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Unsuspected immune arsenal in infants

While completely protected from any infectious germs in their mother's womb, fetuses spontaneously develop, "in advance", an immune defense system ready to react to the bacterial colonization of their digestive tract at birth. This surprising observation made by scientists at the Institut Pasteur and the French National Center for Scientific Research (CNRS) also shows that this same mechanism is capable of regulating its antibacterial activity to allow the installation of intestinal commensal flora and establish the indispensable balance between bacteria and the immune system. This discovery sheds new light on the understanding of mechanisms at the root of auto-immune diseases such as Crohn's disease. This work has been published in *Nature Immunology*.

Before birth, within the sterile conditions of the mother's womb, a fetus is generally not exposed to any kind of infectious agent. Scientists believed that immune defenses were not developed until *ex utero* life on contact with germs – bacteria, viruses, fungi, etc. – from the environment. However, scientists from the Institut Pasteur and the CNRS (Lymphoid Tissue Development Unit) have recently shown in animals that the fetus possesses, well before birth, a strong and spontaneous immune arsenal.

Scientists discovered that this system surprisingly involves particular white blood cells called ILC^[1], from the lymphocyte family. However, contrary to "classic" lymphocytes, these recently discovered cells are involved in innate immunity and not acquired immunity: they are not specific to any pathogenic agent.

After birth however, certain bacteria must progressively colonize the digestive tract to form the endogenous intestinal flora indispensable to our development, health, and nutritional functions. Scientists have shown that ILCs are capable of moderating their antibacterial action and regulating the establishment of this beneficial flora. They then supervise its proliferation, which, without control could become pathogenic.

Scientists at the Institut Pasteur and the CNRS have succeeded in identifying the cellular mechanisms of this balance. They have shown that in the event of infection the ILCs respond by emitting two pro-inflammatory messenger molecules: interleukin 17 and interleukin 22. These molecules force epithelial cells within the intestine to produce small bactericidal proteins to destroy the bacteria before they cross the intestinal wall. Interleukin 17 also activates massive recruitment of neutrophilic white blood cells to digest and thus eliminate bacteria. Once the bacterial threat is controlled the system is repressed.

Uncontrolled neutrophil activation may, in some cases, result in the accidental destruction of the organism's tissues. This phenomenon may be at the root of certain auto-immune diseases, such as Crohn's disease, in which chronic inflammation affects the intestine. The scientists' discovery contributes to further understanding of regulation of the balance between the bacteria in our intestine and the immune response controlling them. It also provides new tools for understanding and treating these diseases.

[1] ILC: Innate Lymphoid Cell

Source

RORyt+ innate lymphoid cells regulate intestinal homeostasis by integrating negative signals from the symbiotic microbiota, *Nature Immunology*, en ligne le 20 février 2011.

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