
In an earlier publication in Cancer Research, Sanders et al. (1) convincingly demonstrated that the adherence of peripheral blood T-lymphocytes and a T-cell clone (8.2) to the Hodgkin’s disease-derived cell line L428 was mediated via two distinct molecular adhesion systems, LFA-3/CD2 and LFA-1/ICAM-1 (2), with the former playing the more dominant role. The significance and nature of the close adhesive associations found between the neoplastic Reed-Sternberg cells of HD and autologous intratumoral T-lymphocytes in Hodgkin’s-involved tissue have been the subject of some debate for several years (3). Whereas the L428 cell line shares several phenotypic features in common with RS cells, it is by no means firmly established whether this cell line really is derived from and therefore representative of RS cells seen in vivo (4). We have recently obtained results suggesting that the mechanism of attachment of autologous T-lymphocytes to the HD cell lines L428 and L591 might be quite different than for autologous intratumoral T-cell attachment to RS cells prepared as single cell suspensions from Hodgkin’s-involved lymph nodes (5). The observed differences are based on the physicochemical requirements for rosette formation by the HD cell lines and for RS cells freshly isolated from involved tissues and are summarized in Table 1. We have clearly demonstrated that divergent cations or the presence of trypsin sensitive HD cell line membrane proteins are not a requirement for lymphocyte attachment to the HD cell lines, findings at complete variance with those of Payne et al. (3), who showed both to be an absolute requirement for autologous lymphocyte attachment to freshly isolated RS cells. Conversely, removal of surface membrane sialic acid from the HD cell lines with neuraminidase completely abolishes their ability to rosette with T-cells, again an observation at variance with observations made for freshly isolated RS cells (3).

Thus, so far as we are able to establish at present, the binding requirements of peripheral blood lymphocytes to both L428 and L591 are identical. This observation perhaps throws some further doubt on the relevance of the in vitro HD cell line/lymphocyte rosetting phenomenon to RS cell/lymphocyte adherence seen in HD, principally because the L591 HD cell line is Epstein-Barr virus positive and is now generally accepted not to be derived from the Hodgkin’s tumor cell population (6). On the other hand, L428 looks increasingly more likely to have originated from the Hodgkin’s tumor cell population and the observed similarities in T-cell adherence requirements for these two essentially dissimilar HD cell lines arguably points against a common adhesion mechanism for the HD cell lines and RS cells in HD. We would therefore urge caution at this juncture in forming any firm conclusions regarding the similar nature of the adhesive interaction taking place between HD cell lines and T-cells and RS cells and T-cells in Hodgkin’s-involved tissues.

A further point we feel it necessary to comment on relates to the adherence of fractionated peripheral blood mononuclear cell populations to both L428 and L591. We can clearly demonstrate that CD8+ and CD4+ T-cells are equally good at forming adhesive associations with both L428 and L591 while CD37+ B-cells are poor, although some B-cells will form attachments. The inefficiency, but not total lack, of B-cell adherence to L428 and L591 can possibly be accounted for by the lack of expression of CD2 on the B-cell, thus disabling the major LFA-3/CD2 adherence pathway but leaving the LFA-1/ICAM-1 system intact to account for the adhesive associations that are seen, as LFA-1 is strongly expressed by B-cell subpopulations. However, we have also demonstrated that peripheral blood monocytes which express high levels of LFA-1 but not CD2, are equally as good as T-cells at forming rosettes with the HD cell lines (5). We feel therefore that there may possibly be yet another alternative mechanism for monocyte adhesion to the HD cell lines. In this regard we have previously demonstrated that anti-major histocompatibility complex Class II antibodies against a monomorphic determinant of the DR β chain (DA6 164) partially inhibit adherence of lymphocytes to L428. We have not yet been able to establish whether only CD4+ T-cells are inhibited from binding. If this were shown to be the case, then Class II molecules which are variably expressed by L428 (and RS/HD tumor cells) may form adhesive interactions with cells expressing surface CD4 (7) which would include peripheral blood monocytes. The mechanisms accounting for T-cell attachment to the HD-derived cell line L428 are clearly due to well-described antigen-independent mechanisms (2). Whether the same adhesion mechanisms are responsible for T-cell attachment to RS/HD cells in vivo remains to be shown.

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References


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1 The abbreviations used are: HD, Hodgkin’s disease; RS, Reed-Sternberg.
2 D. J. Flavell, unpublished observations.

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