Serican Journal of Medicine
2026, VOL. 3, NO. 1, 24938
https://doi.org/10.17161/sjm.v3i1.24938

Blood Levels of Interleukin-17 Family Members in Healthy Individuals and Various Diseases

Ruoxin Lan[1], Sayed Ala Moududee[2], Dongxia Ge[3], Alun R. Wang[4], Yao-Zhong Liu[1,*], and Zongbing You[2,3,*]

[1]Department of Biostatistics and Data Science, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA 70112 USA; [2]Department of Structural and Cellular Biology, Tulane University School of Medicine, New Orleans, LA 70112, USA; [3]Department of Orthopaedic Surgery, Tulane University School of Medicine, New Orleans, LA, USA; [4]Department of Pathology and Laboratory Medicine, Tulane University School of Medicine, New Orleans, LA 70112, USA.

*Correspondence: yliu8@tulane.edu; zyou@tulane.edu

ABSTRACT

The interleukin-17 (IL-17) family of cytokines and receptors plays important roles in host defense, inflammation, autoimmunity, and cancer. This study re-analyzed a pan-disease blood proteomics dataset containing one healthy population (n = 825) and 59 disease populations (n = 5227) classified into cardiovascular, metabolic, cancer, psychiatric, autoimmune, infection, and pediatric classes. Datasets of IL-17A, IL-17C, IL-17D, IL-17F, IL-17RA, and IL-17RB were retrieved from the published report and re-analyzed, focusing on comparisons between diseases and healthy people. We found that IL-17A and IL-17RA blood levels were increased in 55 diseases compared to healthy people. IL-17C, IL-17D, IL-17F, and IL-17RB levels were increased in some diseases but decreased in other diseases. While it was expected that IL-17A, IL-17C, IL-17D, and IL-17F levels were frequently increased in infectious diseases, it was surprising that IL-17RA and IL-17RB levels were remarkably increased in pediatric tumors. Future studies will investigate the roles of IL-17RA and IL-17RB in the pathogenesis of pediatric tumors.

ARTICLE HISTORY
Received: Dec. 24, 2025
Revised: Jan. 21, 2026
Accepted: Jan. 22, 2026

KEYWORDS
blood; plasma; proteomics; IL-17; disease

1. Introduction

Interleukin-17 (IL-17) family includes proinflammatory cytokines IL-17A, IL-17B, IL-17C, IL-17D, IL-17E, and IL-17F [1] and their five receptors IL-17 receptor A (IL-17RA), IL-17RB, IL-17RC, IL-17RD, and IL-17RE [1]. IL-17RA acts as a shared subunit and forms heterodimers with the other four receptors [2]. Homodimers of IL-17A or IL-17F and a heterodimer of IL-17A/IL-17F bind to the IL-17RA/IL-17RC receptor complex. Homodimers of IL-17B or IL-17E bind to the IL-17RA/IL-17RB receptor complex. IL-17C homodimer binds to IL-17RA/IL-17RE receptor complex. It has been reported that IL-17A, but not IL-17F or IL-17A/F, also binds to IL-17RA/IL-17RD receptor complex [3]. IL-17D has been reported to bind CD93 in regulating colon inflammation [4]. Although IL-17B was originally considered as the ligand for IL-17RB, it is commonly believed to be a competitor against IL-17E in binding to IL-17RB [5]. IL-17A and IL-17F are produced by T helper 17 (Th17) cells, γδ T cells, natural killer cells, and other immune cells [6]. Binding of IL-17A or IL-17F to IL-17RA/IL-17RC receptor complex recruits nuclear factor-κB (NF-κB) activator 1 (Act1) through SEFIR (similar expression to fibroblast growth factor genes, IL-17 receptors and Toll–IL-1R) domains of IL-17RA, IL-17RC, and Act1. Act1 acts as an E3 ubiquitin ligase to ubiquitinate tumor necrosis factor receptor-associated factor 6 (TRAF6) through lysine-63-linked ubiquitination [7]. Then, TRAF6 activates transforming growth factor –β-activated kinase 1 (TAK1) and subsequently IκB kinase (IKK) complex, resulting in activation of NF-κB pathway that initiates transcription of a variety of cytokines, chemokines, matrix metalloproteinases (MMP), and growth factors, such as IL-1α, IL-1β, IL-6, tumor necrosis factor α (TNFα), colony stimulating factor (CSF), C-X-C motif ligand 1 (CXCL1), CXCL2, CXCL5, CXCL8, C-C motif ligand 7 (CCL7), S100 Calcium Binding Protein A7 (S100A7), S100A8, S100A9, CCAAT Enhancer Binding Protein Beta (CEBPB), Prostaglandin-Endoperoxide Synthase-2

(PTGS2), MMP1, MMP2, MMP7, MMP9, and MMP13 [8-14]. IL-17 also induces expression of programmed cell death protein 1 (PD-1) ligand 1 (PD-L1), but not PD-L2, in a human prostate cancer LNCaP cell line [15]. IL-17A and IL-17F act through IL-17RA/IL-17RC to induce inflammatory responses that protect humans against a variety of fungal and bacterial infections [16]. Defects in IL-17 signaling, such as mutations in IL-17RA, IL-17RC, or Act1, make humans susceptible to chronic mucocutaneous candidiasis [17-19], while unrestricted IL-17 signaling promotes autoimmune diseases (e.g., psoriasis, lupus, rheumatoid arthritis, multiple sclerosis) [20-24] and a variety of cancers including prostate [12, 25], colon [26-29], skin [30, 31], breast [32], lung [33, 34], and pancreatic cancers [35]. IL-17 signaling must be tightly regulated to maintain its physiological functions and avoid pathological effects.

IL-17 signaling is regulated at multiple levels. At the ligand level, differentiation of T helper 17 (Th17) cells that secrete IL-17 is regulated by a thymus-specific isoform of the retinoid acid receptor-related orphan receptor C (RORC, also called RORγT) [36] and multiple transcription factors [37, 38]. Downstream of the receptor level, Act1 plays a central role in mediating several signaling pathways [39, 40]. Act1 binds to tumor necrosis factor receptor-associated factor (TRAF) 6, TRAF2, and TRAF5 to relay the signaling, thus Act1-TRAF6 and Act1-TRAF2/5 interactions receive regulations from ubiquitin ligases (TRAF3 and TRAF4), deubiquitinases (A20 and ubiquitin-specific peptidase 25), microRNAs [41], and Src homology 2 domain-containing tyrosine phosphatase (SHP2) [42]. At the end of IL-17 signaling cascades, an essential transcription factor, CCAAT enhancer binding protein β (C/EBPβ), is inhibited through phosphorylation by extracellular signal-regulated kinase (ERK) and glycogen synthase kinase (GSK) 3β [43]. IL-17RA but not IL-17RC is phosphorylated by GSK3 (GSK3α and GSK3β) at threonine 780 (T780) [44]. IL-17RA phosphorylation at T780 leads to ubiquitination and proteasome-mediated degradation of IL-17RA, resulting in decreased responses to IL-17 treatment in the cultured cells [44]. Ubiquitination of IL-17RA is mediated by F-box and WD repeat domain-containing 11 (FBXW11) E3 ligase through a lysine 27-linked polyubiquitin chain and requiring IL-17RA protein domain of 665 -804 amino acids [45]. In contrast, inhibition of GSK3 activities by insulin treatment enhanced IL-17-induced gene expression, and knockout of GSK3 enhanced IL-17-induced gene expression [46, 47]. In a high-fat diet-induced obese mouse model, hyperinsulinemia inhibited IL-17RA phosphorylation by GSK3, increasing IL-17RA levels and enhancing IL-17-mediated inflammation. Prostate cancer formation was increased in obese mice with phosphatase and tensin homolog (Pten) knockout backgrounds compared to lean mice [44].

Blood IL-17 levels have been studied previously in a variety of patient populations [48-50]. However, these studies were limited in sample size, and the methods used to quantify IL-17 were different. Thus, it is a challenge to compare the results among the studies. Recently, a study used a pan-disease resource with a harmonized proteomics dataset covering 8262 individuals and up to 5416 proteins [51]. One healthy population and 59 disease populations were investigated. The study found that each disease had characteristic protein profiles with differentially abundant proteins. Many of the identified proteins that were increased in cancer and autoimmune diseases were also increased in patients with infectious diseases, suggesting that these proteins are markers for inflammation rather than for a particular disease. Conversely, many of the proteins whose concentrations went up in hepatocellular cancer were increased in other liver diseases, demonstrating the power of this pan-disease approach to identify proteins with a "cross-disease" pattern [51]. Increased protein levels were observed in five common cancers such as extracellular glycoprotein lacritin (LACRT) in breast cancer, POF1B actin binding protein (POF1B) in colorectal cancer, carcinoembryonic antigen-related cell adhesion molecule 6 (CEACAM6) in lung cancer, crumbs cell polarity complex component 2 (CRB2) in ovarian cancer, and acid phosphatase 3 (ACP3) in prostate cancer [51]. IL-17A was found to be increased across the bacterial infections [51]; however, most IL-17 family members did not come up as noticeable proteins linked to the diseases, though IL-17A, IL-17C, IL-17D, IL-17F, IL-17RA, and IL-17RB were detected in the blood proteome. Therefore, we re-analyzed the blood proteomics dataset with a focus on the blood plasma levels of IL-17 family members among the 59 diseases in comparison to the healthy population.

2. Materials and Methods

Dataset sources

We thank the authors of the recent report who made the large-scale plasma proteomics dataset broadly accessible to the scientific community [51].

We retrieved their supplementary data S4 containing basic features of one healthy population and 59 disease populations, such as age and sex. We calculated the total sample size and abbreviated the disease names for making analyses and figures. The modified data S4 is presented as Table 1 herein, including 825 healthy people and 5227 patients of 59 diseases classified into cardiovascular, metabolic, cancer, psychiatric, autoimmune, infection, and pediatric classes. We retrieved their supplementary data S14 containing the mean, median, the first quartile (Q1), and the 3rd quartile (Q3) of the relative abundance of IL-17A, IL-17C, IL-17D, IL-17F, IL-17RA, and IL-17RB in the plasma proteins. As described by the original authors [51], the plasma samples were collected as a part of several studies both within Sweden and internationally to form the Human Disease Blood Atlas (HDBA) cohort, a pan-disease cohort including 59 diseases and 6074 samples, including approximately 2000 samples from patients with breast, ovarian, prostate, colorectal, and lung cancers from the U-CAN biobank. Next-generation targeted proteomics based on the proximity extension assay (PEA) was used for plasma protein quantification [51]. This method relies on antibodies conjugated to complementary DNA probes, polymerase chain reaction amplification, and readout using next-generation sequencing. Relative protein abundances were reported in normalized protein expression (NPX) units on a log2 scale and were referred to as protein concentrations throughout their study for simplicity. Data normalization was performed by the provider using their intensity normalization procedure before data delivery, which was suited for datasets with randomized sample plate layouts [51]. Due to the nature of the relative protein abundances, some protein concentrations were reported as negative values, which was likely caused by the intensity normalization procedure.

Methods of re-analyses

We retrieved the dataset of IL-17A, IL-17C, IL-17D, IL-17F, IL-17RA, and IL-17RB from the supplementary data S14 of the report [51], which includes mean, median, Q1, and Q3 of each plasma protein. Standard deviation (SD) was estimated using SD = interquartile range (Q3-Q1)/1.35. A one-tailed Student's t-test was used to test the hypothesis that the protein mean was greater or less in the disease samples than that of the healthy samples. P values were calculated using the R software package [R version 4.5.1 (2025-06-13), R Core Team (2025); R: A language and environment for statistical computing, R Foundation for Statistical Computing, Vienna, Austria. https://www.r-project.org/]. $P<0.05$ was considered statistically significant. The results are presented in Tables 2 to 8. To rank the plasma protein levels across the healthy and 59 disease populations, the mean values of the healthy population and 59 types of disease conditions are presented in waterfall plots (Figures 1 to 6).

