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Making sense of Mendelian genes

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An enduring legacy from the heyday of Mendelian genetics is talk of 'genes for'. Such talk suggests straightforwardly that genes make characters. But for over a century, thoughtful biologists have insisted such an understanding is mistaken. For them, a gene is a chromosomal difference that, when internal and external environments are otherwise equal, makes a phenotypic difference; 'genes for' talk is but shorthand for this more complex understanding. This paper examines the remarkable durability of the disowned, deterministic character-making understanding, placing particular emphasis on the role of the traditional, start-with-Mendel curriculum in investing that understanding with a heuristic power which later teaching may never fully displace. The paper also reports on recent experimental work exploring the potential of a reordered curriculum for teaching genetics without bolstering genetic determinism.

Evelyn Fox Keller's *The century of the gene* (2000) is the most famous obituary of the entity forever associated with Gregor Mendel (Keller 2000). But what kind of a life did the Mendelian gene ever really have, anyway? Haven't thoughtful biologists long regarded the idea of it as an oversimplification? Indeed, from early days, all kinds of complexity have been allowed for. At the same time, the power of Mendelian explanations to cut through complexity and expose underlying simplicity has been relentlessly showcased. In the spirit of Keller's subsequent book, *Making sense of life* (2002), I want in what follows both to exhibit this 'ambi-valence' (Keller 2002, 130) and to suggest how crucial it has been in making the Mendelian gene – and the determinism it underwrites – so long-lived. Although my analysis of what has made gene talk so durable will not coincide with hers, our accounts are complementary, to such an extent that that the curriculum reform experiment I shall describe at the end could well be considered applied Kellerism.

The Mendelian gene

Gene concepts are legion.[1] By 'the Mendelian gene,' I mean the entity that does the explaining in elementary genetics, e.g., in explaining why two blue-eyed parents can have only blue-eyed children. On the standard Mendelian explanation, there is a gene for eye colour, and it comes in two versions or 'alleles.' There is the brown-eye allele, which is dominant. And there is the blue-eye allele, which is recessive. The father's sperm and the mother's egg each carry only one allele. If the zygote formed from the union of these gametes brings together a brown-eye allele with another brown-eye allele, then the child will have brown eyes. If the zygote brings together a brown-eye allele and a blue-eye allele, then the child will also have brown eyes, because brown-eye is dominant. Only if the zygote brings together a blue-eye allele with another blue-eye allele will the child have blue eyes. A corollary is that, since blue-eyed parents can only ever contribute blue-eye alleles, two blue-eyed parents will have only blue-eyed children.

Note two features of the entity invoked in this example. First, the gene is either in the form of the dominant allele, responsible for the dominant character-version, brown-eye; or it is in the form of the recessive allele, responsible for the recessive character-version, blue-eye. The Mendelian gene is, in short, binary. Second, it is completely determinative, in the sense that the allelic pairs explain without remainder. There is no need to consider anything other than which allele ends up with which allele.

This definition emerged between 1900 and 1910, largely in the work of William Bateson and his research school at Cambridge. Although Mendel's 1866 paper 'Experiments on plant hybrids' furnished inspiration (Mendel 1866), the Mendelian gene is, it should be emphasized, in no straightforward way Mendel's. Yes, Mendel deliberately started his work with garden-pea varieties selected because they showed binary characters – seed color as either yellow or green, with no intermediates; seed shape as round or wrinkled, with no

intermediates, and so on – which were unaffected by context. And yes, he categorized each member of each character pair as 'dominant' or 'recessive,' depending on whether it was visible in the hybrid. But he did all of that as part of an inquiry not into inheritance but into hybrids, in particular the fate of hybrid characters in plants where such characters are not perpetuated intact. Furthermore, in explaining the patterns he derived, Mendel did not postulate the existence of discrete, paired, gene-like entities, but only character-making material, which mixed and unmixed down the generations. In Robert Olby's famous phrase, Mendel was no Mendelian (Olby 1979).[2]

The Mendelian gene as an idea (not an object)

To leave the matter of definition there, however, is to invite confusion over what, exactly, we are talking about when we talk about the life and death of the Mendelian gene. A distinction of Ian Hacking's comes in handy here, between objects and our ideas about them (Hacking 1999, 21–2).

