Special features of quantification of $CD8^+CD38^+$ T-cells by flow cytometry does not represent a good biomarker to monitor the reactivation of cytomegalovirus infection after allogeneic hematopoietic stem cell transplantation

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CD38 also known as cyclic ADP ribose hydrolase is a surface glycoprotein expressed by several leukocytes, in particular $CD4^+$ and $CD8^+$ T-cells, B-lymphocytes and natural killer cells.[1]

CD38 is part of a large family of nucleotide-metabolizing ectoenzymes that also includes CD26, CD39 and CD73. These molecules are clustered in specialized areas of the cell membrane, playing roles as receptor signaling molecules thus regulating cell activation, defense from pathogens, cell migration, immune synapse formation and also life cycle.[2]

CD38 is a powerful disease biomarker for several human disorders, including leukemias and myelomas, and also directly involved in the pathogenesis and prognosis of human virus infections. Several potential clinical applications of CD38 as a putative laboratorial biomarker in the diagnosis, prognosis and therapy of viral infections have been previously reported.[2]

Elevated CD38 antigen expression on $CD8^+$ T cells has been pointed out as a stronger marker for the risk of chronic HIV disease progression to AIDS.[3] Moreover, recent studies have demonstrated that a parallel decline of $CD8^+CD38^+$ lymphocytes and viremia may occur in treated hepatitis B patients, suggesting its role as a biomarker for active infection.[4]

It has been proposed that monitoring of the $CD8^+CD38^+$ T-cell subset in peripheral blood represents a powerful approach to detect cytomegalovirus (CMV) infections in kidney transplant recipients.[5] More recently, it has been reported that in fact, the monitoring of CD38 high expression in peripheral blood $CD8^+$ lymphocytes is a useful additional diagnostic marker for CMV infection in patients after kidney transplantation, especially when they are at risk of tissue-invasive disease when CMV DNA copies may not be detectable in peripheral blood.[6]

The questions surrounding CD38 are still fascinating and continue to prompt novel investigations. One important matter to be clarified is whether the overexpression of the CD38 molecule by circulating T cells may represent a universal biomarker for CMV infection after all modalities of organ transplantation. In order to address this issue, Lino et al.[7] performed a prospective investigation to clarify the applicability of flow cytometric enumeration of $CD8^+CD38^+$ T-cells in peripheral blood as a laboratorial indicator of CVM infection/reactivation in allogeneic hematopoietic stem cell (HSCT) recipients.

The data presented in this study revealed that, in contrast to those previously published in kidney transplantation, the overexpression of CD38 in circulating $CD8^+$ T cells does not correlate with the presence on CMV antigenemia. The authors present a plausible explanation for this phenomenon, discussing the particularities of CD38 expression during bone marrow repopulation and immune system reconstitution after HSCT. The cyclic nature of CD38 expression during hematopoietic ontogeny may explain the presence of CD38 overexpression even in those HSCT recipients with undetectable antigenemia. It has been reported that CD38 is expressed early in hematopoietic cells, with downregulation during the cell maturation process and re-expression upon cell activation. This knowledge is relevant to aware flow cytometry readers and medical professionals working in the clinical management of transplant recipients that overexpression of CD38 may not be considered a universal biomarker of CMV infection following organ transplantation.

The article is well organized, presenting the technical details necessary to ensure its reproducibility, excellent scientific quality and promises a fruitful reading.

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