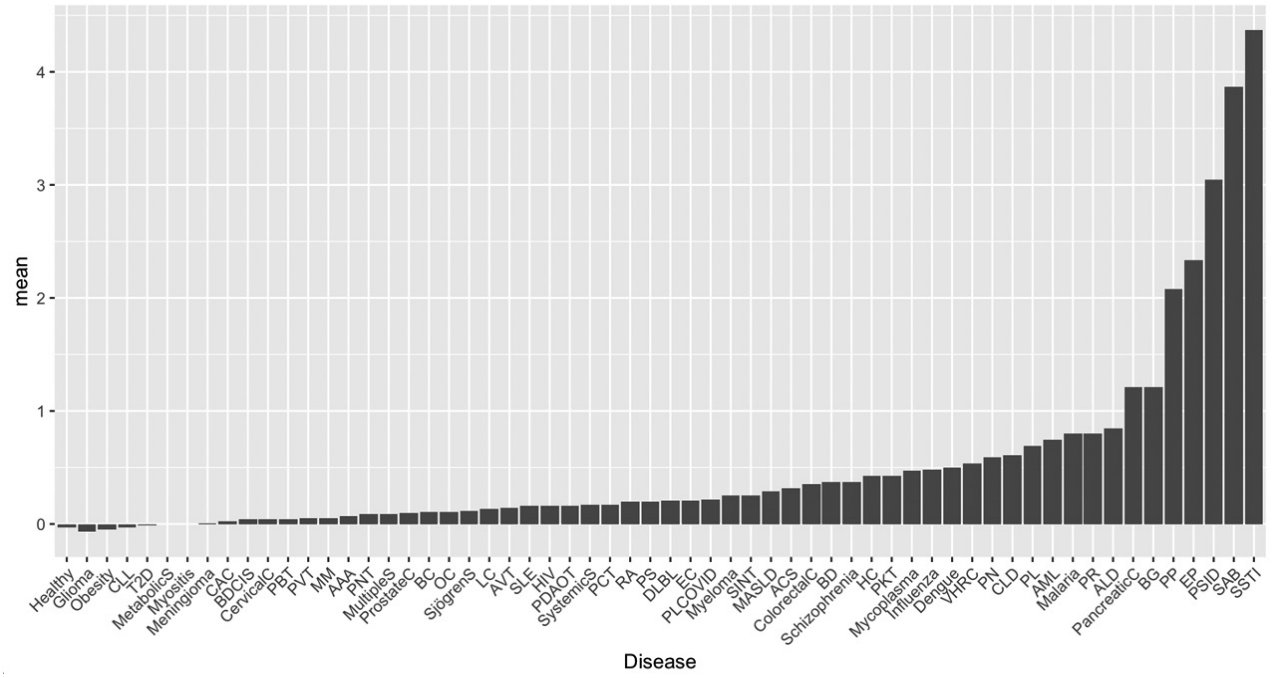

Figure 1. Ranking of plasma levels of IL-17A in healthy individuals and diseases. Abbreviations of disease names are presented in Table 1, including data from 825 healthy people and 5227 patients of 59 diseases. The data are adopted from Supplementary file S14 of Maria Bueno Alvez et al, Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678.

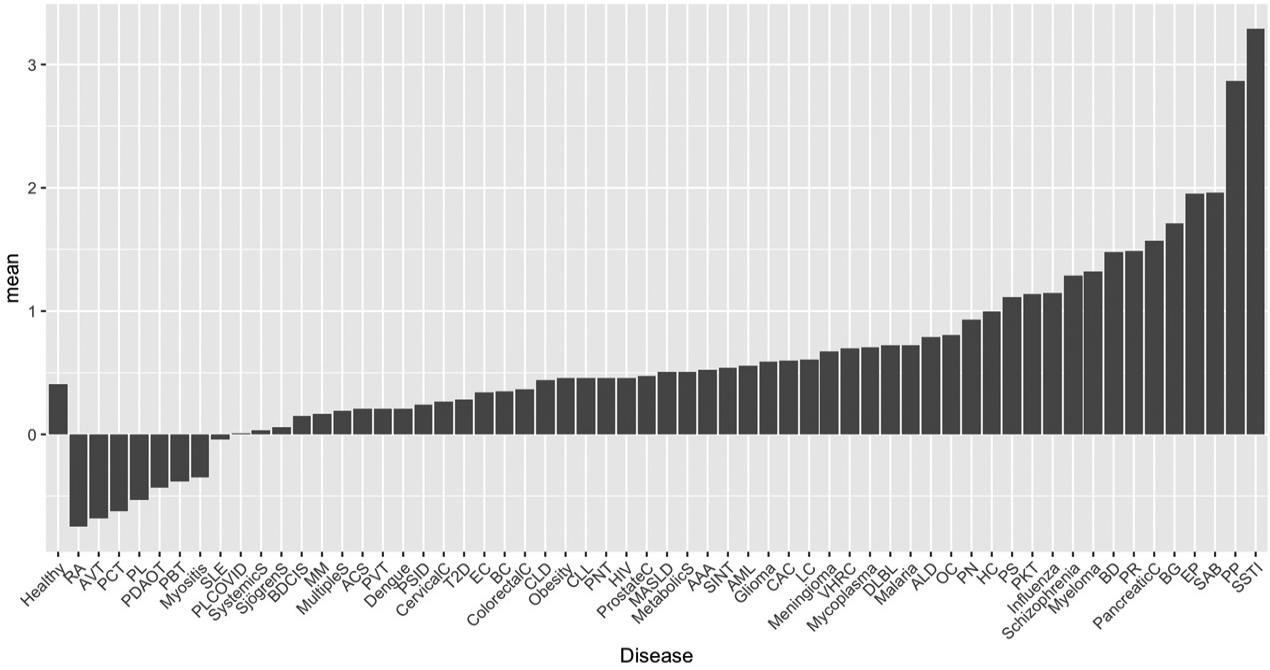

Figure 2. Ranking of plasma levels of IL-17C in healthy individuals and diseases. Abbreviations of disease names are presented in Table 1, including data from 825 healthy people and 5227 patients of 59 diseases. The data are adopted from Supplementary file S14 of Maria Bueno Alvez et al, Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678.

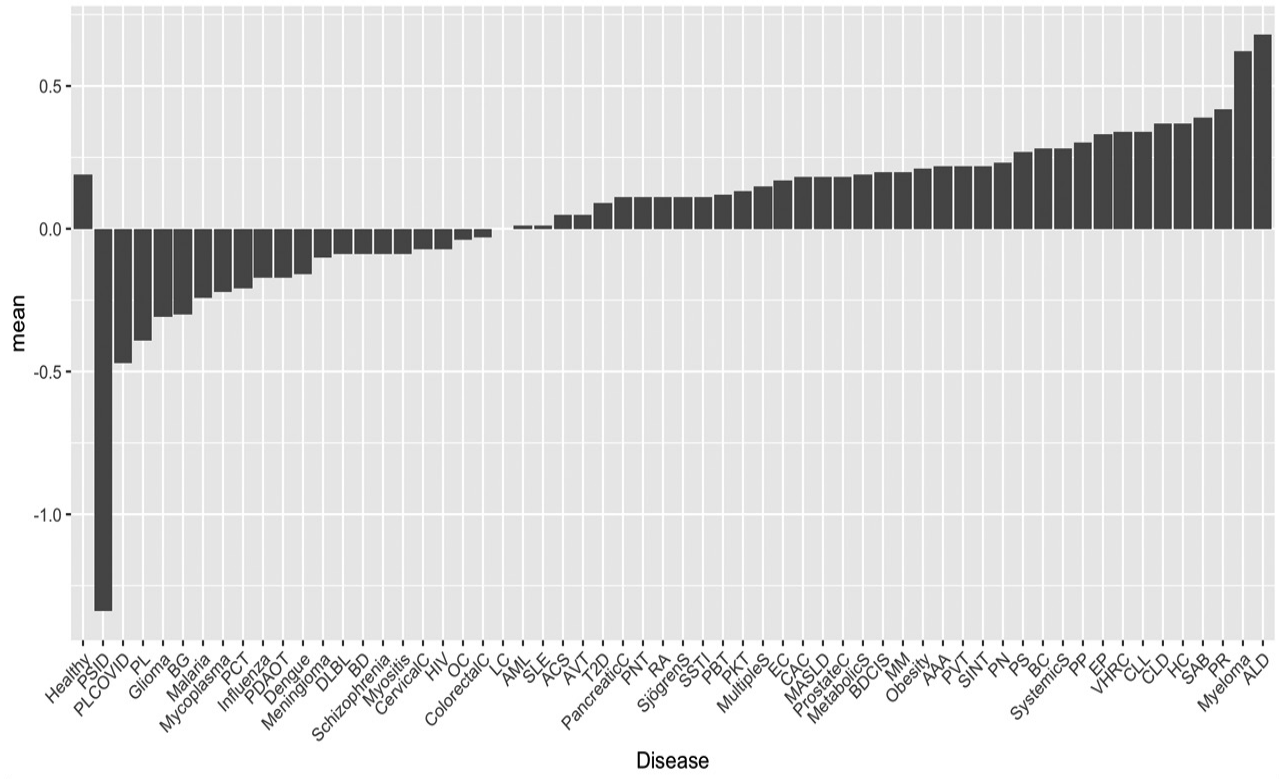

Figure 3. Ranking of plasma levels of IL-17D in healthy individuals and diseases. Abbreviations of disease names are presented in Table 1, including data from 825 healthy people and 5227 patients of 59 diseases. The data are adopted from Supplementary file S14 of Maria Bueno Alvez et al, Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678.

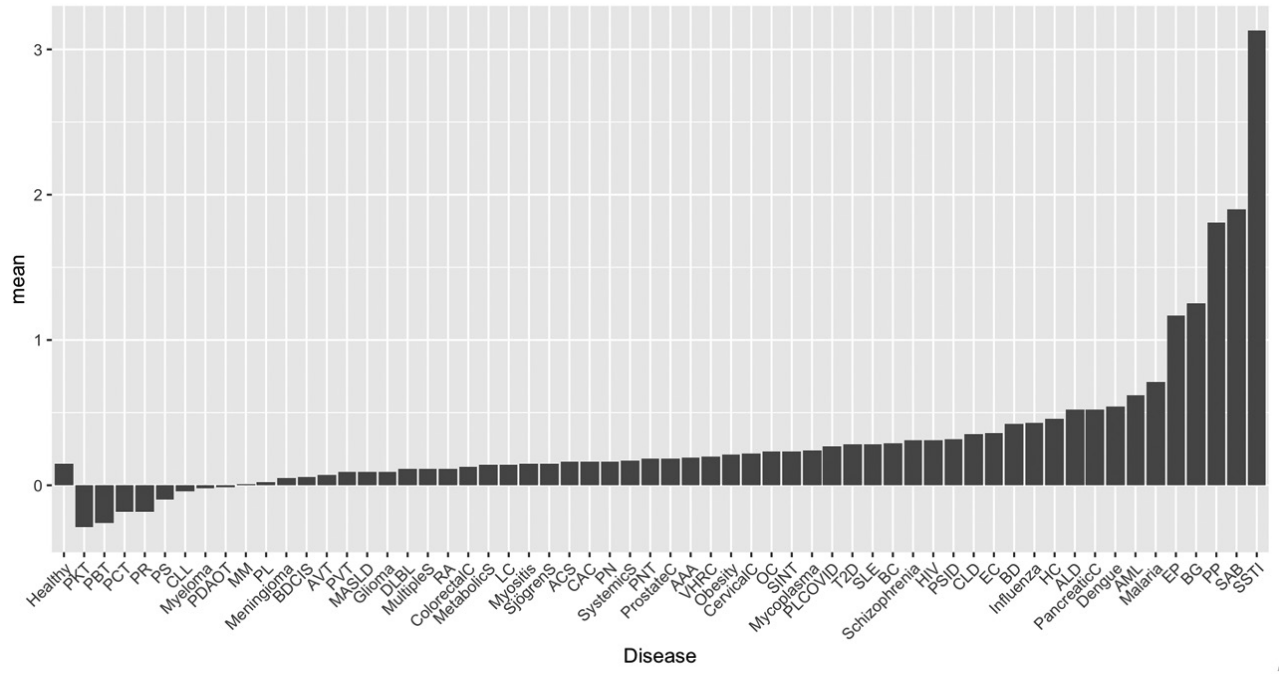

Figure 4. Ranking of plasma levels of IL-17F in healthy individuals and diseases. Abbreviations of disease names are presented in Table 1, including data from 825 healthy people and 5227 patients of 59 diseases. The data are adopted from Supplementary file S14 of Maria Bueno Alvez et al, Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678.