Objects, on Hacking's distinction, are items in the world. They can come into being and pass away, either for science or full stop. In Versailles in November 2018, for example, the platinum-iridium standard kilogram was voted into retirement, to be replaced not by a new hunk of metal but by a value derived from Planck's constant. The standard kilogram ceased to exist for metrology, if not for physics. ('Le grand K,' and its official copies, will remain in their vault, to see whether they lose mass over time.)[3] Since 1980, there has, according to medical officialdom, been no smallpox virus in the wild, thanks to a worldwide eradication program. The smallpox virus, we hope, ceased to exist full stop, outside of a handful of secure government labs at any rate.[4] Where objects are in the world, our ideas about objects are in our heads. Ideas too, of course, can come into being and pass away. The history of science is notoriously full of discarded ideas about objects. The idea of the vortex

atom – the atom understood as a whirl of ether – is now a curiosity of Victorian physics. The idea of the ether itself, as something existing in the world, petered out in the early twentieth century.[5]

Why adopt Hacking's distinction? Because it steers us away from ambiguous talk, about 'the death of the vortex atom,' say, or 'the death of the ether.' On our best current physics, the vortex atom and the ether never existed, and so, strictly speaking, cannot have ceased to be. Rather, what ceased to be were beliefs in the existence of these objects. To disambiguate in this way can itself give life to a new line of questioning about the *interaction* between existence beliefs and the world itself (Hacking 1999, 27–8 & 31–2). The historiography of genetics furnishes a shining instance in Robert Kohler's *Lords of the fly* (1994), about T. H. Morgan's fly room at Columbia (Kohler 1994). Although initially skeptical about the existence of Mendelian 'factors,' Morgan came to preside over the research program that, through fruit-fly crossing experiments, secured the identity of those factors as nothing other than bits of chromosome. (Another Hacking borrowing: if you can map them, then they are real.) At a distance, one might have guessed that what Morgan and his students did was to collect fruitflies and then check, first without and then with the aid of microscopes, whether the patterns of inheritance exhibited fit with Mendelian expectations. Not at all. Wild *Drosophila melanogaster* does not 'Mendelize.' Cleanly binary characters are conspicuous by their absence, so there is little scope for spotting such tell-tale Mendelian signs as uniform dominance in offspring, or the 3-to-1 dominant-to-recessive ratio in the offspring of offspring (Kohler 1994, 28–9). Morgan and his students had to breed Mendelizing fruitflies into existence, by breeding out all of the pattern-wrecking variability (Kohler 1994, ch. 3). The chromosomal Mendelism that the Morgan group set out in *The mechanism of Mendelian heredity* (1915) co-evolved along with the lab-bound fly lineages to which that theory now answered.[6]

Kohler's book should be a permanent reminder that there is a marvellously interactionist history of the Mendelian gene to be told, rich with objects as well as with ideas about objects (Radick 2003, 197–8). Here, however, I will touch on such interactions only incidentally. My concern is mainly with the life and death of the idea of the Mendelian gene. I wish to show how a new interpretation of the nature of the life of this idea throws light on its remarkable ability to elude death.

Two ways of understanding the idea of the Mendelian gene

Although the term 'gene' is not used in *The mechanism of Mendelian heredity*, the Morgan group's discussion there of how Mendelian talk should and should not be construed – and how much scope there is for misconstrual, even among experts – remains peerless. The book's retention throughout of the older term 'factor' was certainly idiosyncratic. As the bibliography testifies, 'gene' had spread rapidly among geneticists after its introduction in 1909 by Wilhelm Johannsen. Morgan's own co-authors, Alfred Sturtevant, Calvin Bridges, and Hermann Muller, had used 'gene' in the titles of cited papers. But *The mechanism of Mendelian heredity*, aiming at a more general biological readership, carried a message for which 'factor' was indeed a better fit than 'gene.' Over and over again, the reader is reminded that whenever chromosomally borne hereditary factors are identified as 'for' a visible character (e.g., eye color), or for a version of a character (e.g., red eye), that identification is limited to situations where the many other factors – hereditary but also developmental and environmental – influencing that character or character-version are held constant. Absent such constancy of background, all bets are off.

