Gene therapy for malaria: Benefits far outweigh the risks

There's a new treatment emerging for malaria, a kind of gene therapy that makes the malaria parasite more susceptible to anti-malaria drugs. It's the work of a team at Yale University, whose lead researcher, Sidney Altman, is famous as a pioneer in molecular genetics. In 1989, he won the Nobel Prize for his discovery that RNA molecules can function as enzymes, understanding of which changed everything in genetics along with research on the origins of life. Now, Altman's team at Yale believes it's possible to alter genetic expression of plasmodium, the malarial parasite, which could amount to a sea change in the war against one of humanity's worst infectious diseases.

And so, there's no way that anyone could be against it, right? Well maybe not. After all, it is a kind of gene therapy and gene therapy scares people, especially those who do not like scientists messing with anyone's genome. Of course they don't all say "genome". Typically, the alarmists say "genetic code". That's what you find in the most alarmist articles, like this one on the quack website Natural News, where Mike Adams, the same guy who recently blamed Beau Biden's death on GMOs and chemotherapy, wrote:

> I'd like to talk about genetic engineering for a moment, but to preface it with the recognition that we, as a society, are nowhere near the level of maturity and ethics required for manipulating the genetic code. I don't believe we are ready for genetic engineering, but at some point we may evolve ethically and spiritually to the point where we can more responsibly grasp this potential technology. So even though I'm in favor of exploring genetic engineering in the long run, I am solidly against it today.

It's almost as if Adams said, "I'm genetically illiterate, but hear me out anyway." Otherwise, he would know that the Genetic Code is not a target of gene therapy. But that's okay; the Genetic Literacy Project is all about facilitating literacy about things that people need to know to navigate issues of biotechnology, things like what is a gene, what is DNA, what is RNA, and what is the Genetic Code.

So let's talk about why "Genetic Code" is capitalized when used correctly, yet is not capitalized when used by those who don't know what they're talking about. The Genetic Code is the language that all living things on Earth–all cells in the human body and any organisms that make humans sick–use to read genes in order to express them. It's not the content that varies from species to species and individual to individual. There are genes coding for the Code itself, but those are the genes that do not get changed. All organisms of all species use the same genetic language, but differ in the genetic content that the language is used to express. Thus, for example, the plasmodium parasite, uses the exact same Genetic Code that our cells use.

The Genetic Code has been around for billions of years. It has not evolved much, and it's needed for genes to work and for gene therapy to work. And so, while initially it may sound as if we're merely being picky about terminology, it's actually about understanding the most important concept in genetics. But get ready to hear more from those concerned about gene therapy, especially from alarmists like Adams who fundamentally don't trust modern medicine, mainstream doctors, and scientists.

The question that comes up now though is whether we have 'evolved ethically' enough to commit to defeating malaria, which kills 500,000-800,000 people, mostly children and mostly in third world countries. Now, because of our exponentiating ability to manipulate, not the Genetic Code but genes and gene products within cells, the Yale team has a novel strategy that may be poised to turn the tides against malaria.

Gene therapy for malaria: How it works

Before delving into the therapy, it's important to talk about what malaria is and why it's such a problem. Plasmodium is a kind of protozoan, a singled-celled creature whose structure and genetics are very similar to those of our own cells. Several species of plasmodium act as parasites in humans. Victims get infected with plasmodium through a mosquito bite and the organism settles in the liver. There, it matures and reproduces for 3-12 days, depending on the species. During this time the victim has no symptoms and for certain plasmodium species this state can continue for a few years. In most cases, however, new immature forms of the parasite spread out from the liver and infect red blood cells and that's when the person gets really sick, with a very high fever, chills, fatigue, and a host of other symptoms. Certain drugs can destroy plasmodium parasites, but there's been growing resistance to the drugs, especially from the worst plasmodium species, called *Plasmodium falciparum*. Additionally, many of the antimalarial drugs will destroy the parasites in blood cells, but not those remaining in the liver, so the person can get sick again.

In a new study published in the *Proceedings of the National Academy of Sciences*, Altman's team from Yale demonstrated how to use specially designed strands of RNA called a morpholino oligomers to strike directly at *P. falciparum*, where the punch can have the greatest effect: the parasite's gene expression. Before a gene in DNA in the cell nucleus can be translated –using the language of the Genetic Code that is the same in all organisms– into a protein that's needed to run a specific function in the cell, the gene is first transcribed into what's called messenger RNA (mRNA).

The mRNA is a kind of intermediate that must travel to a different part of the cell before the genetic message can finally be used. But a specially designed morpholino oligomer can attach to the mRNA, effectively neutralizing it, or it can interfere with how the mRNA is spliced or otherwise processed in order to deliver its message. Thus, while the gene in the nucleus may be switched on so that it's constantly sending out it's message, the message cannot be read, so whatever protein was supposed to be manufactured never does get manufactured. It's kind of like RNA interference that's being used ever more frequently to design new foods.

Since this all happens inside the cells of the parasite, the morpholino oligomer strategy can potentially be far more effective than any drug, if certain key genes are chosen for blocking. Or, the Yale research

suggests, morpholino oligomer can be used to weaken the parasite, such that strains otherwise resistant to antimalarial drugs would become extremely susceptible.

Could there be risks? Of course there could be. To be delivered to plasmodium parasites in red blood cells, liver, and other tissues, morpholino oligomers would have to be sent through the infected patient's blood and people might worry that they might do something to the patient's own cells. Well they might, but then again, they are RNA, not DNA. RNA does not last very long before it's broken down, so there's no reason to think that a morpholino oligomer should have any permanent effect on a human. Perhaps, they could block expression of a human gene that happens to be very similar to a plasmodium gene. But such an unlikely effect would be very temporary, and all in all the most susceptible entity within the person would be the parasite that the morpholino oligomer is designed specifically to kill. So while there's a risk, it's very small, and that must be considered, particularly in context of one of humanity's worst diseases.

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