Make your own monster

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Mutants: On the Form, Varieties and Errors of the Human Body by Armand Marie Leroi
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Jacob's Ladder: The History of the Human Genome by Henry Gee
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I848 an advertisement in the Brooklyn Eagle triumphantly announced a performance by 'the most extraordinary and interesting man in miniature in the known world'. Charles Sherwood Stratton was a perfectly formed 25-inch-tall midget, who weighed only 15 pounds. It had been the idea of the Victorian freak show impresario Phineas Taylor Barnum to present him in the guise of 'General Tom Thumb'. Before long, the general's imitations – 'in full military costume' – of Napoleon Bonaparte and Frederick the Great, and a varied repertoire including a 'Scotch song' and a rendition of the polka, would make him a wealthy man. Following his hugely successful London debut at the Princess's Theatre four years earlier (the Illustrated London News had described him as 'a little monster'), he had received three separate invitations to visit Queen Victoria at Buckingham Palace. His unexpected success spawned a host of copycat acts including 'Anita the Living Doll', 'Leonine the Lion Woman', 'Chang the Chinese Giant', 'Jo-Jo the Dog-Faced Boy' and John Merrick, the 'Elephant Man'. But by the turn of the century, the mood of the public had changed and the public display of such 'human prodigies' – as they preferred to be called – had become unacceptable in many countries. The profession of 'museum freak' was in terminal decline.

Such discontinuous variations on the human form are rare, but we are used to the continuous everyday variations that comprise the full spectrum of the 'normal'. They leave the basic body plan intact, and are the stuff of evolution by natural selection. The more 'monstrous' variations are unlikely to be of direct significance in evolutionary processes, but they do offer invaluable insights into the way animal form is generated.

Unusual characteristics can have environmental causes: the skin of the 19th-century freak show exhibit the 'Blue Man' was 'the colour of a Maltese cat' as the result of the prolonged administration of silver nitrate for dubious medicinal purposes. Most variation in human form, however, occurs because the genes responsible for every part of our internal and external make-up come in different versions. Each of these arises from a process of random gene modification called mutation, which is largely caused by errors of copying, or the damage done by mutagens such as UV light or chemicals. Occasionally, mutations pass permanently into the genetic record. The frequency with which this happens has itself evolved: if too many errors are introduced into the genome of an organism, its core information will melt away; too few, and there would be insufficient variation for evolution to work with.

In Mutants, Armand Marie Leroi argues that in order to understand how people's bodies are constructed, biologists need now to focus their attention on the bestiary of human variation, both normal and extreme. As people are not clocks, we cannot simply take them apart and reassemble them to investigate their inner workings, for both practical and ethical reasons. As a result, we must either study nature's own random 'experiments' on human form, as evidenced in 'normal' variation and developmental errors, or focus our attention on animals. The latter strategy has proved enormously useful; new technologies enable genes to be inserted or deleted as required, so that their effects on form can be studied. The genomes of flies, worms and fish have been randomly mutated using chemicals or radiation so as to generate bestiaries of bizarre mutants whose detailed mechanics can then be unravelled. Such models are the source of the vast majority of what we currently know about the way animals – including humans – are made.

It is true that a mouse or a worm is something short of human, but modern genetics has taught us that all living things share fundamental generative processes and principles. Indeed, some of the genes that control human development work equally well when transplanted into other species. This conservation of generative principles between widely different species reflects their shared evolutionary history; evolution works by tinkering with pre-existing genetic programs. Gene sequencing initiatives have shown, much to our surprise, that humans have almost exactly the same number of genes as organisms of broadly similar structural complexity, such as mice and monkeys. Many of these 25,000 or so genes are, furthermore, similar or near-identical in kind between related species, so that it's worth asking what exactly it is about our own genome that makes us distinctively human.

As the genome project expands, making it possible to compare the human genome with those of distantly related organisms, it becomes easier to assess the extent to which mice, worms, fish and flies provide models for understanding what goes on in humans. It turns out that a little circumspection is needed. A recent study of the coral species Acropora millepora, for example, identified large swathes of genes shared by coral and humans which were not found in common model organisms such as the fruit fly Drosophila melanogaster or the nematode worm Caenorhabditis elegans, even though flies and worms evolved millions of years later than coral. Such findings, which were quite unexpected, suggest that at least some of the genes thought to be the evolutionary innovations of vertebrates have more ancient origins. Animals may in some instances discard genes as they become more complex. It would appear that in order to gain a true understanding of the genetic make-up of human beings, we will need to study a far greater range of organisms.

