Beneficial mutations: real or imaginary?—part 1

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Randomly occurring beneficial mutations lie at the heart of Darwinian evolution. Without them there is no mechanism by which a single originating cell could have diversified into the myriad species that we see on Earth and in the fossil record today. But according to recent reports on the human genome, mutations are being classified into just two categories—'deleterious' and 'functional'. Beneficial mutations are not being catalogued. This surprising result turns out to be in accord with the history of the beneficial mutation concept. The theory was originally developed by R.A. Fisher in his 1930 book *The Genetical Theory of Natural Selection* in an attempt to salvage Darwinism because the only evidence he had was for deleterious mutations. Until recently genetic theorists have perpetuated his practice. Beneficial mutations are simply *assumed* to exist because Darwinian theory *demands* that they exist. The first experiments to characterize the properties of beneficial mutations were published in 2011 and the result contradicted Fisher's theory. This outcome is analyzed in part 2 of this article.

Having been a student of biology for more than 50 years I have never had a problem with the concept of beneficial mutations. I was therefore shocked to discover in recent reports on the human genome that beneficial mutations have not been found. Only 'deleterious' and 'functional' mutations have been documented. On doing some research into the ways that genetic theorists have treated beneficial mutations, and the data they have worked from, I was even more shocked to discover that they have had no data to work from either.

The theory of beneficial mutations was originally developed by English statistician R.A. Fisher, the founding father of neo-Darwinism, in his 1930 book *The Genetical Theory of Natural Selection*.[1] But he had only deleterious mutations to work with and so he came up with his theory of beneficial mutations out of a belief that they must exist. Genetic theorists have followed his example ever since. The stranglehold that neo-Darwinian evolution has achieved over academia and the media today was thus built upon nothing more than imagination and evolutionary necessity.

Darwin's *Origin of Species* started the ball rolling, but while it was widely praised it met fierce opposition from professional scientists.[2] By the beginning of the 20th century the discovery of Mendelian genes and the fact that they could mutate had largely pushed Darwin's ideas aside. By the end of the 1920s the science of genetics and the discovery that known mutations were all deleterious posed a seemingly fatal challenge to Darwinism. But in 1930 a new revolution began. Fisher published his book and he and fellow English mathematician J.B.S. Haldane, together with American geneticist Sewall Wright, then compiled during the 1930s and 1940s a body of mathematics that became known as the 'Modern Synthesis', or neo-Darwinian theory.

This body of theory remained largely academic until a convergence of three further events took place in 1953. Watson and Crick published the double-helix structure of DNA, giving biology its first ever grounding in the hard physical sciences. Bernard Kettlewell, a Research Fellow at Oxford University, began experiments on industrial melanism in the peppered moth. These produced the first ever example of natural selection in the wild[3] and it became textbook orthodoxy as 'evolution in action'. And American geochemist Clair Patterson announced at a conference what was to become a 'universal constant' in the evolutionary worldview—the 4.55-billion-year 'age' of the earth.

Mutations became synonymous with nucleotide changes in DNA. Natural selection re-emerged as all-conquering hero, promoting beneficial mutations, and removing deleterious ones. And the official oodles of time allowed chance to magically transform anything into anything else. Today's educated atheists grew up believing evolution as fact, the media made an industry out of it, and (almost) everybody believed it. But at the IUPS Congress in Birmingham in July 2013, the President, Oxford University Emeritus Professor Denis Noble, announced that "all the central assumptions of the Modern Synthesis … have been disproven."[4]

Beneficial mutations

Despite Noble's critique (and those of others e.g. ReMine,[5] Sanford[6]) the concept of the beneficial mutation remains the centrepiece of evolutionary thinking. The underlying idea has been around since Darwin's time. On p.63 of the final 1876 edition of the *Origin* Darwin said this: "Natural Selection … implies only the preservation

of such variations as arise and are beneficial to the being under its conditions of life." No-one could object to that.

