Neoantigen vaccine generates intratumoral T cell responses in phase Ib glioblastoma trial - DTU Orbit (14/03/2019)

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Neoantigens, which are derived from tumour-specific protein-coding mutations, are exempt from central tolerance, can generate robust immune responses⁴⁻⁶ and can function as bona fide antigens that facilitate tumour rejection⁸. Here we demonstrate that a strategy that uses multi-epitope, personalized neoantigen vaccination, which has previously been tested in patients with high-risk melanoma⁴⁻⁶, is feasible for tumours such as glioblastoma, which typically have a relatively low mutation load⁹ and an immunologically ‘cold’ tumour microenvironmet⁸. We used personalized neoantigen-targeting vaccines to immunize patients newly diagnosed with glioblastoma following surgical resection and conventional radiotherapy in a phase I/Ib study. Patients who did not receive dexamethasone-a highly potent corticosteroid that is frequently prescribed to treat cerebral oedema in patients with glioblastoma-generated circulating polyfunctional neoantigen-specific CD4⁺ and CD8⁺ T cell responses that were enriched in a memory phenotype and showed an increase in the number of tumour-infiltrating T cells. Using single-cell T cell receptor analysis, we provide evidence that neoantigen-specific T cells from the peripheral blood can migrate into an intracranial glioblastoma tumour. Neoantigen-targeting vaccines thus have the potential to favourably alter the immune milieu of glioblastoma.

General information
State: Published
Organisations: Genomic Epidemiology, Department of Bio and Health Informatics, Cancer Genomics, Harvard Medical School, Dana-Farber Cancer Institute, Broad Institute, Brigham and Women's Hospital, Oncovir Inc.
Number of pages: 4
Pages: 234-239
Publication date: 2018
Peer-reviewed: Yes

Publication information
Journal: Nature
Volume: 565
ISSN (Print): 0028-0836
Ratings:
BFI (2019): BFI-level 3
Web of Science (2019): Indexed yes
BFI (2018): BFI-level 3
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 14.59
Web of Science (2017): Impact factor 19.181
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 13.33
Web of Science (2016): Impact factor 19.304
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 14.38
Web of Science (2015): Impact factor 17.184
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 14.22
Web of Science (2014): Impact factor 14.547
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 14.96
Web of Science (2013): Impact factor 15.295