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Journal club

HETEROLOGOUS IMMUNITY MEETS TISSUE-SPECIFIC TRAINING

In 1980, oil exploration in the Peruvian Amazon resulted in contact with the isolated Nahua Indian tribe. Within only a few years, 50% of this previously uncontacted tribe were dead because they lacked adaptive immunity to Western diseases. Based on what we know now about how the immune system responds to infection, these isolated Indian populations also lacked the adaptation of innate immunity and tissue microenvironments that comes with the experience of frequent infections that are passed between individuals in a denser populace. A 2003 report by Selin, Welsh and colleagues in *The American Journal of Pathology* is one of the first to show that a previous infection alters immunity and pathology to the next infection.

It is not simply adaptive immunity that 'adapts'. Transient inflammatory conditions can result in long-lasting changes in tissues. For example, after an inflammatory response, the lungs contain a larger number of macrophages of different types, have higher levels of matrix and apoptotic cell turnover, contain more T cells and acquire isolated B cell follicles. This altered state of the lung tissue has a qualitative effect on the next inflammatory condition. This concept of heterologous immunity was pioneered, in my view, by Chen *et al.*, who showed that the sequence of lung infections can influence the outcome of the next infection. Some sequences of infection were beneficial to later immune responses (for example, influenza virus followed by vaccinia virus), whereas others were harmful (for example, influenza virus followed by lymphocytic choriomeningitis virus), which indicates that early-life infections can sculpt the local tissue microenvironment.

> "adaptation of tissue-specific immunity with infectious experience explains the heterogeneity in the response of humans to infection"

Immunologists can now apply this influence of infections to the recent concept of tissue-specific training of innate immunity (see Further reading). Tissue conditions determine immune reactivity, the response to the pathogen sculpts the tissue microenvironment, the tissue then retrains immunity, such that immunity to the next infection is different, and so the cycle continues. This adaptation of tissue-specific immunity with infectious experience explains the heterogeneity in the response of humans to infection — for example, why some patients with chronic lung diseases such as asthma and COPD develop infectious complications, whereas others do not, and why previously uncontacted isolated communities should be cautious about contact with Western populations.

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ORIGINAL ARTICLE Chen, H. D. *et al.* Specific history of heterologous virus infections determines anti-viral immunity and immunopathology in the lung. *Am. J. Pathol.* **163**, 1341–1355 (2003)
FURTHER READING Netea, M. G. *et al.* Trained immunity: a memory for innate host defense. *Cell Host Microbe* **9**, 355–361 (2011)