Darwin defined what he meant by 'variation' in chapter 2 of *The Origin* as things that could be observed by a careful study of many individuals of the varieties, species, and genera of interest. In other words, natural selection worked on those 'variations' that were already present if one looked closely and systematically enough. But when Mendel's particulate theory of inheritance overtook Darwin's blending theory of inheritance a dramatic change took place in the meaning of the word 'variation'. Mendel's particles (genes) were found to be able to mutate—to change spontaneously into something that had not existed previously. In the new era of genetics a 'variation' was no longer necessarily something that already existed and could be observed by a careful scientist. Mutations gave evolutionists the first solid evidence that something new could arise which had not existed previously. Darwin's definition of 'variation' was no longer in charge!

When genetics came of age in 1953 in DNA's double helix, with its interchangeable information-carrying bases, another change to the meaning of 'variation' took place. Natural variations of Darwin's kind were already known to be produced during the crossing-over stage of meiosis. But when it was discovered that 'random errors' could occur in DNA copying of individual nucleotides these became the factories for the 'something new that had not existed previously'. The neo-Darwinian mantra of 'mutations and natural selection' had now to depend entirely upon random copying errors to produce the new information that microbes-to-mankind evolution required. The 'beneficial mutation' of the early geneticists had turned into a 'beneficial' random DNA copying error.

Something for nothing—the Darwinian dream

In the 1859 first edition of Darwin's *Origin* his first words were a quote from William Whewell's 1833 *Bridgewater Treatise*:

> "But with regard to the material world, we can at least go so far as this—we can perceive that events are brought about not by insulated interpositions of Divine power, exerted in each particular case, but by the establishment of general laws."

In his final chapter, Darwin outlined his vision of life in all its "endless forms most beautiful and most wonderful" as being the result of these 'general laws'.

It sounds laudably scientific, but reading between the lines we find a man wanting to have the privileges and pleasures of life without owing any special debt of honour or gratitude to his Creator (Romans 1:21). The Creator is mentioned, but only as a remote First Cause, the one who impressed laws upon matter and breathed life 'into a few forms or into one' in the beginning. All subsequent forms of life arose as the 'lineal descendants' of the originator(s) via evolution.[7] Darwin wanted to get all the variety of life—including man—'for nothing'. Like the trees and flowers of the English countryside he wanted to see himself as a product of natural law. He did not want to see himself as a special creation in the image and likeness of a personal Creator (Genesis 1:26–28) who became personal Saviour, and one day would return as personal Judge.

Darwin's desire to 'get something for nothing' lies at the heart of the beneficial mutation concept and also at the heart of the world's embrace of evolution. It is biologically complex so I will use a mechanical example from physics to illustrate the point. In the decade following 1859 Scottish physicist James Clerk Maxwell proposed a thought experiment to explore the possibility of violating Lord Kelvin's Second Law of Thermodynamics. If such a thing were possible then we could build a perpetual motion machine and get 'something for nothing' from it in the form of an endless supply of energy! Such machines could power the world indefinitely.

Maxwell imagined a rectangular box partitioned into two compartments with a door in the dividing wall. A benevolent demon (who became known as Maxwell's Demon) guarded one side of the door, and when a hotter-than-average gas molecule approached the door he would let it through to the other side. After a while one side would contain all the hottest molecules, thus violating the Second Law of Thermodynamics which predicted that heat would tend to travel from a hotter to a colder region, not the other way around.

A machine using the principle of Maxwell's Demon has now been created in order to obtain temperatures so close to absolute zero that they are measured in millionths of a degree. Two laser beams take the place of the demon, but the outcome is the same.[8] But rather than violating the Second Law of Thermodynamics and allowing physicists to get 'something for nothing' the machine shows that a great deal of intelligent design, manipulation, and expenditure of energy is required. And the outcome is completely in accord with the Second Law!