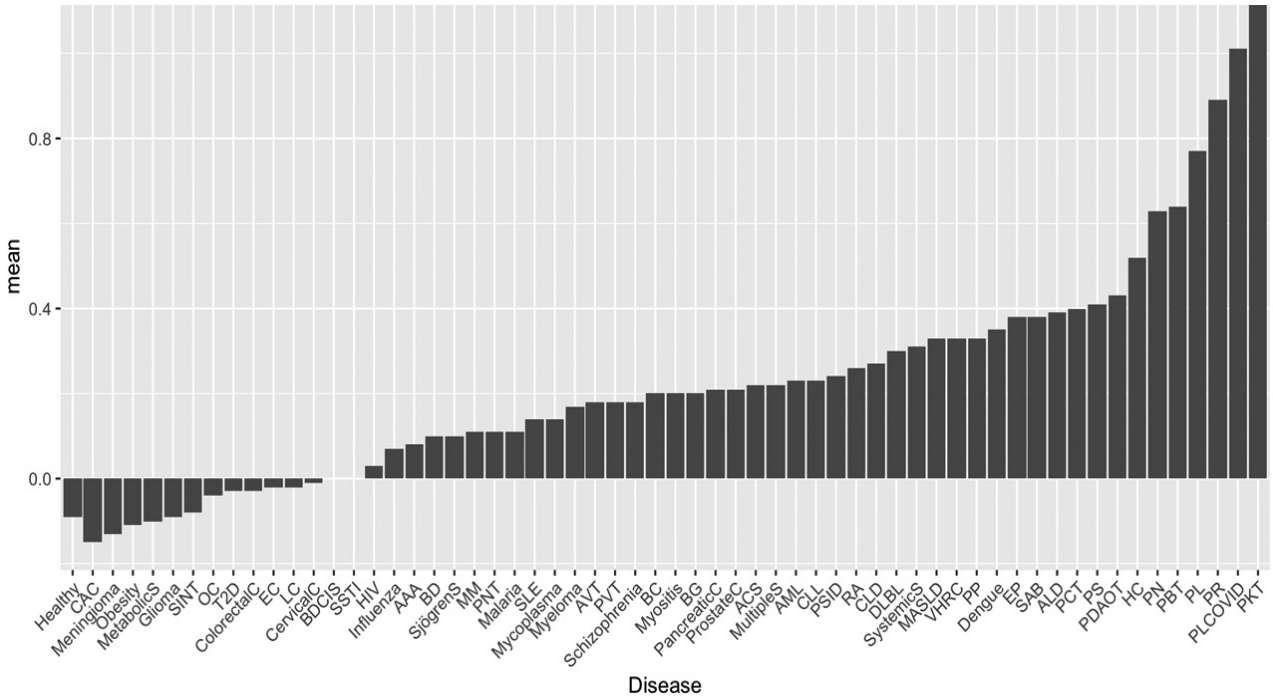

Figure 5. Ranking of plasma levels of IL-17RA in healthy individuals and diseases. Abbreviations of disease names are presented in Table 1, including data from 825 healthy people and 5227 patients of 59 diseases. The data are adopted from Supplementary file S14 of Maria Bueno Alvez et al, Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678.

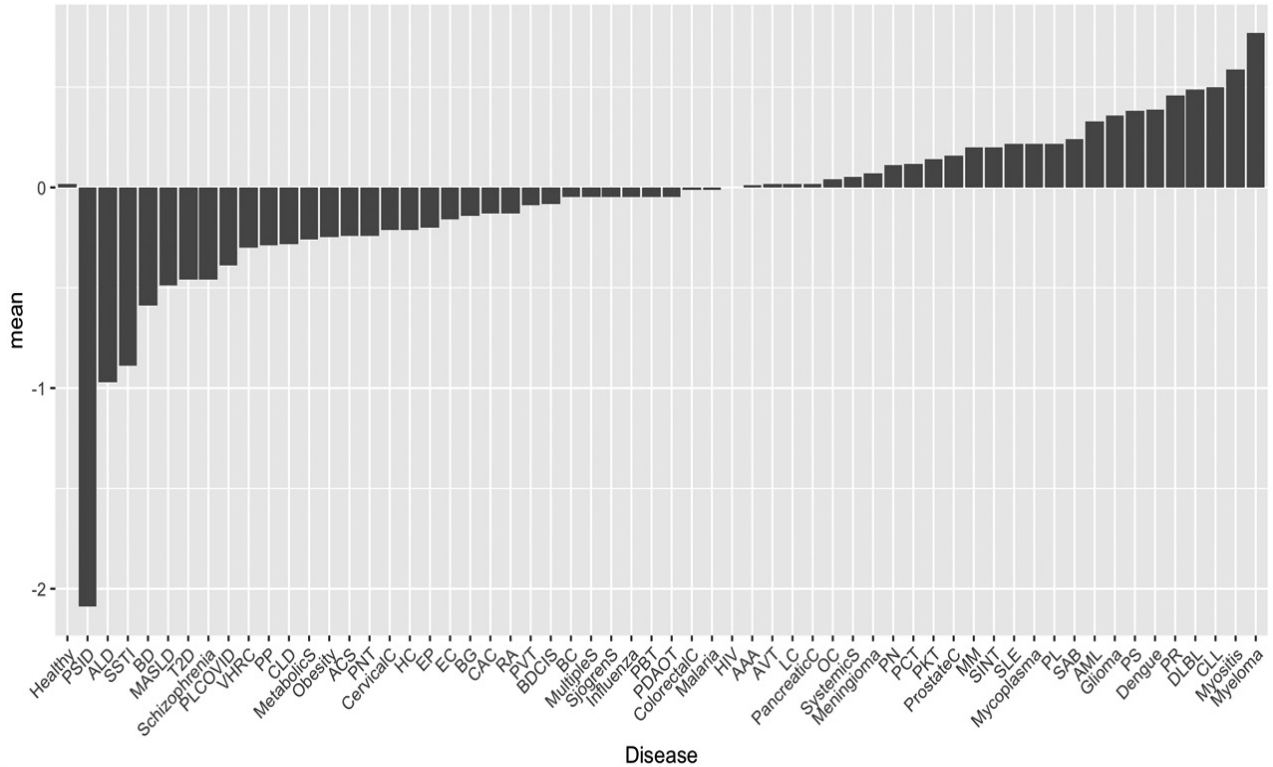

Figure 6. Ranking of plasma levels of IL-17RB in healthy individuals and diseases. Abbreviations of disease names are presented in Table 1, including data from 825 healthy people and 5227 patients of 59 diseases. The data are adopted from Supplementary file S14 of Maria Bueno Alvez et al, Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678.

3. Results

IL-17A and IL-17RA plasma levels are increased in cardiovascular diseases

As shown in Table 2, IL-17A and IL-17RA plasma levels were not detectable in healthy people. IL-17D, IL-17F, and IL-17RB were detected at low levels, while IL-17C was detected at a moderate level in healthy people. IL-17A and IL-17RA plasma levels were significantly increased in cardiovascular diseases, including abdominal aortic aneurysm (AAA), acute coronary syndrome (ACS), acute venous thromboembolism (AVT), coronary artery calcification (CAC), and previous venous thromboembolism (PVT), except that IL-17RA was significantly decreased in CAC. IL-17C significantly decreased in AVT and PVT but significantly increased in CAC. IL-17D was significantly decreased in ACS and AVT. IL-17RB was significantly decreased in CAC.

IL-17A and IL-17RA plasma levels are increased in some metabolic diseases

As shown in Table 3, IL-17A and IL-17RA plasma levels were significantly increased in some metabolic diseases, including alcohol-related liver disease (ALD), chronic liver disease (CLD), metabolic dysfunction-associated steatotic liver disease (MASLD), and viral hepatitis-related cirrhosis (VHRC). IL-17RA was also significantly increased in metabolic syndrome (MetabolicS). In ALD, IL-17C, IL-17D, and IL-17F levels were significantly increased. IL-17C was significantly increased in metabolic syndrome and VHRC. IL-17D was also significantly increased in CLD and VHRC. It was noted that IL-17RB significantly decreased in all metabolic diseases, including ALD, CLD, MASLD, metabolic syndrome, obesity, type 2 diabetes (T2D), and VHRC.

IL-17A and IL-17RA plasma levels are increased in many cancers

As shown in Table 4, IL-17A and IL-17RA plasma levels were significantly increased in many cancers, including acute myeloid leukemia (AML), breast cancer (BC), cervical cancer (CervicalC), colorectal cancer (ColorectalC), diffuse large B-cell lymphoma (DLBL), hepatocellular cancer (HC), lung cancer (LC), metastatic melanoma (MM), myeloma, pancreatic cancer (PancreaticC), pituitary neuroendocrine tumor (PNT), and prostate cancer (ProstateC). IL-17A was also significantly increased in endometrial cancer (EC), ovarian cancer (OC), and small intestine neuroendocrine tumor (SINT). IL-17RA was also significantly increased in glioma. IL-17C was significantly increased in DLBL, glioma, HC, LC, myeloma, OC, and pancreatic cancer, but was significantly decreased in breast ductal carcinoma in situ (BDCIS), meningioma, and MM. IL-17D was significantly increased in BC, CLL, HC, myeloma, but was significantly decreased in AML, cervical cancer, DLBL, glioma, LC, meningioma, and PNT. IL-17F was significantly increased in AML, BC, EC, HC, OC, and pancreatic cancer, but was significantly decreased in CLL, meningioma, MM, and myeloma. IL-17RB was significantly increased in AML, CLL, DLBL, glioma, MM, and prostate cancer, but it significantly decreased in cervical cancer, EC, HC, myeloma, and PNT.

IL-17A and IL-17RA plasma levels are increased in psychiatric diseases

As shown in Table 5, IL-17A and IL-17RA plasma levels significantly increased in bipolar disorder and schizophrenia. IL-17C and IL-17F were also significantly increased in both diseases. In contrast, IL-17D and IL-17RB were significantly decreased in both diseases.

IL-17A and IL-17RA plasma levels increased in autoimmune diseases

As shown in Table 6, IL-17A and IL-17RA plasma levels were significantly increased in autoimmune diseases, including multiple sclerosis (MultipleS), rheumatoid arthritis (RA), Sjögren's syndrome (SjögrenS), systemic lupus erythematosus (SLE), and systemic sclerosis (SystemicS). IL-17RA was also significantly increased in myositis. In contrast, IL-17C was significantly decreased in all autoimmune diseases, and IL-17D was significantly decreased in multiple sclerosis, myositis, RA, and SLE. IL-17F was significantly increased in SLE. IL-17RB was significantly increased in myositis and SLE, but was significantly decreased in multiple sclerosis and RA.

IL-17A and IL-17RA plasma levels increased in infectious diseases

As shown in Table 7, IL-17A and IL-17RA plasma levels were significantly increased in all infectious diseases, including bacterial gastroenteritis (BG), Dengue, E. coli pyelonephritis (EP), human immunodeficiency virus (HIV), influenza, malaria, mycoplasma, pneumococcal pneumonia (PP), and Staphylococcus aureus bacteremia (SAB). IL-17A was also

significantly increased in streptococcal soft tissue infection (SSTI). IL-17C was significantly increased in BG, EP, influenza, malaria, mycoplasma, PP, SAB, and SSTI. IL-17F was significantly increased in BG, Dengue, EP, HIV, influenza, malaria, PP, SAB, and SSTI. In contrast, IL-17D was significantly decreased in many infectious diseases, including BG, Dengue, HIV, influenza, malaria, and mycoplasma, while IL-17RB was significantly decreased in EP, PP, and SSTI.

IL-17A and IL-17RA plasma levels are increased in pediatric diseases

As shown in Table 8, IL-17A and IL-17RA plasma levels were significantly increased in many pediatric diseases, including pediatric CNS tumor (PCT), pediatric lung COVID (PLCOVID), pediatric lymphoma (PL), pediatric neuroblastoma (PN), pediatric retinoblastoma (PR), and pediatric systemic inflammatory disease (PSID). IL-17C was significantly increased in PCT and PR but was significantly decreased in pediatric bone tumor (PBT), pediatric diffuse astrocytic and oligodendroglia tumor (PDAOT), PLCOVID, and PL. IL-17F was significantly increased in PSID but was significantly decreased in PCT, PBT, pediatric kidney tumor (PKT), PR, and pediatric sarcoma (PS). IL-17RB was significantly increased in PR and PS but was significantly decreased in PLCOVID and PSID.

Plasma levels of IL-17 family members are high in most infections and some cancers.

