LETTER TO THE EDITOR

An investigation of germline variants of *HAVCR2* in subcutaneous panniculitis-like T-cell lymphoma and related lesions in a North American population

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SUPPLEMENTAL TABLES AND FIGURES

Table S1. Characteristic features distinguishing SPTCL from Lobular Panniculitis

	SPTCL	Lobular Panniculitis
Clinical Presentation	Multiple subcutaneous nodules with progression (skin ulceration uncommon) Systemic symptoms (fever, malaise, cytopenia) Autoimmune disease or positive autoantibodies HLH in subset of patients	Subcutaneous nodules Usually no systemic symptoms of fever, malaise, cytopenia Autoimmune disease or positive autoantibodies Usually, no HLH
Morphology	T lymphocytes are predominantly CD8+ αβ cytotoxic cells	Mixture of CD4+ and CD8+ T cells
	Fat rimming by tumor cells with cytological atypia	Rare to absent
	Karyorrhexis	Rare to absent
	Low or absent reactive cells (B lymphocytes, plasma cells, plasmacytoid dendritic cells,	Admixed reactive cells (B lymphocytes, plasma cells, plasmacytoid dendritic cells
Genetics		
TCR monoclonality	Yes	Negative or Oligoclonal
***HAVCR2* variants**	Yes	No
Somatic mutations	Uncommon (only in 10-20%)	No

Table S2. HAVCR2 and clonality status of cases with detected somatic mutations

CASE NUMBER	DIAGNOSIS	SOMATIC MUTATIONS*	VAF	INTER-PRETATION	*HAVCR2* STATUS (VAR/WT)**	TRG
Case 22	SPTCL	*TET2*; p.C1135fs*7	2.7%	P	WT	Clonal
Case 33^	SPTCL	*KMT2D*; p.L804delinsPHLSPQPEEL	9%	VUS	VAR: p.I97M het	Polyclonal
Case 35	SPTCL	*BCORL1*; p.P1416L *CREBBP*; p.V1802M	10% 13%	VUS VUS	VAR: p.I97M het	Clonal

*Next Generation sequencing was performed using TruSight ® Oncology 500 (TSO500, Illumina ®) kit. Sequencing was performed using a NextSeq 550Dx system (Illumina ®). Proprietary TruSight Oncology 500 and TruSight Oncology 170 v1.0 local applications (Illumina ®) were used for alignment and variant calling. Resulting vcf file is uploaded to the QIAGEN Clinical Insight (QCI, QIAGEN) for filtering and annotation. This assay has a limit of detection of 1-3% VAF for both small nucleotide variants and 3-5% VAF for indels to 25 nucleotides.

***HAVCR2* c.245A>G, p.Y82C (COSM3683806), c.291A>G, p.I97M and c.302C>T, p.T101I mutational analysis were performed using the custom designed PrimePCR ddPCR Assays (BIO-RAD, Hercules, CA) on a BIO-RAD QX200 droplet digital PCR (ddPCR) system. The presence of mutation and the fractional abundance (FA) of the mutant allele was determined with QuantaSoft v.1.7 (BIO-RAD).

^Case was sequenced by submitter. VAF = variant allele frequency, VAR = variant, WT = Wild Type, het = heterozygous, TRG = T-cell Receptor Gamma Chain, P = Pathogenic, VUS = variant of uncertain significance

Figure S1. Atypical lobular panniculitis with *HAVCR2* germline variants, cases 2 and 3.

Case 2 (Panels A-F): Biopsy from a 61-year-old female shows atypical lobular panniculitis-like infiltrate separated by intact fibrous septae (A, H&E 20X). On high power, a mixed lymphohistiocytic infiltrate is present (B, H&E 200X). Focally, adipocytes are rimmed by perforin+ cytotoxic T cells (C, H&E 200x; D, Perforin immunostain, 200x). ddPCR detected homozygous *HAVCR2* p.T101I variant (E). T-cell gene rearrangement studies were clonal (F), but polyclonal in two other biopsies in two subsequent biopsies (not shown).

Case 3 (Panels G-L): Biopsy from a 56-year-old female shows an atypical lobular panniculitis-like infiltrate (G, H&E 20x). On high power, reactive plasma cells are seen (H, H&E 200X). There is focal adipose rimming by Granzyme+ cytotoxic T cells (I, H&E 200x; J, Granzyme immunostain 200x). ddPCR detected homozygous *HAVCR2* p.I97M germline variant (K). T-cell gene rearrangements were polyclonal (L).