



CREATION^{In} THE CROSSFIRE

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And there was evening and there was morning, the sixth day. Thus the heavens and the earth were completed, and all their hosts....And the water prevailed more and more upon the earth, so that all the high mountains everywhere under the heavens were covered. Gen 1:31-2:1; 7:19

The Next Meeting: May 23, 2009 at 7 PM. John Rajca, former curator of ICR's museum, will speak.

Natural Selection via Malaria Pt 2

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Because we can document natural selection working through malaria, this does not mean evolution produced our present animal world from an ancient, ancestral one-celled organism. Human resistance to malaria is usually the result of a point mutation of the hemoglobin alpha or beta-chains, although there are other point mutations that confer resistance, such as Duffy negative red blood cells. Also, the malaria organisms develop resistance to anti-malarial agents, such as chloroquine, which is the result of two point mutations.

Michael Behe covers the topic of malaria in his book, *The Edge of Evolution*. The edge of evolution is the border between random and nonrandom mutations. One of his salient observations is that over the millennia that humans and malaria species (**plasmodia**) have been locked in a struggle of survival and dominance, plasmodia have never been able to adapt themselves to the mutated variant hemoglobins. This is especially germane to the debate over whether evolution can truly produce new functional cellular machinery. What keeps these organisms from adapting to the human variant hemoglobins that have been around for millennia while they have been able to quickly adapt to all the anti-malarial drugs?

There are many hemoglobin variants that have greater or lesser resistance to malaria, such as sickle cell hemoglobin and hemoglobin C. The establishment of variant hemoglobins in human populations is usually a response to the selective pressure of malaria. Americans generally have no idea how devastating this disease is because few people in our country contract malaria, but in other countries nearly the entire population is exposed to it annually, and children are the most vulnerable victims.

Michael Behe is a leading author in the Intelligent Design movement. Our review of malaria last month

led us to the effectual arguments of Intelligent Design. Michael Behe believes in descent with modification from a common ancestor (evolution), and an old earth (billions of years old).

Behe likens the interplay between the plasmodia and their human hosts as trench warfare rather than as the arms race espoused by Richard Dawkins. The mutations that cause resistance to anti-malarial drugs debilitate the plasmodia to some degree. Likewise, the mutations in hemoglobin variably debilitate humans. The red blood cells and the parasites are nanobots in this war of survival. Winning for either side would mean calling some kind of uneasy truce of mutual tolerance or commensalism. Some invading organisms have developed this kind of relationship. For example, otherwise healthy humans with adequate diets can have a parasitic infestation of ameba or even giardia with no overt clinical symptoms.

With malaria the outcome is often "winner takes all." Either the human annihilates the parasites, sometimes after years of fighting them, or the parasites kill the human host. The plasmodia are mindless nanobots that automatically carry out their programming. They are not concerned with the survival of their hosts. Their life cycle and survival depend on astronomical reproduction within a human host to insure the transfer of mature malarial gametocytes when a mosquito feeds on the infested blood.

In the mosquito's midgut, the ingested gametocytes develop into mature sex cells, which develop into sporozoites that migrate through the salivary ducts into the mosquito's proboscis from which they can be injected into a human victim at the next blood meal.

Behe discusses the development of resistance to anti-malarial drugs to show what he means by "the edge of evolution." He wants to give a sober appraisal of the limits of Darwinian processes, what they can and cannot do to show that edge, i.e., the limits. He makes this crucial point:

If there is not a smooth, gradually rising, easily found evolutionary pathway leading to a biolog-

ical system within a reasonable time, Darwinian processes won't work.

Behe gave an interesting example of what this evolutionary pathway might be like. If you were blindfolded and told to walk from Lubbock, Texas and climb to the top of the Sears Tower in Chicago, with instructions to always climb higher and never to back down, this might be similar to the rugged evolutionary landscape of random mutations and natural selection. This would keep a species...

...staggering down genetic dead-end alleys, getting stuck on the top of small anatomical hills, or wandering aimlessly over physiological plains, never even coming close to winning the biological pot of gold at a distant biological summit.

Behe brings up the problem of the plasmodia developing a mechanism to overcome the problem presented by variant hemoglobins. The plasmodia feed on hemoglobin, but the slight changes in variant hemoglobins make these hemoglobins either unavailable or less digestible. The plasmodia have been staggering down genetic dead-ends for millennia, yet have never come to a solution to their problem. Why can't the plasmodium simply absorb the nutrients it needs from its nutrient-rich host the way bacteria do? This might seem simple, but even this method is very complex, requiring, among other things, the proper membrane pumps for each class of nutrients.

If the solution were a point mutation, the probability would have been strongly in favor of finding that solution unless that mutation is too debilitating to the plasmodium. Another possible solution would have been to build a new enzyme system that would allow the plasmodium to ingest the variant hemoglobin, but this would increase the complexity, which might require Intelligent Design.

The Mathematical Limits of Darwinism

In order to detect the edge of evolution to find the limits of random mutation and natural selection, Behe calculated the probability of a single point mutation that would confer resistance to the anti-malarial drug atovaquone.

A trillion or more malarial parasites infect the average victim. About one billion people are infected with malaria each year. Spontaneous resistance to atovaquone occurs in one out of three victims. That means the probability is relatively high, 1 in 3 trillion. Resistance for chloroquine requires two point mutations, which occurs in about one person every year. A total of a billion trillion parasites is about equal to the proba-

bility for the two necessary mutations, or 1 in a billion trillion.