Random beneficial mutations are the biological equivalent of Maxwell's Demon. They supposedly allow life to reap a harvest of new DNA-based biological information that can create all of life's grand variety without any need for a Creator. Richard Dawkins' metaphor of climbing Mt Improbable deftly illustrates the supposed power of these randomly generated 'beneficial' mutations.[9] Mt Improbable represents the sheer cliff-face of improbability that complex adaptations (e.g. eyes, reproduction, photosynthesis) pose to any naturalistic theory of evolution. That master of spin

took us around the back of Mt Improbable where (he said) there lay an easy stepwise gradation of random 'beneficial' mutations. Each could be selected one at a time and neo-Darwinian life could conquer even the highest peaks of evolutionary improbability in slow and easy stages. When Dawkins was writing for 'the public understanding of science'[10] the molecular evidence was not available to test his claims. But the age of genomics now allows us to examine such claims and evaluate this pivotal assumption in modern evolutionary theory.

Human genome studies

Human genome studies are being carried out all around the world at present and the major findings can be summarized in just a few words: accumulating mutation load and a multitude of associations between mutations and diseases. The Human Gene Mutation Database[11] currently contains records of more than 141,000 mutations. New ones are being discovered at a rate of over 11,000 per year. A September 2012 summary reported that of these about 6,000 constitute 'disease associated' and 'functional' polymorphisms (different versions of a DNA sequence).[12] Notice that the classification recognizes just two categories—mutations are either 'disease associated' or they are 'functional'. There is no category labelled 'beneficial'.

The Online Mendelian Inheritance in Man database[13] catalogues all known mutations that are inherited in the simple Mendelian manner. It's subtitle, 'An Online Catalog of Human Genes and Genetic Disorders', indicates its comprehensive scope. About 6,000 'disease associated' and 'functional' mutations are known to be inherited in this way. There is no reference anywhere to 'beneficial' mutations.

In a sample of 179 genomes from The 1,000 Genomes Project the average healthy person was found to be carrying about 400 'disease associated' mutations and two 'disease causing' mutations.[14] No parallel discoveries have been reported for 'beneficial' mutations. In the 1,092 genomes reported on in October 2012 they had located 38 million single base changes, with each individual carrying on average 3.6 million, 1.4 million 'indels' (where a difference of 1–50 in the number of bases occurs from insertions and/or deletions), and 14,000 large deletions (>50 bases).[15] According to the HGMD mentioned earlier, gross deletions (>20 base pairs) outnumber gross insertions by 5 to 1. A study of human genes contributing to intelligence shows that they are particularly vulnerable to mutation and that we are all carrying at least two or more mutations deleterious to our intellectual and emotional capabilities.[16]

If we truly were evolving in the neo-Darwinian manner then among these millions of mutations we should be carrying at least some 'beneficial associated' mutations. None have been found. It would be REALLY BIG NEWS! Our genomes are accumulating deleterious mutations, not 'beneficial' ones, and they are losing DNA faster than they are gaining it. We are heading towards extinction, as Sanford predicted,[6] not towards new evolutionary heights!

What do the theorists say?

Evolutionary theorists use a concept called the 'fitness landscape' to imagine possible scenarios for the action of natural selection. This landscape consists of peaks, troughs, and plains. Organisms can 'drift' along plains in any direction as long as any mutational changes are not significant enough for selection to work on them. They can fall into troughs by accumulating deleterious mutations, but they can only climb peaks through positive selection of beneficial mutations. But to arrive at any useful conclusions theorists need to know the 'fitness-effects distribution' of the mutations that do occur. They need to know how often large, damaging mutations occur compared with those of small or no effect, and how often large-effect beneficial mutations occur compared to small-effect beneficial mutations. Knowing these distributions allows them to build mathematical models and carry out evolutionary experiments which help to explore the fitness landscape.

