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Team discovers genetic material in blood cells that may affect malaria parasites

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Researchers at Duke University Medical Center may finally have discovered why people with sickle cell disease get milder cases of malaria than individuals who have normal red blood cells.

In a finding that has eluded scientists for years, Duke researchers discovered that genetic material in red blood cells may help alter parasite activity via a novel mechanism that alters parasite gene regulation.

"One of the most interesting findings in our study is that the human microRNA (very small units of genetic material) found in sickle red cells directly participate in the gene regulation of malaria parasites," said Dr. Jen-Tsan Chi, M.D., Ph.D., senior author and associate professor in the Duke Institute for Genome Sciences and Policy and Department of Molecular Genetics and Microbiology. "These microRNAs enriched in the sickle red cells reduce the parasite's ability to propagate, so that certain people stay more protected."

MicroRNAs are small units of RNA, which come from DNA. MicroRNAs are only 20-25 nucleotides long and help to regulate gene expression.

The scientists also showed that when two different microRNAs were introduced at higher levels in normal red cells, the parasite growth also was decreased.

The findings appear in the journal Cell Host and Microbe.

"This finding should lead to greater understanding of the host-parasite interaction and parasite lifecycle, which may eventually develop into a new approach to therapy for malaria, which up to 500 million people develop each year worldwide," Chi said.

Every year about 1.5 to 3 million people die from the disease, most of them children, according to the World Health Organization (WHO). Between 1,000 and 2,000 cases occur in the United States.

"I think this work will expand our understanding of the interaction between the malaria parasite and its human host, given that this is a completely new mode of interaction between them, and will give us a far greater understanding of the parasite life cycle," said lead author Greg LaMonte, a scientist in the Chi laboratory.

The malaria parasites grow in the human red cells, cells that scientists thought lacked any genetic material. Many scientists had looked for the components in sickle cells that could help them resist the parasite, but the Duke researchers found one component by thinking outside of scientific norms.

The Duke team found microRNAs in the red blood cells and showed that their composition is dramatically different in the sickle red blood cells. Counter to what they expected, they showed that these differences directly contribute to the malaria resistance in sickle cell disease.

The scientists also conducted a different experiment that showed blocking these microRNAs (miR-451 and Let-7i is particular) in sickle cells reduced the ability of the cells to protect against malaria.

"If you block the miRNAs, the parasite grows two or three times as well," Chi said.

Another surprise in this investigation was the presence of a chimera, a fusion of human microRNA with the parasites' mRNAs.

"We never expected to find this," Chi said. "The fusion of human and parasite RNA represents a unique form of host-parasite interaction, and may reflect either a novel form of host-cell immunity or a mechanism by which the parasite is able to adapt to the host-cell environment."

Provided by Duke University Medical Center