Title: Differences in the inflammatory proteome of East African and Western European adults and associations with environmental and dietary factors.

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Abstract:

Non-communicable diseases (NCDs) are rising rapidly in urbanizing populations in sub-Saharan Africa. Assessment of inflammatory and metabolic characterstics of an urbanizing African population and the comparison with populations outside Africa could provide insight in the pathophysiology of the rapidly increasing epidemic of NCDs, including the role of environmental and dietary changes. Using a proteomic plasma profiling approach comprising 92 inflammation-related molecules, we examined differences in the inflammatory proteome in healthy Tanzanian and healthy Dutch adults. We show that healthy Tanzanians display a pro-inflammatory phenotype compared to Dutch subjects, with enhanced activity of the Wnt/β-catenin signalling pathway and higher concentrations of different metabolic regulators such as 4E-BP1 and fibroblast growth factor 21. Among the Tanzanian volunteers, food-derived metabolites were identified as an important driver of variation in inflammation-related molecules, emphasizing the potential importance of lifestyle changes. These findings endorse the importance of the current dietary transition in the NCDs epidemic in sub-Saharan Africa and the inclusion of underrepresented populations in systems immunology studies.

Introduction

The human immune response is tightly regulated by a complex and intricate network of pro-and anti-inflammatory cytokines, chemokines and other immuno-metabolic mediators. Prolonged dysregulation of this network may result in an unresolved pro-inflammatory state, which is central to the development of a wide range of non-communicable diseases (NCDs), including cardiovascular disease, diabetes, rheumatic and inflammatory bowel diseases, and even malignancies (Choi et al., 2015; Moore & Tabas, 2011; Seyedsadjadi & Grant, 2021). The inflammatory response is highly variable among healthy individuals as a consequence of genetic and non-genetic factors (Brodin & Davis, 2017); this includes intrinsic factors such as age and sex, as well as environmental exposures such as diet and past infections (Liston, Humblet-Baron, Duffy, & Goris, 2021). Not surprisingly, variation in inflammatory proteins between populations has also been reported (A. Schutte, 2006; A. E. Schutte, Myburgh, Olsen, Eugen-Olsen, & Schutte, 2012). Understanding the nature of this variation and the factors involved is key for understanding the dynamics of infectious as well as immune-mediated pathology across populations.

Worldwide, many communities are currently undergoing a rapid urbanization process with a transition of lifestyle, and diet, characterized by a more sedentary lifestyle and a shift from traditional high-fiber diets to a diet richer in processed foods, animal fat and simple carbohydrates. Also, environmental exposures change from close contact with animals and smoke from burning wood to petrol gasses. This is accompanied by an epidemiologic transition in which the burden of disease shifts from infectious diseases to NCDs (Beaglehole et al., 2011; Unwin et al., 2010). This epidemiologic transition is at least partly mediated through effects on the immune system of individuals across communities. We recently reported that urban-living

Tanzanians display a pro-inflammatory gene signature and higher *ex-vivo* cytokine responses compared to rural-living individuals (Temba et al., 2021) and that food-derived metabolites are an important driver of this difference. In communities in sub-Saharan Africa, this effect may also be more pronounced than in other populations, as the historically high burden of infectious diseases may have resulted in the selection of genotypes favoring a robust immune response (Karlsson, Kwiatkowski, & Sabeti, 2014). Indeed, we recently showed important differences in the genetic regulation of cytokine responses between healthy Tanzanian and Dutch individuals, with enrichment of interferon pathways in the Tanzanians (Boahen et al., 2022). In a context with a declining burden of infectious diseases, alongside a shift to an unhealthy Western-type lifestyle, such a heritable pro-inflammatory phenotype may particularly drive a health-to-disease transition with the onset of NCDs (Bickler et al., 2018).

Studies on non-Western populations outside historically wealthy countries are underrepresented in systems-immunology literature, despite the fact that these populations are representative of the majority of the world's population. In addition, these populations offer unique opportunities to increase our understanding of the pathophysiology of NCDs, including the role of diet and environmental exposures. Our present knowledge of the regulation of the immune system in individuals in sub-Saharan Africa and how this compares to individuals in the industrialized world is limited. We investigated the hypothesis that healthy individuals in East Africa have a pro-inflammatory phenotype in comparison to individuals from North-western Europe and that these differences are partly driven by common environmental factors, including diet. Using a 92-plex proteomic panel based on a proximity extension assay technology, we compared the inflammatory proteome of healthy Tanzanians of African origin residing in Tanzania with that of healthy individuals of Western-European ancestry living in the Netherlands. Next, we studied associations between the proteome with intrinsic factors and environmental exposures, with special emphasis on the food-derived metabolites.

RESULTS

Demographics

Data from plasma samples of 318 Tanzanian and 416 Dutch individuals were included in this study. Characteristics of study participants are summarized in **Table 1 & Supplemental Fig. 1**. The Tanzanians had a significantly higher median (IQR) age (30.2 years; 23.4-39.9) than the Dutch (23.0 years; 21.0-26.0; *P*-value <0.0001) (**Supplemental Fig. 1a**), although both populations were young adults. Tanzanian females also had a higher BMI than Dutch females (25.7; 22.6-29.9 vs. 21.5; 20.4-23.1; *P*-value <0.0001).