A study that addressed the human fitness-effects distribution of deleterious mutations in protein coding genes had no trouble assembling suitable data. Their data showed that more than 50% of new mutations are likely to have 'mild' effects (reducing fitness by between 0.1 and 10%) and less than 15% of new mutations are likely to have strongly deleterious effects.[17] However, in a study of the fitness-effects distribution of beneficial mutations the author was unable to find suitable data and so was forced to estimate the distribution using 'extreme value theory'.[18] This is a statistical method for predicting the frequency of extreme events such as floods and earthquakes when you only have a limited amount of data. You may have data for 100 years but to build something like a nuclear reactor you need to estimate how likely it is that a 1,000-year or 10,000-year event might occur during its lifetime. The

Table 1. Fisher's data on mutations that he presented in his table 1.

	Completely Recessive	Intermediate	Dominant	Total
Autosomal	130	9	0	139
Sex-Linked	78	4	0	82

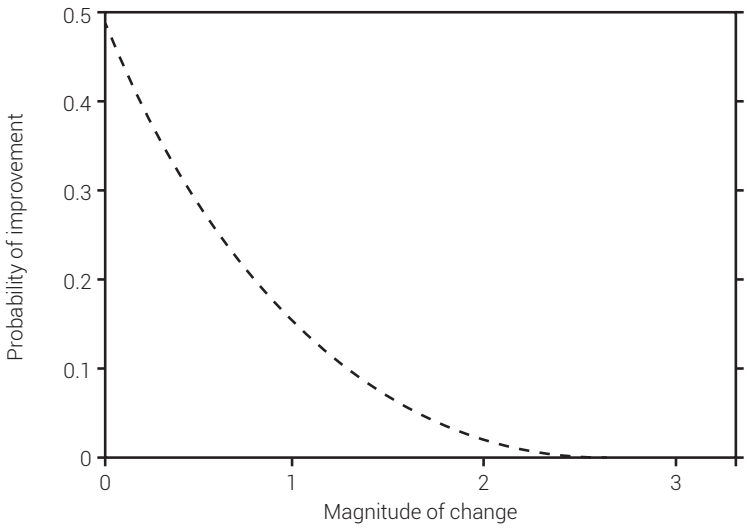

Figure 1. Fisher's expected exponential distribution of benefits from mutation compared with magnitude of mutational change (after figure 3 in Fisher[1]).

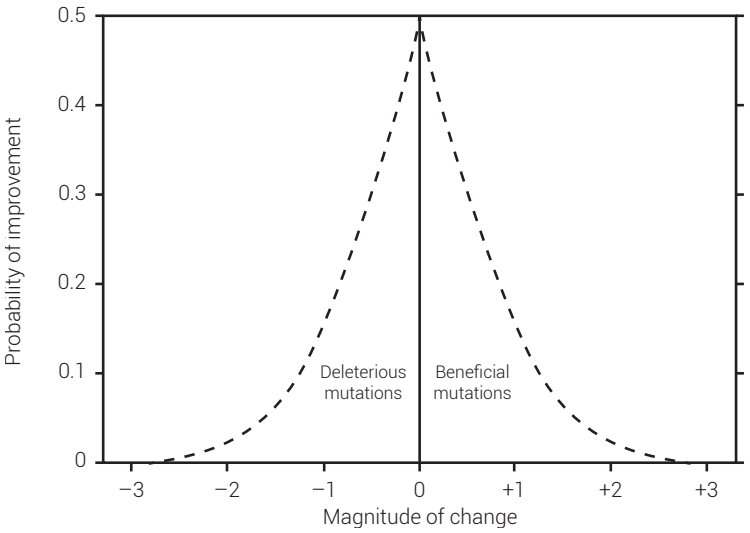

Figure 2. Separating deleterious and beneficial mutations from Fisher's original combined distribution in figure 1.

details of the method are unimportant because the author tells us that there is an established convention in genetics to simply *assume* what is required! So he *assumed* that a wild-type allele (an unmutated DNA sequence) could mutate to 'a small number of beneficial' alternative states. No data were required! 'Beneficial' mutations are a necessary component of neo-Darwinian theory so they are simply *assumed* to exist.

