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Highlights AEDV

In 77TH AAD Congress

1-5 March 2019

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Dermatopathology

Dr. Rafael Botella Estrada

Scientific Initiative of:

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PRAME EXPRESSION IN MELANOCYTIC TUMORS

- PRAME (PReferentially expressed Antigen in Melanoma) is a melanoma-associated antigen that was isolated by autologous T cells in a melanoma patient.
- Expression in 155 primary melanomas, 100 metastatic melanomas and 145 nevi
- Diffuse nuclear immunoreactivity for PRAME was found **in 87% of metastatic and 83.2% of primary melanomas**
  - 94.4% of ALM, 92.5% of SSM, 90% of NM, 88.6% of LMM, and 35% of desmoplastic melanomas
- Of the 140 cutaneous melanocytic nevi, 86.4% were completely negative for PRAME. Immunoreactivity for PRAME was seen, albeit usually only in a minor subpopulation of lesional melanocytes, in 13.6% of cutaneous nevi, including dysplastic nevi, common acquired nevi, traumatized/recurrent nevi, and Spitz nevi.
- It may also be valuable for margin assessment of a known PRAME positive melanoma

TABLE 1. Primary Cutaneous Melanomas With Diffuse (4+) PRAME IHC Expression

Melanoma Type	In Situ Only	Invasive	Total
Superficial spreading	12/12	37/41	49/53
Lentigo maligna	24/27	15/17	39/44
Acral	7/7	10/11	17/18
Nodular	NA	9/10	9/10
Other*	2/2	6/8	8/10
Subtotal†	45/48	77/87	122/135
Desmoplastic‡	NA	7/20	7/20
Total	45/48	84/107	129/155

TABLE 3. PRAME IHC Expression in Melanocytic Nevi

Type of Melanocytic Nevus	Diffuse (4+) IHC PRAME Expression	Focal (1 or 2+) IHC PRAME Expression
Common acquired nevus	0/40	4/40 (1+)
Dysplastic (Clark's) nevus	0/60	10/60 (1+)
		1/60 (2+)
Blue nevus	0/10	0/10
Spitz nevus	1/10	1/10 (1+)
Deep penetrating nevus	0/3	0/3
Traumatized/ recurrent nevus	0/15	1/15 (2+)
		1/15 (1+)
Congenital nevus	0/2	0/2
Nodal nevus	0/5	0/5
Total	1/145	18/145

PRAME Expression in Melanocytic Tumors.
Am J Surg Pathol 2018 Nov;42(11):1456-1465

PAME AS TREATMENT TARGET

The Journal of Clinical Investigation

RESEARCH ARTICLE

A therapeutic T cell receptor mimic antibody targets tumor-associated PRAME peptide/HLA-I antigens

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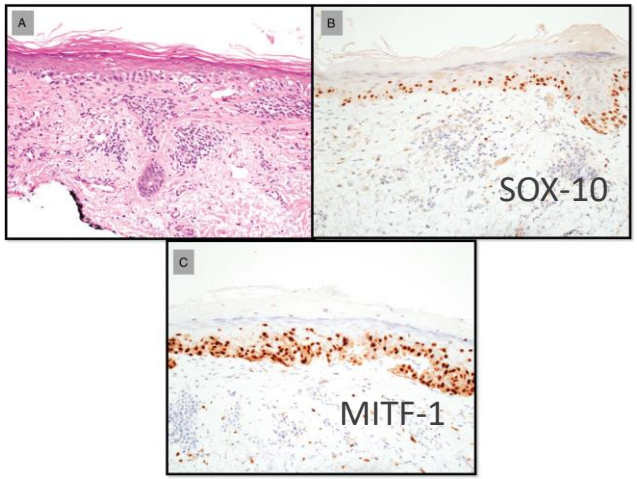
Preferentially expressed antigen in melanoma (PRAME) is a cancer-testis antigen that is expressed in many cancers and leukemias. In healthy tissue, PRAME expression is limited to the testes and ovaries, making it a highly attractive cancer target. PRAME is an intracellular protein that cannot currently be drugged. After proteasomal processing, the PRAME$^{300-309}$ peptide ALYVDSLFFL (ALY) is presented in the context of human leukocyte antigen HLA-A*02:01 molecules for recognition by the T cell receptor (TCR) of cytotoxic T cells. Here, we have described Pr20, a TCR mimic (TCRm) human IgG1 antibody that recognizes the cell-surface ALY peptide/HLA-A2 complex. Pr20 is an immunological tool and potential therapeutic agent. Pr20 bound to PRAME$^+$HLA-A2$^+$ cancers. An afucosylated Fc form (Pr20M) directed antibody-dependent cellular cytotoxicity against PRAME$^+$HLA-A2$^+$ leukemia cells and was therapeutically effective against mouse xenograft models of human leukemia. In some tumors, Pr20 binding markedly increased upon IFN-γ treatment, mediated by induction of the immunoproteasome catalytic subunit β5i. The immunoproteasome reduced internal destructive cleavages within the ALY epitope compared with the constitutive proteasome. The data provide rationale for developing TCRm antibodies as therapeutic agents for cancer, offer mechanistic insight on proteasomal regulation of tumor-associated peptide/HLA antigen complexes, and yield possible therapeutic solutions to target antigens with ultra-low surface presentation.

