Induction of systemic anti-melanoma immunity through intratumoral TLR-7/8 activation

Manisha Singh1*, Hiep Khong1, Zhimin Dai1, John P Vasilakos2, Patrick Hwu1, Willem W Overwijk1

From Society for Immunotherapy of Cancer 29th Annual Meeting
National Harbor, MD, USA. 6-9 November 2014

Purpose
Intratumoral immune activation can induce systemic immunity and anti-tumor activity. Imiquimod is a cream-formulated, TLR-7 agonist that is FDA-approved for the treatment of non-melanoma skin cancers, but has limited activity against melanoma. In the current study, we studied the anti-tumor activity and mechanism of action of a novel injectable TLR 7/8 dual agonist, 3M-052, which remains at the site of injection to avoid systemic distribution.

Experimental design
Mice bearing established B16 melanomas were treated intratumorally with 3M-052 or vehicle. The mechanistic contribution of individual cell types and molecules to the anti-tumor effect was determined using genetically engineered mice and antibody blockades. Immune cell infiltrates were analyzed by flow cytometry.

Results
Intratumoral administration of 3M-052 generated systemic anti-tumor immunity and suppressed both injected and distant uninjected wild-type B16.F10 melanomas. Treated tumors showed increased level of CCL2 chemokines and CCL2 dependent infiltration of M1 phenotype-shifted macrophages which could kill tumor cells directly through production of nitric oxide. CD8+ T cells, B cells, Type I IFN, IFN-g, and pDCs contributed to efficient tumor suppression whereas perforin, NK cells and CD4 T cells were not required.

Conclusion
Induction of effective innate and tumor specific adaptive immunity by intratumoral treatment of TLR7/8 agonist, 3M-052 is a promising approach for the treatment of metastatic cancer.

Authors’ details
1Department of Melanoma Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA. 23M Drug Delivery Systems Division, 3M Company, St. Paul, MN, USA.

Published: 6 November 2014
doi:10.1186/2051-1426-2-S3-P176

Submit your next manuscript to BioMed Central and take full advantage of:
• Convenient online submission
• Thorough peer review
• No space constraints or color figure charges
• Immediate publication on acceptance
• Inclusion in PubMed, CAS, Scopus and Google Scholar
• Research which is freely available for redistribution

Submit your manuscript at www.biomedcentral.com/submit

© 2014 Singh et al.; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.