This convention was established by Fisher in his 1930 book. He had no evidence at all for beneficial mutations so he had to imagine them. Once he had imagined them, he then had to imagine all the details of their nature and every mode of their action. The only data he presented is in table 1. All of these mutations were known by their effects to be deleterious; the majority were recessive and none of them were dominant. Only dominant and beneficial mutations are useful to evolution so Fisher had to devise a strategy for turning recessive deleterious mutations into dominant beneficials. Being arguably the greatest statistician of all time he had little trouble in carving out a rather tortuous route to this end, and it is a story that should be told. For this article, however, we will focus just on some of the landmarks on his journey.

First, he assumed that deleterious and beneficial mutations were equally likely to occur. This is an astonishing denial of the truth that lay before him in his table of data! Then he started referring to deleterious mutations as 'less advantageous' and beneficial mutations as 'more advantageous' respectively. So with just a few carefully chosen weasel words he produced a beneficial fitness landscape where previously there was none! He then assumed that the distribution of fitness effects of all mutations compared with their size would follow an exponential curve, reproduced here in figure 1.

He imagined that small mutations would have a higher chance of improving the fitness of the species than would large mutations, so the curve is high on the left and it diminishes towards zero on the right as the magnitude of change increases. Fisher's expectation of an exponential distribution remained in place for the next 80 years.

To expose his fabrication we need to separate deleterious from beneficial mutations, which he had bundled together in figure 1. We can do this by taking a copy of figure 1, flipping it horizontally, and joining it to the original, as in figure 2.

This is Fisher's model—both deleterious mutations (on the left) and beneficial mutations (on the right) have mostly small or zero effect on fitness, and mutations of large effect are increasingly rare. The fallacy of his model can then be seen in figure 3 where the beneficial mutations have been removed because he had none!

The whole foundation of neo-Darwinian theory was built upon Fisher's imaginary notion that small *deleterious* mutations could turn any form of life into any other.

Why would a world-class scholar like Fisher stoop to such depths of self-deception as to deny the reality of his own data? Part of the answer is given on p. 53 of his book:

> "... unless we are to abandon altogether the evolutionary conception of the modification of species by the occasional substitution of one gene for the predecessor from which it arose … [Darwin's theory] requires that the successful new gene should in some way *become* dominant to its competitors, and if back mutations occur, to its predecessor also [emphasis in original]."

Fisher's commitment to evolution forced him to believe that beneficial mutations *must* exist, and since he had no evidence for their existence then he had to invent them! Another part of the answer is given in the last five chapters of his book. They were devoted to eugenics, a subject to which he was deeply committed. His personal worldview was the cause of his self-deception, and he deceived the world.

Let's now put some flesh on figure 3 to illustrate the truth that Fisher was so keen to deny. A summary of the average human genome data is presented in figure 4.

Fisher's genetic theory—when reduced to the data it was based on—and human genome studies agree that beneficial mutations do not exist!

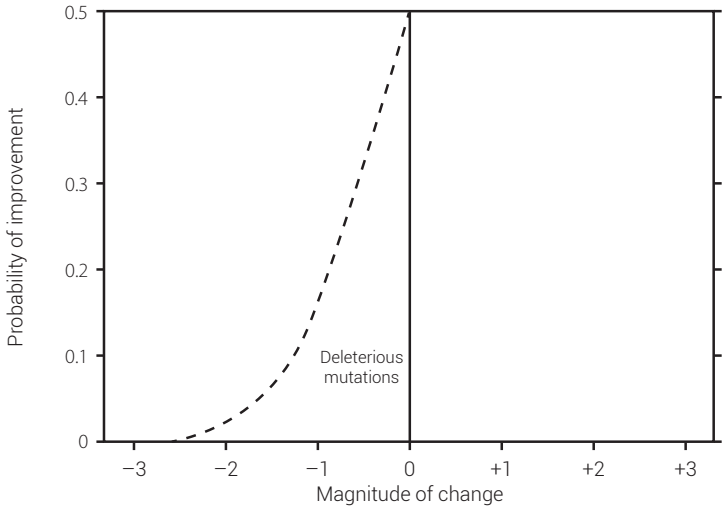

Figure 3. Fisher only had deleterious mutations to work with. Neo-Darwinian theory was built entirely upon the imaginary notion that small deleterious mutations could turn a microbe into every other form of life!

