Peptide binding characteristics of the non-classical class Ib MHC molecule HLA-E assessed by a recombinant random peptide approach

ABSTRACT

The specificity of HLA-E is possibly not as exquisite as previously thought because it appears to refold around a random peptide library in comparison to the results obtained with classical class Ia MHC molecules, namely RT1-A1c and RAu, and can associate with synthetic peptides carrying an HIV sequence, suggesting that it could bind different phenotypes and present them to T lymphocytes.

INTRODUCTION

The MHC MHC-binding genes are the most important molecular loci in the human genome. They have been the focus of intense research in recent years, particularly in the field of molecular genetic engineering (MGE). MGE has been highly successful in developing gene-editing techniques such as CRISPR/Cas9, so it seems appropriate to investigate whether other MHC-binding genes might also be useful for the development of gene-editing techniques.

We used the MHC-E titeling approach to identify the non-classical class of HLA-E molecule (HLA-E-B) that binds to the HLA-E binding site of the HLA-E-B gene.

Methods: The non-classical MHC class Ib molecules are not only closely homogeneous but also have low cell surface expression and limited polymorphism. These molecules possess important roles in regulating cell activity, as evidenced by their conservation status across species. However, some class III molecules, such as HLA-E, Qa-1, and RT.BM1 have been found to play highly specialized roles within different classes of molecules. However, not all leader sequences from human class I MHC molecules contain peptides that can bind to HLA-E. For instance, sequence of the Hla-B alleles containing a threonine for methionines substitution at position P4 did not able to 'bind' HALA-H2 as described in an in vitro binding assay, and other studies showed that the crystal structure of HLAS-EB confirmed that zygotic phenotypes could rea The objective of our current research was to determine the specificity of peptide binding for HLA-E using a biochemical approach, with an in vitro refolding system. This requires not only access to sufficient material but also specialized antibodies that can purify the class I molecule from other cellular components. While previous work has been successful, attempts to obtain p53 have been hindered by low expression and the lack of such spherical antibodies.

CONCLUSION

Remarkable conclusions Our research has proven that the recombinant bacterially produced HLA-E can provide a binding motif for the non-classical class Ib MHC molecule, which can be used to determine the binding affinity of specific peptides when there is no cell-based assay available. While this motif confirmed that Hla-EFH (human immunoglobuline aromatic hydrophobic endothelial monocytogene) favors hydrophilic residues at most positions, it appears unlikely that this molecules' requirements are not so