After a first chapter introducing the pairing and segregation of chromosomes as underpinning the pairing and segregation of Mendelian factors, the second chapter, misleadingly entitled 'Types of Mendelian heredity,' drives home how phenomenally complex the relationship between a factor and an associated character can be. It is not merely, as Bateson had stressed, that simple 'dominance'/'recessive' relationships cannot be counted on, or that a single factor can affect multiple characters, or that a single character can be affected by multiple factors. A change in temperature, for example, can change the character associated with a given genetic constitution, as Erwin Baur had found in work with primroses. Raised at around 20º C, the white primrose, P. alba, produces white flowers and the red primrose, P. rubra, produces red flowers. But when the temperature rises to 30º C, P. rubra produces not red flowers but white ones. The lesson drawn is as much linguistic as biological:

> Strictly speaking, we should say, not as we generally do for brevity's sake, that the difference between the two races is that one has white, the other red flowers, but we should say rather that P. rubra reacts at 20º by producing red, at 30º by forming white flowers; P. alba, on the other hand, reacts both at 20º and at 30º by producing white flowers. The constant difference between these races is not their color, but in the possibility of producing specific colors at certain temperatures. (Morgan et al. 1915, 38–9)

More examples follow, of environmental influences but also developmental influences, glossed expansively:

> ‘Age,’ too, is in a sense an environmental condition, which influences the development of characters. Thus a white flower may change to purple as the plant gets older, or the flaxen hair of a child may turn to brown when he becomes a man. But, as in the case of other ‘environmental’ conditions, age may not have the same effect on individuals with different factors; in this way it comes about that animals or plants which differ by certain factors may show a difference in character only at certain ages, or may not show the same difference at all ages. (Morgan et al. 1915, 42)

The Morgan group has acquired a reputation for relegating development to the sidelines, as no business of geneticists, whose job is to understand transmission. But that is at best unfair caricature. They stressed that if, as seemed clear, each cell in a developing organism receives the same set of factors, then embryological differentiation can take place only if, as regional peculiarities establish themselves, factors are differentially affected. No less than temperature differences or age differences, then, the chemical differences distinguishing one region from other regions could be necessary for a factor’s expression. (‘Thus when we speak of factors for eyes or for legs, we really mean factor-differences which can produce effects only in the eye, the leg, or other regions of the body’ (Morgan et al. 1915, 44–5.) Yet another context that could matter was the complex of other factors present in an organism. Without the factors required to make an eye, say, an eye-color factor can have no effect; and such effects as it does have can be different depending on interactions with other eye-color factors present.

Brilliantly, these complications come across not as problems for chromosomal Mendelism but as taken-for-granted presuppositions. It is precisely because everything is interacting with everything else, all the time, with the most complex consequences, that we

need to study heredity in the Mendelian manner, using organisms purged of variability and raised in controlled environments. Anyone who understands that, as Morgan and company put it at the end of the chapter, 'every character is the realized result of a reaction of hereditary factors with each other and with their environment,' will grasp the wisdom of a method of inquiry which imposes constancy on the factorial and environmental background in order to investigate how differences at a single locus of a single chromosome can affect a body (Morgan et al. 1915, 46).

Of course, there is a catch: the need not to forget all the contrived homogeneity behind Mendelian 'factor for' and 'unit character' talk and, conversely, the need to remember the status of that talk as abbreviating much more cumbersome talk about what was observed when, against a backdrop of factorial, developmental, and environmental constancy in a particular set of organisms, a particular change took place at one locus. Concern that new Mendelians, like some old ones, might need extra coaching in order to keep the limitations in mind surfaces throughout the rest of the book. A discussion of the 'sex factor' known to be carried in the X chromosome, for example, goes out of its way to disabuse the reader of the notion that the factor is, in any non-simple way, for sex:

> As in the case of sex limited characters, so in the case of sex itself there must be many factors in the fertilized egg that are as essential to the development of sex as are the sex factors themselves, but as they are distributed to all individuals alike, they are not thought of as differentiators, but as forming the chemical background on which the single or the double amount of the sex factor gives its result. It is quite conceivable that one or more of these other factors might so change that the sex differentiators would become inoperative or even change so that those other factors themselves become the differentiators that determine sex.