As shown in Figure 1, the top ten highest levels of IL-17A were found in infection diseases (SSTI, SAB, PSID, EP, PP, BG, and malaria), two tumors (pancreatic cancer and pediatric retinoblastoma), and ALD. The top ten highest levels of IL-17C were found in infection diseases (SSTI, PP, SAB, EP, and BG), three tumors (pancreatic cancer, pediatric retinoblastoma, and myeloma), and two psychiatric diseases (bipolar disorder and schizophrenia) (Figure 2). The top ten highest levels of IL-17D were found in some tumors (myeloma, pediatric retinoblastoma, hepatocellular cancer, and chronic lymphocytic leukemia), liver diseases (alcohol-related liver disease, chronic liver disease, and viral hepatitis related cirrhosis), and infectious diseases (SAB, EP, and PP) (Figure 3). The top ten highest levels of IL-17F were found in infection diseases (SSTI, SAB, PP, BG, EP, malaria, and Dengue), two tumors (acute myeloid leukemia and pancreatic cancer), and alcohol-related liver disease (Figure 4). The top ten highest levels of IL-17RA were found in all pediatric tumors (pediatric kidney tumor, pediatric retinoblastoma, pediatric lymphoma, pediatric bone tumor, pediatric neuroblastoma, pediatric diffuse astrocytic and oligodendroglia tumor, pediatric sarcoma, and pediatric CNS tumor), hepatocellular cancer, and pediatric lung COVID (Figure 5). The top ten highest levels of IL-17RB were found in some tumors (myeloma, chronic lymphocytic leukemia, diffuse large B-cell lymphoma, pediatric retinoblastoma, pediatric sarcoma, glioma, and acute myeloid leukemia), myositis, Dengue, and Staphylococcus aureus bacteremia (Figure 6). Since the levels of IL-17A, IL-17F, IL-17RB, and IL-17RA were very low and almost undetectable in the healthy population, any diseases with reduced levels of them are unlikely to have any clinical relevance, as they would not be detectable (Figures 1, 4, 5, and 6). IL-17C levels were the highest among the IL-17 family in the healthy population, and their levels were remarkably decreased in rheumatoid arthritis, acute venous thromboembolism, pediatric CNS tumor, pediatric lymphoma, pediatric diffuse astrocytic and oligodendroglia tumor, pediatric bone tumor, and myositis (Figure 2). IL-17D levels were detectable in the healthy population, and its levels were remarkably decreased in pediatric systemic inflammatory disease, pediatric lung COVID, pediatric lymphoma, glioma, bacterial gastroenteritis, malaria, mycoplasma, pediatric CNS tumor, influenza, and pediatric diffuse astrocytic and oligodendroglia tumor (Figure 3).

4. Discussion

Blood plasma levels of IL-17A, IL-17F, and IL-17RA are usually very low and often undetectable in healthy people, as shown in Table 1. IL-17A and IL-17F are secreted by immune cells in the tissues where natural defense against pathogens is needed, such as in the intestines and lungs. They are quickly used by the local tissues with little entering the blood circulation. As proinflammatory cytokines, IL-17A and IL-17F are secreted by immune cells upon infection or any conditions causing inflammation. IL-17RA is a transmembrane protein. There is no prior report showing that IL-17RA is secreted to the blood. A speculative reason to have increased IL-17RA levels in the blood is that apoptotic cells and tissues may leak IL-17RA into the blood [51], or increased levels of IL-17RA may lead to the release of IL-17RA with extracellular vesicles of an average size of about

100 nm in diameter known as exosomes. Detection of IL-17RA in plasma by PEA does not distinguish between the intact, signaling-competent receptor and nonfunctional fragments or vesicle-associated proteins. Therefore, the biological activity of circulating IL-17RA cannot be inferred from detected values alone. Through re-analysis of the blood proteomics dataset, we found that IL-17A and IL-17RA plasma levels significantly increased in 55 of 59 diseases included in the study. The only four exceptions are obesity, type 2 diabetes, breast ductal carcinoma in situ, and meningioma. Previous studies using traditional assay methods have found that obese people had increased circulating levels of IL-17 [52] and patients with T2D had increased serum levels of IL-17 [53]. Suffice it to say, IL-17A and IL-17RA plasma levels are increased in almost all common diseases. As discussed in a recent review article [54], the IL-17 family, particularly IL-17A acting through IL-17RA, plays very important roles in human health. The underlying reason why IL-17A and IL-17RA levels were generally elevated in so many diseases is unknown. One speculation is that it is well-known that most diseases have an inflammatory component in pathogenesis, so IL-17, as a key inflammatory cytokine, might be upregulated during the onset and progression of diseases.

Unlike IL-17A and IL-17RA, other IL-17 family members (IL-17C, IL-17D, IL-17F, and IL-17RB) were found to have either increased or decreased plasma levels in the 59 diseases. In some diseases, IL-17C and IL-17D levels were increased together with IL-17A, such as ALD, VHRC, and HC. However, in other diseases, IL-17C and IL-17D levels were decreased despite increased IL-17A, such as AVT, cervical cancer, multiple sclerosis, SLE, pediatric lung COVID, and pediatric lymphoma. It is unknown whether IL-17C and IL-17D play any roles different from those of IL-17A. We speculate that they may play specific roles in each disease in a context-dependent manner. IL-17F was increased together with IL-17A in many diseases, including ALD, CLL, AML, BC, HC, OC, pancreatic cancer, BD, schizophrenia, SLE, all infectious diseases, PR, and PSID. However, IL-17F was decreased in the presence of increased IL-17A in some diseases, such as MM, PCT, and PR. These findings suggest that IL-17F mostly works together with IL-17A to activate IL-17RA signaling, as both IL-17A and IL-17F are secreted by the same type-17 immune cells. IL-17RB decreased in most diseases, including ACS, CAC, ALD, CLD, MASLD, metabolic syndrome, obesity, T2D, VHRC, cervical cancer, EC, HC, myeloma, PNT, BD, schizophrenia, multiple sclerosis, RA, EP, PP, SSTI, pediatric lung COVID, and PSID. There were a few diseases in which IL-17RB was increased, such as AML, glioma, MM, prostate cancer, myositis, SLE, PR, and PS. As most diseases have increased IL-17RA that heterodimerizes with IL-17RC to mediate IL-17A and/or IL-17F functions, the decreased IL-17RB, which also heterodimerizes with IL-17RA, may yield more IL-17RA to IL-17RC, thus enhancing IL-17A/F signaling. In cases where both IL-17RA and IL-17RB are increased, IL-17E signaling may be enhanced in addition to IL-17A/F signaling.

The plasma levels of IL-17A, IL-17C, IL-17D, and IL-17F were remarkably high in infectious diseases such as SSTI, SAB, EP, PP, BG, and malaria, suggesting that all of them are proinflammatory cytokines that are responsible for host defense against pathogens. IL-17A and IL-17C levels were also remarkably high in pancreatic cancer and pediatric retinoblastoma. Pancreatic cancer may initiate from the background of pancreatitis with increased levels of proinflammatory cytokines. Pediatric retinoblastoma involves mutational deactivation of both alleles of a retinoblastoma suppressor gene (RB1), which rarely involves inflammation; the roles of increased IL-17A and IL-17C are unknown. IL-17RA levels were remarkably high in all pediatric tumors, and IL-17RB levels were also high in pediatric retinoblastoma and pediatric sarcoma. It would be intriguing to investigate whether pediatric tumors share a common inflammatory pathogenesis involving IL-17RA and IL-17RB.

There are several limitations of this re-analysis study. First, the IL-17 family includes six cytokines and five receptors. For an unknown reason, only six members were included in the published dataset [51], though antibodies against other members are commercially available. Second, the PEA technology used by the original authors involved PCR and next-generation sequencing, which was high-throughput but without standard controls of IL-17 family members; the protein concentrations were relative abundance of proteins rather than the absolute concentrations. Many negative values of protein concentrations were included, which were included in our analyses, but their usefulness in clinical detection is limited. Third, the technical details of how data normalization was performed by the provider using their intensity normalization procedure were not described in the published report [51]. The information may be avail-

able at https://doi.org/10.17044/scilifelab.28577390.v1 [51], which requires some procedures to access it. Therefore, we only retrieved the values published in supplementary data S14 of the report [51] for our re-analyses. Finally, this re-analysis of one-timepoint data does not reveal a biological process and cannot provide any predictive values for clinical diagnosis; further studies are required to assess the roles of the IL-17 family in the associated diseases.

In summary, our re-analyses of the published blood proteomics dataset of one healthy and 59 disease populations found that IL-17A and IL-17RA plasma levels were increased in 55 diseases compared to healthy people. IL-17C, IL-17D, IL-17F, and IL-17RB levels were increased in some diseases but decreased in other diseases. While it was expected that IL-17A, IL-17C, IL-17D, and IL=17F levels were frequently increased in infectious diseases, it was surprising that IL-17RA and IL-17RB levels were remarkably increased in pediatric tumors. Future studies will investigate the roles of IL-17RA and IL-17RB in the pathogenesis of pediatric tumors.

Acknowledgements: We thank Maria Bueno Alvez and other co-authors of the article published in Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678, for making the data available to the public.

Author's disclosure: The authors disclose no conflicts of interest.

Funding resources: Dr. Dongxia Ge received a pilot grant from Tulane University School of Medicine.

5. References

1. Moseley TA, Haudenschild DR, Rose L, Reddi AH: Interleukin-17 family and IL-17 receptors. Cytokine Growth Factor Rev 2003, 14(2):155-174. doi:10.1016/s1359-6101(03)00002-9:
2. McGeachy MJ, Cua DJ, Gaffen SL: The IL-17 Family of Cytokines in Health and Disease. Immunity 2019, 50(4):892-906. doi:10.1016/j.immuni.2019.03.021: PMC6474359.
3. Su Y, Huang J, Zhao X, Lu H, Wang W, Yang XO, Shi Y, Wang X, Lai Y, Dong C: Interleukin-17 receptor D constitutes an alternative receptor for interleukin-17A important in psoriasis-like skin inflammation. Sci Immunol 2019, 4(36):eaau9657. doi:10.1126/sciimmunol.aau9657:
4. Huang J, Lee HY, Zhao X, Han J, Su Y, Sun Q, Shao J, Ge J, Zhao Y, Bai X et al: Interleukin-17D regulates group 3 innate lymphoid cell function through its receptor CD93. Immunity 2021, 54(4):673-686.e674. doi:10.1016/j.immuni.2021.03.018:
5. Goepfert A, Lehmann S, Blank J, Kolbinger F, Rondeau JM: Structural Analysis Reveals that the Cytokine IL-17F Forms a Homodimeric Complex with Receptor IL-17RC to Drive IL-17RA-Independent Signaling. Immunity 2020, 52(3):499-512.e495. doi:10.1016/j.immuni.2020.02.004:
6. McAleer JP, Kolls JK: Directing traffic: IL-17 and IL-22 coordinate pulmonary immune defense. Immunol Rev 2014, 260(1):129-144. doi:10.1111/imr.12183:
7. Liu C, Qian W, Qian Y, Giltiay NV, Lu Y, Swaidani S, Misra S, Deng L, Chen ZJ, Li X: Act1, a U-box E3 ubiquitin ligase for IL-17 signaling. Sci Signal 2009, 2(92):ra63. doi:2/92/ra63 [pii]10.1126/scisignal.2000382:
8. Onishi RM, Gaffen SL: Interleukin-17 and its target genes: mechanisms of interleukin-17 function in disease. Immunology 2010, 129(3):311-321. doi:IMM3240 [pii]10.1111/j.1365-2567.2009.03240.x:
9. Shen F, Ruddy MJ, Plamondon P, Gaffen SL: Cytokines link osteoblasts and inflammation: microarray analysis of interleukin-17- and TNF-alpha-induced genes in bone cells. J Leukoc Biol 2005, 77(3):388-399. doi:jlb.0904490 [pii]10.1189/jlb.0904490:
10. Li Q, Liu L, Zhang Q, Liu S, Ge D, You Z: Interleukin-17 Indirectly Promotes M2 Macrophage Differentiation through Stimulation of COX-2/PGE2 Pathway in the Cancer Cells. Cancer Res Treat 2014, 46(3):297-306. doi:10.4143/crt.2014.46.3.297crt-46-3-297 [pii]:
11. You Z, Ge D, Liu S, Zhang Q, Borowsky AD, Melamed J: Interleukin-17 induces expression of chemokines and cytokines in prostatic epithelial cells but does not stimulate cell growth in vitro. Int J Med Biol Front 2012, 18(8):629-644.
12. Zhang Q, Liu S, Ge D, Xue Y, Xiong Z, Abdel-Mageed AB, Myers L, Hill SM, Rowan BG, Sartor O et al: Interleukin-17 promotes formation and growth of prostate adenocarcinoma in mouse models. Cancer Res 2012, 72(10):2589-2599. doi:0008-5472.CAN-11-3795 [pii]10.1158/0008-5472.CAN-11-3795:

13. Zhang Q, Liu S, Parajuli KR, Zhang W, Zhang K, Mo Z, Liu J, Chen Z, Yang S, Wang AR et al: Interleukin-17 promotes prostate cancer via MMP7-induced epithelial-to-mesenchymal transition. Oncogene 2017, 36(5):687-699. doi:onc2016240 [pii]10.1038/onc.2016.240:
14. Li X, Bechara R, Zhao J, McGeachy MJ, Gaffen SL: IL-17 receptor-based signaling and implications for disease. Nat Immunol 2019, 20(12):1594-1602. doi:10.1038/s41590-019-0514-y:
15. Wang X, Yang L, Huang F, Zhang Q, Liu S, Ma L, You Z: Inflammatory cytokines IL-17 and TNF-alpha up-regulate PD-L1 expression in human prostate and colon cancer cells. Immunol Lett 2017, 184:7-14. doi:10.1016/j.imlet.2017.02.006: PMC5362328.
16. Ye P, Garvey PB, Zhang P, Nelson S, Bagby G, Summer WR, Schwarzenberger P, Shellito JE, Kolls JK: Interleukin-17 and lung host defense against Klebsiella pneumoniae infection. Am J Respir Cell Mol Biol 2001, 25(3):335-340. doi:10.1165/ajrcmb.25.3.4424:
17. Puel A, Cypowyj S, Bustamante J, Wright JF, Liu L, Lim HK, Migaud M, Israel L, Chrabieh M, Audry M et al: Chronic mucocutaneous candidiasis in humans with inborn errors of interleukin-17 immunity. Science 2011, 332(6025):65-68. doi:-science.1200439 [pii]10.1126/science.1200439:
18. Ling Y, Cypowyj S, Aytekin C, Galicchio M, Camcioglu Y, Nepesov S, Ikinciogullari A, Dogu F, Belkadi A, Levy R et al: Inherited IL-17RC deficiency in patients with chronic mucocutaneous candidiasis. J Exp Med 2015, 212(5):619-631. doi:10.1084/jem.20141065: PMC4419340.
19. Boisson B, Wang C, Pedergnana V, Wu L, Cypowyj S, Rybojad M, Belkadi A, Picard C, Abel L, Fieschi C et al: An ACT1 mutation selectively abolishes interleukin-17 responses in humans with chronic mucocutaneous candidiasis. Immunity 2013, 39(4):676-686. doi:10.1016/j.immuni.2013.09.002: PMC3873857.
20. Lowes MA, Kikuchi T, Fuentes-Duculan J, Cardinale I, Zaba LC, Haider AS, Bowman EP, Krueger JG: Psoriasis vulgaris lesions contain discrete populations of Th1 and Th17 T cells. J Invest Dermatol 2008, 128(5):1207-1211. doi:10.1038/sj.jid.5701213:
21. Chabaud M, Page G, Miossec P: Enhancing effect of IL-1, IL-17, and TNF-alpha on macrophage inflammatory protein-3alpha production in rheumatoid arthritis: regulation by soluble receptors and Th2 cytokines. J Immunol 2001, 167(10):6015-6020.
22. Lock C, Hermans G, Pedotti R, Brendolan A, Schadt E, Garren H, Langer-Gould A, Strober S, Cannella B, Allard J et al: Gene-microarray analysis of multiple sclerosis lesions yields new targets validated in autoimmune encephalomyelitis. Nat Med 2002, 8(5):500-508. doi:10.1038/nm0502-500:
23. Park H, Li Z, Yang XO, Chang SH, Nurieva R, Wang YH, Wang Y, Hood L, Zhu Z, Tian Q et al: A distinct lineage of CD4 T cells regulates tissue inflammation by producing interleukin 17. Nat Immunol 2005, 6(11):1133-1141. doi:10.1038/ni1261: PMC1618871.
24. Langrish CL, Chen Y, Blumenschein WM, Mattson J, Basham B, Sedgwick JD, McClanahan T, Kastelein RA, Cua DJ: IL-23 drives a pathogenic T cell population that induces autoimmune inflammation. J Exp Med 2005, 201(2):233-240. doi:jem.20041257 [pii]10.1084/jem.20041257:
25. Zhang Q, Liu S, Xiong Z, Wang AR, Myers L, Melamed J, Tang WW, You Z: Interleukin-17 promotes development of castration-resistant prostate cancer potentially through creating an immunotolerant and pro-angiogenic tumor microenvironment. Prostate 2014, 74(8):869-879. doi:10.1002/pros.22805:
26. Wu S, Rhee KJ, Albesiano E, Rabizadeh S, Wu X, Yen HR, Huso DL, Brancati FL, Wick E, McAllister F et al: A human colonic commensal promotes colon tumorigenesis via activation of T helper type 17 T cell responses. Nat Med 2009, 15(9):1016-1022. doi:nm.2015 [pii]10.1038/nm.2015:
27. Chae WJ, Bothwell AL: IL-17F deficiency inhibits small intestinal tumorigenesis in ApcMin/+ mice. Biochem Biophys Res Commun 2011, 414(1):31-36. doi:S0006-291X(11)01587-7 [pii]10.1016/j.bbrc.2011.09.016:
28. Chae WJ, Gibson TF, Zelterman D, Hao L, Henegariu O, Bothwell AL: Ablation of IL-17A abrogates progression of spontaneous intestinal tumorigenesis. Proc Natl Acad Sci U S A 2010, 107(12):5540-5544. doi:0912675107 [pii]10.1073/pnas.0912675107:
29. Hyun YS, Han DS, Lee AR, Eun CS, Youn JH, Kim HY: Role of IL-17A in the development of colitis-associated cancer. Carcinogenesis 2012, 33(4):931-936. doi:bgs106 [pii]10.1093/carcin/bgs106:

30. Xiao M, Wang C, Zhang J, Li Z, Zhao X, Qin Z: IFNgamma promotes papilloma development by up-regulating Th17-associated inflammation. Cancer Res 2009, 69(5):2010-2017. doi:0008-5472.CAN-08-3479 [pii]10.1158/0008-5472.CAN-08-3479:
31. Wang L, Yi T, Zhang W, Pardoll DM, Yu H: IL-17 enhances tumor development in carcinogen-induced skin cancer. Cancer Res 2010, 70(24):10112-10120. doi:70/24/10112 [pii]10.1158/0008-5472.CAN-10-0775:
32. Novitskiy SV, Pickup MW, Gorska AE, Owens P, Chytil A, Aakre M, Wu H, Shyr Y, Moses HL: TGF-beta Receptor II Loss Promotes Mammary Carcinoma Progression by Th17 Dependent Mechanisms. Cancer Discov 2011, 1(5):430-441. doi:10.1158/2159-8290.CD-11-0100:
33. Chang SH, Mirabolfathinejad SG, Katta H, Cumpian AM, Gong L, Caetano MS, Moghaddam SJ, Dong C: T helper 17 cells play a critical pathogenic role in lung cancer. Proc Natl Acad Sci U S A 2014, 111(15):5664-5669. doi:1319051111 [pii]10.1073/pnas.1319051111:
34. Xu B, Guenther JF, Pociask DA, Wang Y, Kolls JK, You Z, Chandrasekar B, Shan B, Sullivan DE, Morris GF: Promotion of lung tumor growth by interleukin-17. Am J Physiol Lung Cell Mol Physiol 2014, 307(6):L497-508. doi:ajplung.00125.2014 [pii]10.1152/ajplung.00125.2014:
35. McAllister F, Bailey JM, Alsina J, Nirschl CJ, Sharma R, Fan H, Rattigan Y, Roeser JC, Lankapalli RH, Zhang H et al: Oncogenic Kras activates a hematopoietic-to-epithelial IL-17 signaling axis in preinvasive pancreatic neoplasia. Cancer Cell 2014, 25(5):621-637. doi:S1535-6108(14)00122-6 [pii]10.1016/j.ccr.2014.03.014:
36. Villey I, de Chasseval R, de Villartay JP: RORgammaT, a thymus-specific isoform of the orphan nuclear receptor RORgamma / TOR, is up-regulated by signaling through the pre-T cell receptor and binds to the TEA promoter. Eur J Immunol 1999, 29(12):4072-4080. doi:10.1002/(SICI)1521-4141(199912)29:12<4072::AID-IMMU4072>3.0.CO;2-E [pii]:
37. Ciofani M, Madar A, Galan C, Sellars M, Mace K, Pauli F, Agarwal A, Huang W, Parkurst CN, Muratet M et al: A validated regulatory network for Th17 cell specification. Cell 2012, 151(2):289-303. doi:S0092-8674(12)01123-3 [pii]10.1016/j.cell.2012.09.016:
38. Chen RY, Fan YM, Zhang Q, Liu S, Li Q, Ke GL, Li C, You Z: Estradiol inhibits Th17 cell differentiation through inhibition of RORgammaT transcription by recruiting the ERalpha/REA complex to estrogen response elements of the RORgammaT promoter. J Immunol 2015, 194(8):4019-4028. doi:jimmunol.1400806 [pii]10.4049/jimmunol.1400806:
39. Qian Y, Liu C, Hartupee J, Altuntas CZ, Gulen MF, Jane-Wit D, Xiao J, Lu Y, Giltiay N, Liu J et al: The adaptor Act1 is required for interleukin 17-dependent signaling associated with autoimmune and inflammatory disease. Nat Immunol 2007, 8(3):247-256. doi:ni1439 [pii]10.1038/ni1439:
40. Leonardi A, Chariot A, Claudio E, Cunningham K, Siebenlist U: CIKS, a connection to Ikappa B kinase and stress-activated protein kinase. Proc Natl Acad Sci U S A 2000, 97(19):10494-10499. doi:10.1073/pnas.190245697190245697 [pii]:
41. Amatya N, Garg AV, Gaffen SL: IL-17 Signaling: The Yin and the Yang. Trends Immunol 2017, 38(5):310-322. doi:10.1016/j.it.2017.01.006: PMC5411326.
42. Luo Q, Liu Y, Shi K, Shen X, Yang Y, Liang X, Lu L, Qiao W, Chen A, Hong D et al: An autonomous activation of interleukin-17 receptor signaling sustains inflammation and promotes disease progression. Immunity 2023, 56(9):2006-2020 e2006. doi:10.1016/j.immuni.2023.06.012:
43. Shen F, Li N, Gade P, Kalvakolanu DV, Weibley T, Doble B, Woodgett JR, Wood TD, Gaffen SL: IL-17 receptor signaling inhibits C/EBPbeta by sequential phosphorylation of the regulatory 2 domain. Sci Signal 2009, 2(59):ra8. doi:2/59/ra8 [pii]10.1126/scisignal.2000066:
44. Liu S, Zhang Q, Chen C, Ge D, Qu Y, Chen R, Fan YM, Li N, Tang WW, Zhang W et al: Hyperinsulinemia enhances interleukin-17-induced inflammation to promote prostate cancer development in obese mice through inhibiting glycogen synthase kinase 3-mediated phosphorylation and degradation of interleukin-17 receptor. Oncotarget 2016, 7(12):13651-13666. doi:7296 [pii]10.18632/oncotarget.7296:
45. Jin B, Moududee SA, Ge D, Zhou P, Wang AR, Liu YZ, You Z: SCF(FBXW11) Complex Targets Interleukin-17 Receptor A for Ubiquitin-Proteasome-Mediated Degradation. Biomedicines 2024, 12(4):755. doi:10.3390/biomedicines12040755:

46. Chen C, Zhang Q, Liu S, Lambrechts M, Qu Y, You Z: AZD5363 inhibits inflammatory synergy between interleukin-17 and insulin/insulin-like growth factor 1. Front Oncol 2014, 4:343. doi:10.3389/fonc.2014.00343:
47. Ge D, Dauchy RT, Liu S, Zhang Q, Mao L, Dauchy EM, Blask DE, Hill SM, Rowan BG, Brainard GC et al: Insulin and IGF1 enhance IL-17-induced chemokine expression through a GSK3B-dependent mechanism: a new target for melatonin's anti-inflammatory action. J Pineal Res 2013, 55(4):377-387. doi:10.1111/jpi.12084:
48. Wong CK, Ho CY, Ko FW, Chan CH, Ho AS, Hui DS, Lam CW: Proinflammatory cytokines (IL-17, IL-6, IL-18 and IL-12) and Th cytokines (IFN-gamma, IL-4, IL-10 and IL-13) in patients with allergic asthma. Clin Exp Immunol 2001, 125(2):177-183. doi:cei1602 [pii]:
49. Molet S, Hamid Q, Davoine F, Nutku E, Taha R, Page N, Olivenstein R, Elias J, Chakir J: IL-17 is increased in asthmatic airways and induces human bronchial fibroblasts to produce cytokines. J Allergy Clin Immunol 2001, 108(3):430-438. doi:S0091-6749(01)20382-0 [pii]10.1067/mai.2001.117929:
50. Ziolkowska M, Koc A, Luszczykiewicz G, Ksiezopolska-Pietrzak K, Klimczak E, Chwalinska-Sadowska H, Maslinski W: High levels of IL-17 in rheumatoid arthritis patients: IL-15 triggers in vitro IL-17 production via cyclosporin A-sensitive mechanism. J Immunol 2000, 164(5):2832-2838. doi:ji_v164n5p2832 [pii]:
51. Alvez MB, Bergstrom S, Kenrick J, Johansson E, Aberg M, Akyildiz M, Altay O, Skold H, Antonopoulos K, Apostolakis E et al: A human pan-disease blood atlas of the circulating proteome. Science 2025, 390(6779):eadx2678. doi:10.1126/science.adx2678:
52. Sumarac-Dumanovic M, Stevanovic D, Ljubic A, Jorga J, Simic M, Stamenkovic-Pejkovic D, Starcevic V, Trajkovic V, Micic D: Increased activity of interleukin-23/interleukin-17 proinflammatory axis in obese women. Int J Obes (Lond) 2009, 33(1):151-156. doi:ijo2008216[pii]10.1038/ijo.2008.216:
53. Fatima N, Faisal SM, Zubair S, Siddiqui SS, Moin S, Owais M: Emerging role of Interleukins IL-23/IL-17 axis and biochemical markers in the pathogenesis of Type 2 Diabetes: association with age and gender in human subjects. Int J Biol Macromol 2017, 105(Pt 1):1279-1288. doi:S0141-8130(17)32518-7 [pii]10.1016/j.ijbiomac.2017.07.155:
54. Deng G, Guo M, Fan J, Wang W, Jiang ML, Zhang CJ: Interleukin-17 family in health and immune diseases: From origin to clinical implications. Neural Regen Res 2026, 21(5):1809-1833. doi:10.4103/NRR.NRR-D-25-00026: PMC12694644.