It took decades for falciparum to become resistant to chloroquine even though probability was strongly in favor of once a year. The protein discovered in falciparum that confers resistance is PfCRT (for *P. falciparum* chloroquine resistance trait). The methods and thinking employed to discover this protein are among the most elegant I've seen.

Thomas Wellems and his group at the National Institutes of Health did a series of genetic studies on the parasite. They discovered that the mutation responsible for resistance to chloroquine was one of approximately 5300 proteins that the parasite's DNA encodes. This was an enormous job. The parasite's genome is about 100 million nucleotides long. They narrowed it down to a 400,000-nucleotide region on one of 14 chromosomes. Finally they found a 36,000-nucleotide region and discovered a previously unknown gene. From that they were able to determine the amino acid sequence of the protein that had the mutation.

Once they had determined the protein's amino acid sequence, they realized that it had a hydrophobic section, which meant it was probably in a cell membrane. They decided that this protein was probably a protein pump. They found that this protein was located in the membrane of the parasite's digestive vacuole. They think this mutated protein allows chloroquine to leak out of the vacuole through the pump. When the plasmodia digest hemoglobin, toxic heme molecules are released. Heme is not a protein and the parasite cannot digest it. If the heme accumulates in its digestive compartment the organism will die. Normally waste heme is transformed into hemozoin and is removed, but chloroquine interferes with the waste removal process, letting the toxicity of heme to build.

PfCRT contains 424 amino acid residues. The two mutations that make this protein able to confer resistance are at positions 76 and 220.

...we saw that changes in human genes in the wake of malarial attacks were diminishment—beneficial only in dire circumstances, but detrimental in normal times. *P. falciparum*, however, greatly outnumbers humans and reproduces much more rapidly, and therefore has many more opportunities for lucky genetic accidents. By standard Darwinian theory, it ought to make the next step in the arms race very early. Standard Darwinian logic predicts that malaria will mutate more, and sift its mutations more effectively than humans. So are the changes in the mutated PfCRT an improvement? Is the parasite

strengthening in an absolute sense, and evolving new “advanced and complex machinery,” as Richard Dawkins might expect? It appears not. When chloroquine is no longer used to treat malaria patients in a region, the mutant strain of *P. falciparum* declines and the original strain makes a comeback, indicating that the mutant is weaker than the original strain in the absence of the toxic chloroquine. Apparently, much like human thalassemia or sickle hemoglobin or G6PD deficiency, the mutant malarial protein is a new plus only in desperate circumstances—in trench warfare.

Trench Warfare

The struggle between the plasmodia and humans is not an arms race according to Behe. Some scientists refer to the development of antimicrobial resistance and human ingenuity for developing new antibiotics as an arms race. When the parasite or the human produces a mutation, the over-all vitality of the mutant offspring decreases. Mutant hemoglobin almost always produces some anemia and other side effects. A person with sickle cell trait has mildly decreased hemoglobin content. Coupled with iron deficiency or a bacterial infection, the health of carriers would deteriorate more rapidly than someone with normal hemoglobin.

Many of the variant hemoglobins confer some kind of protection to malaria. As mentioned last time, sickle cell disease is cruel beyond the imagination of most people. To see it in action is heartrending. The same is true of the severe thalassemias.

If these mutations were an arms race, the side producing the mutation would benefit from its protection, but because the mutation produces degeneration of a normal functioning molecule, the effect is to weaken the individual. The parasite or person experiences decreased health. This kind of response, then, is not an arms race, but trench warfare where sacrifices are made to improve survivability at the expense of critical resources.

Hemoglobin C-Harlem vs. Hemoglobin S

Behe says it is crystal clear that the spread of the sickle gene is the result of Darwinian evolution—natural selection acting on random mutation. He also said that hemoglobin C-Harlem, discovered in a New York City resident, doesn't form sickle cells. According to the European Network for Rare and Congenital Anemias (ENERCA), it does produce sickling when deoxygenated. www.newbornscreening.com says that the RBCs of children with HbSC-Harlem do sickle.

C-Harlem has HbS's mutation at the 6th position of the beta chain, but it has a second mutation at the 73rd position. Behe seemed excited to report C-Harlem has almost all the protection HbS has but has none of the bad effects of sickle cell disease. Behe wondered why HbC-Harlem wasn't more prevalent in Africa. Possibly, the reason is that combining HbC-Harlem with HbS could be as troublesome as HbSS, conferring no more advantage. HbC-Harlem parents would have to mate with HbS spouses in order to replace HbS as the dominant gene.

Intelligent Design does not necessarily favor Biblical creation however. Intelligent Design advocates purport to apply scientific methods and principles to determine whether something is the product of an intelligent designer. A vanishingly small probability does not guarantee that something was designed. Rather, those things that are complex and cannot happen as a result of random events, have an extremely low probability and, especially if they meet Behe's criterion of irreducible complexity, are designed. Behe's criterion of irreducible complexity. The plasmodias' inability to develop an enzyme system that would allow them to digest variant hemoglobins properly seems to indicate the edge of evolution where random mutation and natural selection will always fail to provide a solution.

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