EMBnet.journal
Bioinformatics in Action

You want it darker*

Vivienne Baillie Gerritsen

We are highly adaptable. We have been for the past few million years, and continue to be so on a daily basis. Whichever way you look at it, the art of adaptation really is just a way of preserving your integrity – physical or psychological – and coping the best way possible with the environment you are evolving in. Throughout the animal world and over the aeons, the capacity to adapt has always been Nature's answer to predators and hostile physical, geographical or climatic conditions. In short, adaptation is the best way to survive and Charles Darwin was the first to explain animal diversity in this way in his Origin of Species. Ever since, the study of fossils or more recently genomes is a constant support to Darwin's theory of what was then coined 'natural selection'. But it all remained very theoretical; it is difficult to observe animal adaptation within a man's lifetime when it occurs over thousands or even hundreds of years. However, there is a moth in Great Britain, known as the Peppered Moth which, over a relatively short period of time, adapted to the effects of pollution resulting from the Industrial Revolution by changing the colour of its body and wings. The protein involved in this change was recently discovered and named 'the cortex protein'.

* Title taken from Leonard Cohen's latest album, "You Want It Darker"

"Standing figures and telegraph poles"
by Theodore Major (1908-1999).

By the early 20th century, air pollution caused by the Industrial Revolution had begun to hit parts of Europe and, in particular, parts of Great Britain quite hard. Following decades of manufacturing, soot had settled on buildings, walls, fences and trees and gradually painted towns and the nearby countryside a dull grey. Needless to say, it had a profound effect on plant and animal life living close to industrial centres. During this period, amateur naturalists and moth collectors couldn't help but notice that a moth known as *Biston betalaria*, or more commonly the peppered moth, was changing colour: the original black-speckled white moth was gradually becoming only black. It wasn't due to the deposit of soot on their wings, but seemed to be an actual modification in the colour of their wings and bodies. The phenomenon was termed 'industrial melanism' to describe the blackening of the moths' colour – as opposed to melanochroism which is the darkening of any given colour. Many theories attempting to explain the process emerged, while in the wake of Charles Darwin's Origin of Species published in 1859, evolutionists saw the change as an example of natural selection taking place before their very eyes. For camouflage purposes, the peppered moths were slowly adopting a darker colour, less conspicuous when resting against the bark of a tree or on a soot-darkened wall. However, their theory needed evidence.rest of the ESCRT complex – and membrane scission is an activity scientists are also very eager to understand at the molecular level.

The English entomologist J.W.Tutt (1858-1911) was one of the first to describe the colour change in peppered moths. He saw it as a form of crypsis, i.e. an animal's ability to make itself discreet – invisible to predators for instance – by means of camouflage or mimicry. The normally occurring light-coloured lichen on trees was gradually being killed off by soot and leaving the bark of trees, bare and dark. In the presence of predators, the original peppered moth would have been very visible on such a surface, while the all black version – named *carbonaria* today – would be unnoticed. In the 1950s, the British geneticist and lepidopterist H.B.D. Kettlewell (1907- 1979) carried out a few elegant investigations which by Theodore Major (1908-1999) "standing figures and telegraph poles" showed that the change of colour in the moths was not a case of crypsis but instead a case of natural selection where the original light-coloured peppered moth had been gradually replaced by carbonaria in industrial areas. He demonstrated this by placing both types of moth first on dark and then on light surfaces. In each experiment, most of the moths he managed to recapture were those whose colour matched the colour of the backgrounds, thus supporting the theory of natural selection. On a dark background, predators went straight for the original peppered moths, while on a light background their black kin were caught.

What was happening on the molecular level? The wing patterns of butterflies and moths (*Lepidoptera*) – of which there are hundreds of thousands of different species worldwide – are, in fact, a striking example of diversity brought about by natural selection. The different colours observed are a combination of the quantity of melanin in the cells – known as scale cells – that form the patterns seen on lepidopteran wings, and the cells' optics. The cortex protein, or simply cortex, has a direct role in the amount of melanin present in scale cells. Cortex belongs to a fast-evolving subfamily of cell-cycle regulators, and may well regulate pigmentation during early wing disc development, perhaps by regulating scale cell development itself. As such, cortex will have become a major target for natural selection involved in pigmentation; pattern variation in *Lepidoptera*, and its expression does indeed vary significantly between butterflies and moths with different wing patterns. The first reported sighting of *carbonaria* is said to have occurred in 1848 in Manchester, though previous sightings seem to have been made. This would imply that the mutation linked to industrial pollution would have appeared shortly before soot levels rose – although it could also have existed undetected at a low frequency for hundreds of years...

Cortex controls melanism in the peppered moth. But what is the exact nature of the mutation? Breeding experiments in the early 20th century had already suggested that industrial melanism was the consequence of an inherited form of a single dominant or semi-dominant gene. It wasn't before the 21st century that the molecular identity of the mutation was unveiled, and came as a bit of a surprise. It turned out to be the doings of a large tandemly repeated transposable element which inserts itself into the non-coding part of the cortex gene. Statistical inference based on the distribution of *carbonaria* haplotypes has even pinpointed the transposition event to the year 1819 – which would be consistent with the historical record. As for the effects of the mutation on cortex itself, the protein is expressed more abundantly in *carbonaria* than it is in the light-coloured peppered moth.

Driven by the intense industrialisation of a nation, over a relatively short period of time the colour of the peppered moth shifted from black-speckled to black. The inserted transposable element increases the abundance of cortex in scale cells causing them to darken in the process, though how exactly remains a mystery. Cortex has thus proved to have an important role in a spectacular story of rapid adaptation in the peppered moth. However, it is rare that a protein acts on its own. Industrialisation didn't happen on the same scale everywhere either. Up until the 18th century, London was the most industrialised and polluted city in Britain. Later, other places were hit although a few have since stepped back and are considered rural nowadays. The atmospheric pollution in these areas has also varied, as did the darkening of surfaces, food abundance and predators. Migration too can influence frequency changes... So, it is difficult to explain industrial melanism on the sole basis of the cortex protein. What can be said with certainty, however, is that it did play a major role, and what happened to the peppered moth offers an elegant and classical example of natural selection induced by human activity and driven by selective predation, over a brief and observable period of time.

Cross-references to UniProt

Protein cortex, *Biston betularia* (peppered moth) : P0DOC0

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