Leroi, however, believes that if we are to understand human beings, we should pay more attention to human variation than to what other organisms can tell us. He illustrates his thesis with accounts of conjoined twins, developmental disorders of eyes, faces, fingers and limbs, skeletal abnormalities, giants, midgets, dwarfs, albinos, abnormalities of sexuality and excessive hair growth. Each deviation is supplied with a specific historic example. Thus we encounter Catherine de Medici, who in the 16th century tried to create a race of miniature humans by arranging a marriage between two dwarfs; and Ritta and Christina Parodi, the conjoined twins whose dissection soon after their death on 23 November 1829 enthralled Paris, at the same time provoking moral outrage from the critic Jules Janin that anatomists could 'bring this monster to the level of ordinary men'. Leroi, in characteristic fashion, follows this story with a discussion of the molecular genetic mechanisms thought to underlie such abnormalities. Tellingly, though, as is almost always the case, these were elucidated in animals – in this instance newts and mice – rather than in humans.

Leroi's book is clever and greatly entertaining, but not, in the end, entirely satisfying. While it is undoubtedly true that mutations are, collectively, 'a Rosetta stone that enables us to translate the hidden meaning of genes', there is no new revelation here, and the importance of human mutations has not, as might be inferred, entirely escaped the attention of contemporary biologists. Great efforts have been made to document human genetic diversity, in particular that of indigenous populations, in order to identify the SNPs (single nucleotide polymorphisms) that underlie many of the common differences between individuals. Once gene sequencing technology is sufficiently advanced, it will be possible to assemble huge databases of complete genomes gleaned from thousands and eventually millions of individuals, so as comprehensively to determine the genetic basis of individual variation and susceptibility to disease.

But in the end, the key information pertaining to the generation of human form will almost certainly come from the further study of animals rather than human mutants. Leroi's project is a recapitulation of Francis Bacon's in his Novum organum of 1620: 'We must make a collection or particular natural history of all the monsters and prodigious products of nature, of every novelty, rarity or abnormality.' But unlike Bacon, who emphasised the utility to which such a collection might be put, arguing that 'once a nature has been observed in its variations, and the reason for it has been made clear, it will be an easy matter to bring that nature by art to the point it reached by chance,' Leroi skirts the issue. In unravelling the mechanisms by which nature constructs living things, we are, surely, constructing the platform on which we will one day redesign life from first principles and create our own 'monsters'. Leroi's decision not to address this possibility is disappointing; he chooses instead to conclude with an entertaining but trivial discussion of beauty.

The quest for the secrets of biological form, which we have now located in the genome, can itself be traced back to antiquity. In his immensely enjoyable new book, Jacob's Ladder, Henry Gee concerns himself with the forces 'that take a formless speck and shape it into what is recognisable as a human being'. It is Gee's contention that the 'history of biology can be retold as the story of the search for this agency, the genome'. This history is often told as if it began with Charles Darwin. In Gee's account, Darwin assumes an important but not singular role in the evolution of our understanding of how living things are made.

The common evolutionary history shared by humans and other creatures is reflected in certain aspects of an embryo's development. Gee describes, for example, how at one point the human embryo is rolled out flat like a piece of dough, before promptly rolling up again. There is no obvious reason why this should happen, but that the process also occurs in reptiles indicates either that it reflects a fundamental constraint of vertebrate development or that ancient, probably superfluous genetic programs, configured long before humans first appeared, continue to operate at the earliest stages of our construction. Such observations are fuel for debate in theoretical biology, and occasionally lead to influential errors such as Ernst Haeckel's in his Generelle Morphologie der Organismen (1866), where he argued that the development of an organism follows its evolutionary history; or, more succinctly, that 'ontogeny recapitulates phylogeny.' Mutations that alter the genetic programs determining development are responsible for the major deviations from human form that occur from time to time. Occasionally such mutations are 'atavistic', indicating the continued existence of ancient programs that are normally suppressed by more recently evolved genetic controls. The embryos of modern horses have three toe buds, for example, but only the middle one grows to any size. The occasional appearance in nature of horses with three functional toes – one such is depicted as a unicorn in a 16th-century woodcut, The Triumph of Caesar – is the result of a mutation that allows the lateral buds to continue growing.

