Malaria sporozoites injected in the skin reach the blood vessels and enter the blood circulation. They reach the liver, invade hepatocytes and develop into liver stages.

The circumsporozoite protein (CSP), expressed on the surface of sporozoites is believed to play an important role in sporozoite motility in the skin and invasion of the liver.

MAM01 is a human monoclonal antibody that recognizes the central repeats (NPNA) and the minor NVDPNANP containing repeats of the falciparum CSP.

Anti-CSP monoclonal antibodies like MAM01 bind CSP, and the hypothesized mechanism of action is inhibition of sporozoite motility.

To better understand the mechanism of action of MAM01 and its functional properties, in vivo, intravitral microscopy was used to characterize the effect of MAM01 on in vivo motility of sporozoites.

Methods

- Mice were passively immunized with 10 μg, 30 μg, 100 μg and 300 μg of MAM01.
- 16 hours later transgenic sporozoites expressing full P. falciparum CSP (PfPf full CSP) and mCherry expressing were dissected in L15 media, adjusted to 5,000-10,000 parasites/μl and inoculated intradermally with multiple injections into the ear pinna.
- Parasites in the skin were imaged with a 10X objective on an inverted Zeiss Axio Observer Z1 microscope with a Yokogawa CSU22 spinning disk. Mice were kept in a microscope chamber warmed at 28°C.
- Ten minutes after the inoculation, 5-minute videos were recorded to evaluate motility, speed and net displacement. At least 4 videos per condition were recorded.
- Speed and net displacement were automatically tracked from recorded videos and the percent of motile and non-motile total sporozoites were manually counted.

Conclusions

- Sporozoite motility was severely affected in mice passively immunized with MAM01 antibody.
- Sporozoite net displacement and average speed were parameters also affected in immunized mice.
- The data support MAM01’s mechanism of action to be alteration of sporozoite motility.