Table 1. Descriptive characteristics of study participants

	Tanzanians	Dutch	*P*-value
Number	318	416	
Sex, females	163 (51.3)	214 (51.4)	ns
Age, years	30 (23-40)	23 (21-26)	<0.0001
Age category			<0.0001
18-30 years	155 (48.7)	351 (85.8)	
31-40 years	84 (26.4)	15 (3.7)	
41-50 years	50 (15.7)	4 (1.0)	
50-60 years	25 (7.9)	13 (3.2)	
≥60 years	4 (1.3)	26 (6.4)	
BMI	23.8 (21.4-27.3)	22.3 (20.7-24.3)	<0.0001
BMI category			<0.0001
≤ 24.9	194 (61.0)	337 (84.0)	
≥ 25- 29.9	76 (23.9)	57 (14.2)	
≥30	48(15.1)	7 (1.7)	
BMI by sex			
Male	22.8 (20.8-24.9)	23 (21.7-24.6)	ns
Female	25.7 (22.6-29.9)	21.5 (20.4-23.1)	<0.0001
Smoking (N, %)	50 (15.7)	57 (13.7)	ns
Study characteristics only relevant for the Tanzanian cohort			
Residency (N, %)			
Urban	250 (78.6)		
Rural	68 (21.4)		
Highest level of education (N, %)			
Primary	119 (37.4)		
Secondary	69 (21.7)		
College	61 (19.2)		
University	25 (7.9)		
In training	44 (13.8)		
Occupational status (N, %)			
Student	57 (17.9)		
Employed with qualification	66 (20.8)		
Service or shop sales worker	133 (41.8)		
Elementary occupation	62 (19.5)		
Toilet facility (N, %)			
Pit latrine	75 (23.6)		
Water closet	243 (76.4)		
Cooking fuel (N, %) [#]			
Smoky	113 (35.5)		
Non-smoky	205 (64.5)		
Exposure to animals, yes (N, %)	138 (43.4)		

The course of antibiotics in the past year (N, %)	
1-3 courses	164 (50.8)
> 3 courses	28 (8.7)
None	131 (40.6)
Last time antibiotic use (N, %)	
3-6 months ago	44 (13.6)
6-12 months ago	65 (20.1)
12 months ago,	83 (25.7)
None	131 (40.6)
Access to clean water (N, %)	
Tap water	314 (97.2)
Well/canal/river water	9 (2.8)

Comparison between Tanzanians and Dutch characteristics was done using Chi-square and, Mann-Whitney U tests; for categorical and continuous variables respectively. [#]categories of cooking fuel include firewood, charcoal or kerosene (smoky), or gas and electrical (non-smoky).

Differences in inflammatory proteome between Tanzanians and Dutch

The inflammatory proteome was measured simultaneously in samples from the Tanzanian and Dutch participants using the Olink 'inflammation' panel, which targets 92 cytokines, chemokines and other inflammation and metabolism-related proteins (Olink® Proteomics AB, Uppsala, Sweden). Relative protein concentrations are reported as normalized protein expression (NPX) units, which are on a Log2 scale. Eighteen proteins were excluded from further analysis because their value was below the lower limit of detection in more than 25% of samples in both cohorts (**Supplemental Fig. 2**). Principal component analysis (PCA) of the remaining 74 proteins revealed a clear separation between Tanzanian and Dutch samples **(Fig. 1a).** A volcano plot of differentially expressed proteins **(Fig. 1b)** showed that 35 (47%) proteins were significantly higher in the Tanzanians and 20 (27%) lower at an FDR P<0.05, with correction for age and sex and BMI. The most prominently (fold change (FC)) upregulated proteins were two regulators of metabolism: the mTOR substrate and translational repressor 4E-BP1 ($\log_2$ FC 1.9; FDR $P=1.3 \times 10^{-60}$) and FGF21 (fibroblast growth factor 21; $\log_2$ FC 1.3; $P=1.3 \times 10^{-30}$), a hormone produced by the liver that functions as a major regulator of glucose and lipid homeostasis. Obesity and excess carbohydrate and/or insufficient protein intake were reported to increase FGF21 concentrations (Hill, Berthoud, Münzberg, & Morrison, 2018). Other prominently upregulated proteins in the Tanzanians were interleukin (IL)-17A ($\log_2$ FC 0.7; P=9.6 x 10^{-34}) and IL-17C ($\log_2$ FC 0.7; P=1.1 x 10^{-74}), and the CC-chemokine family members CCL11/eotaxin (eosinophil chemoattractant; $\log_2$ FC 0.7; P=7.3 x 10^{-63}), CCL3/MIP-1α (macrophage inflammatory protein-1α; $\log_2$ FC 0.6; P=5.6 x 10^{-10}), CCL7/MCP3 (monocyte chemotactic protein 3; $\log_2$ FC 0.6; P=7.4 x 10^{-42}) and CCL8/MCP2 ($\log_2$ FC 0.5; P=8.4 x 10^{-23}). The cytokines Tumour Necrosis Factor (TNF), IL-6, IL-10, and IL-18, as well as oncostatin-M (OSM) and adenosine deaminase (ADA) were also significantly higher in the Tanzanians.

The most prominently downregulated proteins in Tanzanians were ST1A1 (sulfotransferase 1A1; $\log_2$ FC -0.8; P=2.2 x 10^{-16}) and AXIN1 (axis inhibition protein 1; $\log_2$ FC -0.7; P=6.5 x 10^{-18}). ST1A1 is a cytosolic sulfotransferase that catalyzes the sulfonation of endogenous and exogenous compounds (Wang, Cook, & Leyh, 2016). AXIN1 is a negative regulator of the Wnt/β-catenin signaling pathway (Kikuchi, 1999). This pathway is increasingly recognized to play an important role in inflammatory diseases, diabetes and cancer (Das, Das, Kalita, & Baro, 2021; Jridi, Canté-Barrett, Pike-Overzet, & Staal, 2021). Conversely, CDCP1 (CUB domain-containing protein 1), a transmembrane receptor that is a Wnt signaling promoter (He et al., 2020) was significantly up-regulated ($\log_2$ FC 0.7; P=1.8 x 10^{-61}) in the Tanzanian cohort, suggesting enhanced activity of the Wnt/β-catenin signaling pathway in the Tanzanian participants. Finally, Tanzanians had lower levels of the CXC chemokine family members CXCL1, CXCL5, CXCL6, and CXCL8 (IL8). These chemokines mediate among others neutrophil trafficking (Palomino & Marti, 2015).

