we set forth to identify viral genome in the endothelium of the vasculitic lesions. Cell-mediated immune (CMI) dysfunction, including defective natural killer cell function has been documented in patients with XLP, and defective CMI may result in altered EBV tissue tropism as we suggest. We agree that many more patients, as well as controls, would need to be studied to definitively answer this issue. The functionality of EBV-specific CTL remains a subject for debate. Normal EBV-specific CTL function, as has been detected in some patients with XLP, might indeed explain the targeted assault and damage of the infected vascular structures that we have demonstrated.

Rusung Tan, Jan Dutz, Loralyn Benoit, Derek de Sa, and Anne Junker

Correspondence: Rusung Tan, Departments of Pathology and Laboratory Medicine, University of British Columbia and BC’s Children’s Hospital, 4480 Oak St, Vancouver, BC, Canada, V6H 3V4

References


To the editor:

Langerhans cells and the cells of Langerhans cell histiocytosis do not express DC-SIGN

Geissmann and colleagues recently reported that cells of Langerhans cell histiocytosis (LCH) in osseous and/or chronic lesions have an immature dendritic cell phenotype. In addition to CD1a, LCH cells in all 25 cases examined expressed Langerin, a recently described C-type lectin that appears to be restricted entirely to Langerhans cells.

An increasing number of dendritic cell lectins, such as dendritic cell–specific ICAM-grabbing nonintegrin (DC-SIGN), dendritic cell immunoreceptor (DCIR), DEC-205, and CD23, are now recognized. We consider it important to determine whether these lectins are expressed on dendritic cells in the context of LCH. To this end, we set forth to identify viral genome in the endothelium of the vasculitic lesions. Cell-mediated immune (CMI) dysfunction, including defective natural killer cell function has been documented in patients with XLP, and defective CMI may result in altered EBV tissue tropism as we suggest. We agree that many more patients, as well as controls, would need to be studied to definitively answer this issue. The functionality of EBV-specific CTL remains a subject for debate.

Normal EBV-specific CTL function, as has been detected in some patients with XLP, might indeed explain the targeted assault and damage of the infected vascular structures that we have demonstrated.

Rusung Tan, Jan Dutz, Loralyn Benoit, Derek de Sa, and Anne Junker

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References


C-type lectins, Langerin and DC-SIGN, may have analogous properties on separate dendritic cell subsets with respect to, for example, their capacity to bind T lymphocytes and lentiviruses.

Elizabeth J. Soilleux and Nicholas Coleman

Correspondence: Elizabeth J. Soilleux, Department of Molecular Histopathology, Addenbrooke's Hospital, Hills Road, Cambridge, CB2 2QQ United Kingdom; e-mail: ejs17@cam.ac.uk

References


To the editor:

Phenotype and genotype expression in pseudohomozygous R2 factor V

Factor Va is the important cofactor for prothrombinase. Factor Va is inactivated by activated protein C (APC) following 3 cleavages of the heavy chain at Arg306, Arg506, and Arg679. Cleavage of normal factor Va by APC at these sites results in the production of M4, 45 000, M3, 30 000, M2, 22 000 and 20 000 fragments. In plasma, following the addition of APC and a synthetic membrane surface (phosphatidylcholine phosphatidylserine [PCPS]), appearance of the M3, 30 000 fragment demonstrates cleavage of normal factor V at Arg306 and Arg506. The M3, 30 000 fragment can be detected in plasma by using an anti–human factor V monoclonal antibody that recognizes an epitope located between residues 307 and 506 of the molecule.

The R2 haplotype in factor V is characterized by an A4070G substitution (His1299Arg) in the factor V molecule and is associated with mild APC resistance, but the underlying molecular mechanism remains unclear. We have recently described a thrombotic family with 4 symptomatic members. One of them (I3) was doubly heterozygous for the factor V HR2 haplotype and for the factor V Tyr1702Cys mutation, causing CRM–factor V deficiency. Since the factor V allele predicting the Tyr1702Cys substitution is not expressed at the protein level, the plasma of this patient contains only R2 factor V, in accordance with her reduced factor V levels (FV:Ag 43%; FV:C 36%; normal range 70%-130%) and mild APC resistance (nAPC-sr 0.72, normal values > 0.84). We have concluded that while the His1299Arg substitution in factor V induces APC resistance, the presence of the Tyr1702Cys mutation was responsible for absence of expression of the corresponding allele (previously reported to result in CRM–factor V deficiency). This particular condition (pseudohomozygosity for the factor V HR2 haplotype) offers the opportunity to study the APC-mediated inactivation of R2 factor Va in plasma, which is otherwise possible only in the rare (~0.4% of the general population) homozygous individuals.

Molecular investigations were undertaken in this thrombotic patient (I3, see Castoldi et al). The patient was found to be heterozygous, at both the DNA and messenger RNA (mRNA) levels, for the His1299Arg and Asp2194Gly substitutions, characterizing the HR2 haplotype as well as for the Tyr1702Cys mutation in factor V. No mutation, in addition to the polymorphic
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