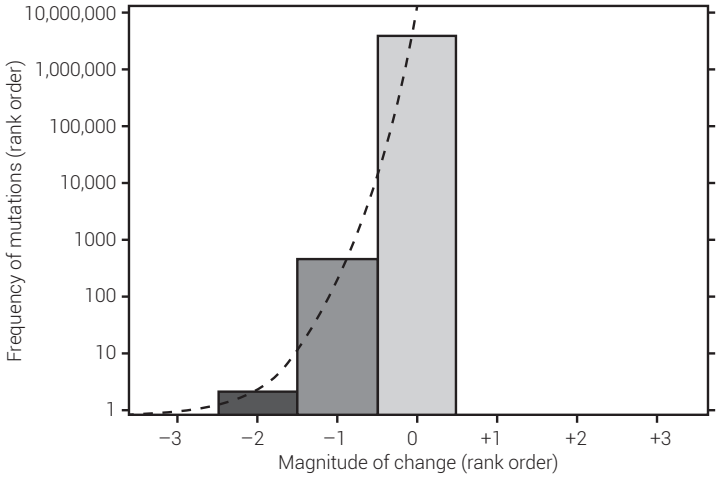

Figure 4. The fitness effects distribution of mutations from human genome studies. The average healthy human carries about 4 million single nucleotide changes of unknown effect (grey bar at zero), about 400 disease-associated changes (darker bar at −1) and about 2 disease causing changes (darkest bar at −2). The expected exponential distribution (dashed line) fits well, but note the logarithmic scale. There are no known beneficial mutations (no positive values on the right of zero).

Objection! Objection!

At this point Darwinists will make a lot of noise about numerous experiments which demonstrate beyond doubt that some mutations can lead to increased fitness, both in humans and in experimental populations. This is certainly true. A recent example is the discovery that a single nucleotide change in ethnic Tibetans (compared with Han Chinese) has allowed them to cope with the chronically low oxygen levels that occur on the high Tibetan plateau.[19] A wiki that lists other examples can be found here.[20]

Why then don't the genetic theorists use this data and these kinds of experiments to derive their fitness-effects distributions for beneficial mutations? The answer to this question is very revealing—because there is a whole lot more to life than just 'mutation and natural selection'! It's an admission that neo-Darwinian theory really only tinkers with life around the edges, not with its central components. This subject is taken up in more detail in part 2 of this article.

Before leaving this part, however, consider the following example. One of the largest studies that went looking for beneficial mutations in the human genome came up with the following results: 27–29% of amino-acid-changing mutations are neutral or nearly neutral, 30–42% are moderately deleterious, and nearly all the remainder (~36%) are highly deleterious or lethal.[21] Nevertheless, they asserted that:

"Our results are consistent with 10–20%

of amino acid differences between humans and chimpanzees having been fixed by positive selection [i.e. they were beneficial] with the remainder of differences being neutral or nearly neutral."

In other words, they could not find beneficial mutations when they went looking through the data for them, but if they assumed that humans and chimpanzees evolved from a common ancestor then they *could* find the evidence. So it was only the *assumption* of evolution that produced any evidence for beneficial mutations, just as we discovered in Fisher's work.

Conclusions

Are beneficial mutations real? They are not being catalogued in systematic studies of human genomes, even though individual examples of benefit have been documented. The catalogues only contain 'deleterious' and 'functional' categories of mutations. The genetic theory of beneficial mutations was made up by R.A. Fisher in 1930 out of nothing more than deleterious mutations and the demands of evolution. His theory has ruled biology for over 80 years and it is the primary cause behind the contemporary stranglehold that neo-Darwinian evolution exerts over academia, the media, and even the church. Recent experiments have finally revealed the long sought after characteristics of beneficial mutations, but they are not at all what Fisher expected. This is dealt with in part 2 of this article.