Table 1. Basic features of human blood protein samples.

Class	Disease (abbreviation)	Age (range)	Males (n)	Females (n)	Total samples (n)
Healthy	Healthy (Healthy)	56.98 (50 - 65)	343	482	825
Cardiovascular	Coronary artery calcification (CAC)	59.67 (50 - 65)	210	65	275
	Abdominal aortic aneurysm (AAA)	64.72 (64 - 67)	100	0	100
	Previous venous thromboembolism (PVT)	55.34 (25 - 70)	69	29	98
	Acute coronary syndrome (ACS)	62.67 (46 - 74)	32	22	54
	Acute venous thromboembolism (AVT)	56.65 (19 - 89)	26	22	48
Metabolic	Type 2 diabetes (T2D)	57.83 (50 - 65)	43	34	77
	Metabolic syndrome (MetabolicS)	57.89 (50 - 65)	183	169	352
	Obesity (Obesity)	56.92 (50 - 65)	83	156	239
	Viral hepatitis-related cirrhosis (VHRC)	51 (18 - 80)	51	26	77
	Alcohol-related liver disease (ALD)	58.2 (42 - 66)	13	2	15
	Chronic liver disease (CLD)	47.51 (17 - 68)	18	21	39
	Metabolic dysfunction-associated steatotic liver disease (MASLD)	51.67 (13 - 79)	67	39	106
Cancer	Metastatic melanoma (MM)	64.68 (24 - 86)	66	38	104
	Lung cancer (LC)	67.24 (46 - 76)	117	160	277
	Ovarian cancer (OC)	61.83 (40 - 80)	0	157	157
	Glioma (Glioma)	59.04 (30 - 81)	87	72	159
	Cervical cancer (CervicalC)	48.74 (35 - 74)	0	110	110
	Acute myeloid leukemia (AML)	64.17 (35 - 83)	29	23	52
	Colorectal cancer (ColorectalC)	65.73 (45 - 75)	133	108	241
	Pituitary neuroendocrine tumor (PNT)	55.55 (17 - 85)	32	17	49
	Prostate cancer (ProstateC)	65.54 (45 - 75)	170	0	170
	Breast cancer (BC)	61.32 (45 - 75)	0	164	164
	Small intestine neuroendocrine tumor (SINT)	62.17 (45 - 74)	34	20	54
	Myeloma (Myeloma)	65.71 (46 - 75)	26	15	41
	Diffuse large B-cell lymphoma (DLBL)	61.2 (46 - 73)	31	24	55
	Chronic lymphocytic leukemia (CLL)	70.04 (50 - 85)	28	22	50
	Meningioma (Meningioma)	62.53 (41 - 75)	22	29	51
	Breast ductal carcinoma in situ (BDCIS)	62.96 (46 - 74)	0	49	49
	Endometrial cancer (EC)	65.71 (47 - 75)	0	107	107
	Hepatocellular cancer (HC)	59.25 (20 - 80)	67	13	80
	Pancreatic cancer (PancreaticC)	65.99 (27 - 85)	39	34	73
Psychiatric	Schizophrenia (Schizophrenia)	39.38 (19 - 66)	75	25	100
	Bipolar disorder (BD)	38.12 (18 - 66)	18	32	50
Autoimmune	Multiple sclerosis (MultipleS)	41.14 (18 - 81)	100	134	234
	Sjögren's syndrome (SjögrenS)	53.21 (20 - 82)	8	91	99
	Rheumatoid arthritis (RA)	61.21 (29 - 91)	24	60	84
	Systemic lupus erythematosus (SLE)	37 (17 - 62)	17	82	99
	Systemic sclerosis (SystemicS)	55.63 (21 - 80)	14	86	100
	Myositis (Myositis)	57.02 (19 - 83)	80	130	210

Infection	Human immunodeficiency virus (HIV)	41.1 (22 - 72)	54	33	87
	Influenza (Influenza)	50.86 (18 - 98)	55	77	132
	E.coli pyelonephritis (EP)	62 (21 - 91)	13	40	53
	Pneumococcal pneumonia (PP)	65.61 (27 - 91)	34	17	51
	Staphylococcus aureus bacteremia (SAB)	63.71 (18 - 90)	21	0	21
	Streptococcal soft tissue infection (SSTI)	57.74 (28 - 90)	37	40	77
	Malaria (Malaria)	39.69 (20 - 62)	58	20	78
	Mycoplasma (Mycoplasma)	43.42 (18 - 72)	16	15	31
	Bacterial gastroenteritis (BG)	37.22 (22 - 61)	20	12	32
	Dengue (Dengue)	38.74 (22 - 66)	11	8	19
Pediatric	Pediatric central nervous system (CNS) tumor (PCT)	7 (1 - 15)	10	5	15
	Pediatric bone tumor (PBT)	11.55 (1 - 17)	6	5	11
	Pediatric retinoblastoma (PR)	0.14 (0 - 1)	4	3	7
	Pediatric lymphoma (PL)	13.6 (8 - 17)	4	6	10
	Pediatric neuroblastoma (PN)	2.54 (0 - 7)	5	8	13
	Pediatric sarcoma (PS)	2.57 (0 - 7)	3	4	7
	Pediatric kidney tumor (PKT)	3.62 (0 - 10)	5	3	8
	Pediatric diffuse astrocytic and oligodendroglial tumor (PDAOT)	8.81 (1 - 16)	12	9	21
	Pediatric long coronavirus disease 2019 (PLCOVID)	1.94 (0 - 5)	3	14	17
	Pediatric systemic inflammatory disease (PSID)	4.03 (0 - 17)	25	13	38

Note: The data are adopted from Supplementary file S4 of Maria Bueno Alvez et al, Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678.

Table 2. Plasma IL-17 family members and cardiovascular diseases.

Healthy (N=825)						Abdominal aortic aneurysm (AAA, N=100)				
Protein	mean	median	Q1	Q3		mean	median	Q1	Q3	*p* value
IL17A	-0.03	-0.09	-0.33	0.18		0.07	0.01	-0.26	0.3	0.008
IL17C	0.41	0.31	-0.09	0.75		0.52	0.41	0.04	1	0.061
IL17D	0.19	0.15	-0.03	0.37		0.22	0.21	0.02	0.41	0.150
IL17F	0.15	0	-0.33	0.4		0.19	-0.04	-0.4	0.43	0.258
IL17RA	-0.09	-0.04	-0.42	0.28		0.08	0.19	-0.32	0.49	0.002
IL17RB	0.02	-0.01	-0.35	0.36		0.01	0.01	-0.42	0.41	0.435
Acute coronary syndrome (ACS, N=54)						Acute venous thromboembolism (AVT, N=48)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.32	0.22	-0.23	0.64	3.29006E-05	0.14	0.05	-0.14	0.28	7.66172E-05
IL17C	0.21	-0.07	-0.58	0.63	0.051	-0.68	-0.79	-1.19	-0.18	2.93896E-24
IL17D	0.05	0.07	-0.2	0.24	0.0008	0.05	0.07	-0.32	0.32	0.020
IL17F	0.16	0.03	-0.37	0.65	0.461	0.07	0.06	-0.38	0.3	0.136
IL17RA	0.22	0.34	-0.11	0.59	5.58125E-06	0.18	0.24	-0.15	0.55	0.0002
IL17RB	-0.24	-0.31	-0.68	0.34	0.006	0.02	-0.01	-0.5	0.43	0.500
Coronary artery calcification (CAC, N=275)						Previous venous thromboembolism (PVT, N=98)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.02	-0.05	-0.28	0.3	0.027	0.05	-0.03	-0.26	0.27	0.022
IL17C	0.6	0.5	0.01	0.95	3.01869E-06	0.21	0.05	-0.25	0.55	0.0004
IL17D	0.18	0.15	-0.03	0.33	0.267	0.22	0.24	-0.06	0.48	0.229
IL17F	0.16	-0.03	-0.3	0.37	0.369	0.09	-0.1	-0.4	0.31	0.129
IL17RA	-0.15	-0.06	-0.52	0.22	0.035	0.18	0.23	-0.13	0.53	2.28573E-08
IL17RB	-0.13	-0.16	-0.5	0.25	3.77711E-06	-0.09	0.03	-0.62	0.36	0.067

Note: The data are adopted from Supplementary file S14 of Maria Bueno Alvez et al, Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678. P value is for the comparison between disease and healthy groups. P values in red indicate significantly increased levels; p values in green indicate significantly decreased levels; and p values in white indicate no significant differences.

Table 3. Plasma IL-17 family members and metabolic diseases.

Healthy (N=825)						Alcohol-related liver disease (ALD, N=15)				
Protein	mean	median	Q1	Q3		mean	median	Q1	Q3	*p* value
IL17A	-0.03	-0.09	-0.33	0.18		0.85	0.63	0.53	0.86	1.74154E-44
IL17C	0.41	0.31	-0.09	0.75		0.79	0.58	0.34	1.22	0.012
IL17D	0.19	0.15	-0.03	0.37		0.68	0.62	0.4	0.82	5.30512E-10
IL17F	0.15	0	-0.33	0.4		0.52	0.28	0.03	0.81	0.007
IL17RA	-0.09	-0.04	-0.42	0.28		0.39	0.63	0.08	0.76	0.0001
IL17RB	0.02	-0.01	-0.35	0.36		-0.97	-1.15	-1.39	-0.27	1.90355E-06
Chronic liver disease (CLD, N=39)						Metabolic dysfunction-associated steatotic liver disease (MASLD, N=106)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.61	0.47	0.1	1.02	2.24745E-09	0.29	0.22	-0.1	0.53	8.33348E-13
IL17C	0.44	0.2	-0.07	0.76	0.380	0.51	0.48	-0.04	0.9	0.070
IL17D	0.37	0.26	-0.01	0.56	0.004	0.18	0.15	-0.09	0.45	0.398
IL17F	0.35	0.37	-0.17	0.57	0.011	0.09	0.04	-0.41	0.39	0.149
IL17RA	0.27	0.26	-0.02	0.58	2.11341E-07	0.33	0.39	-0.01	0.65	4.58124E-19
IL17RB	-0.28	-0.37	-0.89	0.34	0.020	-0.49	-0.51	-1	-0.09	3.36093E-15
Metabolic syndrome (MetabolicS, N=352)						Obesity (N=98)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0	-0.04	-0.3	0.2	0.064	-0.05	-0.07	-0.32	0.16	0.289
IL17C	0.51	0.43	0.02	0.9	0.002	0.46	0.38	-0.06	0.84	0.229
IL17D	0.19	0.18	-0.02	0.37	0.500	0.21	0.17	-0.04	0.36	0.252
IL17F	0.14	-0.03	-0.37	0.39	0.388	0.21	0	-0.38	0.35	0.136
IL17RA	-0.1	-0.06	-0.36	0.28	3.19089E-14	-0.11	-0.05	-0.44	0.21	0.340
IL17RB	-0.26	-0.27	-0.67	0.12	1.38999E-19	-0.25	-0.28	-0.6	0.09	8.49773E-08
Type 2 diabetes (T2D, N=77)						Viral hepatitis-related cirrhosis (VHRC, N=77)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	-0.01	-0.08	-0.24	0.17	0.282	0.54	0.24	-0.07	0.63	2.55073E-22
IL17C	0.28	0.22	-0.18	0.73	0.045	0.7	0.66	0.02	1.17	0.001
IL17D	0.09	0.05	-0.12	0.27	0.001	0.34	0.38	0.06	0.66	0.002
IL17F	0.28	0.05	-0.33	0.61	0.051	0.2	0.15	-0.3	0.51	0.232
IL17RA	-0.03	-0.03	-0.38	0.32	0.155	0.33	0.33	0.04	0.79	1.63496E-11
IL17RB	-0.46	-0.53	-0.8	-0.15	1.08618E-18	-0.3	-0.25	-0.88	0.36	0.001

Note: The data are adopted from Supplementary file S14 of Maria Bueno Alvez et al, Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678. P value is for the comparison between disease and healthy groups. P values in red indicate significantly increased levels; p values in green indicate significantly decreased levels; and p values in white indicate no significant differences.