> The environment – the outer world – is also one of the components that enters into the development of every individual. A specific environment is one of the conditions of development. Why then, it may be asked, may not the environment turn the scale and determine sex? As a general proposition this must be acceded to at once – it is entirely a matter of proof. If there is an internal mechanism to determine sex in a normal environment it is quite conceivable that it might be supplanted in a new world. It is a question of evidence as to how often, if ever, this occurs. It is furthermore quite conceivable that some animals have no internal mechanism to regulate sex but depend on difference in their medium. If such an environment can be discovered it would be sex determining in the same sense in which the term is here employed when the sex differentiators are hereditary factors. (Morgan et al. 1915, 95–6)

Morgan and company even declare at one point that it makes no odds to their 'factorial hypothesis of sex determination' whether, in a given case, the sex-determining factor can be proved to be environmental rather than genetic (Morgan et al. 1915, 106–7). For them, to be a student of inheritance is to be interested in differences that make a difference, whatever the source – though, for the student of Mendelian inheritance, chromosomal differences must take pride of place.

The book's concluding chapter, entitled 'The factorial hypothesis,' reinforces all these lessons and then some. Using the factor for red eye in flies as an example, it begins by setting out two ways of expressing the relations between factor and character. On the first way, a factor is a segregating, intra-gametic something whose effects, upon combination and recombination, explain the 3-to-1 ratio of red-eyed flies to white-eyed flies in the second hybrid generation. On the second way, there are gametes which produce red eyes and

gametes which produces white eyes, and these gametes differ by just one factor-difference. We go on to learn that, like pretty much every character, eye color in flies is under the influence of multiple loci (25 were known by 1915). Can we nevertheless talk of a mutation associated with, say, pink eye as 'the cause of pink'? Yes, because 'we use cause here in the sense in which science has always used the expression, namely, to mean that a particular system differs from another system only in one special factor' (Morgan et al. 1915, 208–9). And again, the chemical ramifications of a change at a single locus may affect multiples characters, not just the character where the effect is so conspicuous as to tempt ill-advised talk of a 'unit character.' ('So much misunderstanding has arisen among geneticists themselves through the careless use of the term "unit character" that the term deserves the disrepute into which it is falling' (Morgan et al. 1915, 210).)

So there are two ways of understanding 'factor,' but they are not equal, since the first, factors-for-unit-characters way needs the second, differences-that-make-a-difference way in order not to be misleading unto falseness. As the Morgan group put it, by way of sharpening the contrast between their Mendelian picture of development-and-inheritance and the Weismannian picture, with its vestigial preformationism:

> [t]he factorial hypothesis does not assume that any one factor produces a particular character directly and by itself, but only that a character in one organism may differ from a character in another because the sets of factors in the two organisms have one difference. This point is not likely to be misunderstood by any one who grasps the meaning of the factorial hypothesis. (Morgan et al. 1915, 211–2)

As to how, exactly, factor-differences manifest themselves developmentally as character-differences, they acknowledged not merely the interest of the problem for experimental

embryology but the possibility that whatever would be learned would help improve understanding of heredity. Even so, there was, in their view, no need to wait for that future science of development in order to proceed with the current science of heredity, since, understood as they understood it, Mendel's law 'stands as a scientific explanation of heredity, because it fulfils all the requirements of any causal explanation' (Morgan et al. 1915, 227).

Ambi-valence analyzed

By 1915, then, we find, among elite practitioners of Mendelian genetics, exasperated acknowledgement that the Mendelian gene had all too often been mistaken, even by geneticists, for a simple character-maker rather than a complex difference-maker. To talk of a 'gene for a character' was, for the Morgan group, to use shorthand for a causal relationship manifest only when, against a particular genetic, developmental, and environmental background, differences at a chromosomal locus produce differences in a character. Change something in the background, and you may well change, or even eliminate, the effect on the character. When the chromosomal differences produce character differences so cleanly differentiated as to be binary – red or white eyes in flies, blue or brown eyes in humans – that is an artifact, contrived or accidental, of the system, not an intrinsic property of the allele pair.

