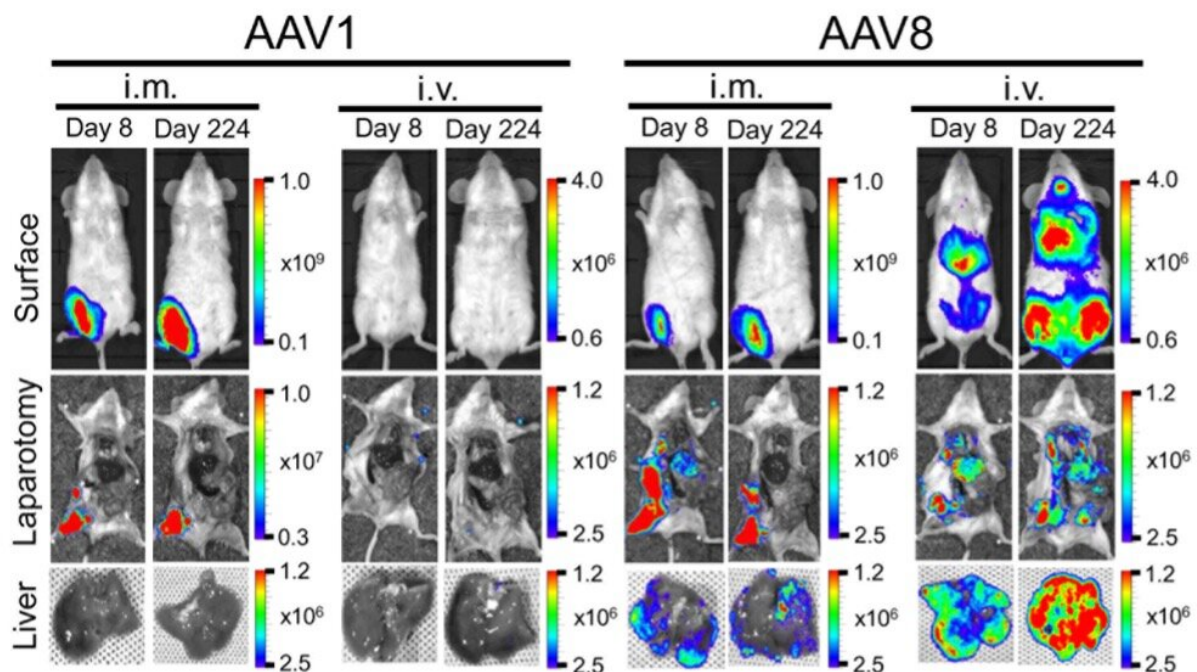


A novel malaria vaccine vector that targets the liver

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The IVIS imaging results for the livers collected from mice on day 8 or day 224 post-administration of AAV-Luc showed that systemic administration of AAV8 induced ~24–43 times better liver luciferase enzyme activity when compared with i.m. administration. Credit: Kanazawa University

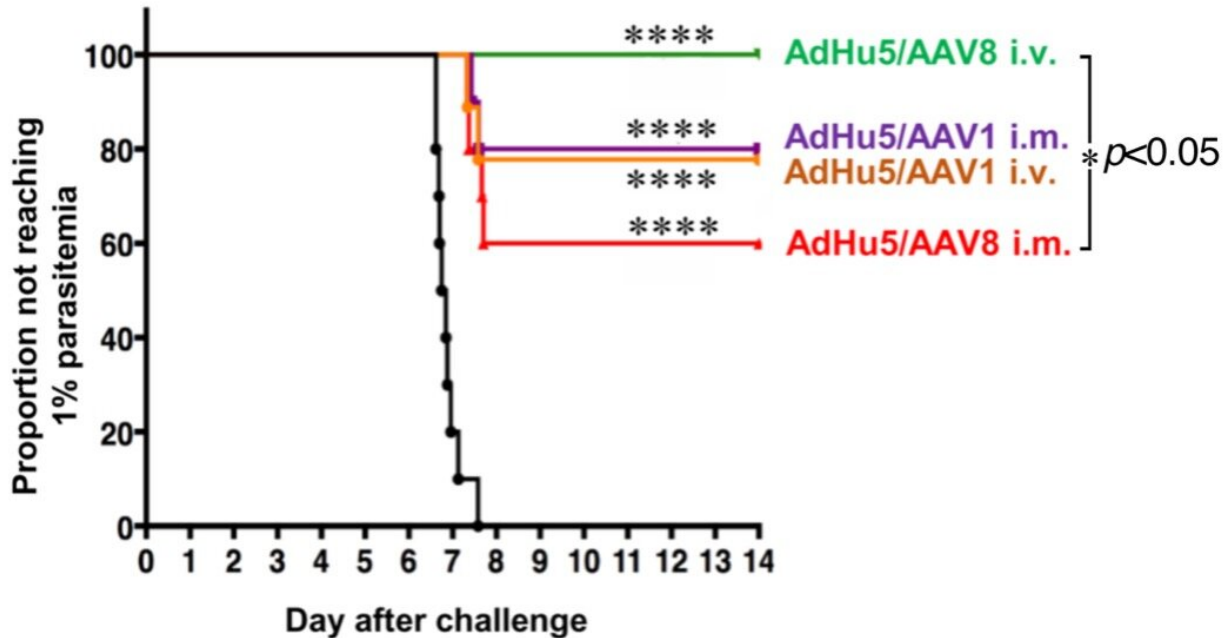
Malaria remains a deadly disease that affects people worldwide, particularly in Africa. Caused by a parasite that can enter the human bloodstream via mosquito bite, the parasites can then infect and

