PRAME Zeta-Antibody ZR383 is getting Under the Skin

A **ZETA Corporation** White Paper

Authors: Dr. rer. nat. Andreas Herrmann and Peiguo Chu M.D. *March, 2024*

SUMMARY:

The predominantly nuclear residing protein PRAME is significantly overexpressed restricted to malignant melanoma and premalignant melanocytic lesions. The PRAME Zeta-Antibody clone ZR383 readily assesses the PRAME antigen in tissue microsections preserved in paraffin with reduced liabilities of antigen cross presentation and potentially could facilitate the reliable determination of skin melanocytic malignancies.

The soluble but also membranous factor PRAME, belonging with MAGE, BAGE, GAGE, NY-ESO1, and LAGE-1 to the CTA gene family, is not expressed in healthy tissue but preferentially in melanoma, which coined its name **(Fig. 1)**.[1] Herein, high expression of PRAME is observed in 88% of primary melanoma tissue and in 95% of advanced and metastatic tissue in melanoma.[2]

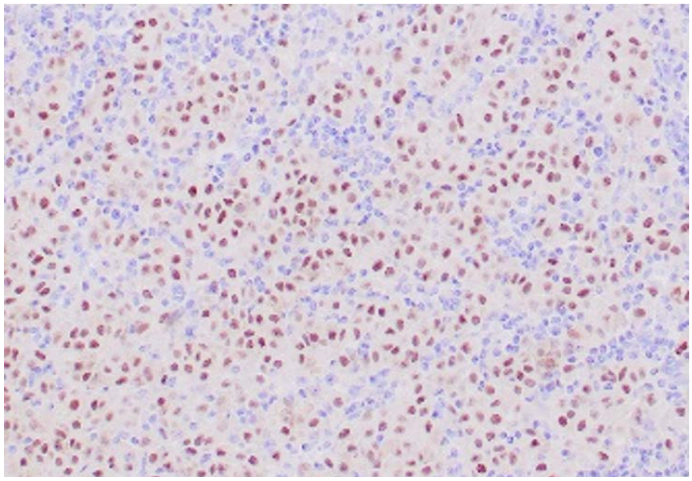

Figure 1: PRAME Zeta-Antibody ZR383. IHC staining of PRAME in human melanoma. Image property of Zeta Corporation.

The factor PRAME has been emphasized to inhibit retinoic acid/retinoic acid receptor RA/RAR signal transduction circuitries thereby contributing to melanoma tumorigenesis and other skin lesions.[1,3]

Moreover, PRAME contributes to the degradation of cell cycle inhibitor p14^{ARF} conferring a cell proliferative advantage.[4]

Interestingly, PRAME belongs to the CTA gene family encoding antigen peptides recognized by T lymphocytes, which elevated the attention on PRAME and other gene family members for therapeutic approaches dramatically.[5]

The PRAME Zeta-Antibody ZR383 maps to the C-terminal moiety of the PRAME antigen that encodes for the interface critical for interaction with the RA/RAR signal transduction circuitries **(Fig. 2)**.

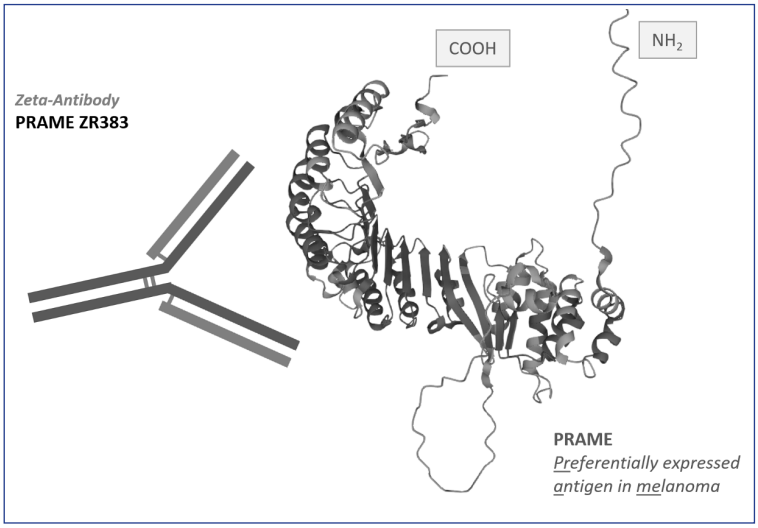

Figure 2: PRAME Zeta-Antibody ZR383 epitope mapping to PRAME C-terminus. Antigen recognition by ZR383 illustrated.[6]

Thus, PRAME Zeta-Antibody clone ZR383 readily assesses PRAME protein expression in premalignant melanocytic lesions and malignant melanoma.

References:

1. Xu, Y. *et al.* The role of the cancer testis antigen PRAME in tumorigenesis and immunotherapy in human cancer. *Cell Prolif* **53**:e12770 (2020).

2. Ikeda, H. *et al.* Characterization of an antigen that is recognized on a melanoma showing partial HLA loss by CTL expressing an NK inhibitory receptor. *Immunity* **6**:199-208 (1997).

3. Epping, M.T. *et al.* The human tumor antigen PRAME is a dominant repressor of retinoic acid receptor signaling. *Cell* **122**:835-847 (2005).

4. Zhang, W. *et al.* Tumor-associated antigen Prame targets tumor suppressor p14/ARF for degradation as the receptor protein of CRL2Prame complex. *Cell Death Differ* **28**:1926-1940 (2021).

5. Goodison, S. *et al.* The cancer testis antigen PRAME as a biomarker for solid tumor cancer management. *Biomark Med* **6**:629-632 (2012).

6. https://www.uniprot.org/uniprotkb/P78395/entry#function