Medical Xpress

Managing cellular security systems

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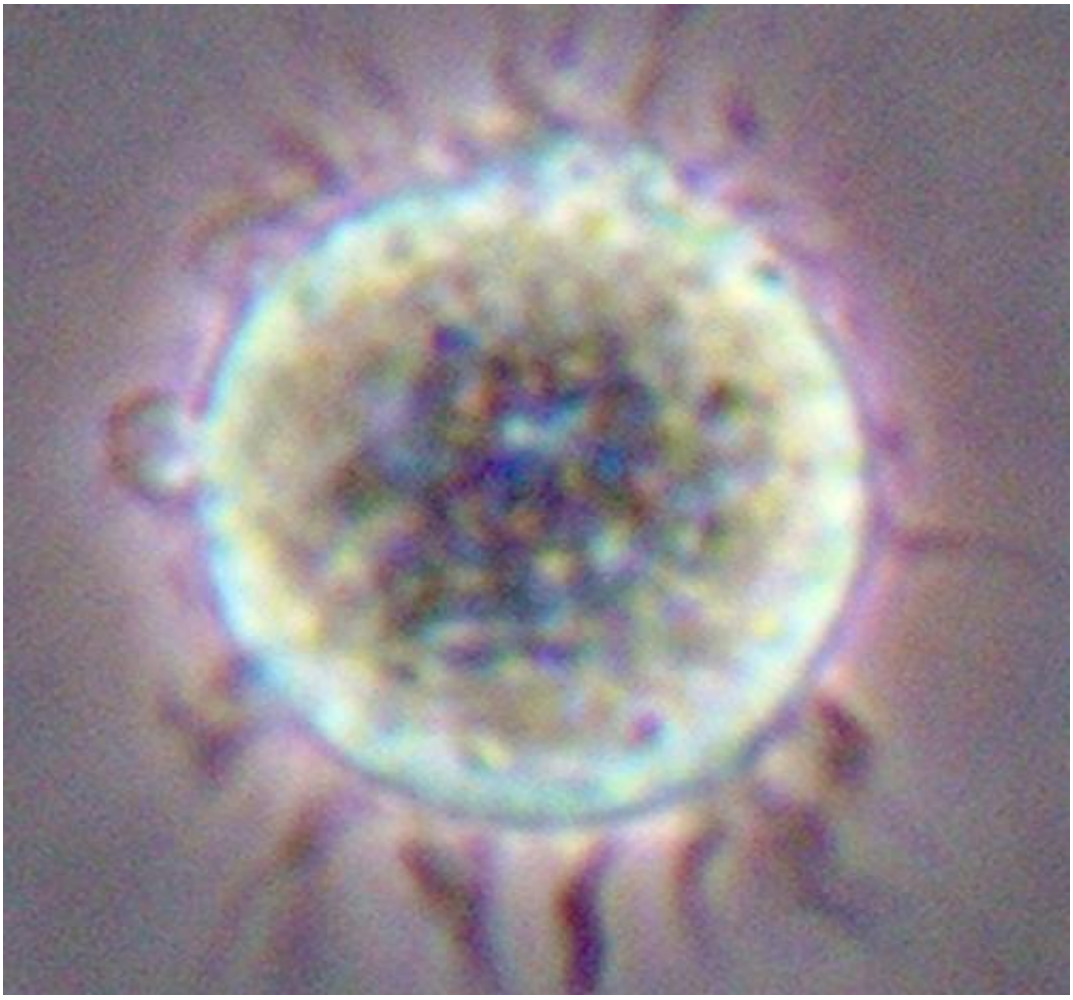

Microscopic image of a mouse cDC. Credit: 2012 Katsuaki Sato, RIKEN Research Center for Allergy and Immunology

Conventional dendritic cells (cDCs) are the immune system's patrol. They recognize foreign threats and trigger a defensive response, while

restraining immune reactions against inappropriate targets like host proteins. They achieve the former via a mechanism called cross-presentation, which displays pieces of pathogens to cytotoxic T lymphocytes (CTLs)—the immune system's 'attack dogs'—while the latter function relies on cDC interactions with regulatory T (T_{reg}) cells.

Katsuaki Sato's group at the RIKEN Research Center for Allergy and Immunology in Yokohama recently identified a subset of cDCs with an especially important role in fighting infection. These cells can be classified based on the proteins they show on their surface and Sato's team became especially interested in cDCs featuring a protein called CD205. "$CD205^+$ cDCs are more efficient in the cross-presentation of cell-bound or soluble antigens to CTLs than other dendritic cell subsets," explains Sato. "However, their role in the immune system under physiological conditions was unclear."

To clarify the function of these cDCs, Sato and colleagues genetically engineered mice in which $CD205^+$ cDCs could be quickly and selectively killed off via injection with diphtheria toxin. This depletion lasted for several days, giving the researchers a powerful way to study the specific contribution of these cells to immune function. Initial experiments with the mice provided compelling evidence that $CD205^+$ cDCs are required to marshal an effective CTL response. Loss of these cells also resulted in abnormal T_{reg} levels in various tissues, indicating that $CD205^+$ cDCs are required to maintain appropriate levels of other T cell populations throughout the body.

Animals infected with high doses of the pathogenic bacterium *Listerium monocytogenes* normally perish quickly due to septic shock resulting from immune overreaction, but $CD205^+$ cDC-deficient animals proved resistant to septic shock and tended to survive longer, revealing a crippled inflammatory response. In the end, however, these animals were more vulnerable to bacterial infection and proliferation, resulting from

impaired cDC cross-presentation of bacterial antigens to CTLs. The researchers observed similar effects with viral infection.

These results position CD205$^+$ cDCs at a critical juncture for regulating overall immune system function as well as directed counterattacks against pathogens and the researchers see clear potential for exploiting these cells in clinical applications. "Further elucidation of CD205$^+$ cDC function might provide insights into immune regulation and pathology and aid therapeutic interventions for infectious diseases as well as autoimmune and inflammatory disorders," says Sato. "For example, we would like to develop vaccines that selectively target CD205$^+$ cDCs with bacterial and viral antigens."

More information: Fukaya, et al. Conditional ablation of CD205+ conventional dendritic cells impacts the regulation of T-cell immunity and homeostasis in vivo. *Proceedings of the National Academy Sciences* 109, 11288–11293 (2012). www.pnas.org/content/109/28/11 … df-aeca-bd12e8ea4a9a

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