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SUPPLEMENTARY INFORMATION

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Germline *HAVCR2* mutations altering TIM-3 characterize subcutaneous panniculitis-like T cell lymphomas with hemophagocytic lymphohistiocytic syndrome

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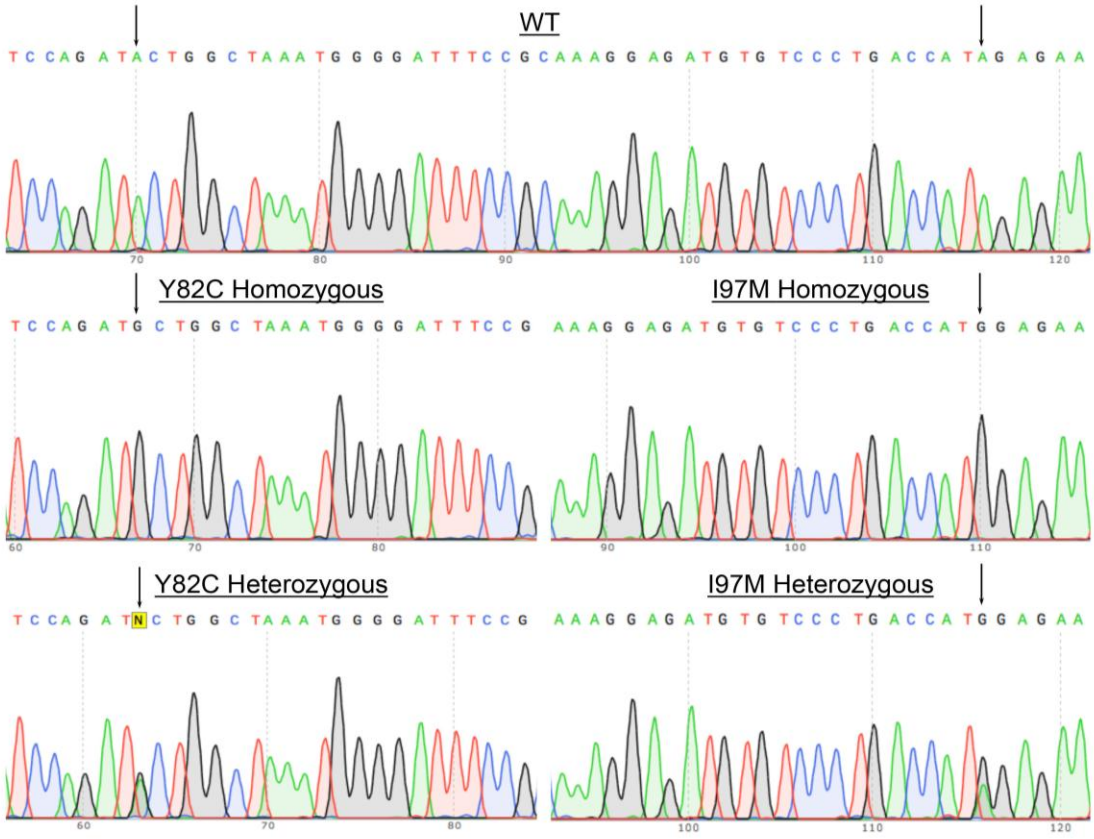


Supplementary Figure 1

Sequencing chromatograms showing *HAVCR2* mutations from homozygous affected individuals and heterozygous healthy relatives compared to wild-type *HAVCR2* from a healthy control.

a

Population frequency of HAVCR2 Y82C (SNP rs184868814)

Population	AA Reference Homozygotes	AG Heterozygotes	GG variant homozygotes	Allele Frequency	HWE Exact P-value
East Asia	9434	397	3	0.02104	0.5706
Latino	17209	366	1	0.01063	0.5
European (Finnish)	12896	127	0	0.004924	0.576
European (Non-Finnish)	63350	43	0	0.0003394	0.9319
South Asian	15391	48	0	0.001559	0.8466
African	12018	1	0	0.0000416	0.9964
Ashkenazi Jewish	5076	0	0	0	NA
Other	3233	16	0	0.002474	0.8881

Population frequency of HAVCR2 I97M (SNP rs35960726)

Population	AA Reference Homozygotes	AG Heterozygotes	GG variant homozygotes	Allele Frequency	HWE Exact P-value
East Asia	9432	0	0	0	NA
Latino	17208	20	0	0.0005811	0.9392
European (Finnish)	12897	61	0	0.002365	0.7883
European (Non-Finnish)	63338	626	0	0.004942	0.2136
South Asian	15391	0	0	0	NA
African	12016	10	0	0.0004161	0.9636
Ashkenazi Jewish	5076	62	0	0.006107	0.6635
Other	3233	27	0	0.004176	0.8123

b

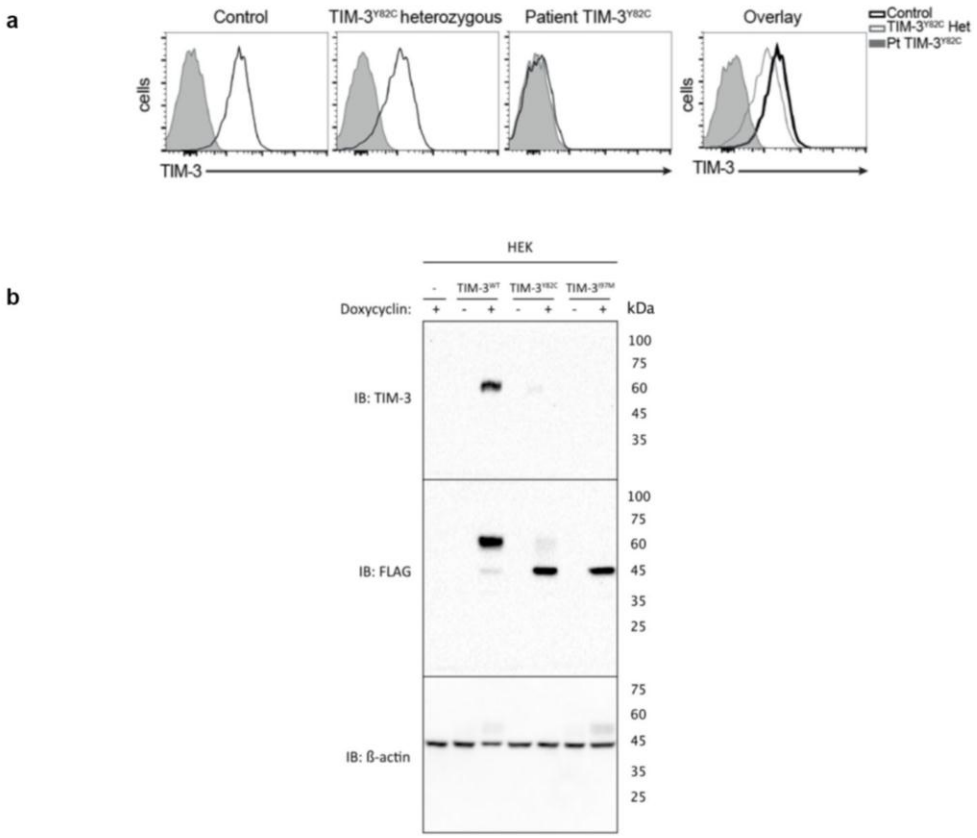
Frequency of HAVCR2 Y82C (SNP rs184868814) in the Tahiti Population

