



**Figure 1 | Compartmentalization of adaptive immunity in vertebrates.** **a**, In jawed vertebrates, a haematopoietic stem cell differentiates into a common lymphoid progenitor, and then into three lineages: T cells, which are responsible for the cellular immune response; B cells, responsible for the humoral response; and natural killer cells (not shown). On T cells, the receptor is the T-cell antigen-binding receptor and on B cells it is membrane-bound immunoglobulin. Alternative RNA processing changes membrane-bound immunoglobulin to a secreted antibody of the same specificity in a plasma cell. **b**, In jawless vertebrates, an as-yet-undefined precursor is thought to give rise to two lineages of lymphocyte-like cells defined by their expression of variable lymphocyte receptor (VLR) A or B. As Guo *et al.*<sup>1</sup> show in the lamprey, VLRA is expressed only on the cell surface; VLRB is expressed initially on the cell surface and is also secreted. The molecular mechanisms by which adaptive immunity is compartmentalized into cellular and humoral responses in jawed and jawless vertebrates are fundamentally different. But in both cases there was evidently evolutionary pressure to create specific lineage-restricted immune systems.

adaptive immune specificity in the lamprey and hagfish is mediated by variable lymphocyte receptors (VLRs) that are unrelated to immunoglobulin-type molecules<sup>4</sup>.

Much is now known about the structure and genetic diversification of VLRs, which consist of variable and invariant portions. On the basis of this, they are classified as VLRA and VLRB<sup>4,5</sup>, and the complex immune repertoires of both types are somatically derived through a gene-conversion-like mechanism that recombines relatively short DNA sequences encoding leucine-rich repeats<sup>6,7</sup>. A very different form of somatic recombination gives rise to diversified immunoglobulins and TCRs in the lymphocytes of jawed vertebrates.

But VLRs are produced by cells in the lamprey that morphologically resemble the lymphocytes seen in jawed vertebrates<sup>8,9</sup>. Gou *et al.*<sup>1</sup> illustrate further parallels between VLR-bearing cells and conventional T and B cells. First, transfection of complementary DNAs encoding VLRA and VLRB into mammalian cell lines revealed that VLRB is both expressed at the cell surface and secreted, whereas VLRA is only surface expressed (Fig. 1b). The tissue distribution of VLRA is more anatomically restricted than that of VLRB. A known stimulant of T-cell proliferation in jawed

vertebrates acts on VLRA-expressing cells to a greater degree than on VLRB-expressing cells. Putative orthologues of transcription products expressed in conventional T and B cells are associated with cell populations that are respectively restricted to VLRA and VLRB expression. Finally, two types of AID/APOBEC deaminase enzyme, both of which could potentially be involved in the generation of somatic variability<sup>7</sup>, are expressed selectively in the two lineages.

However, the relationship of the VLRA- and VLRB-expressing cell populations to the lymphocyte lineages in jawed vertebrates is far from clear. Confounding factors are the absence of conventional T- and B-cell receptors, which are the defining lineage-specific markers, and of their respective co-receptors. And there are no equivalents of those members of the major histocompatibility complex (MHC) family that interact specifically with T cells in jawed vertebrates.

The results of Gou *et al.*<sup>1</sup> constitute a convincing case for the compartmental differentiation of immune functions in jawless as well as in jawed vertebrates. But the possible relationships between the VLR lymphocyte-like cells and the mediators of adaptive immunity in jawed vertebrates have probably



## 50 YEARS AGO

A general investigation has been in progress for some time in this Department into certain aspects of the chemistry of *Ulex europaeus*. This common furze has a local reputation as a supplementary animal foodstuff ... No previous results are available on the carotene content of the green matter (spines) of furze and its seasonal variation, which are now reported ... From October to February or March — when furze is fed to stock — the average carotene content is 126 mgm./kgm., indicating that it is a very good, and freely available, source of carotene. The relatively high values during the summer months point to the possibility of using dried furze meal as a supplementary source of carotene in animal feeding. The problem of retention of carotene in dried furze is being investigated.

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## 100 YEARS AGO

The interesting problem of the dew-pond still awaits a definite solution. That these ponds are mainly fed by mist, and not dew, can hardly be doubted by anyone who has visited them at night, situated as they are on the topmost ridges of the Downs. In the driest summer the prevailing south-west wind, as it comes up from the sea, forms on these heights after dark thick clouds of mist, which soak everything that comes into contact with them ... The source of the water in these ponds, therefore, seems evident, but the mechanism by which the mist is precipitated into the ponds is not so apparent ... It appears to me that the only possible explanation is that the particles of mist must bear charges of electricity differing in potential from that of the earth. The charge on the earth would, of course, be most dense at the summits of the hills. Hence the tendency for the mist to deposit on the top of the ridge.

From *Nature* 10 June 1909.

50 & 100 YEARS AGO