J Clin Invest 2017;127:2705

MITF-1 AND SOX10 TO DISTINGUISH MELANOMA IN SITU AND ACTINIC KERATOSIS

- Melanoma in situ may occasionally be confused with intraepidermal melanocytic hyperplasia on sun-damaged skin
- 70 cases were retrospectively chosen, including:
  - 50 cases of melanoma in situ
  - 20 cases of actinic keratoses
- MITF-1 and SOX10 can be used to differentiate melanoma in situ from actinic keratosis with melanocytic hyperplasia
- MITF-1 exhibits slight superior sensitivity and seems to be a more effective immunostain than SOX10 for the identification and quantification of melanocytes in the setting of melanoma in situ

MIS, LM



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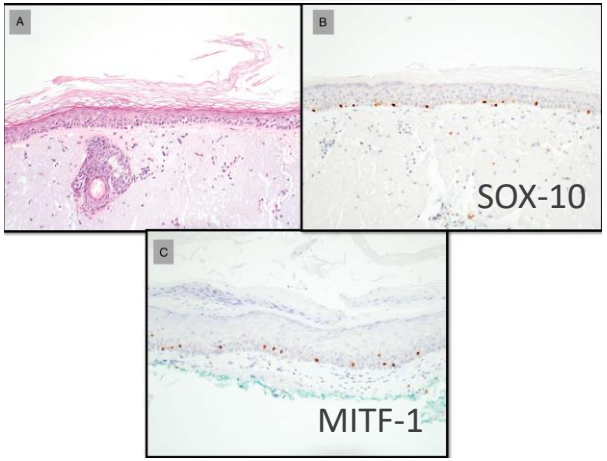
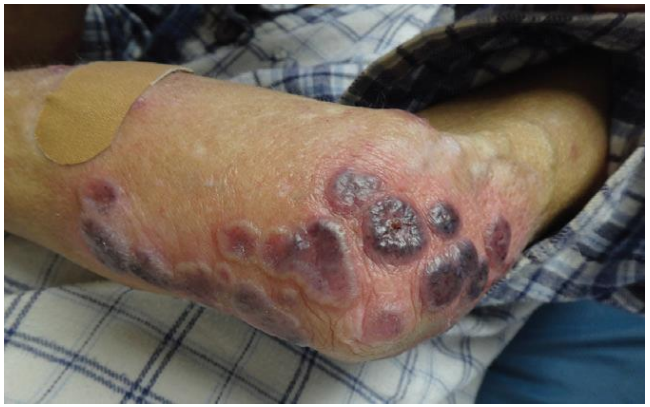
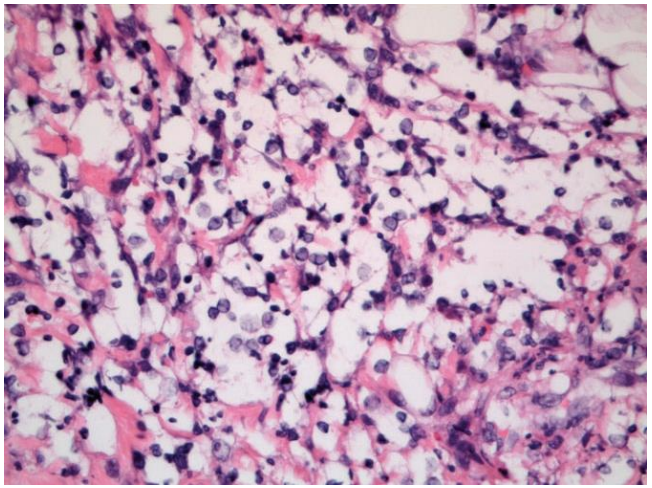


Diagnostic Utility and Comparative Immunohistochemical Analysis of MITF-1 and SOX10 to Distinguish Melanoma In Situ and Actinic Keratosis: A Clinicopathological and Immunohistochemical Study of 70 Cases
Am J Dermatopathol 36:124-30

CRYPTOCOCCOID/MOLLUSCOID SWEET SYNDROME

- Histology: Superficial to mid dermal infiltrate with many vacuolated spaces, scattered neutrophils, and larger mononuclear cells resembling histiocytes
- High power exam revealed basophilic yeast-like bodies within the spaces, concerning for disseminated cryptococcal infection
- Immunohistochemical staining revealed the pseudo-capsular spaces to be vacuolated myeloperoxidase-positive cells, leading to a diagnosis of Sweet's syndrome
- Staining and tissue culture were negative for bacteria, fungi and mycobacteria.





Cryptococcoid Sweet's syndrome: Two reports of Sweet's syndrome mimicking cutaneous cryptococcosis. J Cutan Pathol 2017;44:413-419

SWEET SYNDROME: UNUSUAL PRESENTATIONS

- Giant cellulitis-like Sweet´s syndrome:
  - Older (age>50)
  - Obese
  - Fever + leukocytosis
  - Paraneoplastic

- Vital organ involvement in Sweet's syndrome
  - Aortic valve
  - Atrioventricular valves
  - Endocardium
  - Myocardium
  - Great cardiac vessels can be involved

ADULT ONSET STILL DISEASE. HISTOLOGICAL FEATURES ASSOCIATED WITH WORSE PROGNOSIS

- Multicentric study 34 pts AOSD
- Atypical persistent skin eruption:
  - Face involvement
  - Ferritin level >1500 ng/mL
  - Number of lines of treatment to achieve complete remission
  - Histological features: acanthosis, spongiosis, superficial necrotic keratinocytes, and abundant neutrophilic infiltrates

- Cases reported with findings similar to dermatomyositis (with basal vacuolization) also associated with worse prognosis

Increased severity and epidermal alterations in persistent versus evanescent skin lesions in adult-onset Still disease
J Am Acad Dermatol 2018;79:969-71