The immunogenicity of Bcr-Abl expressing dendritic cells is dependent on the Bcr-Abl kinase activity and dominated by Bcr-Abl regulated antigens.

Abstract:
In Ph(+) chronic myeloid leukemia (CML), the constitutively active Bcr-Abl kinase leads to the up-regulation and activation of multiple genes, which may subsequently result in the expression of leukemia-associated antigens. In this study, we investigated the immunogenicity of Bcr-Abl-regulated antigens by stimulating CD8(+) T lymphocytes with autologous dendritic cells transfected with RNA coding for Bcr-Abl wild-type or a kinase-deficient mutant. Significant HLA class I-restricted T-cell responses were detected against antigens regulated by the Bcr-Abl kinase, but not toward the Bcr-Abl protein itself. The T-cell repertoire of a patient with CML in major molecular remission due to imatinib mesylate was also dominated by T cells directed against Bcr-Abl-regulated antigens. These results encourage the development of immunotherapeutic approaches against Bcr-Abl-regulated antigens for the treatment of CML patients with residual disease following therapy with Bcr-Abl kinase inhibitors.