Population	AA Reference Homozygotes	AG Heterozygotes	GG variant homozygotes	Allele Frequency	HWE Exact P-value
Tahiti	107	8	0	0.03738	0.6879

Supplementary Figure 2

Frequencies of the Y82C and I97M variants in different populations according to their ethnic origin.

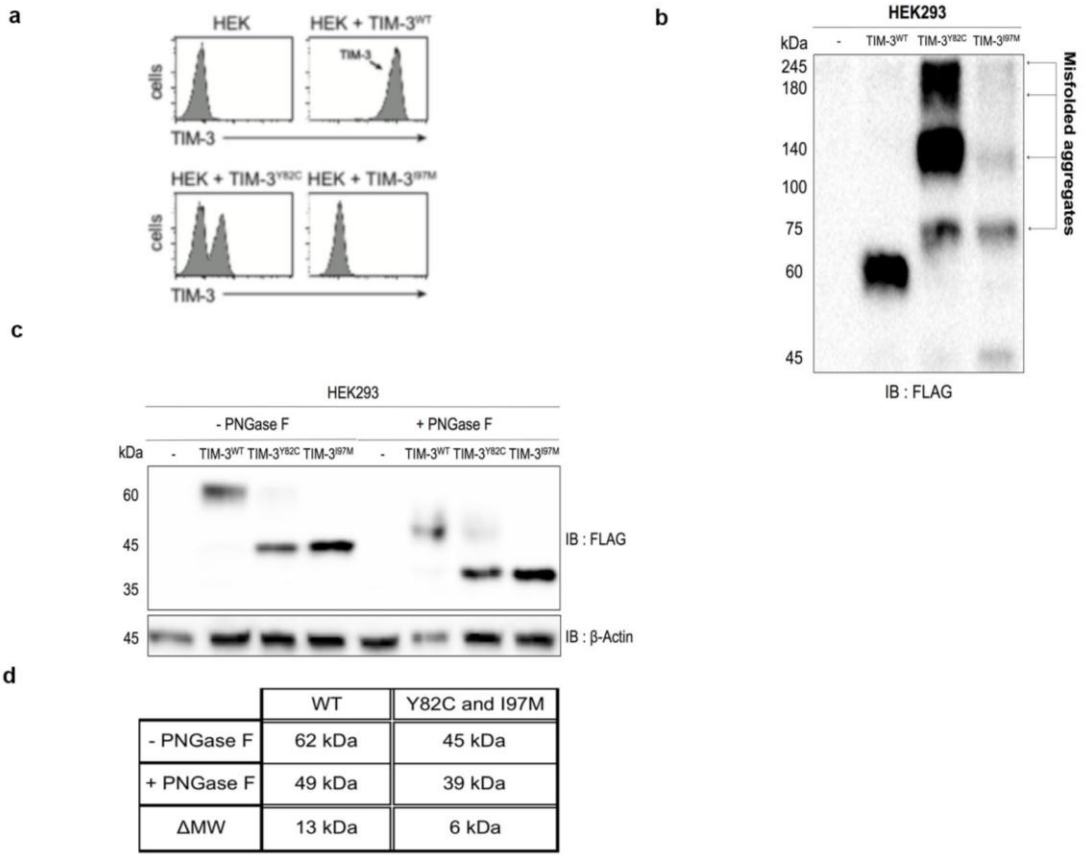
a, Distributions of the Y82C and I97M variants across all gnomAD populations. **b**, Frequency of the Y82C variant in the Tahiti population from Polynesia. The chi-squared test was used to calculate Hardy–Weinberg equilibrium (HWE) *P* values.



Supplementary Figure 3

Expression of TIM-3 mutants in SPTCL patients and stably transfected HEK-293 cells.

a, Flow cytometry of TIM-3 expression on monocytes ($CD14^{+}$) from a Y82C TIM-3 heterozygous individual shows an intermediate level of expression as compared to TIM-3 expression on patient and control cells. One representative experiment of the four heterozygous individuals analyzed is provided. **b**, Complete image of the western blot shown in Fig. 3c.