It was, and remains, hard to make this more complex gloss on the Mendelian gene stick.[7] Why? An important clue lies, I think, with the nature of the ties binding 'gene for' talk to the gene-as-difference-maker notion. Those ties are not, on inspection, straightforwardly those of an abbreviation to what it abbreviates. Abbreviations do not, after all, usually cut loose semantically. No one who understands English is in danger of mistaking, say, 'USA' for anything other than the United States of America, or 'USB' for anything other than the sort of computer port so labelled (though only experts – along with non-experts who read instruction manuals – will know that the label is an acronym of

Universal Serial Bus). Furthermore, abbreviations typically arrive on the scene *after* what they abbreviate. In the case of the Mendelian gene, however – and as Morgan and company well knew – it was the early critics of Mendelism, among them Morgan, who had insisted that, contrary to Mendelian emphases on the factorial and the binary, the same hereditary factor could have different effects under different internal and external conditions.[8] In *The mechanism of Mendelian heredity*, the Morgan group were fighting a rearguard action in declaring entrenched genes-as-character-makers talk to be shorthand for genes-as-difference-makers talk.

But if the relationship between the two kinds of talk isn't as intimate as that between an abbreviation and what it abbreviates, neither is it as distant as that between two meanings arbitrarily yoked together under a single term. One of Evelyn Fox Keller's most illuminating reflections on the semantic lives of 'gene,' and her own analyses of it, occurs in an endnote in *Making sense of life*:

> My principal claim in *The century of the gene* was that the term gene has now acquired so many different meanings that its continued usefulness is in doubt, whereas here I argue for the productivity of linguistic imprecision. The question thus arises, when is imprecision productive and when counter-productive? My answer is this: imprecision is productive in the absence of literal meanings, and ceases to be productive either when literal meaning is in manifest conflict with implicit meanings (as happened with 'gene action' once the chemical identity of the genetic material was agreed upon) or when two or more different literal meanings have been established (as is now the case today for the gene). (Keller 2002, 321, first note 7)

Interpreting the above in light of the content of *The century of the gene* and *Making sense of life*, I take the point to be something like this. When a science is just getting going, and even well into its maturity, a central term's having multiple meanings – and so becoming 'ambi-valent,' as she puts it – may be not just unproblematic but valuable, notably when those meanings supply the metaphors that can keep a research community moving forward until, thanks to that forward motion, eventually the metaphors are no longer needed.[9] So, 'gene' coming to mean both something stable, like an atom, and something active, like an organism, served geneticists tolerably well through the first three quarters of the twentieth century. To be sure, there was a price to be paid occasionally, e.g., the inability of the community to do anything with the Morgan group's insights into the variable nature of gene expression during development (which Morgan again highlighted in the 1930s).[10] But progress since the 1960s did not so much literalize the metaphors as replace them with molecular knowledge for which the metaphors were wholly inapt. Functional stretches of DNA, it turns out, are nothing like atoms, and do not act in anything like the way organisms act. There are, it turns out, no such things as those durably nuggety yet easily dominated entities called 'alleles for blue eyes' in humans. There is just DNA across a large number of loci which, for any number of reasons, result in sufficiently low quantities of melanin for an iris to look some shade of blue.[11] Hence Keller's obituary for the gene, and her hope for new concepts, expressed in new language, the better to realize the promise of the new knowledge.

Returning to the character-maker versus difference-maker understandings of the Mendelian gene, they are, it seems to me, neither metaphoric nor in tension with each other. But Keller's larger claim about 'gene' as corralling together different conceptions, in a way that brought cognitive benefits as well as costs, seems to me spot-on, as does her related claim that, whatever the benefits in the past, the costs now outweigh them.

