T-cell Responses to Oncogenic Merkel Cell Polyomavirus Proteins Distinguish Patients with Merkel Cell Carcinoma from Healthy Donors

Purpose: Merkel cell carcinoma (MCC) is a highly aggressive skin cancer with strong evidence of viral carcinogenesis. The association of MCC with the Merkel cell polyomavirus (MCPyV) may explain the explicit immunogenicity of MCC. Indeed, MCPyV-encoded proteins are likely targets for cytotoxic immune responses to MCC as they are both foreign to the host and necessary to maintain the oncogenic phenotype. However, to date only a single MCPyV-derived CD8 T-cell epitope has been described, thus impeding specific monitoring of T-cell responses to MCC. Method: To overcome this limitation, we scanned the MCPyV oncoprotein large T and small T antigens and the virus capsid protein VP1 for potential T-cell epitopes, and tested for MHC class I affinity. We confirmed the relevance of these epitopes using a high-throughput platform for T-cell enrichment and combinatorial encoding of MHC class I multimers. Results: In peripheral blood from 38 patients with MCC and 30 healthy donors, we identified 53 MCPyV-directed CD8 T-cell responses against 35 different peptide sequences. Strikingly, T-cell responses against oncoproteins were exclusively present in patients with MCC, but not in healthy donors. We further demonstrate both the processing and presentation of the oncoprotein- derived epitopes, as well as the lytic activity of oncoprotein-specific T cells toward MHC-matched MCC cells. Demonstrating the presence of oncoprotein-specific T cells among tumor-infiltrating lymphocytes further substantiated the relevance of the identified epitopes. Conclusion: These T-cell epitopes represent ideal targets for antigen-specific immune therapy of MCC, and enable tracking and characterization of MCPyV-specific immune responses. (C) 2014 AACR.

General information
Publication status: Published
Organisations: University Hospital Herlev, Medical University of Graz, Seattle Cancer Center Care Alliance
Pages: 1768-1778
Publication date: 2014
Peer-reviewed: Yes

Publication information
Journal: Clinical Cancer Research
Volume: 20
Issue number: 7
ISSN (Print): 1078-0432
Ratings:
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 8.13 SJR 4.947 SNIP 2.084
Web of Science (2014): Impact factor 8.722
Web of Science (2014): Indexed yes
Original language: English
DOIs: 10.1158/1078-0432.CCR-13-2697

Bibliographical note
Supplementary data for this article are available at Clinical Cancer Research Online (http://clincancerres.aacrjournals.org/)
Source: FindIt
Source ID: 260949668
Research output: Contribution to journal › Journal article – Annual report year: 2014 › Research › peer-review