マラリア原虫の免疫逃避

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マラリアは最も深刻な感染症の一つであり、毎年約 50 万人が死亡している。これまでにアルテミシニンを初め様々な抗マラリア薬が発見されてきたが、効果的なワクチンの実用化には至っていない。これはマラリア原虫が抗原変異と抗原多型を利用し、巧みに宿主の獲得免疫を回避しているからだと考えられてきた。今回、荒瀬らは、新たな免疫逃避機構として、マラリア原虫が赤血球上に RIFIN というタンパク質を発現させて、積極的に宿主の免疫反応を抑制することを見出した。これは、がん細胞が PD-L1 を発現して T 細胞の PD-1 と結合し、免疫にブレーキをかける仕組みとよく似ており、抗マラリア薬・マラリアワクチンの開発においても「免疫チェックポイントの阻害」が切り札になることを示した画期的な報告である。

紹介論文

Immune evasion of *Plasmodium falciparum* by RIFIN via inhibitory receptors.
Saito F, et al & Arase H* (Biken, Osaka univ.)
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要旨

Malaria is among the most serious infectious diseases affecting humans, accounting for approximately half a million deaths each year. *Plasmodium falciparum* causes most life-threatening cases of malaria. Acquired immunity to malaria is inefficient, even after repeated exposure to *P. falciparum*, but the immune regulatory mechanisms used by *P. falciparum* remain largely unknown. Here we show that *P. falciparum* uses immune inhibitory receptors to achieve immune evasion. RIFIN proteins are products of a polymorphic multigene family comprising approximately 150–200 genes per parasite genome that are expressed on the surface of infected erythrocytes. We found that a subset of RIFINs binds to either leucocyte immunoglobulin-like receptor B1 (LILRB1) or leucocyte-associated immunoglobulin-like receptor 1 (LAIR1). LILRB1-binding RIFINs inhibit activation of LILRB1-expressing B cells and natural killer (NK) cells. Furthermore, *P. falciparum*-infected erythrocytes isolated from patients with severe malaria were more likely to interact with LILRB1 than erythrocytes from patients with non-severe malaria, although an extended study with larger sample sizes is required to confirm this finding. Our results suggest that *P. falciparum* has acquired multiple RIFINs to evade the host immune system by targeting immune inhibitory receptors.