pharmacological treatments and interventions that could be proposed to at-risk populations. Finally, in a context dominated by clinical and biomedical approaches to health, the difficulties confronting these French social epidemiologists as they work to reinforce a socio-political imaginary supporting the study of the biological incorporation of social environments are reminders that social epigenetics can, in theory, feed competing imaginaries and potentially reinforce the notions of risk factors, individual responsibility for one's health, and behavioral prescription.

Declarations

Conflict of interest The authors do not have any competing interests—intellectual or financial—in the research detailed in the manuscript.

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François Romijn is a FNRS research fellow in sociology at the Université Libre de Bruxelles (LAMC Research Laboratory). He completed his Ph.D. (2018) at the School for the Advanced Studies in the Social Sciences (EHESS) & the Université libre de Bruxelles.

Séverine Louvel is associate professor in the sociology of science at Sciences Po Grenoble, member of the PACTE research laboratory and a junior member of the Institut Universitaire de France. In her current work she explores the research cultures of and sociopolitical expectations towards environmental epigenetics.