The Olink platform used in this study does not contain adipocytokines and provides relative, rather than absolute, protein concentrations. Therefore, we measured absolute concentrations of a selection of cytokines using an ELLA microfluidics platform, and concentrations of adipocytokines by ELISA. The data have been reported previously (Temba et al., 2022), and confirm that Tanzanian participants have significantly higher plasma concentrations of IL-1 receptor antagonist (IL-1Ra), IL-6, and IL-18, together with significantly higher leptin and lower adiponectin concentrations than Dutch participants after correcting for age, sex and BMI **(Fig. 1c)**. In addition, Tanzanian females regardless of BMI had higher plasma concentrations of leptin compared to Dutch females (**Supplemental Fig. 3**) in line with the previous findings (Abbas, Lutale, & Ahren, 2004). There were no significant differences in plasma concentrations of resistin and alpha-1 antitrypsin (AAT).

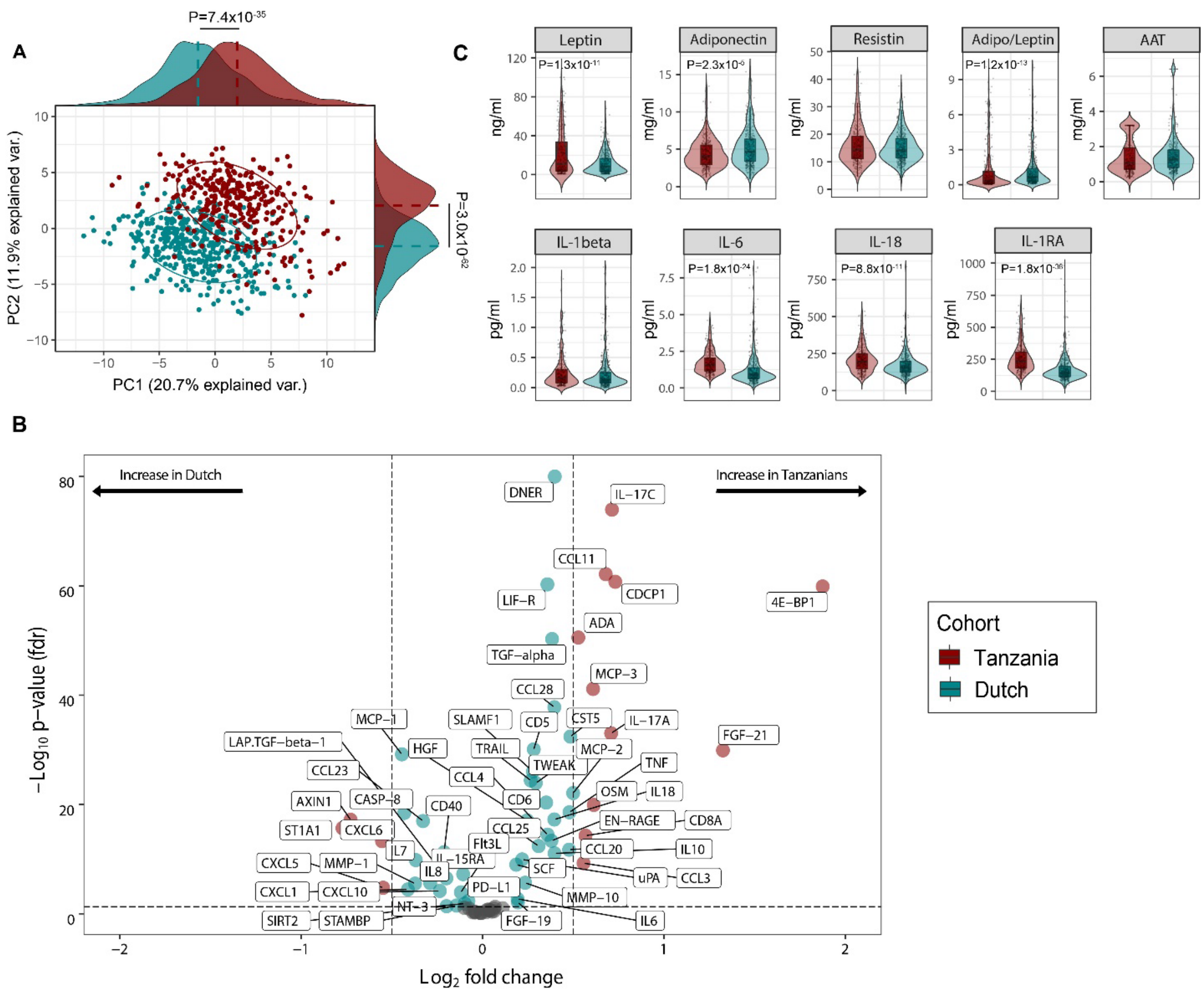

Figure 1. Differentially expressed inflammatory protein profiles among Dutch and Tanzanian participants. (A) Principal component analysis depicting the sample distribution of Dutch (N=416) vs. Tanzanian (N=318) healthy individuals across PC1 and PC2, **(B)** Volcano plot of the Dutch and Tanzanian cohorts showing differentially expressed protein (DEPs) analyzed by Limma (linear models for microarray data) R package (Dutch cohort; N=74 and Tanzanian cohort N=72 inflammatory proteins). Presented in the x-axis is the Log_2 fold change (Log2 FC) of the normalized protein expression (NPX) while the y-axis presents the -Log_{10} of the adjusted p-values (FDR <0.05), dotted lines represent the cut-off value Log2FC <.5 and >.5 **(C)** Violin plots showing the mean (linear regression corrected for age, sex and BMI) differences of the circulating inflammatory cytokines and adipokines in the Dutch and Tanzanian participants (also previously reported (Temba et al., 2022)). Dark red and turquoise colors indicate higher concentrations in the Tanzanian vs. Dutch participants respectively. Results were declared significant after correcting for multiple testing using False discovered rate (FDR); p-value <0.05(*), <0.005(**), and <0.0001(***). Abbreviation: AAT; alpha-1 antitrypsin; BMI; Body Mass Index