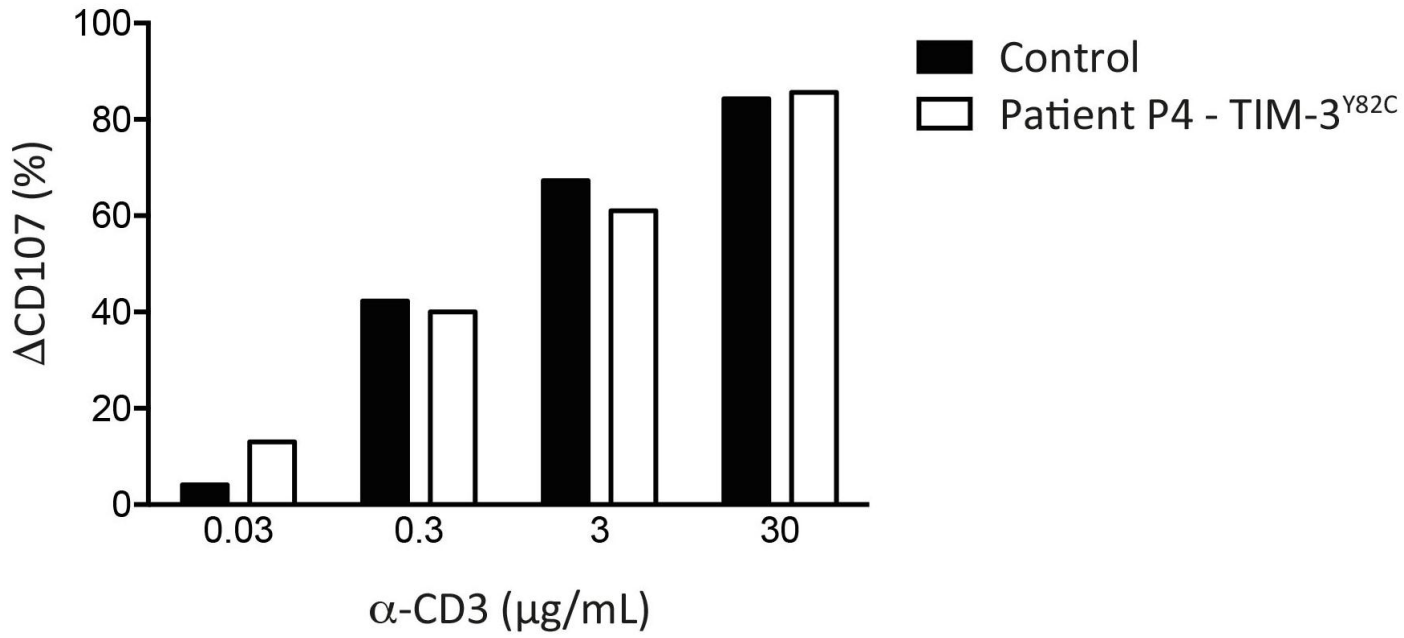
d

	WT	Y82C and I97M
- PNGase F	62 kDa	45 kDa
+ PNGase F	49 kDa	39 kDa
ΔMW	13 kDa	6 kDa

Supplementary Figure 4

Y82C and I97M lead to TIM-3 protein misfolding and impaired surface expression.

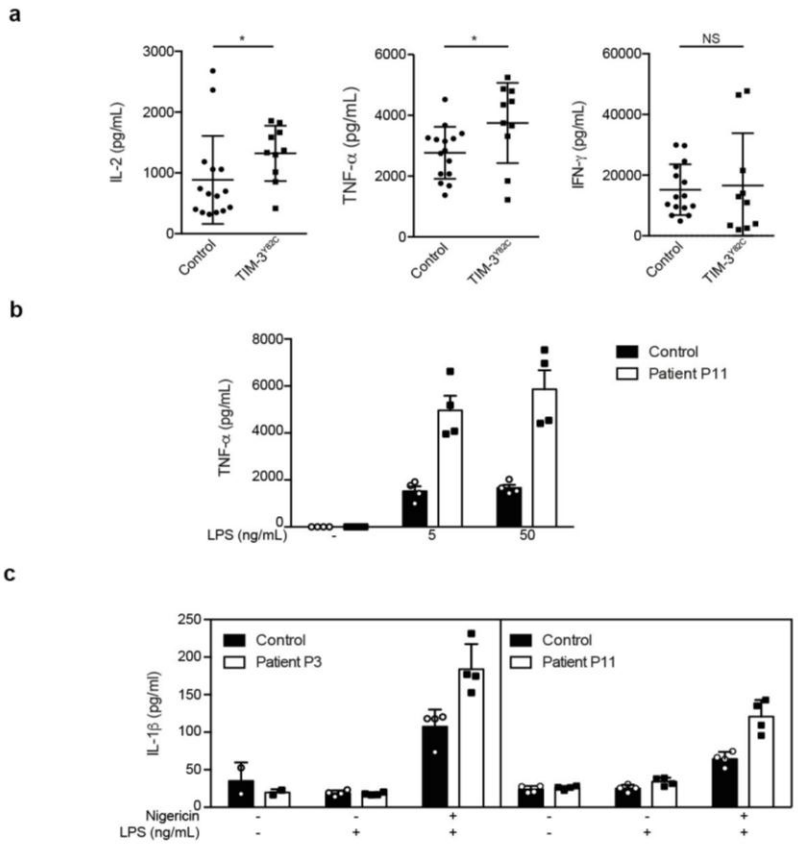
a, Plot showing the impaired surface expression of the two TIM-3 mutants on the same HEK-293T cells as in Fig. 3d, using flow cytometry analysis, by APC-conjugated TIM-3 antibody or isotype control antibody. **b**, Cell lysates from wild-type and Y82C or I97M TIM-3-transfected HEK-293 cells were put on a 7.5% native gel and immunoblotted against α-FLAG. Misfolded aggregates are highlighted with arrows. **c**, The same lysates from **b** were submitted to an N-deglycosylation assay using the PNGase F enzyme and following the manufacturer's denaturation protocol. These lysates as well as control lysates (without PNGase F) were immunoblotted with α-FLAG and α-β-actin. Experiments in **b** and **c** were repeated three times, and representative gels are shown. **d**, Analysis of the wild-type and mutant (Y82C and I97M) bands before and after PNGase F treatment. MW, molecular weight.



Supplementary Figure 5

Cytotoxic lymphocytes from P4 display similar degranulation activity to control lymphocytes.