reproduce within the person's liver. Significant effort has been made to develop an anti-malaria vaccine; unfortunately, previous vaccine candidates have had low-to-modest efficacies. Now, in an article in *Frontiers in Immunology*, researchers at Kanazawa University have identified a new vaccine platform as a potentially better-performing inducer of anti-malaria immunity in the liver.

Malaria vaccines are often designed to generate an [immune response](#) to the Plasmodium falciparum circumsporozoite protein (PfCSP), which is present at pre-erythrocytic stages. Plasmodium falciparum is the specific parasite that causes the deadliest form of malaria. Because of the nature of this parasite's biology, previous attempts have indicated that a successful vaccine needs to induce a T cell-mediated response in the [liver](#) that can clear the infection within a week of beginning—and thus before the parasites have multiplied, matured, and re-entered the bloodstream.

The research team published earlier results targeting PfCSP using a vaccine backbone known as adeno-associated virus serotype 1 (AAV1). AAV1 worked best when used as a booster. However, the group hypothesized that another type of backbone, AAV8, would be more effective.

"AAV8 is a hepatotropic virus, which means it specifically targets the liver," explains Mohammad Shahnaij, lead author of the study. "We believed it would address the timing concerns associated with suboptimal anti-malaria vaccine candidates."



Mice primed by i.m. injection with the AdHu5-PfCSP vaccine followed by an i.m. or i.v. booster vaccine dose of AAV1 or AAV8 were challenged with transgenic PfCSP-Tc/Pb sporozoites. The immunization regimen of i.m. AdHu5-PfCSP/i.v. AAV8-PfCSP provided 100% protection. Credit: Kanazawa University

The researchers created a vaccine that expresses PfCSP with AAV8 as the backbone. Lab mice were primed with another vaccine known as human adenovirus type 5-PfCSP. Then, one group of mice was given AAV8-PfCSP intravenously (IV), while another group was treated with it intramuscularly (IM). AAV8-PfCSP served as a booster shot in these experiments.

"IV injection caused the vaccine to be about 2.5 times better at entering the mouse liver [cells](#) than IM injection," explains Shigeto Yoshida, senior author. "We also found that an IV booster shot with AAV8-PfCSP was significantly more efficacious than an IM booster

with this [vaccine](#), and more effective than using either an IM or IV dose of AAV1-PfCSP."

The group also examined immune cell responses following a single IV dose of AAV8-PfCSP. Notably, T cells were significantly recruited to the liver compared with mice injected with a saline solution.

"We observed a large population of cytotoxic T cells, especially effector memory T cells, in the livers of mice given IV injections of AAV8-PfCSP," says Shahnaij. "These cells are extremely important for removing parasites and infected liver cells."

These findings may revolutionize the field of anti-malaria therapy and potentially help save the lives of countless people living in parts of the world ravaged by this disease.

More information: Mohammad Shahnaij et al, Liver-Directed AAV8 Booster Vaccine Expressing Plasmodium falciparum Antigen Following Adenovirus Vaccine Priming Elicits Sterile Protection in a Murine Model, *Frontiers in Immunology* (2021). [DOI: 10.3389/fimmu.2021.612910](#)

Provided by Kanazawa University

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