Associations between inflammation-related proteins and intrinsic and environmental factors

Next, we investigated associations between the inflammation-related proteins with host intrinsic factors such as age and sex, BMI and environmental exposures relevant to the Tanzanian setting. The analyses were variously corrected for age, sex and BMI to assess the impact of one specific factor. In high-income countries, age is a potent driver of immune variation with a shift toward a pro-inflammatory state (*25, 26*). In the Dutch participants, advancing age was indeed associated with an increase in inflammation-related proteins, including inflammatory cytokines (IL-6, IL-7, IL-18), IL-15RA, monocyte chemoattractant proteins (MCP2-4), matrix metalloprotease1 (MMP1), the chemokine IL-8 and hepatocyte growth factor (HGF) (Bielinski et al., 2017). In contrast, these significant associations were largely absent in the Tanzanians (**Fig. 2 & Table S2**). An exception was a strong significant positive association of advancing age with CDCP1, CCL11 and CCL25, which was also observed in the Dutch cohort. Overall, these results show that the association between advancing age and inflammatory markers is much weaker in the Tanzanians. Females in both cohorts overall had lower concentrations of inflammatory proteins than males **(Fig. 2)**, which is consistent with our earlier findings that females had lower *ex vivo* cytokine responses (Temba et al., 2021; Ter Horst et al., 2016). Results also showed that Tanzanian females had significantly higher concentrations of TNF-beta (TNFB), IL12-beta and CCL28 than Tanzanian males.

Finally, since environmental exposures are potential drivers of inflammation, we determined the relationship between relevant exposures for Tanzanians and the proteome. Such exposures included type of toilet, exposure to wood smoke for cooking, farm-animal exposure, access to clean water, previous infections and prior use of antibiotics (**Table 1**). Our results did not show a significant association between inflammatory proteins with one of these exposures.

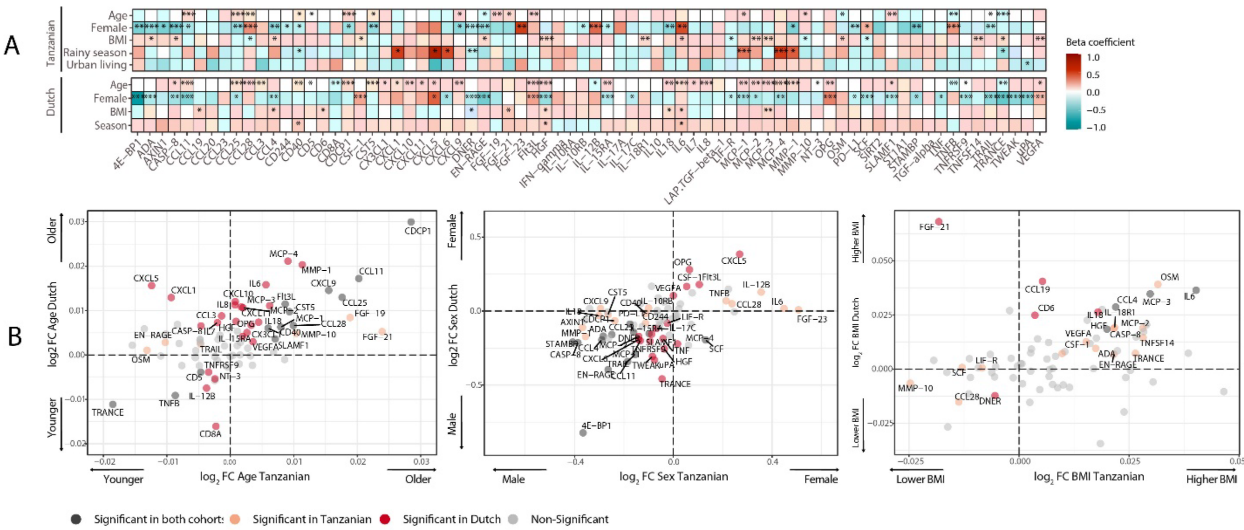

Figure 2: Associations of age, BMI, sex and seasonality with inflammatory proteins in the Dutch and Tanzanian participants. A) Heat maps showing the regression beta-coefficient of the plasma inflammatory proteins with host and environmental factors in the Dutch and Tanzanian cohorts. Dark red colors indicate higher concentrations of the inflammatory proteins with advanced age, higher BMI and higher in males, whereas turquoise color indicated lower concentration of inflammatory proteins with advanced age, higher BMI and higher concentrations in females in both cohorts. Depicted are p- values of the significant associations and results were declared significant after correcting for multiple testing using False discovered rate (FDR); p-value <0.05(*), <0.005(**), and <0.0001(***). B) Four-quadrant plot depicting the association between the inflammatory protein expression with either age, sex or BMI in the Dutch and Tanzania cohorts related to panel A

Associations with food-derived metabolites and dietary habits

We recently reported that diet, and especially the transition between a rural traditional diet to an urban Western-type diet, had a major influence on *ex vivo* cytokine immune responses in the Tanzanian cohort (Temba et al., 2021). We postulated that diet also explained part of the variation in inflammatory proteins. To test this hypothesis, we selected food-derived metabolites (n=288) from an untargeted plasma metabolome, as previously described (Temba et al., 2021). Using these metabolites, we first performed unsupervised hierarchical clustering, which yielded two different clusters (food-metabolome clusters one and two) **(Supplemental Fig. 4a)**. Weekly food consumption was associated with these food-metabolome clusters: participants in cluster one more frequently consumed ugali (a traditional porridge made from maize), plantain (cooking banana) and green vegetables, and less frequently rice and fried potato chips **(Supplemental Fig. 4b)**. Next, we performed unsupervised clustering of the inflammatory proteome with age, sex, BMI, geolocation (i.e., rural vs. urban living), seasonality and the food-metabolome clusters as input variables. This analysis revealed two significant inflammatory proteome clusters: one with lower and one with higher expressed inflammatory proteins **(Fig. 3)**. Participants belonging to food-metabolome cluster one (i.e., more 'traditional' Tanzanian diet) were overrepresented in the cluster with lower-expressed inflammatory proteins, whereas participants belonging to cluster two were overrepresented in the cluster of higher-expressed inflammatory proteins (**Table S3**). Other factors such as age, sex or season were not associated with the inflammatory clustering.

