pattern of γδ T cells must be an important clue to the function of this T cell sublineage[16]. However, the distinctive tissue localization pattern is not strictly an epithelial tropism. The preferential homing of γδ T cells to the epidermis that is seen in the mouse, is not observed in either chickens or humans. Furthermore, we have observed a selective homing pattern in the spleen that is phylogenetically conserved. In both chickens and humans[4,15] the γδ T cells preferentially localize in the splenic red pulp rather than the periarteriolar lymphoid sheath, which contains the majority of the splenic αβ T cells. Since the relationship of the splenic red pulp to a system of epithelial defence is not obvious, these observations suggest a more general function for γδ T cells rather than a defence role restricted to the epithelial boundaries of the body.

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SIR—We would like to contribute to the discussion concerning the preferential localization of γδ T cells in human epithelia. In the murine system it has been observed that γδ T cells are present in epidermis and intestinal epithelium in much higher frequency than αβ T cells. Janeway in particular, has elaborated on this finding and put forward the general suggestion that γδ T cells could play a particular role in immunosurveillance at these sites[5,16].

We have looked into the distribution of γδ T cells versus αβ T cells in a variety of normal human tissues of lymphoid and non-lymphoid nature. Serial sections of freshly frozen tissue were acetone fixed, incubated with anti-CD3, anti-TCR γδ-1 (ref. 9) and βF1 (anti-TCR αβ) (ref. 17) monoclonal antibodies and stained according to a highly sensitive immuno-alkaline phosphatase method. We studied bone marrow; fetal and neonatal liver; fetal and neonatal thymus; fetal, neonatal and adult lymph nodes; adult spleen and tonsil; neonatal and adult skin[18,21], oesophagus, stomach, small and large intestine, lung and trachea, testis, epididymis, uterus, vagina, kidney and brain.

At all sites within these organs αβ T cells constituted over ninety per cent of $CD3^+$ cells. γδ T cells comprised less than ten per cent of CD3 cells. Therefore, we conclude that there is no evidence for preferential homing or localization of γδ T cells in human epithelia. However, in none of the organs were γδ T cells observed in lymph follicles (of lymph nodes, tonsil, spleen, Peyer's patches or lung). Also, the percentage of γδ T cells in epidermis seemed on average higher than in papillary dermis. Therefore, there may still be a difference in migration of γδ versus αβ T cells, but this does not result in their preferential localization in epithelia. With respect to morphology of γδ T cells and αβ T cells, we find that generally they cannot be distinguished, but occasional $CD3^+$ cells with dendritic appearance always proved to express γδ TCR.

In view of these findings, great caution should be taken in ascribing a special function to γδ T cells in immunosurveillance of human epithelia. Future intensive and thorough investigation should reveal what contribution these cells make to the immune system.

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JANEWAY REPLIES—The above letters raise two questions. First, do T cells bearing γδTCR have a special tropism for epithelia, and second, is this tropism seen in man? In addition, the letters appear to contain a misapprehension of the content of two articles[5,16] that I have written on this topic. These articles propose that one role γδ T cells might have is defence of epithelia from intracellular infection and/or transformation, and that such cells might recognize not foreign antigen but an alteration in the host cell surface induced by infection. Both articles clearly state that such T cells are also found in other sites where they must mediate other functions. Thus, I do not take issue with the conclusion of the above letters that epithelial defence is not the only role such cells play. There are, however, strong data arguing that some T cells of this class exhibit this specialization.

Since this proposal was made, we and others have shown that T cells bearing γδTCR are in fact the dominant population in murine intestine[2,3]. More importantly, we have shown that such cells express receptors encoded by the $V_{\gamma 7}$ gene V_γ not expressed by γδ T cells in any other tissue[3,19]. S. Tonegawa *et al.* have shown that the $V_{\gamma 6}$ gene, again not expressed by γδ T cells in other tissues, is used in reproductive epithelium (personal communication), while Allison *et al.*[20] have shown that the $V_{\gamma 5}$ gene is expressed only by γδ T cells in epidermis. Thus, in addition to tropism to epithelia, there is a marked restriction in the specificity of γδ T cells found in these tissues. This does not prove that T cells with γδTCR are specialized for epithelial defence, but it certainly is most readily explained in the context of our earlier hypothesis. Recently, experiments with mice transgenic for γδTCR show that epithelial homing is a property of the γδ T cell lineage and not of particular γδTCR specificities. Specificity appears to reflect ligand recognition in the epithelia (M. Bonneville *et al.* personal communication). This further supports a functional role for those γδ T cells in epithelia. Perhaps studies of *V*-gene usage in γδTCR in humans would show similarly specific localization.

The human studies cited show predominance of T cells with αβTCR in intestinal epithelium. From examining photographs of such sections, however, Bucy notes (above) that the T cells with γδTCR show tropism for the epithelial layer whereas T cells with αβTCR do not. Thus, the human data on tropism of γδTCR-bearing cells to epithelia do not conflict with those in the mouse. Rather, this tropism is masked by the presence of large numbers of T cells with αβTCR found in humans but not mice or chickens, where similar studies show 20–40% of T cells with αβTCR. Thus, the obvious species difference may reflect differences in the behaviour of αβ cells and/or differences in the actual γδ receptors, rather than differences in function or tropism of T cells with γδTCR. Until these issues are resolved, it is as unwise to state that T cells with γδTCR are *not* specialized for epithelial immunity as it is to state that this is their only function, or that only γδ T cells can perform such functions, neither of which I have claimed (although such claims have been attributed to me).

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