The 'gene for' locution is, I submit, straightforwardly shorthand for genes-as-character-makers talk and only unstraightforwardly shorthand for genes-as-difference-makers talk. In principle, becoming educated in genetics involves the displacing of the character-makers conception by the difference-makers conception, even as 'gene for' talk remains constant. In practice, however, the situation is much trickier, and not just because some people go further in their genetics educations than others. The very structure of a typical genetics education endows the character-makers conception with independent life, by investing it with heuristic power. Begin your education in genetics with Mendel's peas, and you will learn not merely about a case where, you are told, binary characters are determined by genes for those characters, and by nothing else. You will learn too that many apparently more complicated cases can be made tractable by treating them in the first instance like Mendel's peas. (And if you don't learn that, you won't pass.)[12] Of course you will go on to learn about all sorts of exceptions to your rule of thumb, and the reasons why those exceptions are the way they are: the effects of other genes, epigenetic modifications, the interplay of development and environment, chance. By the end of your education, you will know, of course, that 'it's not all in the genes,' and become annoyed with anyone who suggests that you think otherwise. But the Mendelian, treat-'em-like-the-peas rule of thumb will remain in place. It will guide your reasoning and even – in the way of heuristics – perhaps your unreasoned reflections and reactions too, with much reinforcement from the wider culture in the form of gene-personifying 23-and-Me ads, 'gene for' discovery stories, jargon talk of what is in an organization's DNA, and so on. You will affirm genes-for-characters determinism in your actions and attitudes while rejecting it if asked about it, because you know that it's false.[13]

'Again and again,' writes Theodore Porter in his recent study of the role of insane asylums in the making of the science of heredity, 'geneticists acknowledged the inadequacy

of single-gene explanations in one breath and then proceeded in the next as if heredity could mean nothing else' (Porter 2018, 321). That was the situation in 1930. And now, in the age of proliferating –omics, including personalized genomics? Consider Siddhartha Mukherjee's bestselling *The gene: An intimate history*, published in 2016.[14] Over and over again, Mukherjee emphasizes that context determines what a gene determines, in mini-essays on everything from race and IQ to breast cancer. But he also has a contrary and, as the book proceeds, increasingly thumping message. Underlying all this surface complexity and diversity there is a deep simplicity, just as Mendel found. If a gene is in version *A*, you get character A; if the gene is in version *B*, you get character B. In a minor but telling way this dismissiveness of context, and the jarring incoherence it introduces, show up in his mini-essay on the genetics of schizophrenia. Genes are, we learn, part of the causal mix behind schizophrenia, becoming 'genes for schizophrenia' only with the collaboration of environment and chance. Schizophrenia itself is not one but many, and so are the relevant genes: over a hundred genomic regions have been implicated, and, according to Mukherjee, 'no single gene stands out as the sole driver of the risk' – a risk which may in any case be of enhanced creativity as much as of diminished sanity. But then, in a long footnote added at proof stage, Mukherjee appears to take it all back, reporting excitedly about a then brand-new study that found a single gene strongly associated with schizophrenia: if you have the trouble-making variant, then you will get schizophrenia, other things being equal; and if you don't have the variant, you won't (Mukherjee 2016, 298–300, 441–6, quotation on 445–6).

What the psychologist Steven Heine calls 'switch thinking' is persistent under binary Mendelism (Heine 2017, 27). So is category thinking generally. With humans, racial categories have figured prominently from the start. In a paper on eugenics in 1905, Francis Galton wondered whether 'a study of Eurasians, that is, of the descendants of Hindoo and English parents, might not be advocated . . . both on its own merits as a topic of national

importance and as a test of the applicability of the Mendelian hypotheses to men' (Galton 1906, 16). When, three years later, the German anatomist Eugen Fischer joined an expedition to what is today Namibia, it was to check for Mendelian patterns in the families sprung from Boer men and Hottentot women. Fischer went on to become the boss of Nazi racial anthropology, while Mendelism went on to lend crucial legitimatory lustre to Nazi racial laws and policies.[15] Even today, when official biology repudiates the reality of race, the categories – and the homogenizing they encourage (this race goes with these genes, that race with those genes) – cling on, not least in medical training. A child shows up in your clinic with fluid in the lungs. She is not white, so it can't be cystic fibrosis, right? Maybe you slow down and interrogate that conclusion. Or maybe you don't. In Angela Saini's *Superior: The return of race science* (2018), we learn about a black child whose cystic fibrosis went undiagnosed for years until an X-ray of her chest happened to be seen by a radiologist who didn't know what color she was (Saini 2019, 259).