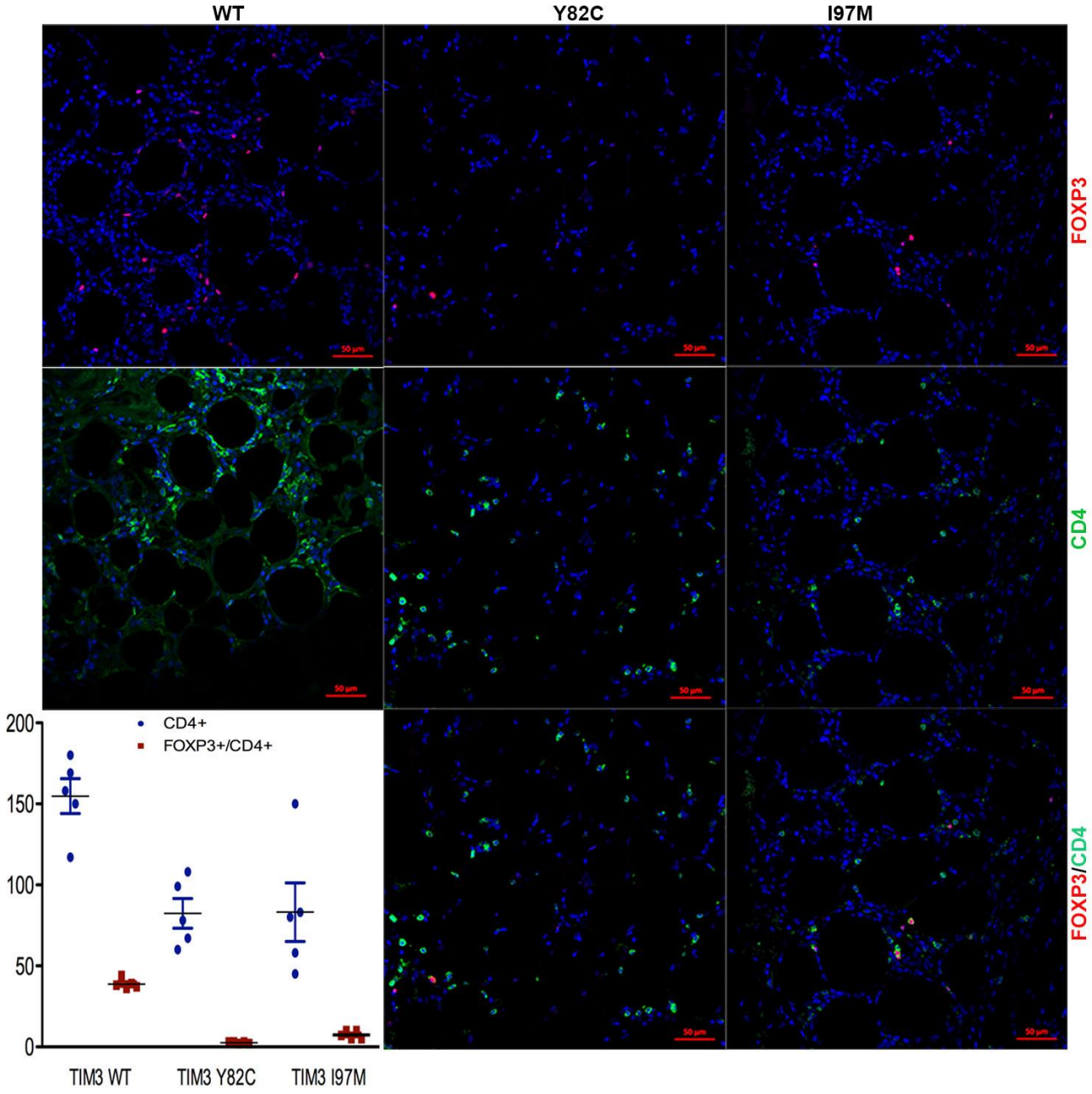
One representative experiment over four patients analyzed (P1–P4) is shown.



Supplementary Figure 6

Increased secretion of inflammatory cytokines by TIM-3-deficient leukocytes.

a, Cytokine production by T lymphoblasts from Y82C TIM-3 patients as compared to controls. TNF-α, IL-2 and IFN-γ were quantified by CBA (*P < 0.05). Data are means ± s.d. from three different patients (P3, P4, P11). Data represent the results of different independent experiments performed with different biological samples (cell cultures from cells obtained at different time points) obtained from different controls and three different TIM-3 Y82C patients. An unpaired *t* test was used to determine statistical significance between control (n = 15) and Y82C (n = 10) samples. **b**,**c**, Increased TNF-α production (**b**) and IL-1β production (**c**) by macrophages from patients (P3 and P11) with Y82C TIM-3, as compared to wild-type TIM-3 controls, in response to TLR4 (LPS) and NLRP3 (nigericin) activation (as done in Fig. 4). Graphs represent means ± s.e.m. from two independent experiments in duplicate (*P < 0.05).



Supplementary Figure 7

FOXP3^{+}CD4^{+} T_{reg} cells are significantly decreased in panniculitis from TIM-3-mutant (Y82C, I97M) SPTCL as compared to TIM-3-wild-type SPTCL.

Immunofluorescence using anti-CD4 and anti-FOXP3 antibodies was performed on consecutive slides from a wild-type (WT) SPTCL sample for TIM-3 (left) or the same slide for Y82C (middle) and I97M (right) TIM-3-mutant SPTCL samples. Cells positive for FOXP3 and CD4 staining were counted using Fiji software, and graphs represent means ± s.e.m. for CD4^{+} and FOXP3^{+}CD4^{+} cells from five different fields (lower left). A significantly decreased number of CD4^{+} and FOXP3^{+}CD4^{+} cells in TIM-3-mutant SPTCL was observed when comparing TIM-3-mutant to TIM-3-wild-type SPTCL ($P < 0.001$, one-way ANOVA). Representative images mounted using Photoshop are shown.

