Bark scorpion toxin loses its bite

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Bark scorpion (*Centruroides* spp.) toxin is known to be intensely painful and potentially lethal. It provides the scorpion with a defence against predators; those that survive are unlikely to attack again. However, with grasshopper mice (*Onychomys* spp.) the toxin actually behaves as an analgesic. When stung, grasshopper mice will lick the wound for a few seconds before resuming the attack and devouring the scorpion.

Recent research has elucidated some fascinating details of this phenomenon.[1] There are multiple voltage-gated sodium (Na^+) channels in mammals. One, known as Nav1.7, is the target of the toxin and initiates the pain signal that is then sent to the brain. At first it was suspected that changes to this protein would be responsible for the resistance of grasshopper mice to the toxin. After all, it was recently found that naked mole rats were insensitive to acid-induced pain because of amino acid differences in this protein. This allows them to live underground where there is a high concentration of carbon dioxide.

However, researchers found that variation in a second Na^+ channel, Nav1.8, is responsible for the unusual reaction of grasshopper mice. Normally, Nav1.8 is responsible for transmitting signals of pain to the central nervous system. In grasshopper mice it binds to the bark scorpion toxin which blocks the signal of pain in a dose-dependent manner. In fact, after being exposed to the toxin, other painful stimuli, such as formalin, also have less of an effect. This was ascertained by measuring the amount of time spent licking the injection site after administration.

Grasshopper mice have multiple amino acid variants in the Nav1.8 protein compared to house mice (*Mus musculus*). Those making a major contribution to venom sensitivity are localized in one region (domain II). In particular, the amino acids at positions 859 and 862 are switched. In grasshopper mice the hydrophilic glutamine (Q^{859}) precedes the acidic glutamic acid (E^{862}). The house mouse has the reverse (E^{859}; Q^{862}). The position of the acidic E^{862} appears essential to inhibit Na^+ current, though the additional amino acid replacements may contribute as well.

The researchers compared the residues at these two positions with those of Nav1.8 proteins in other rodents and non-rodent mammals. In all 18 species investigated, only glutamic acid (E) and glutamine (Q) were found. Seven of the 10 rodent species and one primate carried E^{862} which is critical for blocking Na^+ current in grasshopper mice. Two of the rodents (*Mesocricetus auratus*, *Cavia porcellus*) and the primate (*Otolemur garnetti*) also carried Q^{859}.

Is anyone selecting?

Evolutionists assume that genetic changes are essentially random and that non-random patterns are attributable to natural selection. Based on finding only two amino acid variants at these two positions, they conclude that these amino acids play a critical role in the structure and function of the Nav1.8 domain II. They also suggest that the pattern found in the grasshopper mouse evolved under selection pressure unrelated to scorpion venom, in some distant mammalian ancestor. This would mean that mice already resistant to the toxin exploited scorpions as a food source.

In the creation model, it is uncertain if all rodents share common ancestry. However, primates would definitely be considered to be from a different baramin (created kind) than mice.[2] It is very reasonable to conjecture that the amino acids at these positions play critical roles, but there is no reason to believe the pattern is from natural selection. Population genetics models show that natural selection is not a powerful force in vertebrates. In most circumstances natural selection is not powerful enough to remove deleterious mutations; neither is it powerful enough to preserve most beneficial ones.[3]

Given that natural selection is not a mathematically plausible explanation for the pattern in mammals, there are likely to be genetic mechanisms, including repair mechanisms, which maintain these amino acids at these positions. It is quite reasonable to believe that grasshopper mice had the means (by carrying at least the E^{862} and perhaps Q^{859}) to exploit the scorpions as a food source. Further genetic changes could have been effected through genetic mechanisms, including biased gene conversion.[4] Thus, though one can imagine a creative story involving natural selection to explain why grasshopper mice carry these amino acid variants, it probably has little or nothing to do with what is really going on.

Channels for change

Evolutionists have noted that genetic loci coding for proteins which interface with the environment are frequently the targets of 'evolution'.[5] While one needs to be cautious because universal common ancestry is assumed in their model, creationists have noted intrabaraminic (within a created kind) examples of this in genes affecting insecticide resistance[6], coat colouration[7], olfaction, and other traits.[8] Clearly sodium channel genes are involved with environmental interaction, and they also have been involved in some adaptive responses.