What is to be done?

The question is, of course, Lenin's. But it is also Keller's, used as the title of her final chapter in *The mirage of a space between nature and nurture* (2010). There she recommended greater attention to trait malleability, to the functional roles of non-coding as well as of coding DNA, and to inheritance beyond the genome as helpful ways of dispelling that mirage (Keller 2010, ch. 4). Amen, I say. But, given my analysis above of the heuristic power of the character-making understanding of the Mendelian gene, and the insulation of that understanding from ordinary criticism, I think a more fundamental change is called for.

As we saw, the character-making understanding arrived before the difference-making understanding: a chronology, I suggested, which counts against the Morgan group's claim that the former is shorthand for the latter. But what if the order had been reversed? What if,

from the start, it had been not the critics of Mendelism – the Oxford biologist W. F. R. Weldon most incisively and implacably, but also Morgan, and others – who stressed the role of context in shaping the effects that a gametically inherited something can have, but the Mendelians themselves? So that every presentation of Mendel's results by his followers began with discussions of, for example, the variability of inherited characters as typically spanning a wide spectrum, except where selection, by nature or by humans, narrows it; the role of nuclear and cytoplasmic contexts ('ancestry'), inherited within a lineage along with individual factors, in modifying the effects of those factors on character variability; the comparable modifying role of wider physical and chemical environments; and the way that Mendel, for his purposes, deliberately tried to minimize all of those influences, the better to detect the character difference when he introduced a gametic difference. Then, I think, anyone listening or reading would have at least the possibility of emerging from acquaintance with the case of Mendel's peas without taking the character-making understanding, as a permanent, immutable heuristic, with them.

In a limited way, I've actually done the experiment, in collaboration with Dr Jenny Lewis and Dr Annie Jamieson. In the autumn of 2013 at the University of Leeds, we ran an elective introduction-to-genetics module organized as if it had come from the Weldonian past that never was: the past in which Weldon lived to complete and publish the amazing *Theory of Inheritance* manuscript left unfinished at his death in 1906. In this counterfactual past, there was Mendel, for sure, but no Mendelism. Thus our module opened with just those emphases on contexts and variability just described, and hammered away at them throughout, so that students saw them not as complications to the main story but as the main story in its own right. Before and after teaching we set the students – who were doing non-science degrees – a questionnaire to determine their levels of genetic determinism. We did the same with a group of biology students taking the standard, start-with-Mendel introductory module

in genetics. What we found was that, whereas students taking the Mendelian module were on average just as determinist about genes at the end as they were at the beginning (suggesting that, as some teachers of genetics fear, all their qualifying 'it's not all in the genes' pleading goes in one ear and out the other), students taking the Weldonian module were on average less determinist, and to a statistically significant degree.[16]

Between the small size of our study (28 students in each group) and the large number of incomparabilities between the two modules as well as between the two student groups, our findings can be no more than suggestive. Happily, however, the Weldonian curriculum is now being put through its paces much more robustly, within a new, three-year study now underway in collaboration with the education psychologist Brian Donovan, the biologist-educationalist Michelle Smith, and over fifty genetics teachers at colleges and universities throughout the US.[17] The aim is to examine, through a combination of randomized controlled trials and cognitive 'think alouds' (in which students talk through their reasoning processes), how different ways of learning about multifactorial genetics affect not only levels of genetic determinism but willingness to challenge racial and gender prejudice, on the hypothesis that the more fully students grasp trait malleability, the less prone they will be to essentialism and the complacency it engenders. So that is to come. For now, it is pleasing to think that an old debate, counterfactually investigated, is helping to create a new kind of scientific education, factually investigated, and maybe even to create students who will someday wonder how anyone could ever have seen a space between nature and nurture.

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Making Sense of Genes; and to Evelyn Fox Keller for her endlessly inspiring work and example.

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[1] For an excellent introductory survey see Griffiths and Stotz 2013.

[2] On early Mendelism and its relationship to Mendel see Bowler 1989, chs. 5 & 6.

[3] On the retirement of the International Prototype Kilogram, see Leicester 2018 and Robinson et al. 2019.