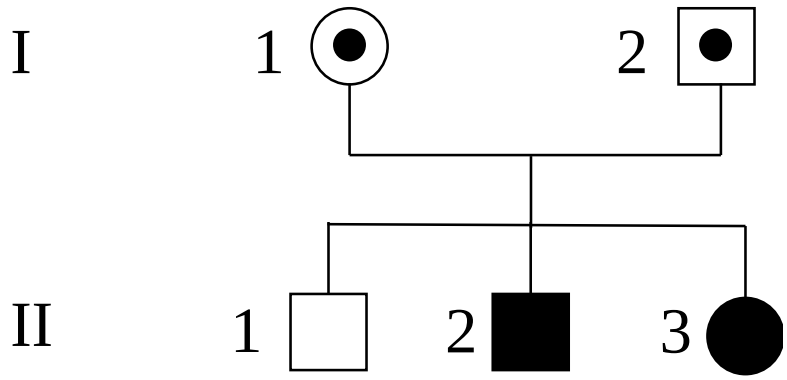
Supplementary Note

Patient samples and case reports

This study was approved by the Institutional Review Board of all participating institutions where samples were obtained following informed consent for all subjects included in this series. A total of 27 patients with institutional diagnosis of SPTCL were recruited, including three families, two from East Asia with two affected siblings (P1 and P2; P10 and P11), whose parents are healthy, and another from French Polynesia with one affected child (P4) and seemingly unaffected family members. Family of P10 and P11 came from a Vietnamese village where both paternal and maternal grand-fathers died of a hematologic disease with sub-cutaneous nodules, enlarged lymph nodes, anemia, high fevers and weight loss evocative of SPTCL. Matched normal blood samples were available for thirteen cases of the 27 patients included in this series. The tumor samples are composed of 22 FFPE samples and 4 fresh frozen tissues, and one blood sample for P11 for whom we did not have available material from a skin biopsy. Patient's age ranged from 1 to 90 years (median 19 years) and their ethnic backgrounds include Caucasian (n=12), Polynesian (n=8), East Asian (n=4), African (n=2) and South American (n=1). The pedigree, family history and case report of the 16 TIM-3 mutant SPTCL patients are presented below. In all pedigrees, a circle represents a female and a square indicates a male, a dot in the middle of the symbol indicates a carrier. The black shaded symbols are the affected patients. Symbols filled with light gray color indicate individuals lost to follow up.

P1 & P2

Pedigree



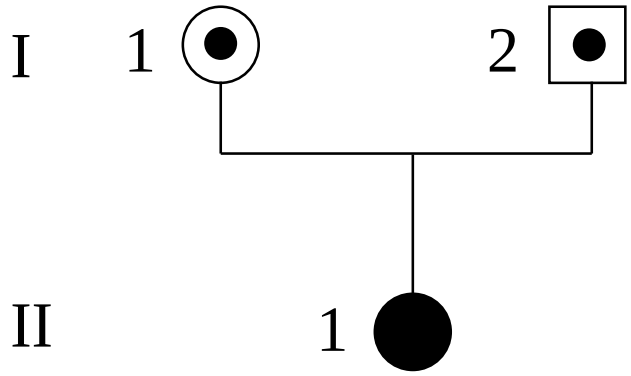
Family History : There is no family history of lymphoma, autoimmunity or other disorders associated with this pathology.

Case Reports :

The East Asian family (F1) was comprised of five individuals, all previously healthy with no relevant family history. Parents were unrelated from China and Cambodia. Two siblings presented one year apart at respectively 11- and 9-years of age with typical HLH and panniculitis. The 11-year old boy (P1, II-2) presented with facial swelling and HLH, which was initially misdiagnosed as sepsis, and a 6- month history of fatigue, night sweats and fever. Initial biopsy of the bone marrow for pancytopenia showed infiltrate of pleomorphic predominantly CD3+/CD8+ T-cells in both sites with rimming of individual adipocytes consistent with SPTCL. He rapidly developed subcutaneous nodules on the trunk and extremities with SPTCL identified in subcutaneous tissue. Molecular studies showed T-cell receptor β-chain gene rearrangement consistent with skin lesions. The child underwent 2 cycles of chemotherapy and had progressive disease with continuous signs of HLH, despite subsequent use of other chemotherapeutic agents. Importantly, he was put in near-remission following the sole use of Cyclosporine A (CsA) shortly before a successful HLA-identical allogeneic HSCT from his HLA-matched older brother (II-1). His sister (P2, II-3) presented one year later with similar facial swelling and typical HLH preceding the panniculitis on her legs and buttocks. Sub-cutaneous nodule biopsies showed clonal T-cell receptor (TCR) β-chain gene rearrangement. Corticosteroids and CsA therapy induced significant reduction in her symptoms, and she then underwent a successful unrelated HSCT. There was no evidence of a pathogen or another trigger in both cases despite intensive investigations. Both siblings are alive and disease free at the last follow-up 2 and 3-year post transplant.

P3

Pedigree



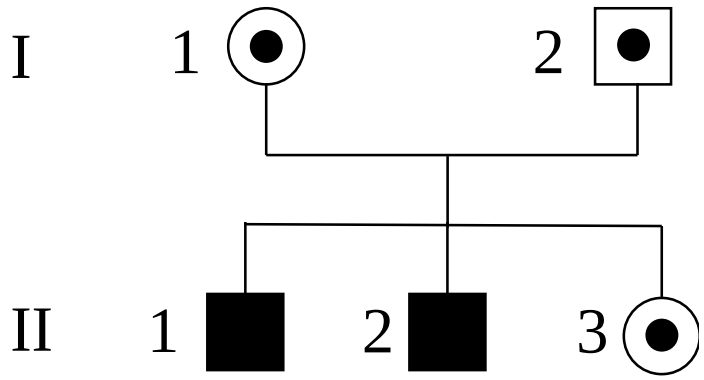
Family History : There is no family history of lymphoma, autoimmunity or other disorders associated with this pathology.

Case Report

P3 is a teenage girl (II-1) from French Polynesia born from non-consanguineous healthy parents of Maori ancestry. Her past medical history was uneventful until the age of 13 when she presented persistent mild fever and painful left flank with incomplete HLH (4/8 criteria) (fever, no splenomegaly, hypofibrinogenemia, hypertriglyceridemia, hyper ferritinemia, normal liver enzymes, mild anemia, normal neutrophils and platelets counts, hemophagocytosis on bone marrow aspirate). Infectious screening was negative and there were no obvious signs of autoimmunity. Positron emission tomography PET-CTSCAN revealed diffuse enhancement of sub-cutaneous tissues. Profound skin biopsy displayed panniculitis with oligoclonal TCRβ chain rearrangement. Short course steroids (6 weeks) and CsA (8 months) allowed long term remission. At last follow up, at the age of 14.5, while the patient has been off immunosuppressive drugs for the last 6 months, the patient was in complete remission as attested by normal physical exam, biological results and PET-CT Scan.

