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The Effect of Autoimmunity and Skin Melanization on the Resistance to Murine Malaria

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Introduction: Plasmodium falciparum has exerted tremendous selective pressure on genes that improve survival in severe malarial infections. Systemic lupus erythematosus (SLE) is an autoimmune disease that is six to eight times more prevalent in women of African descent as compared to women of European descent, which usually present lower levels of cutaneous melanin. In our studies we evaluated the effect of genetic changes that increase the susceptibility to SLE and the effects of melanin production on the response to malaria. To evaluate the effect of melanin on malaria, we tested three different murine malaria models in congenic mice that only differed on the gene that encodes for the enzyme involved in mammalian melanin biosynthesis. To this end, we infected albino C57B6.Tyr$^{-/-}$ mice with either the cerebral malaria model *Plasmodium berghei* ANKA, the severe anemia model *Plasmodium yoelii* 17XL or the chronic infection model *Plasmodium c. chabaudi* AS. To investigate the effect of autoimmunity on the response to malaria we infected mice deficient in FcϒRIIB and/or overexpressing TLR7 with *P. berghei* ANKA or *P. yoel*ii 17XL. **Results:** Mice that are prone to SLE due to a deficiency in FcϒRIIB, or to overexpression of TLR7, are protected from death due to cerebral malaria. Protection appears to be by immune mechanisms that allow SLE-prone mice to better control their overall inflammatory responses to parasite infections. Albino mice lacking tyrosinase do not present different clinical outcomes than regular C57B6 mice.

Discussion: These findings suggest that the high prevalence of SLE in woman of African descent, living outside of Africa, may be due to the inheritance of genes that are beneficial in the immune control of cerebral malaria, but in the absence of malaria, contribute to autoimmune disease. Melanin does not affect the response to malaria infection, suggesting that melanization was not selected because of malaria.

Keywords: autoimmunity, malaria, melanin, systemic lupus erythematosus