Table 4. Plasma IL-17 family members and cancer.

Healthy (N=825)						Acute myeloid leukemia (AML, N=52)				
Protein	mean	median	Q1	Q3		mean	median	Q1	Q3	*p* value
IL17A	-0.03	-0.09	-0.33	0.18		0.75	0.53	0.04	1.15	3.93753E-12
IL17C	0.41	0.31	-0.09	0.75		0.56	0.47	-0.21	1.1	0.132
IL17D	0.19	0.15	-0.03	0.37		0.01	-0.04	-0.29	0.37	0.004
IL17F	0.15	0	-0.33	0.4		0.62	0.41	-0.04	1.01	6.57583E-06
IL17RA	-0.09	-0.04	-0.42	0.28		0.23	0.17	-0.19	0.66	0.0001
IL17RB	0.02	-0.01	-0.35	0.36		0.33	0.39	-0.14	0.79	0.0006
Breast cancer (BC, N=164)						Breast ductal carcinoma in situ (BDCIS, N=49)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.11	0.05	-0.22	0.33	5.39529E-06	0.04	-0.09	-0.35	0.09	0.066
IL17C	0.35	0.16	-0.24	0.87	0.175	0.15	0	-0.39	0.41	0.001
IL17D	0.28	0.26	0.03	0.49	0.0004	0.2	0.22	0.05	0.45	0.407
IL17F	0.29	0.08	-0.27	0.5	0.0008	0.06	-0.06	-0.49	0.31	0.144
IL17RA	0.2	0.24	-0.17	0.52	1.84933E-13	0	0.13	-0.23	0.32	0.061
IL17RB	-0.05	-0.08	-0.48	0.36	0.075	-0.08	-0.12	-0.44	0.2	0.070
Cervical cancer (CervicalC, N=110)						Chronic lymphocytic leukemia (CLL, N=50)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.04	-0.07	-0.25	0.25	0.024	-0.03	-0.07	-0.33	0.24	0.500
IL17C	0.27	0.16	-0.35	0.69	0.028	0.46	0.33	-0.36	1.14	0.375
IL17D	-0.07	-0.07	-0.26	0.14	1.73565E-20	0.34	0.34	0.04	0.51	0.001
IL17F	0.22	0.07	-0.2	0.51	0.081	-0.04	-0.17	-0.42	0.34	0.009
IL17RA	-0.01	0.02	-0.27	0.33	0.030	0.23	0.28	0.04	0.53	2.27214E-10
IL17RB	-0.21	-0.29	-0.69	0.24	0.0002	0.5	0.5	-0.11	0.98	1.31283E-05
Colorectal cancer (ColorectalC, N=241)						Diffuse large B-cell lymphoma (DLBL, N=55)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.35	0.24	-0.07	0.61	5.55678E-32	0.21	-0.01	-0.29	0.41	0.0003
IL17C	0.37	0.12	-0.32	0.85	0.237	0.72	0.58	-0.01	1.17	0.004
IL17D	-0.03	-0.04	-0.27	0.18	6.17001E-25	-0.09	-0.06	-0.37	0.22	1.01009E-06
IL17F	0.13	0.03	-0.28	0.4	0.269	0.11	0.09	-0.35	0.4	0.297
IL17RA	-0.03	0	-0.34	0.31	0.027	0.3	0.2	-0.04	0.63	2.80808E-09
IL17RB	-0.01	0.02	-0.4	0.42	0.222	0.49	0.33	-0.18	1.31	0.0008
Endometrial cancer (EC, N=107)						Glioma (N=159)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.21	0.17	-0.15	0.41	1.08335E-09	-0.07	-0.08	-0.35	0.18	0.099
IL17C	0.34	0.25	-0.2	0.83	0.171	0.59	0.33	-0.2	1.16	0.012
IL17D	0.17	0.16	-0.09	0.36	0.267	-0.31	-0.35	-0.58	-0.07	7.87005E-63
IL17F	0.36	0.09	-0.26	0.82	0.003	0.09	0	-0.4	0.35	0.087
IL17RA	-0.02	0.01	-0.43	0.31	0.093	-0.09	-0.04	-0.39	0.28	0.500
IL17RB	-0.16	-0.22	-0.57	0.17	0.0003	0.36	0.34	-0.08	0.88	8.2526E-10
Hepatocellular cancer (HC, N=80)						Lung cancer (LC, N=277)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value

IL17A	0.43	0.35	-0.06	0.8	5.28393E-11	0.13	-0.02	-0.29	0.36	1.59476E-08
IL17C	1	0.79	0.26	1.55	1.6704E-08	0.61	0.29	-0.24	1.15	0.0006
IL17D	0.37	0.35	0.08	0.69	0.0002	0	0	-0.26	0.22	2.95343E-19
IL17F	0.46	0.22	-0.26	0.66	2.3641E-05	0.14	0.03	-0.3	0.37	0.369
IL17RA	0.52	0.49	0.08	1.05	1.55797E-14	-0.02	0	-0.31	0.31	0.006
IL17RB	-0.21	-0.34	-0.91	0.3	0.011	0.02	0.02	-0.42	0.42	0.500
Meningioma (N=51)						Metastatic melanoma (MM, N=104)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.01	-0.08	-0.29	0.16	0.196	0.05	-0.05	-0.26	0.22	0.011
IL17C	0.67	0.43	-0.04	1.23	0.024	0.17	0.08	-0.37	0.67	0.0007
IL17D	-0.1	-0.12	-0.48	0.14	3.24954E-06	0.2	0.21	-0.12	0.51	0.413
IL17F	0.05	-0.04	-0.29	0.23	0.032	0.01	-0.09	-0.39	0.26	0.002
IL17RA	-0.13	-0.06	-0.37	0.15	0.229	0.11	0.16	-0.24	0.47	5.26318E-05
IL17RB	0.07	0.14	-0.46	0.55	0.317	0.2	0.12	-0.26	0.72	0.006
Myeloma (N=41)						Ovarian cancer (OC, N=157)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.25	0.16	-0.13	0.58	0.0003	0.11	0.01	-0.25	0.28	3.94343E-06
IL17C	1.32	1.27	0.15	2.04	1.57715E-05	0.81	0.54	-0.15	1.51	2.29073E-05
IL17D	0.62	0.62	0.17	1	3.76147E-06	-0.04	-0.04	-0.4	0.21	8.97329E-11
IL17F	-0.02	-0.02	-0.22	0.14	2.23257E-05	0.23	-0.07	-0.41	0.41	0.049
IL17RA	0.17	0.15	-0.25	0.51	0.002	-0.04	0	-0.36	0.27	0.090
IL17RB	0.77	0.46	0.01	1.42	2.13295E-06	0.04	0.06	-0.39	0.51	0.354
Pancreatic cancer (PancreaticC, N=73)						Pituitary neuroendocrine tumor (PNT, N=49)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	1.21	1.06	0.44	1.97	4.45991E-21	0.09	0.03	-0.13	0.23	0.0008
IL17C	1.57	1.32	0.51	2.21	1.76564E-15	0.46	0.43	-0.11	1	0.335
IL17D	0.11	0.14	-0.22	0.37	0.059	0.11	0.14	-0.15	0.25	0.029
IL17F	0.52	0.29	-0.13	0.91	2.03397E-05	0.18	0	-0.3	0.39	0.341
IL17RA	0.21	0.29	-0.17	0.57	1.46184E-06	0.11	0.19	-0.23	0.46	0.003
IL17RB	0.02	0.02	-0.46	0.45	0.500	-0.24	-0.32	-0.58	0.19	0.0007
Prostate cancer (ProstateC, N=170)						Small intestine neuroendocrine tumor (SINT, N=54)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.1	0.07	-0.24	0.35	5.25787E-05	0.25	0.13	-0.17	0.54	4.57137E-05
IL17C	0.47	0.32	-0.13	0.81	0.131	0.54	0.26	-0.1	0.87	0.092
IL17D	0.18	0.16	-0.03	0.39	0.338	0.22	0.14	-0.14	0.35	0.272
IL17F	0.18	0.07	-0.3	0.48	0.249	0.23	0.07	-0.24	0.54	0.155
IL17RA	0.21	0.2	-0.14	0.62	1.85123E-12	-0.08	-0.08	-0.33	0.29	0.436
IL17RB	0.16	0.17	-0.25	0.53	0.0008	0.2	0.11	-0.34	0.8	0.059

Note: The data are adopted from Supplementary file S14 of Maria Bueno Alvez et al, Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678. P value is for the comparison between disease and healthy groups. P values in red indicate significantly increased levels; p values in green indicate significantly decreased levels; and p values in white indicate no significant differences.

Table 5. Plasma IL-17 family members and psychiatric diseases.

Healthy (N=825)						Bipolar disorder (BD, N=50)				
Protein	mean	median	Q1	Q3		mean	median	Q1	Q3	*p* value
IL17A	-0.03	-0.09	-0.33	0.18		0.37	0.26	-0.03	0.71	1.23496E-07
IL17C	0.41	0.31	-0.09	0.75		1.48	1.31	0.65	1.89	8.81263E-17
IL17D	0.19	0.15	-0.03	0.37		-0.09	-0.1	-0.28	0.1	1.00454E-12
IL17F	0.15	0	-0.33	0.4		0.42	0.16	-0.33	0.79	0.011
IL17RA	-0.09	-0.04	-0.42	0.28		0.1	0.06	-0.33	0.45	0.010
IL17RB	0.02	-0.01	-0.35	0.36		-0.59	-0.55	-1.03	-0.19	2.07214E-12
Schizophrenia (N=100)										
Protein	mean	median	Q1	Q3	*p* value					
IL17A	0.37	0.25	0	0.58	6.3709E-21					
IL17C	1.29	1.14	0.65	1.86	4.7012E-23					
IL17D	-0.09	-0.13	-0.36	0.09	2.23239E-17					
IL17F	0.31	0.16	-0.26	0.46	0.001					
IL17RA	0.18	0.2	-0.12	0.52	6.15731E-09					
IL17RB	-0.46	-0.39	-1.02	-0.11	5.36204E-13					

Note: The data are adopted from Supplementary file S14 of Maria Bueno Alvez et al, Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678. P value is for the comparison between disease and healthy groups. P values in red indicate significantly increased levels; p values in green indicate significantly decreased levels; and p values in white indicate no significant differences.

Table 6. Plasma IL-17 family members and autoimmune diseases.