P4

Pedigree



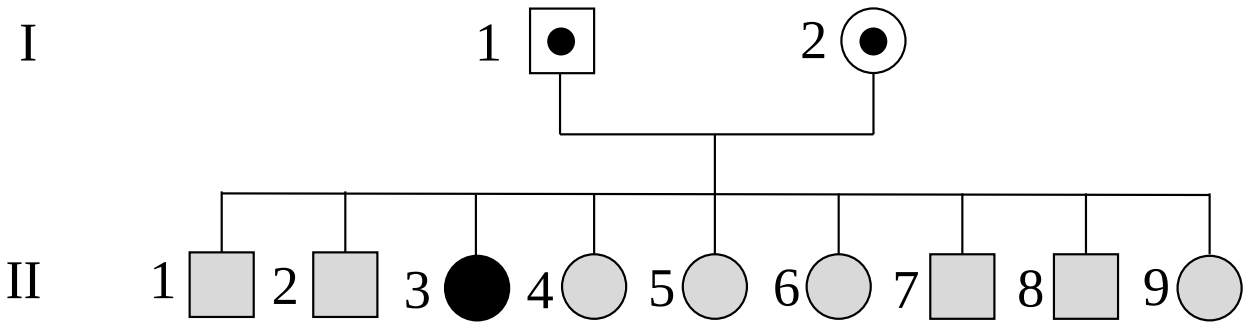
Family History : There is no family history of lymphoma, autoimmunity or other disorders associated with this pathology.

Case Report

P4 (II-2) is a teenage boy from French Polynesia born from non-consanguineous healthy Maori parents; his brother and sister are healthy, including II1 who was investigated at the age of 19 His blood work-up showed increased IgE level and positive anti-DNA antibodies. P4 past medical history was uneventful until the age of 11, when he presented persistent fever and pain in the right flank. HLH was diagnosed with 5/8 positive criteria (fever, no splenomegaly, pancytopenia, hyper ferritinemia, hypofibrinogenemia and hemophagocytosis on bone marrow aspirate). He was treated with steroids, CsA, 4 doses of VP16 and one intrathecal MTX injection allowing complete remission. Steroids were tapered and stopped after 6 weeks, CsA was discontinued after 8 months with complete clinical and biological remission. Infectious screening was negative, there were no obvious signs of autoimmunity and genetic studies of genes associated with familial hemophagocytic lymphohistiocytosis, *SAP* and *XIAP* by Sanger sequencing were negative. At the age of 13, he presented a relapse of HLH with painful redness of right flank. PET-CT scan showed diffuse enhancement of sub-cutaneous tissues revealing panniculitis histologically confirmed with monoclonal TCRβ chain rearrangement. CsA was reinitiated allowing partial remission with intermittent fever requiring several courses of steroids. Abatacept (20 mg/kg every 2 weeks) was tried in addition during 6 months without benefit. Anakinra 100 mg in daily sub cutaneous injection has been initiated in the last 3 months with clinical improvement.

P5

Pedigree



Family History : There is no family history of lymphoma, autoimmunity or other disorders associated with this pathology.

Case Report

P5 (II-3) is a 12-year-old girl born from non-consanguineous healthy Maori parents. Familial history of her 8 brothers and sisters and her personal history were uneventful until the age of 12 when she presented with facial swelling. Skin lesions progressively spread to mandible and periorbital region and became erythematous and warm despite empirical antibiotic treatment. The child became concomitantly febrile. Lesions spread to thighs, back, chest and face, and were palpable bruise-like lesions with induration, erythema and sometimes skin necrosis. Biological assessment was suggestive of mild HLH. Anti-neutrophil cytoplasmic antibodies were positive (1/640). The MRI showed extensive subcutaneous edema with no evidence of dermatomyositis. The skin biopsy showed lobular panniculitis with predominantly lymphocytic inflammation and lichenoid features. Diagnosis of lupus erythematous profundus was proposed and she was initially treated with steroids (IV methylprednisolone pulse) with remarkable clinical improvement. When corticosteroids were tapered and stopped 4 months later, relapse occurred promptly with skin lesions of overlying ulcerations, fever and full-blown HLH. Repeated skin biopsies were consistent with alpha/beta SPTCL. She was then referred to the Oncology department. She initially received two courses of CHOP with transient response on the skin lesions and HLH. She then received two courses of ICE with a near complete metabolic response on FDG-PET and resolution of the HLH. Her treatment was then consolidated with high-dose BEAM followed by autologous hematopoietic stem cell transplantation. She is now in complete remission two years post-autograft, with scarred lipodystrophy in previous SPTCL areas.

P6

Pedigree : Family tree is not available for this patient.

Family History : There is no family history of lymphoma, autoimmunity or other disorders associated with this pathology.

Case Report

P6 is a Polynesian male born from non-consanguineous parents. Familial and personal medical histories were uneventful until the age of 12 months when he presented with subcutaneous lesions of the left orbit, the chest anterior wall and left thigh, associated with incomplete HLH (3/6 criteria evaluated - fever, splenomegaly, hemophagocytosis on bone marrow aspirate). A diagnosis of panniculitis was confirmed on the skin biopsy, and the patient commenced on a HLH treatment (HLH-94 protocol). The skin T-cell lymphoma was then treated based on a modified BFM95 protocol with good response. He has completed the treatment and is in complete remission with a follow-up of 6 years.

P7

Pedigree : Family tree is not available for this patient.

Family History : There is no family history of lymphoma, autoimmunity or other disorders associated with this pathology.

Case Report

Patient P7 was a young Maori female diagnosed at 16-year-old with no significant past medical history. At the time of diagnosis, she also presented an incomplete macrophage activation syndrome (2/2 criteria evaluated). There was no obvious sign of autoimmunity (anti-nuclear antibodies 1/160). She was initially treated with oral CsA with good disease control on the skin lesions and the hemophagocytic syndrome. Treatment was switched to tacrolimus after 4 years due to renal impairment, hypertension and migraine. She received 6 cycles of CHOP 6 years post-initial diagnosis and achieved complete response. However, one year after chemotherapy, the skin lesions reappeared. Tacrolimus was restarted with good control of the disease despite occasional flares. She remains dependent to tacrolimus 10 years post-diagnosis.