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References

1. Fisher, R.A., *The Genetical Theory of Natural Selection*, Oxford University Press, London, 1930.
2. Hull, D.L., *Darwin And His Critics: The Reception of Darwin's Theory of Evolution by the Scientific Community*, University of Chicago Press, 1973.
3. Controversy over the validity of Kettlewell's experiments is dealt with at the Kettlewell Archive at Oxford University, www.wolfson.ox.ac.uk/library/archives/kettlewell/links, 2 October 2013. I found this note interesting: "Kettlewell's research data and experimental notes have not been found. If anyone knows the whereabouts of these papers, please inform the Librarian, Wolfson College, Oxford." 21 August 2013.
4. Noble, D., Physiology is rocking the foundations of evolutionary biology, *Experimental Physiology* on-line pre-print doi:10.1113/expphysiol.2012.071134, 9 July 2013.
5. ReMine, W.J., *The Biotic Message: Evolution vs Message Theory*, St Paul Science, St Paul, MN, 1993.
6. Sanford, J.C., *Genetic Entropy and the Mystery of the Genome*, 3rd edn, FMS Publications, New York, 2008.
7. *On the Origin of Species*, 1st edn, pp. 489–491, ch. xiv, conclusion, 1859, darwin-online.org.uk, accessed 9 July 2013.
8. Castelvecchi, D., How Maxwell's Demon Cools a Gas to Microkelvin Temperatures [Animation], *Scientific American,* 7 February 2011, www.scientificamerican.com/article.cfm?id=raizen-entropy-cooling-experiment-interactive, accessed 8 July 2013.
9. Dawkins, R., *Climbing Mt Improbable*, Norton, New York, 1996.
10. Dawkins was Oxford University's Professor for Public Understanding of Science from 1995 until 2008, en.wikipedia.org/wiki/Simonyi_Professorship_for_the_Public_Understanding_of_Science.
11. The Human Gene Mutation Database at the Institute of Medical Genetics in Cardiff, www.hgmd.cf.ac.uk, accessed 9 September 2013.
12. Stenson, P.D. *et al.,* The Human Gene Mutation Database (HGMD) and its exploitation in the fields of personalized genomics and molecular evolution, *Current Protocols in Bioinformatics* **39**:1.13.1–1.13.20, 2012.
13. Online Mendelian Inheritance in Man, www.omim.org/, accessed 1 April 2013.
14. Yali Xue *et al.,* Deleterious- and disease-allele prevalence in healthy individuals, *The American J. Human Genetics* **91**:1022–1032, 2012.
15. The 1,000 Genomes Project Consortium, An integrated map of genetic variation from 1,092 human genomes, *Nature* **491**:56–65, 2012.
16. Study suggests humans are slowly but surely losing intellectual and emotional abilities, medicalxpress.com/news/2012-11-humans-slowly-surely-intellectual-emotional.html, accessed 8 July 2013.
17. Eyre-Walker, A. *et al.,* The distribution of fitness effects of new deleterious amino acid mutations in humans, *Genetics* **173**:891–900, 2006.
18. Orr, H.A., The distribution of fitness effects among beneficial mutations, *Genetics* **163**:1519–1526, 2003.
19. Yi, X. *et al*., Sequencing of 50 human exomes reveals adaptation to high altitude, *Science* **329**:75–78, 2010.
20. List of Beneficial Mutations in Humans, sciphi.wikkii.com/wiki/List_of_Beneficial_Mutations_in_Humans, accessed 16 September 2013.
21. Boyko, A.R. *et al*., Assessing the evolutionary impact of amino acid mutations in the human genome, *PLoS Genetics* **4**(5):e1000083, 2008.

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