Not only are there toxins in nature targeting voltage-gated sodium channels, but insecticides such as

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Figure 1. The bark scorpion (left) sting is known for being extremely painful and sometimes lethal. The toxin it delivers affects Nav1.7 receptors, initiating a strong pain impulse to the brain. Normally this impulse is conducted to the central nervous system by Nav1.8. Amino acid variants in the Nav1.8 protein of the grasshopper mouse (right) cause it to bind the toxin and block transmission of the signal, enabling these mice to make a meal out of the scorpion.

pyrethroids and DDT target them as well. Unfortunately, resistance to these insecticides has arisen multiple times in various species of insects. A recent study investigating the development of resistance in mosquitoes had some surprising findings. In addition to three non-synonymous mutations (i.e. involving amino acid changes) that appear to be important in conferring resistance in the mosquitoes studied, six synonymous mutations were also correlated. This study and others suggest that synonymous mutations may play a significant role in altering gene functions. This may include gene expression, protein folding and substrate interaction.[9]

Not all change is good

While adaptive changes in sodium channels occur in insects and some mammals, there are other documented changes that are not associated with a clear benefit and, in some cases, are associated with pathology. In humans certain mutations in Nav1.7 and Nav1.8 are associated with altered pain sensitivity, including painful peripheral neuropathy. A possum phenotype has been described in mice carrying a chemically induced mutation in Nav1.8 where simply pinching the skin at the back of the neck results in whole-body immobilization for several minutes.[10]

While the ability to adjust proteins that communicate with the environment may explain much of why creatures have been able to adapt as they have reproduced and filled the earth since the time of the Flood (Genesis 8:17), obviously there are some constraints. Pain perception is essential to avoid injury. Excessive sensitivity can be debilitating. So in a way it is rather surprising that pathways even exist by which these proteins can be adjusted in an adaptive way.

Another issue to address is the cost associated with the changes. For example, sickle cell anemia is a disease. However, carrying the sickle cell trait has allowed people inhabiting malaria-infested regions of the world to survive. So is the underlying mutation in the hemoglobin gene an accident, or was it a costly genetic change implemented in response to a harsh environmental reality? Hemoglobin happens to be one of the proteins involved in interfacing with the environment where adaptive mutations have been noted.[5] A detailed review of adaptation to high altitude suggests that naturalistic mechanisms (random mutation plus natural selection) cannot account for the observed patterns in mammals and birds.[11]

Understanding adaptation in a biblical model

Historically, creationists have often used neo-Darwinism as a means to understand changes that occur within created kinds in the world today. In other words, all genetic changes are viewed as errors and natural selection is the means by which traits increase or decrease in populations. Intrabaraminic diversity is assumed to result from created diversity and operation of these

naturalistic mechanisms. However, when patterns of intrabaraminic diversity are interpreted within the biblical framework that accepts the reality of a global Flood (imposing a severe population bottleneck), it is obvious more must be involved. In retrospect, given that God provides for his creatures, and that the amazing physiologic adjustments creatures can make in response to changes in their environment reflect this, it should not be surprising that God provided a means to make targeted (non-random) genetic changes as well when necessary to aid in adaptation.[6-8, 11]

While evolutionists have noted that pathways exist for adaptive changes, they have no viable reason in their model for how they came into being.[5] Further, how were these adaptive pathways maintained even in creatures that supposedly diverged long ago? After all, adaptive changes in a protein may significantly affect the possibility of future adaptive changes, especially when they involve interrupting a complex network (e.g. some colour variations or antibiotic resistance).[7,12] On the other hand, creationists recognize a Creator, and a design that allows for future useful changes indicates the foresight of the awesome Designer. It is important that creation models today are built on a realistic understanding of what is observed in the world around us. When this is done it brings glory to God because aspects of his character will be recognized in what He has created.[13]

One reason it may have been tempting to use neo-Darwinian mechanisms to explain intrabaraminic genetic diversity is that a number of genetic changes are known to result in disease. Disease is clearly a result of the Curse. It seems it was then inferred that all genetic changes were accidents, a reflection of the Curse. Yet the burgeoning scientific literature makes it evident that genetic changes directly causing disease are the exception, not the rule.

Evidence of the Curse can be seen in the fact that there can be a cost for genetic adaptation in our world today. It can be minor, with a slightly increased risk of a certain disease. Other times it can be more significant, such as with the sickle cell trait. From a medical standpoint, it is important to recognize what is really going on with genetic changes. If the body is attempting to respond to environmental challenges, then prevention of genetic diseases from *de novo* mutations may be linked to removing the challenges. Also, individuals adapted to one environment may be at greater risk when moving to a different environment, since a genetic change appears to be more of a long-term, committed adjustment to a specific environment.

These observations can also provide a basis for understanding natural evil, including the venoms seen in creatures today. It seems they can be explained in part by the fact that a pathway existed to allow for them to arise.[14] There is clearly some advantage to the possessor in terms of survival in a fallen world. Originally, all creation was in harmony and interaction between creatures and their environment brought no harm.[15] So, natural evil can be understood as a breakdown in communication (with the environment and/or creatures in it) that resulted from the sinful choice of Adam and Eve to disregard God's command.[16] Creatures no longer respond in a consistently harmonious way. While God still provides, he upholds the world in such a way that all creatures suffer and die so we can be reminded of the fact that we need a Saviour and Redeemer. Those who put their trust in Christ can look forward to a future restoration of that harmony.[17]

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