P8

Pedigree : Family tree is not available for this patient.

Family History : There is no family history of lymphoma, autoimmunity or other disorders associated with this pathology.

Case Report

P8 is a Vietnamese male diagnosed at the age of 67. He did not present any remarkable past medical history. The first skin lesions appeared 9 months before diagnosis and he had B symptoms for 2 months (fever, malaise, fatigue, weight loss) before presentation. The skin biopsy confirmed the diagnosis of SPTCL. The patient was initially treated with oral prednisolone with good response. Two episodes of flare occurred two and three years' post-diagnosis and were treated with electron beam radiation and continued use of steroids. He is now in complete remission for a year with slow taper of steroids.

P9

Pedigree : Family tree is not available for this patient.

Family History : There is no family history of lymphoma, autoimmunity or other disorders associated with this pathology.

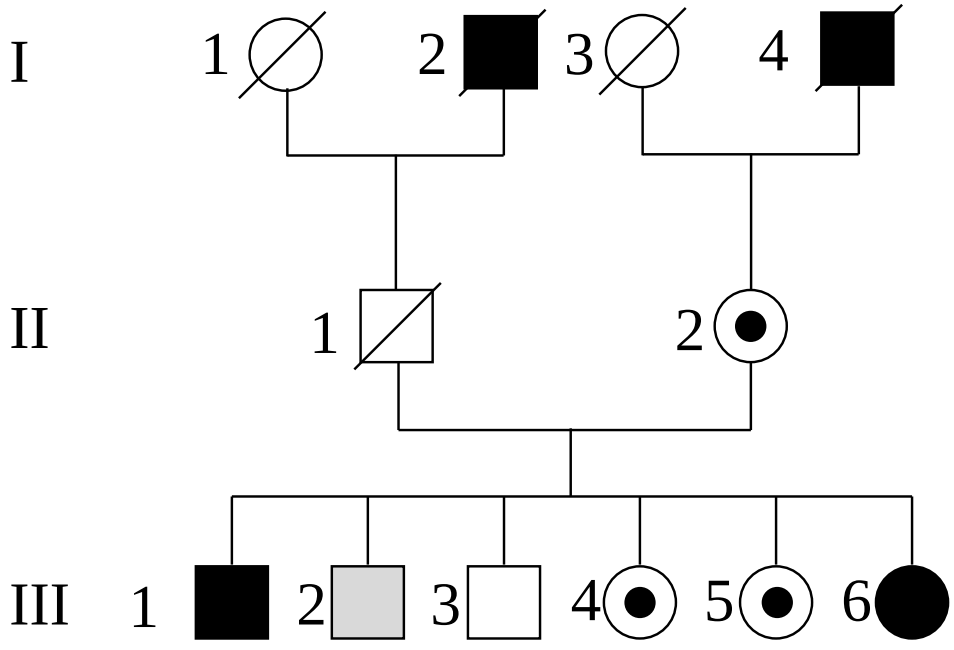
Case Report

P9 is a 22-year-old Polynesian woman with a medical history of recurrent hemophagocytic lymphohistiocytosis, cytolytic hepatitis and a histiocytic and cytophagic panniculitis diagnosed at the age of 16. She was first treated with 4 courses of CHOP chemotherapy without any response. She then received high dose corticosteroid with etoposide and CsA, and achieved first remission 6 months after onset of symptoms. She presented a new outbreak of HLH 6 months later and was treated with corticosteroid. She relapsed one year later and was treated with chemotherapy and corticosteroid, with partial response. She finally received high dose corticosteroid for a new outbreak 3 years later. Seven years after the onset of the disease, she relapsed with HLH and new nodular panniculitis lesions from limb, trunk and face. Panniculitis was associated with splenomegaly, hepatomegaly

and general symptoms (fever, asthenia and weight loss). Biological analysis revealed elevated liver enzymes, elevated lactate dehydrogenase and hypertriglyceridemia. Anti-DNA antibodies were positive and associated with elevation of angiotensin conversion enzyme and of β2-microglobulin. A new skin biopsy showed adipocytes rimming and necrosis. A bone marrow biopsy confirmed the presence of hemophagocytosis without cytotoxic T cell infiltration of bone marrow and adipocyte rimming by inflammatory cells. She was first treated with chemotherapy followed by autologous hematopoietic stem cell transplantation. She reached complete remission but relapsed 3 months later. She was then treated with corticosteroid and low dose methotrexate. HLH symptoms slowly decreased and panniculitis lesions disappeared. She then achieved complete remission 11 months later. Treatment was maintained for seven years. Due to the persistence of CR, methotrexate was discontinued and corticosteroids slowly tapered. The patient is still in remission 16 years after SPTCL diagnosis.

P10 & P11

Pedigree



Family history

P10 and P11 are from the same family from a small vilage in Vietnam. Familial history includes two cases of nodular cutaneous lesions associated with multiple lymph nodes involvement, asthenia and weight loss in both

paternal and maternal grand-fathers (I-2 and I-4). They died from these hematological malignancies. Unfortunately, no biological material was available for additional analysis (died in Vietnam). II-1 was healthy before accidental death at age 54. II-2 is healthy at the age of 84 years. There is no information on III-2 but this brother is reported to be healthy. III-3-4-5 are healthy with the exception of lichen planus that occurred in III-4 who also has antinuclear antibodies at 1/40 and, anti parietal gastric cells at 1/1600.