Next, we performed a correlation analysis to assess the relationship between diet-related metabolites and inflammatory proteins. Results show different negative associations between plant-derived polyphenols (apigenin, naringenin, cyanidin 3-(6-caffeoyl glucoside) 5-glucoside, licoagrodin, shoyuflavone C and phenolic acids such as gallic acid) and inflammatory proteins, particularly the MCP and CXCL families (**Fig. 4**). In contrast, positive associations were observed between inflammatory proteins, and especially members of the MCP and CXCL families, with plasma metabolites belonging to the following classes: carboxylic acids and derivatives (for example, aminobutanoic acid-ABA), organooxygen compounds (for example, triose), and prenol lipids such as resveratrol 4"-(6-) galloylglucoside (**Fig. 4 & Table S4**). The detailed classifications of various diet-derived metabolites and their correlations with various inflammatory proteins are presented in T**able S4**. Overall, these findings support the notion that a traditional plant-based

Tanzanian diet in healthy Tanzanians has an important impact on circulating inflammatory proteins.

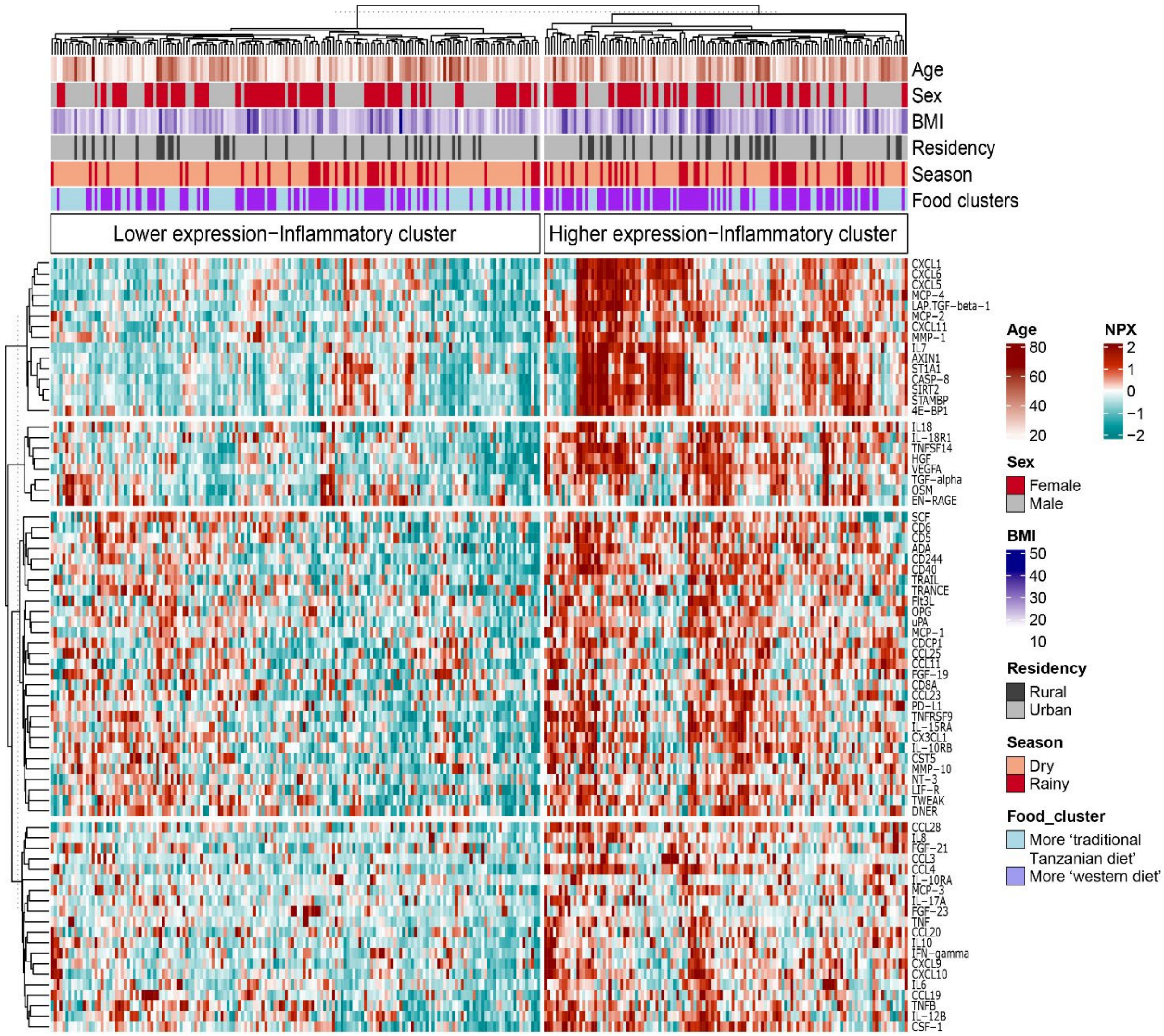

Figure 3. Association between food-derived plasma metabolites with inflammation-associated proteins. Unsupervised k-means clustering of individuals from the Tanzanian cohort (N= 318) according to the inflammatory proteins (N=72 inflammatory proteins). Data are shown as normalized protein expression (NPX). The color code indicates the relative expression of the inflammatory protein across the samples of the two compared groups. Dark red and turquoise colors indicate higher and lower expressions, respectively. Presented are annotations for age, sex, BMI, seasonality, geographical location (i.e rural vs. urban) and food-derived metabolite cluster. Results were considered significant after correcting for multiple testing using False discovered rate (FDR); p-value <0.05(*), <0.005(**), and <0.0001(***). Abbreviations: NXP; normalized protein expression; BMI; body mass index.

