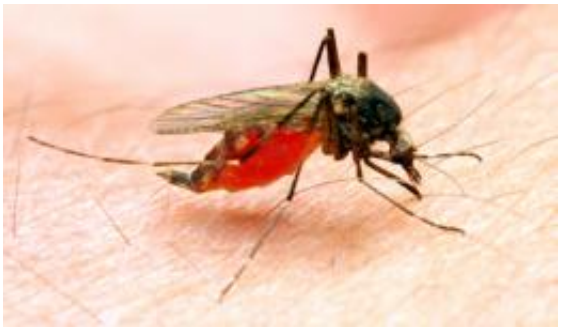
How malaria evades the body's immune response

July 12 2012, By Helen Dodson



(Medical Xpress) -- The parasites that cause human malaria and make it particularly lethal have a unique ability to evade destruction by the body's immune system, diminishing its ability to develop immunity and fight the infection, a Yale study has found. The study appears in the Online Early Edition of the *Proceedings of the National Academy of Sciences*.

One of the biggest problems in controlling malaria in regions of high transmission, where it continues to account for over one million deaths yearly, is that protective immunity against re-infection does not occur. It is believed that inadequate formation and maintenance of infection-fighting memory T-cells are at the root of this immune malfunction. This phenomenon also frustrates efforts to develop effective malaria

vaccines.

It's known that malaria causes a highly inflammatory response in infected individuals that leads to the deadly clinical complications of anemia and cerebral disease. The Yale research team learned that the parasites produce their own version of a human cytokine, or immune hormone, which directs the inflammatory response during malaria. They also discovered that this cytokine, called PMIF, incapacitates the anti-malaria, memory T-cell immune response.

Using a genetically modified strain of the malaria parasite in mice, the Yale team found that PMIF causes host T-cells to develop into short-lived effector cells rather than protective memory cells. The short-lived cells die during the infection, and the long-lived memory T-cells are not produced in adequate numbers to combat the infection or to protect from re-infection, which occurs repeatedly in malaria-endemic regions.

"These findings indicate that malaria parasites actively interfere with the development of immunological memory, and may account for the inhibition of protective immune responses in human malaria," said Rick Bucala, M.D., professor of internal medicine, pathology, and epidemiology and public health at Yale School of Medicine. "This knowledge will help us identify specific therapies that can protect anti-malarial T-cells from death and improve an individual's immune response to infection or to vaccination."

More information: *PNAS* paper: www.pnas.org/content/early/201 … 573109.full.pdf+html

The published work was the graduate thesis of Yale student Tiffany Sun. Additional authors are Thomas Holowka, Yan Song, Swen Zierow, Lin Leng, Jason Griffith and Elias Lolis of Yale; Yibang Chen and Huabao Xiong of Mount Sinai School of Medicine; Mehdi Nouraie and Victor R.

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The research was supported by the National Science Foundation, the National Institutes of Health, and the Netherlands Organization for Scientific Research.

Provided by Yale University