Gee traces our modern understanding of the process of development to the physician William Harvey, who, under the patronage of Charles I, was allowed to dissect pregnant does culled from the royal deer parks. The results enabled Harvey to refute the prevailing Aristotelian doctrine that menstrual blood was sparked into life by semen. Harvey's view, as outlined in the Exercitationes (1651), was that everything comes from the egg: 'Ex Ovo, Omnia'. Although he couldn't account for how form emerged from the featureless matter in an egg, he coined the word 'epigenesis' to describe the process. In 1674, Nicolas Malebranche proposed his theory of preformation, according to which the ovaries of females were filled with vast numbers of microscopic but fully-formed embryos. These, he supposed, had passed down directly from Eve and contained all future generations. Twenty years later, Nicolas Hartsoeker speculated that with a powerful microscope, it would be possible to see embryos rolled up inside the heads of sperm. Trembley's discovery in the early 1740s that polyps, when sliced, could regenerate intact polyps from the fragments, gave the lie to preformationism, but it wasn't until the early 19th century that it was realised eggs and sperm are uniquely specialised 'germ' cells.

The transition from a premodern to an essentially modern conception of animal development, as Gee says, was brokered by the Naturphilosophie movement of the late 18th century. Goethe, one of its most enthusiastic proponents, invented the term 'morphology', the science of form. Naturphilosophie's combination of German Romanticism – according to which the unconscious spirit (Geist) of 'lower' creatures struggled progressively to attain the conscious state of man – and scientific empiricism set the agenda for modern biological thought. Despite its mystical element, the movement was important for its insistence that a genetic program was responsible for biological form, not the elaboration of preformed homunculi.

Darwin's great achievement was to strip away the mysticism and any concept of guided 'progression' from evolutionary theory. His undoing, on the other hand, was his failure to connect with the work of Gregor Mendel, who uncovered distinct patterns of inheritance by combining biological experimentation with mathematical analysis. Darwin had made it acceptable to believe that species had natural rather than metaphysical origins, but he had no insight into the mechanisms of heredity, and no experimental method for addressing the issue. Although Mendel remained unrecognised in his lifetime (the poor response to his work eventually led him to switch his attention to beekeeping and meteorology), he had demonstrated that the agents of heredity were discreet particulate entities, modifications to which resulted in variation within and between species.

In the end, it was the study of one of nature's simplest creatures, a bacteriophage (a virus that preys on bacteria), which finally pinned down the generative force behind humans and all other life. Genes were not, it turned out, made from the structurally complex proteins found in living things, but from a relatively simple, repetitive molecule, DNA. Gee describes this final part of the story well, though he makes an error in attributing a famous 1952 experiment by Alfred Hershey and his knitting-obsessed technician Martha Chase – which finally persuaded sceptics such as Linus Pauling that the hereditary molecule was DNA and not a protein – to Avery, MacLeod and McCarty, who had earlier worked on the same problem.

Once the genetic function of DNA had been discovered, it was only a matter of years before variation and monstrosity came to be understood in terms of gene mutation. From this point onwards it is possible to discern renewed attention to a strand of thought that had, perhaps, always been present in Enlightenment philosophy: the possibility of the construction of new life and modification of the old. We must now take seriously the notion that our own and other forms need not be dictated by chance and natural selection, and that artificial man may be within our reach. This new Enlightenment enterprise, represented for the moment in the language of medical progress and debates over modified foodstuffs, will redefine our understanding of what it is to be human.

Although, like Leroi, Gee steers clear of such issues, he does complete his book with an intelligent account of the post-genomic landscape. If we try to distinguish ourselves from our close animal relatives on the basis of the number of genes we have in common, he points out, we will be sorely disappointed. It may be just about unsurprising that we share 99 per cent of our genes with monkeys, but it is more salutary to learn that we share almost the same number with mice and puffer fish. If it is not the number of genes we possess that gives us our humanity, it must be something else. That something else is, more likely than not, to be found in the unique programs that determine how, where and when individual genes are switched on and off. Gee concludes, correctly, that once the developmental logic of life is laid bare, it will be possible to generate working models of living systems on computers.