Figure 4. Association between inflammatory proteins and the food-derived metabolites within the Tanzanian cohort. Heat map showing associations between inflammatory proteins and food-derived metabolites within the Tanzanian participants. Depicted are β coefficients of the multiple linear regression model, including age and sex as covariates. Red and turquoise colors indicate positive and negative correlations, respectively. results were declared significant after correcting for multiple testing using False discovered rate (FDR); p-value <0.05(*), <0.005(**), and <0.0001(***).

DISCUSSION

Genetic and environmental variations, including diet, lifestyle and infectious diseases burden, are important for modulating immune responses and may result in differences in immune phenotypes across populations. Our analysis of the inflammatory proteome shows that healthy Tanzanians have a more prominent pro-inflammatory phenotype compared to healthy Dutch individuals. Among the Tanzanians, food-derived metabolites were identified as an important driver of variation in inflammation-related proteins, emphasizing the potential importance of lifestyle changes.

In the same European and African cohorts, we recently showed remarkable differences in the genetic regulation of immune responses, with ancestry-specific pathways regulating induced cytokine responses and significant enrichment of the interferon pathway in the Tanzanians (Boahen et al., 2022). From a historical perspective, the natural selection of genotypes that mediate a strong inflammatory response offers an obvious advantage in areas with a high infectious diseases burden such as sub-Saharan Africa. In addition, epigenetic regulation as a conduit that mirrors environmental exposure (e.g., diet, lifestyle or exposure to infectious diseases) may also promote an inflammatory signature. However, while a strong inflammatory response can be advantageous in the host's response against infections, it may become disadvantageous when the environment changes with a reduction in the infectious burden and a shift toward an unhealthy lifestyle. Many areas in sub-Saharan Africa are currently witnessing such changes and this is one of the important drivers of the rapid increase in non-communicable diseases and other inflammation-associated pathologies.

A healthy diet is an important component of a healthy lifestyle. In the present study, we show that Tanzanians who consumed more traditional staple foods, such as ugali (porridge made from maize or millet) or plantain, as well as green vegetables, had lower concentrations of inflammation-related proteins. We also observed several significant associations between food-derived metabolites and inflammatory proteins. Specifically, plant-derived polyphenols were negatively associated with members of the MCP and CXCL families. Especially gallic acid, a natural phenic acid with different health benefits, which is present in mangos and other edible plants (Kim et al., 2021), had different negative associations with immune-derived proteins. These data confirm our earlier findings that diet has an important impact on cytokine responses (Temba, 2021 #287) as well as plasmatic coagulation (Temba et al., 2022). Traditional foods, particularly plant-based diets, are increasingly recognized for their cardiovascular health benefits (Hemler & Hu, 2019), and our findings support the notion that promoting traditional diets may be a viable public health strategy for curbing the NCDs epidemic. Other environmental exposures may potentially confound the diet-inflammation associations, for example, individuals with a traditional diet may also use more frequently a pit latrine or smoky fuels and may have more infections, but we found no significant associations between inflammatory proteins and any of these other environmental exposures.

An interesting observation was the limited number of associations between advancing age and inflammation-related proteins in the Tanzanians. In historically wealthy countries, aging is associated with a blunted response of immune cells to stimulation, while having a chronic low-inflammation state (Guarner & Rubio-Ruiz, 2015; Liberale, Montecucco, Tardif, Libby, & Camici, 2020), as also observed in Dutch in this study. Cytokine responses decline in the Tanzanians with advancing age (Temba et al., 2021), similar to Europeans, but the reasons why systemic inflammation does not increase remain uncertain. Possible explanations are the already present inflammatory signature at a younger age, possibly because of higher cumulative exposure to infections or other environmental insults, or those older participants in Tanzania manage to control the inflammatory state by a healthier lifestyle.

The two most upregulated proteins in the Tanzanians, 4E-BP1 and FGF21, are regulators of metabolism. FGF21 has received much attention recently as an endocrine regulator of glucose, lipid and energy metabolism (Hill et al., 2018). FGF21 is an insulin sensitizer, and its secretion is increased by a high intake of carbohydrates and low dietary protein intake (Lundsgaard et al., 2017; Maekawa et al., 2017). FGF21 inhibits age-associated metabolic syndrome and protects against diabetic cardiomyopathy (Yan et al., 2021). FGF21, therefore, acts differently from classic energy balance signals like leptin (Hill et al., 2018). Traditional Tanzanian diets are high in carbohydrates and low in proteins, which may explain the high FGF21 among the Tanzanians. FGF21 was also reported to be higher in obesity (X. Zhang et al., 2008), but we did not find an association with BMI. Tanzanians also had higher leptin and lower adiponectin concentrations than the Dutch. This is in line with the results of an earlier study among non-obese and obese subjects with type 2 diabetes in Tanzania and Sweden, which showed that leptin concentrations were 50% higher in the Tanzanians (Abbas et al., 2004). This supports the importance of potential ethnic differences in metabolic profiles and adipocytokines (Mente et al., 2010). To our knowledge, this study is the first to compare FGF21 levels between healthy individuals from sub-Saharan Africa and Europe.

Another interesting finding was the significant differences in CDCP1 and AXIN1, pointing towards an enhanced activity of the Wnt/β-catenin pathway in the Tanzanians. The Wnt/β-catenin pathway is a key regulator of inflammation, playing a role in both the inflammatory and anti-inflammatory pathways (Ma & Hottiger, 2016). Dysregulated activation of the Wnt/β-catenin pathway is increasingly recognized to play a role in the pathogenesis of chronic inflammatory diseases, metabolic inflammatory diseases and cancer (Jridi et al., 2021). Mice fed on a high-fat Western-type diet expressed high concentrations of Wnt2 protein in atherosclerotic lesions, suggesting that the Wnt/β-catenin pathway also contributes to atherosclerosis (J. Zhang et al., 2021).

