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Tracking the Battle: Immune Cells vs HIV in Humanized Mice

HIV is a human-specific pathogen. The discovery of humanized mice with high HIV susceptibility opened a new chapter in HIV research. In fact, we were the first to report on this novel humanized HIV mouse model over a decade ago. Humanized mice are generated by transplantation of hematopoietic stem and progenitor cells into severely immunocompromised mice. These mice develop an immune system of human origin. We used this HIV mouse model, among other things, to investigate novel drugs, genetic engineering methods for producing HIV-resistant immune cells, and the pathogenetic significance of macrophages. Macrophages were long considered a mere HIV reservoir with no further pathogenetic significance in HIV. We had previously found that macrophages in HIV-infected humanized mice are less susceptible to clearing bacterial products, explaining the sustained HIV-associated immune activation. However, these data did not account for the complex and plastic nature of macrophages. Using a sophisticated humanized mouse model, we found that macrophages exhibit anti-HIV activity, most likely through the secretion of soluble factors. Finally, I will illustrate the value of humanized mice for investigating immunotherapies to control HIV without antiretroviral treatment, umanized represent a breakthrough in studying HIV research.

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