Healthy (N=825)						Multiple sclerosis (MultipleS, N=234)				
Protein	mean	median	Q1	Q3		mean	median	Q1	Q3	*p* value
IL17A	-0.03	-0.09	-0.33	0.18		0.09	0.03	-0.22	0.33	3.30805E-06
IL17C	0.41	0.31	-0.09	0.75		0.19	0.17	-0.34	0.62	1.10871E-06
IL17D	0.19	0.15	-0.03	0.37		0.15	0.12	-0.14	0.32	0.036
IL17F	0.15	0	-0.33	0.4		0.11	0	-0.34	0.38	0.126
IL17RA	-0.09	-0.04	-0.42	0.28		0.22	0.28	-0.11	0.61	3.01677E-19
IL17RB	0.02	-0.01	-0.35	0.36		-0.05	0.01	-0.43	0.37	0.0354
Myositis (N=210)						Rheumatoid arthritis (RA, N=84)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0	-0.07	-0.32	0.28	0.164	0.2	0.07	-0.17	0.34	1.20287E-08
IL17C	-0.35	-0.59	-1.06	0.17	6.11658E-34	-0.75	-0.9	-1.31	-0.19	6.77035E-38
IL17D	-0.09	-0.17	-0.48	0.19	1.47037E-16	0.11	0.1	-0.2	0.36	0.039
IL17F	0.15	0.03	-0.41	0.45	0.500	0.11	-0.02	-0.36	0.31	0.230
IL17RA	0.2	0.3	-0.13	0.57	2.64118E-16	0.26	0.31	-0.1	0.64	2.42742E-09
IL17RB	0.59	0.53	0.02	1.11	7.24746E-25	-0.13	0	-0.36	0.37	0.006
Sjögren's syndrome (SjögrenS, N=99)						Systemic lupus erythematosus (SLE, N=99)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.12	0.09	-0.18	0.38	0.0002	0.16	0.12	-0.22	0.36	5.40641E-06
IL17C	0.06	-0.06	-0.56	0.36	1.60972E-07	-0.04	-0.14	-0.76	0.45	2.93426E-07
IL17D	0.11	0.17	-0.23	0.43	0.052	0.01	-0.09	-0.44	0.3	0.0005
IL17F	0.15	-0.05	-0.33	0.35	0.500	0.28	0.13	-0.28	0.57	0.020
IL17RA	0.1	0.17	-0.23	0.46	0.0001	0.14	0.18	-0.14	0.46	1.30898E-07
IL17RB	-0.05	-0.07	-0.42	0.42	0.132	0.22	0.24	-0.24	0.67	0.002
Systemic sclerosis (SystemicS, N=100)										
Protein	mean	median	Q1	Q3	*p* value					
IL17A	0.17	0.14	-0.23	0.44	2.79061E-05					
IL17C	0.03	-0.1	-0.66	0.65	4.50094E-05					
IL17D	0.28	0.24	-0.11	0.57	0.037					
IL17F	0.17	0.1	-0.39	0.56	0.388					
IL17RA	0.31	0.32	-0.01	0.71	3.19089E-14					
IL17RB	0.05	-0.02	-0.29	0.46	0.295					

Note: The data are adopted from Supplementary file S14 of Maria Bueno Alvez et al, Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678. P value is for the comparison between disease and healthy groups. P values in red indicate significantly increased levels; p values in green indicate significantly decreased levels; and p values in white indicate no significant differences.

Table 7. Plasma IL-17 family members and infection.

Healthy (N=825)						Bacterial gastroenteritis (BG, N=32)				
Protein	mean	median	Q1	Q3		mean	median	Q1	Q3	*p* value
IL17A	-0.03	-0.09	-0.33	0.18		1.21	1.05	0.49	1.7	2.5163E-15
IL17C	0.41	0.31	-0.09	0.75		1.71	1.58	1.16	2.24	1.92107E-20
IL17D	0.19	0.15	-0.03	0.37		-0.3	-0.36	-0.54	-0.06	3.19876E-15
IL17F	0.15	0	-0.33	0.4		1.25	1.03	0.52	1.72	1.27655E-12
IL17RA	-0.09	-0.04	-0.42	0.28		0.2	0.19	-0.07	0.55	0.0002
IL17RB	0.02	-0.01	-0.35	0.36		-0.14	-0.15	-0.57	0.23	0.063
Dengue (N=19)						E.coli pyelonephritis (EP, N=53)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.5	0.37	0.13	0.75	2.44844E-07	2.33	2.04	1.25	3.38	6.47426E-28
IL17C	0.21	0.15	-0.42	0.42	0.081	1.95	1.86	1.15	2.81	3.83749E-20
IL17D	-0.16	-0.17	-0.53	0.12	0.0008	0.33	0.3	-0.14	0.75	0.061
IL17F	0.54	0.45	0.06	0.65	5.0171E-05	1.17	1.11	0.42	1.8	1.8751E-13
IL17RA	0.35	0.41	0.18	0.67	6.31783E-08	0.38	0.28	0.01	0.73	7.01361E-11
IL17RB	0.39	0.39	-0.27	1.06	0.051	-0.2	-0.21	-0.58	0.27	0.006
Human immunodeficiency virus (HIV, N=87)						Influenza (N=132)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.16	0.06	-0.16	0.46	5.69663E-05	0.48	0.3	0.02	0.76	5.69647E-27
IL17C	0.46	0.49	-0.1	1.04	0.290	1.15	1.06	0.37	1.84	2.90707E-15
IL17D	-0.07	-0.07	-0.38	0.12	2.91915E-11	-0.17	-0.24	-0.66	0.12	4.07499E-13
IL17F	0.31	0.26	-0.2	0.69	0.012	0.43	0.23	-0.23	0.78	8.54413E-06
IL17RA	0.03	0.06	-0.36	0.54	0.047	0.07	0.11	-0.22	0.42	5.27504E-05
IL17RB	0	-0.06	-0.67	0.67	0.426	-0.05	-0.06	-0.6	0.44	0.148
Malaria (N=78)						Mycoplasma (N=31)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.8	0.54	0.24	1.04	1.89946E-35	0.47	0.47	0.21	0.69	2.44579E-15
IL17C	0.72	0.74	0.12	1.42	0.002	0.71	0.63	0.3	1.16	0.004
IL17D	-0.24	-0.13	-0.53	0.12	1.54222E-15	-0.22	-0.33	-0.57	0.02	8.78726E-08
IL17F	0.71	0.3	-0.01	1.03	6.81323E-11	0.24	0.07	-0.13	0.74	0.218
IL17RA	0.11	0.18	-0.51	0.43	0.006	0.14	0.2	-0.04	0.46	0.0003
IL17RB	-0.01	0	-0.53	0.42	0.353	0.22	0.23	-0.23	0.7	0.053
Pneumococcal pneumonia (PP, N=51)						Staphylococcus aureus bacteremia (SAB, N=21)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	2.08	1.69	1.12	2.92	6.46371E-30	3.87	4.31	2.12	4.92	3.44019E-18
IL17C	2.87	2.69	1.95	4.25	3.12258E-25	1.96	1.92	0.9	2.96	1.6209E-06
IL17D	0.3	0.43	-0.27	0.83	0.168	0.39	0.43	-0.11	1	0.132
IL17F	1.81	1.8	0.68	2.68	6.12218E-16	1.9	1.94	1.27	2.24	3.15774E-29
IL17RA	0.33	0.43	-0.2	0.59	1.4833E-07	0.38	0.27	-0.14	0.79	0.0009
IL17RB	-0.29	-0.31	-0.69	0.21	0.0005	0.24	0.17	-0.26	0.66	0.070
Streptococcal soft tissue infection (SSTI, N=77)										
Protein	mean	median	Q1	Q3	*p* value					

IL17A	4.37	4.42	2.52	5.73	1.36296E-59
IL17C	3.29	3.21	1.81	4.93	3.92222E-28
IL17D	0.11	0.13	-0.36	0.59	0.159
IL17F	3.13	2.74	1.69	4.2	3.14202E-45
IL17RA	0	-0.08	-0.33	0.42	0.078
IL17RB	-0.89	-0.86	-1.28	-0.45	7.15545E-39

Note: The data are adopted from Supplementary file S14 of Maria Bueno Alvez et al, Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678. P value is for the comparison between disease and healthy groups. P values in red indicate significantly increased levels; p values in green indicate significantly decreased levels; and p values in white indicate no significant differences.

Table 8. Plasma IL-17 family members and pediatric diseases.

Healthy (N=825)						Pediatric CNS tumor (PCT, N=15)				
Protein	mean	median	Q1	Q3		mean	median	Q1	Q3	*p* value
IL17A	-0.03	-0.09	-0.33	0.18		0.17	0.08	-0.15	0.35	0.018
IL17C	0.41	0.31	-0.09	0.75		-0.62	-0.89	-1.09	-0.38	1.66183E-14
IL17D	0.19	0.15	-0.03	0.37		-0.21	-0.24	-0.44	0.04	6.58966E-06
IL17F	0.15	0	-0.33	0.4		-0.18	-0.18	-0.4	0.07	0.0001
IL17RA	-0.09	-0.04	-0.42	0.28		0.4	0.43	0.27	0.7	1.27602E-09
IL17RB	0.02	-0.01	-0.35	0.36		0.12	-0.09	-0.54	0.85	0.353
Pediatric bone tumor (PBT, N=11)						Pediatric diffuse astrocytic and oligodendroglial tumor (PDAOT, N=21)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.04	0	-0.53	0.4	0.368	0.16	-0.08	-0.29	0.45	0.056
IL17C	-0.38	-0.3	-0.89	0.28	0.001	-0.43	-0.58	-1.39	0.11	0.0003
IL17D	0.12	-0.21	-0.43	-0.06	0.198	-0.17	-0.19	-0.35	0.17	9.22176E-06
IL17F	-0.26	-0.32	-0.58	-0.05	0.0003	-0.01	0.14	-0.44	0.36	0.108
IL17RA	0.64	0.58	0.29	1.09	2.19752E-05	0.43	0.63	0.13	0.74	6.68435E-08
IL17RB	-0.05	-0.03	-0.28	0.2	0.257	-0.05	-0.01	-0.25	0.19	0.163
Pediatric kidney tumor (PKT, N=8)						Pediatric long COVID (PLCOVID, N=17)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.43	0.08	-0.15	1.21	0.098	0.22	0.22	0.07	0.32	1.30183E-08
IL17C	1.14	1.14	0.16	2.06	0.071	0.01	-0.07	-0.59	0.51	0.022
IL17D	0.13	0.1	-0.03	0.21	0.170	-0.47	-0.53	-0.71	-0.24	2.71873E-15
IL17F	-0.29	-0.53	-0.69	-0.09	0.003	0.27	0.28	-0.35	0.66	0.254
IL17RA	1.15	1.26	1.07	1.32	2.71341E-80	1.01	0.99	0.73	1.37	5.5083E-22
IL17RB	0.14	0.14	-0.12	0.29	0.132	-0.39	-0.2	-0.8	0.29	0.018
Pediatric lymphoma (PL, N=10)						Pediatric neuroblastoma (PN, N=13)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.69	0.56	0.24	0.68	1.4166E-12	0.59	0.66	0	0.97	0.0009
IL17C	-0.53	-0.84	-1.13	0.13	0.0007	0.93	0.75	0.24	1.78	0.050
IL17D	-0.39	-0.39	-0.57	-0.16	7.74502E-10	0.23	0.2	-0.27	0.52	0.403
IL17F	0.02	0.09	-0.28	0.31	0.173	0.16	-0.16	-0.4	0.89	0.485
IL17RA	0.77	0.92	0.58	0.99	1.70416E-19	0.63	0.77	0.13	1.02	4.11249E-05
IL17RB	0.22	0.08	-0.47	0.57	0.206	0.11	0.09	-0.08	0.19	0.052
Pediatric retinoblastoma (PR, N=7)						Pediatric sarcoma (PS, N=7)				
Protein	mean	median	Q1	Q3	*p* value	mean	median	Q1	Q3	*p* value
IL17A	0.8	0.74	0.35	1.21	0.0003	0.2	0.36	-0.19	0.47	0.107
IL17C	1.49	2.12	0.5	2.22	0.012	1.11	0.7	-0.53	2.11	0.172
IL17D	0.42	0.43	0.06	0.67	0.089	0.27	0.24	0.02	0.65	0.325
IL17F	-0.18	-0.32	-0.46	-0.04	0.003	-0.1	-0.12	-0.27	0.03	0.002
IL17RA	0.89	0.95	0.73	1.22	4.54825E-13	0.41	0.4	0.28	0.55	1.86558E-11
IL17RB	0.46	0.57	0.3	0.66	6.34192E-06	0.38	0.29	0.12	0.44	2.93179E-05
Pediatric systemic inflammatory disease (PSID, N=38)										

Protein	mean	median	Q1	Q3	*p* value
IL17A	3.05	3.3	1.58	4.21	9.60647E-23
IL17C	0.24	0.06	-0.71	1.09	0.216
IL17D	-1.34	-1.41	-1.66	-1.18	2.4143E-155
IL17F	0.32	0.13	-0.19	0.46	0.015
IL17RA	0.24	0.29	0.07	0.53	1.18553E-09
IL17RB	-2.09	-2.27	-2.71	-1.68	1.81172E-65

Note: The data are adopted from Supplementary file S14 of Maria Bueno Alvez et al, Science, Vol 390, Issue 6779, December 18, 2025; DOI: 10.1126/science.adx2678. P value is for the comparison between disease and healthy groups. P values in red indicate significantly increased levels; p values in green indicate significantly decreased levels; and p values in white indicate no significant differences.