To summarize, our findings reveal significant differences in inflammatory and metabolic proteins and pathways between healthy individuals living in East Africa and individuals living in Western Europe. This is especially important in light of the current epidemiological transition and lifestyle changes in sub-Saharan Africa, which coincides with a sharp increase in non-communicable diseases in the region. Our study also endorses the importance of including underrepresented populations in systems-immunology studies.

Material and Methods

Study Design and Population

The present study used samples from two cross-sectional cohorts of healthy volunteers: the 300-Tanzania-FG (300TZFG) and the Dutch 500FG. Both cohorts were enrolled within the Human Functional Genomics Project (https://www. humanfunctionalgenomics.org). The demographic characteristics of both cohorts have been described previously (Temba et al., 2021; Ter Horst et al., 2016). Briefly, the 300TZFG cohort consists of 323 healthy Tanzanian individuals aged between 18 and 65 years residing in the Kilimanjaro region in Northern Tanzania. The cohort was enrolled between March and December 2017. Exclusion criteria were participants with any acute or chronic disease, use of antibiotics or anti-malaria medication in the three months before blood sampling, tuberculosis in the past year, a blood pressure ≤ 90/60mmHg or ≥140/90mmHg, or random blood glucose >8.0 mmol/L. Pregnant, postpartum, or breastfeeding females were excluded. The 500FG cohort consists of 534 Dutch individuals of Western-European background, aged 18 years and older. Data was collected between August 2013 and December 2014 at the Radboud university medical center (Radboudumc) in the Netherlands. Exclusion criteria were: the use of any medication in the past month and acute or chronic diseases at the time of blood sampling. Pregnant, postpartum, or breastfeeding females were excluded.

Sample collection and preparation

The current study is part of the Human Functional Genomics Project (HFGP; humanfunctionalgenomics.org), which employs standardized procedures for sample collection, handling, and pre-processing. Blood was obtained in the morning via antecubital puncture into ethylenediaminetetraacetic acid (EDTA) tubes (Monoject^{TM}; Covidien, Ireland). Within two to three hours after blood collection, plasma was collected by centrifugation at 3800rpm for 8 minutes at room temperature. The obtained plasma were stored at −80°C, as recommended by the ISBER biobanking organization (Garcia, Bracci, Guevarra, & Sieffert, 2014). Plasma samples for the Tanzania cohort were shipped to the Netherlands on dry ice.

Inflammatory proteome

Plasma proteins were measured with the Olink 92 Inflammation panel using proximity extension technology (Olink® Proteomics AB, Uppsala, Sweden)(Assarsson et al., 2014). This panel includes 92 inflammation-related proteins. This assay utilizes the binding of target proteins by paired oligonucleotide antibody probes, followed by hybridization and amplification. Data are reported as normalized protein expression values (NPX), which is an arbitrary unit in a Log2 scale that is calculated from normalized Ct values. Validation data of the assay are available on the Olink website (www.olink.com). All samples were measured in the same batch in a single run. Proteins were excluded from analysis when values were both below the detection limit in more than 25% of all samples. Plasma samples from the Tanzanian and Dutch cohorts were on their first and second freeze-thawed cycles, respectively. Pre-analytical processing such as freeze-thawed cycles and storage time has limited influence on the measured proteins reported in this study (Enroth, Hallmans, Grankvist, & Gyllensten, 2016; Lee, Kim, & Shin, 2015; Shen et al., 2018).

Measurement of the circulating inflammatory mediators

Plasma concentrations of the cytokines IL-6, IL-1β, IL-1 receptor antagonist (IL-1Ra) and IL-18 (lot number Bio-Tech/R&D; SPCKC-PS-001559) and IL-18 binding protein (IL-18BPa) (lot number Bio-Tech/R&D; SPCKB-PS-000502) were measured in EDTA plasma using the Simple Plex™ cartridges run on the Ella™ platform (Protein Simple, San Jose, USA) following the manufacturer's instructions.

Plasma metabolome

Plasma samples of the Tanzanian cohort were measured using the untargeted metabolomics workflow by General Metabolics (Boston, MA) with procedures as previously described (Fuhrer, Heer, Begemann, & Zamboni, 2011). In short, metabolites were measured by a high throughput mass spectrometry technique using the Agilent Series 1100 LC pump coupled to a Gerstel MPS2 autosampler and the Agilent 6520 Series Quadrupole Time-of-flight mass spectrometer (Agilent, Santa Clara, CA). The selection of food-derived metabolites was performed based on the ontology given in the HMDB (https://www.hmdb.ca/) as described previously (Temba et al., 2021).

Ethical statement

The 300TZFG study was approved by the Ethical Committees of the Kilimanjaro Christian Medical University College (CRERC) (No 2443) and the National Institute for Medical Research (NIMR/HQ/R.8a/Vol. IX/2290 and NIMR/HQ/R.8a/Vol.IX/3318) in Tanzania. The 500FG cohort study was approved by the Ethical Committee of the Radboud University Medical Centre Nijmegen, the Netherlands (NL42561.091.12, 2012/550). Subject recruitment and experimental procedures were conducted according to the principles mentioned in the Declaration of Helsinki. Written informed consent was obtained from all subjects.

Statistical analysis

The proteomic data from the Dutch and Tanzanian cohorts were normalized using inter-plate controls for batch variation correction and presented in the $\log_2$ scale. Data values below the limit of detection (LOD) were handled using the actual measured values to increase the statistical power and give a complete data distribution. Outliers detection were done using principal component analysis (PCA) in which data points that fall in more than 3 standard deviations from the mean of principal component one (PC1) and two (PC2) were excluded. This pre-analytical process led to exclusion of 12 participants (N=7 Dutch and N=5 Tanzanians) as potential outliers. Proteins with >25% data values below LOD in both cohorts were excluded (N=18 in the Duch and N=20 in the Tanzania cohorts), leaving 74 and 72 inflammatory proteins for the downstream data analysis in the Dutch and Tanzanian cohorts respectively. In total, 416 Dutch and 318 Tanzania participants were available after the pre-analytical process. Details of preanalytical steps for both cohorts are described in Supplementary figure 1.