[4] On the eradication of smallpox see Bhattacharya 2011.

[5] On the vortex atom, see Kragh 2002. On ether physics and its fate, see Navarro 2018.

[6] My allusion is to Hacking 1983, 23, but my understanding of the way that the theories of laboratory sciences answer not to the world but to the versions which exist only in laboratories owes more to Hacking 1992.

[7] For Richard Dawkins' defense, in the wake of controversy over *The selfish gene*, of his use of 'gene for X' as professionally conventional shorthand for 'a genetic contribution to variation in X', and his disavowal of the determinism attributed to him by critics, see Dawkins 1982, ch. 2, esp. 21–3. According to Dawkins, anyone prepared to speak 'of a gene for tallness in Mendel's peas' should also be prepared to speak of a gene for reading in humans, 'because the logic of the terminology is identical in the two cases' (23). Previous tracings of the difference-maker understanding to the Morgan group can be found in Kampourakis (2017, 31–4) and Waters (1994, 406).

[8] For Morgan's thinking along these lines up to 1910, see Schwartz 2008, ch. 9, esp. 172–3.

[9] I have recommended a dose of Keller on productive ambi-valence before, in an article on the history of the term 'heredity' and Hilary Putnam's notion of a division of linguistic labor, in which scientific progress and semantic clarification are presumed to go together; see Radick 2012, 723.

[10] For the later Morgan passages see Keller 2002, 132–47; also Keller 2000, 56–7.

[11] For eye color as among the 'myths of human genetics,' see McDonald 2011, 34–6. Blue-eyed parents can, in fact, have brown-eyed children.

[12] See Jamieson and Radick 2013, 592, for analysis of a textbook problem whose successful solution depends on treating reasonableness in humans like yellowness or greenness in peas.

[13] The classic study of the gene as 'cultural icon' is Nelkin and Lindee 1995. There is, alas, no classic study of the treat-'em-like-the-peas heuristic. The psychological research bearing on genetics and heuristics has tended to concentrate on the mesh between genetic explanations and more basic explanatory biases, favoring, e.g., essences (Dar-Nimrod & Heine 2011), or inherent features (Cimpian & Salomon 2014), or causes that are proximate, stable, and powerful (Lynch et al. 2018). In the philosophy of science, meanwhile, heuristics belongs to Heinz Post, who, by way of countering what he saw as Kuhn's relativism, stressed the conservation of heuristics across supposedly revolutionary changes (Post 1971). My broadly Kuhnian concern with the heuristic power of Mendelian reasoning is thus a poor fit with both bodies of specialist scholarship. Nevertheless two elements in the general discussion of heuristics by the subject's maestro, Daniel Kahneman, in his *Thinking, fast and slow* (2011), strike me as congenial. First, in a rough and ready way, thinking about genes as character-makers can be considered fast-thinking genetics, while thinking about genes as difference-makers can be considered slow-thinking genetics. Second, after defining 'heuristic' as 'a simple procedure that helps find adequate, though often imperfect, answers to difficult questions,' Kahneman quoted the mathematician George Pólya's advice from *How to solve it*: 'If you can't solve a problem, then there is an easier problem you can solve: find it' (Kahneman 2011, 98) Maybe, in learning, á la Kuhn, to extend the initial Mendelian pea-crosses exemplar to ever more complex problems, you are learning too, á la Pólya, that a good bet for making headway on a problem, however complex-looking, is to start by treating it like the peas.

[14] The remainder of this paragraph is taken from my essay review of the book in the *Times Literary Supplement*: Radick 2016a and used here with permission.

[15] See Teicher 2020. On Fischer's study, published in 1913, as 'seen in Germany as the first large-scale proof for the general applicability of Mendel's laws for human racial crosses,' see 35–41, quotation on 39.

[16] Jamieson and Radick 2017; also Radick 2016b and, in abbreviated form, Radick 2016c.

[17] *Honoring the complexity of genetics: Exploring how undergraduate learning of multifactorial genetics affects belief in genetic determinism*, NSF Award ID 1914843. Also working with us on the project are Dennis Lee, Kelly Schmid, Awais Syed, and Monica Weindling.