Case Report

P10

P10 (III-6) is a 41 years old Vietnamese woman with a medical history of hepatitis C, treated with interferon and ribavirin. She then developed an interferon-induced hyperthyroidism. At the age of 29, she had breast implants without any complication. 12 years later, she developed subcutaneous nodular lesions surrounding breast prosthesis, associated with fever and myalgia. Breast prosthesis were removed and subcutaneous lesions biopsied. Pathological analysis confirmed the diagnosis of SPTCL and revealed adipocytes necrosis and rimming with CD8+CXCL13-CD2-CD5-CD7-CD3+CD30-EBER-Ki67high T cells. PET-TDM highlighted multiples lesions from the trunk and the limbs. Circulating blood lymphocytes were mainly composed of CD4+ T cells (35%), CD8+ T cells (26%) and B cells (37%), with a selective NK cell lymphopenia (1%). Lactate deshydrogenase and β2-microglobulin were elevated. Bone marrow biopsy was normal. She first received corticosteroids that enabled a small improvement of her general condition. She was then treated with 4 courses of CHOP chemotherapy and obtained a complete response. Treatment was continued with an autologous HSCT after Busulfan, etoposide, melphalan (BAM) conditioning regimen. She relapsed during the autologous HSCT with new subcutaneous lesions of the limb. She then received successive courses of vinblastine, doxorubicine and bendamustine without any response. She was finally treated with dexamethasone and lenalinomide and reached complete response. She received a sibling-identical allogeneic HSCT after fludarabine and melphalan conditioning regimen. She subsequently relapsed despite having a 100% donor chimerism. Further analysis oriented by this case series identified the brother to be homozygous for Y82C-TIM3. She is on ciclosporine therapy with disease control for the last 6 months.

P11

Case Report

P11 (III-1) is a 48 year old with a medical history of hepatitis C, treated with interferon. He had blood test two years as a potential donor for his sister (P10) before diagnosis, which showed normal blood count, liver-function tests and ferritinemia. He then developed asthenia and weight loss, with multiple skin plaques/nodules that were treated with topical corticosteroids. He then developed hepatomegaly and splenomegaly and recurrent bouts of fever. Blood test revealed biological evidence of HLH with hyperferritinemia (8058 microgram/L, N=30-400), hypertriglyceridemia (4.1mmol/L, N=0.5-1.5), liver cytolysis and icteric cholestasis. Lactate deshydrogenase levels were also elevated. No auto-antibodies were detected. Total IgE level was increased at 796 kUI/L (N=0-114kUI/L).

P12

Pedigree : Family tree is not available for this patient.

Family History : There is no family history of lymphoma, autoimmunity or other disorders associated with this pathology.

Case Report

P12 was a 31 years old Maori from New Zealand when he was diagnosed. His main medical history was a Kawasaki disease during childhood. A few months before presentation, a thigh subcutaneous lesion appeared and was associated with fever and fatigue, decreased blood counts and hyperferritinemia. After diagnosis on the skin biopsy, he was treated with oral methotrexate and ciclopsorine A (CsA) with good response. 18 months post-diagnosis, the disease is stable on CsA.

P13

Pedigree : Family tree is not available for this patient.

Family History : There is no family history of lymphoma, autoimmunity or other disorders associated with this pathology.

Case Report

P13 is a 90 years Caucasian woman with no significant medical history. She consulted for two nodular lesions of arm and limb. She had no other associated symptoms. Complete surgical tumor excision was performed. Histological analysis revealed adipocytes rimming and necrosis, angiocentrism, cytophagia and mitosis and a diagnosis of SPTCL. CT-Scans did not reveal other disease sites and bone marrow biopsy was normal. She was then treated with local radiotherapy and then was lost to follow-up one month after treatment.

P14

Pedigree : Family tree is not available for this patient.

Family History : There is no family history of lymphoma, autoimmunity or other disorders associated with this pathology.

Case Report

P14 is a Caucasian girl born to non-consanguineous parents. Her familial and personal medical histories were uneventful until the age of 15.5 when she presented unilateral groin induration with persistent fever, weight loss and asthenia. Biological assessment showed mild leucopenia, normal hemoglobin and platelets counts, no excess of activated T cells, normal fibrinogen and ferritinemia, mild increased triglyceridemia (3.32 mmol/l) and of liver enzymes (ALT 31 IU/L, AST 143 IU/L). Biospy was consistent with SPTCL. Because initial treatment with cortico-steroids and weekly vinorelbine was only partially efficient, 6 months intensive chemotherapy with the ALCL99 protocol was administered followed by 18 months of maintenance therapy with 6 mercaptopurine and methotrexate. She is currently in complete remission 3 years post treatment cessation.

P15

Pedigree : Family tree is not available for this patient.

Family History : There is no family history of lymphoma, autoimmunity or other disorders associated with this pathology.

Case Report

P15 is a 23-year-old Caucasian young man who presented at the age of 11 years with multi-focal panniculitis and HLH following a story of intermittent fevers, rashes and weight loss in the last 6 months. Skin biopsy confirmed the diagnosis of SPTCL and bone marrow biopsy showed involvement on his bone marrow with similar adipocyte rimming of CD3+CD8+Tcells. He was first treated with 2 courses of CHOP without significant response and switched to ABVD. Based on refractory disease he received high-dose chemotherapy followed by autologous-HSCT. He relapsed 9 years later with similar symptoms and HLH-SPTCL which proved refractory to multiple lines of chemotherapy. He recently underwent allogeneic HSCT and is in remission 6 months post-transplant and being progressively weaned off CsA and other transplant-related medications.

P16

Pedigree : Family tree is not available for this patient.

Family History : The patient's mother and aunt have a history of lupus.

Case Report

P15 is a 31 years old woman with a medical history of systemic lupus, pancreatitis and recurrent fever since the age of 11 years old. She was first treated with hydroxychloroquine for 2 years. She then received colchicine for one year, followed by corticosteroids, colchicine, hydroxychloroquine and CsA for 2 years. She was finally treated with azathioprine for 4 years. Between the age of 22 and 30, she received multiple courses of corticosteroids. At the age of 31 years old, she consulted for the appearance of multiple nodular lesions on the face, arms, limbs and trunk. She had fever, weight loss and asthenia, no adenopathy, splenomegaly nor hepatomegaly. CBC revealed a mild lymphopenia and an isolated anemia. Coombs test was positive. Antinuclear and anti-cardiolipin antibodies were positive. Complement was normal. Skin biopsy revealed cytotoxic T cell infiltration with adipocyte rimming and necrosis, cytophagia, angiocentrism and vasculitis. She

was treated with corticosteroids and low dose methotrexate once a week. She achieved complete remission three months later and is still in CR seven years after the SPTCL diagnosis.