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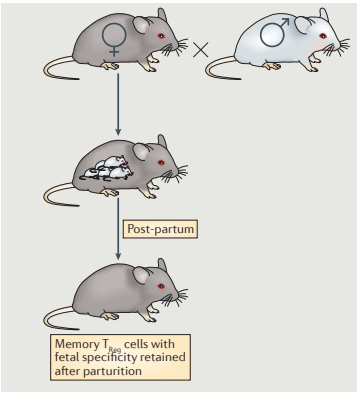

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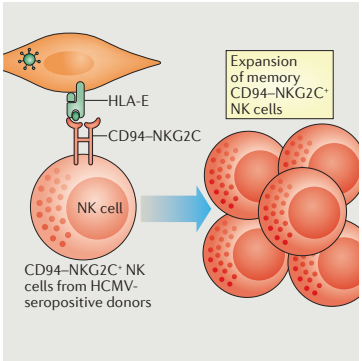

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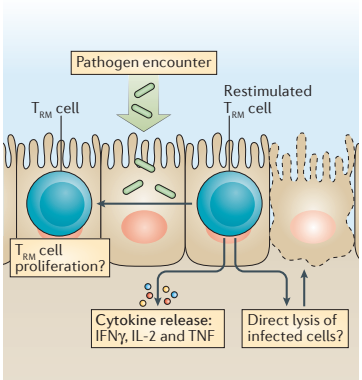

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When Edward Jenner introduced vaccination against smallpox in 1796 — which led ultimately to the worldwide eradication of the disease by 1979 — he understood almost nothing about the immune mechanisms responsible for the health benefits. We now know that vaccination, which has revolutionized modern medicine, depends on the phenomenon of immune memory, and we define this as a quantitatively and qualitatively enhanced immune response upon rechallenge. This textbook view considers immune memory to be a hallmark of adaptive immunity, and decades of research has investigated the memory properties of B cells and T cells with a view to enhancing vaccine design. For example, it is becoming increasingly clear that $CD4^+$ T cells are essential for the formation of protective memory $CD8^+$ T cells following infection or immunization. A greater understanding of the signals that influence the quantity and quality of memory $CD8^+$ T cells will be crucial for the design of vaccines able to elicit T cell-mediated immunity. Furthermore, we have learnt recently that the specialization of some memory T cells into tissue-resident subsets gives the host enhanced regional immunity. Can vaccines be designed to safely and effectively induce local specialists to prevent reinfection at a particular target site? In turn, such studies of 'classical' immune memory have paved the way for a broadening of the field away from its original definition. In addition to enhancing secondary immune responses, T cells — in the form of memory regulatory T cells — can also protect against aberrant secondary responses, which has implications for autoimmunity, antimicrobial host defence and maternal–fetal tolerance. As evidence of regulatory T cell memory emerges in humans, it will be important to factor the balance between effector and regulatory memory into vaccine design. Immunologists are also now beginning to turn their attention to 'memory' outside of the adaptive immune system. It has been shown that natural killer (NK) cells can exert memory after encounter with certain stimuli, which offers potential in terms of targeting NK cells for the therapy of infectious diseases and cancer. This discovery of memory behaviour in NK cells has catalysed research to determine whether other types of innate immune cell have the capacity for some form of immune memory. At such an exciting time in the field, *Nature Reviews Immunology* is proud to present a Focus issue on immune memory that reviews all of these new areas of research and discusses controversial ideas in the field that have led some to re-evaluate the textbook definition of memory. As we look to the future, it will be important to continue expanding our view of immune memory to tackle the worldwide burden of chronic infections such as AIDS and hepatitis.