Human Pathology (2016) **53**, 82–90

ELSEVIER

Human PATHOLOGY

www.elsevier.com/locate/humpath

Original contribution

Neurofibromin protein loss in desmoplastic melanoma subtypes: implicating *NF1* allelic loss as a distinct genetic driver?☆

Alexander Kadokura BS[a,1], Noah Frydenlund MS[b,1], Dominick A. Leone MPH[c], Shi Yang MD[d], Mai P. Hoang MD[e], April Deng MD, PhD[f], Marier Hernandez-Perez MD[g], Asok Biswas MD, FRCPath, DipRCPath[h], Rajendra Singh MD[i], Ron Yaar MD, PhD[j], Meera Mahalingam MD, PhD, FRCPath[k,*]

[a]*Division of Graduate Medical Sciences, Boston University School of Medicine, Boston, MA 02118*
[b]*University of Iowa Carver College of Medicine, Iowa City, IA 52240*
[c]*Boston University School of Public Health, Boston, MA 02118*
[d]*Department of Pathology, Boston University of Medicine, Boston, MA 02118*
[e]*Department of Pathology, Massachusetts General Hospital, Boston, MA 02118*
[f]*Department of Pathology, University of Massachusetts Medical School, Worcester, MA 01601*
[g]*Miraca Life Sciences, Newton Upper Falls, MA 02458*
[h]*Department of Pathology, Western General Hospital, Edinburgh, Scotland EH13 9QW*
[i]*Department of Pathology and Dermatology, Icahn School of Medicine Mount Sinai, New York, NY 10001*
[j]*Aurora Diagnostics GPA Laboratories, Greensboro, NC 27401*
[k]*Dermatopathology Section, Department of Pathology and Laboratory Medicine, VA Consolidated Laboratories, West Roxbury, MA 02132*

Received 15 December 2015; revised 28 January 2016; accepted 10 February 2016

Keywords:
Desmoplastic melanoma subtypes;
Pure variant;
Mixed variant;
Neurofibromin;
RETp

Summary Loss of the *NF1* allele, coding for the protein neurofibromin, and polymorphism in the proto-oncogene *RET* (*RETp*) are purportedly common in desmoplastic melanoma (DM). DM is categorized into pure (PDM) and mixed (MDM) subtypes, which differ in prognosis. Most *NF1* mutations result in a truncated/absent protein, making immunohistochemical screening for neurofibromin an ideal surrogate for *NF1* allelic loss. Using antineurofibromin, our aims were to ascertain the incidence of neurofibromin loss in DM subtypes and to evaluate the relationship with *RET*, perineural invasion (PNI) and established histopathologic prognosticators. A total of 78 archival samples of DM met criteria for inclusion (54 cases of non-DM serving as controls). Immunohistochemistry was performed for neurofibromin, whereas direct DNA sequencing was used for *RETp* and *BRAF* mutation status. Statistical analyses included χ^2 test as well as Fisher exact test. Neurofibromin loss was more common in DM than non-DM (69% versus 54%; $P = .02$). In DM, significant differences in neurofibromin loss

☆ Disclosures: The authors have no conflicts of interest, financial or otherwise.

* Corresponding author at: Dermatopathology Section, Department of Pathology and Laboratory Medicine (113),VA Consolidated Laboratories, 1400 VFW PKWY, West Roxbury 02132, MA. Tel.: +1 857 203 5992; fax: +1 857 203 5623.
E-mail address: me@meeramahalingam.com (M. Mahalingam).

[1] Both authors contributed equally.

http://dx.doi.org/10.1016/j.humpath.2016.02.012
0046-8177/Published by Elsevier Inc.