To analyze the similarities and dissimilarities between the samples, unsupervised PCA was performed using 'prcomp' function in R package. Heatmap of unsupervised hierarchical clustering (k-nearest neighbors with 100 repetitions) of the samples was generated using 'ComplexHeatmap' R package by calculating the matrix of Euclidean distances from the $\log_2$ NPX value. Limma (linear models for microarray data) R package was used for differential expression analysis of plasma inflammatory proteins between cohorts. Proteins with adjusted P-value (FDR) < 0.05 were selected as significantly differentially expressed (DE). Proteins with a positive and negative value of $\log_2$-fold-change were considered as upregulated and downregulated, respectively.

Data availability

Anonymized metadata of the Tanzanian participants and the circulating inflammation markers are available in an open access registry (DANS registry; https://doi.org/10.17026/dans-xgx-zuht) Untargeted plasma metabolome data have been deposited to the EMBL-EBI MetaboLights database (http://www.ebi.ac.uk/metabolights/); study identifier MTBLS2267. The source data of the proteomics analysis are provided in Supplemental Table 5. Publicly available databases used for this study include KEGG (https://www.genome.jp/kegg/), HMDB (https://www.hmdb.ca/) and ChEBI (https://ebi.ac.uk/chebi/). All other data is available in the main text and supplementary materials.

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Declaration of interests: The authors declare no competing interests.

Author contributions

Q.d.M., A.V., M.G.N., L.A.B.J., R.K., J.L.S., and B.T.M contributed to the conceptualization, study design, data interpretation and lead the project; G.S.T., V.K., R.K., and B.T.M., contributed to participants recruitment, data collection and laboratory analyses; G.S.T and N.V performed statistical analysis and graphics of the proteome, inflammatory and metabolome data; G.S.T and Q.d.M. wrote the original draft of the manuscript; and G.S.T., N.V., T.P., V.K., B.T.M., R.K., L.A.B.J., J.L.S., A.V., M.G.N., and Q.d.M., contributed in writing-review and editing the manuscript.

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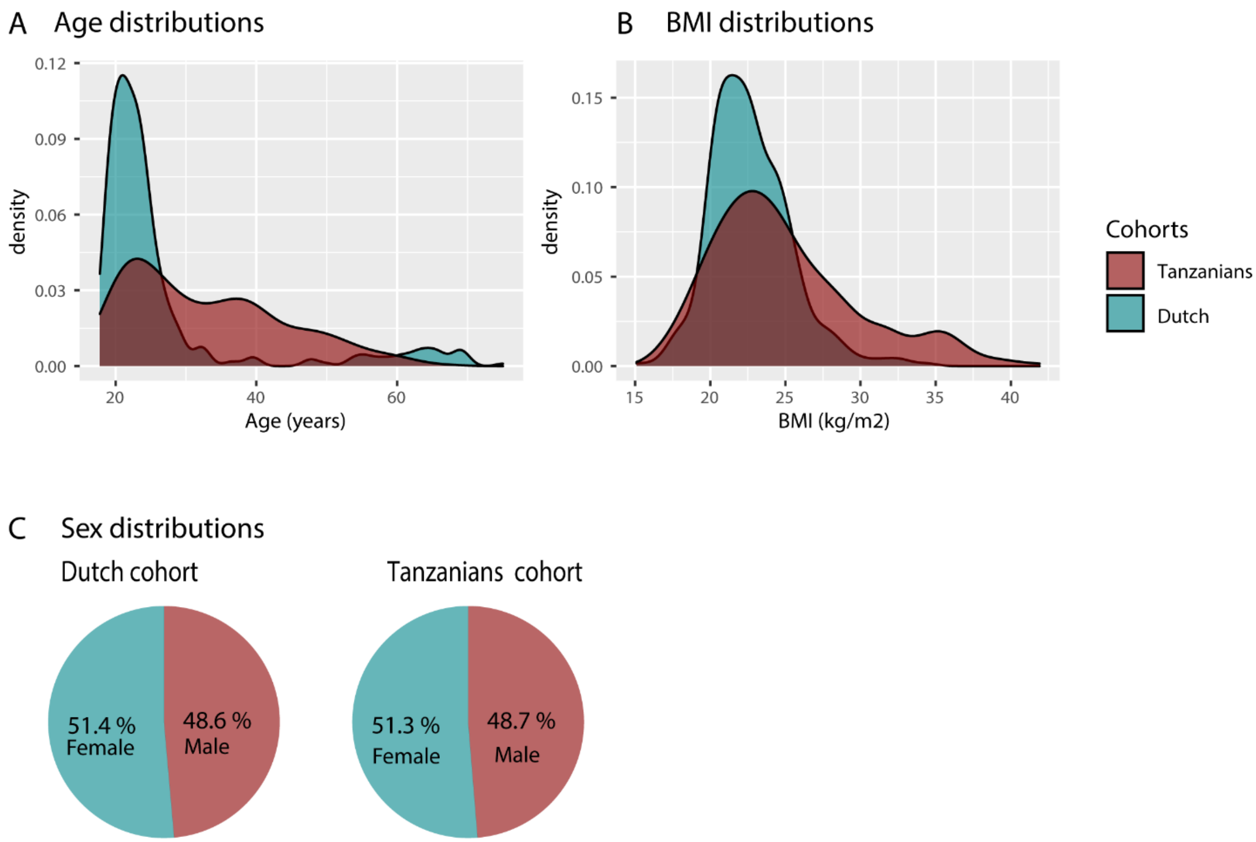
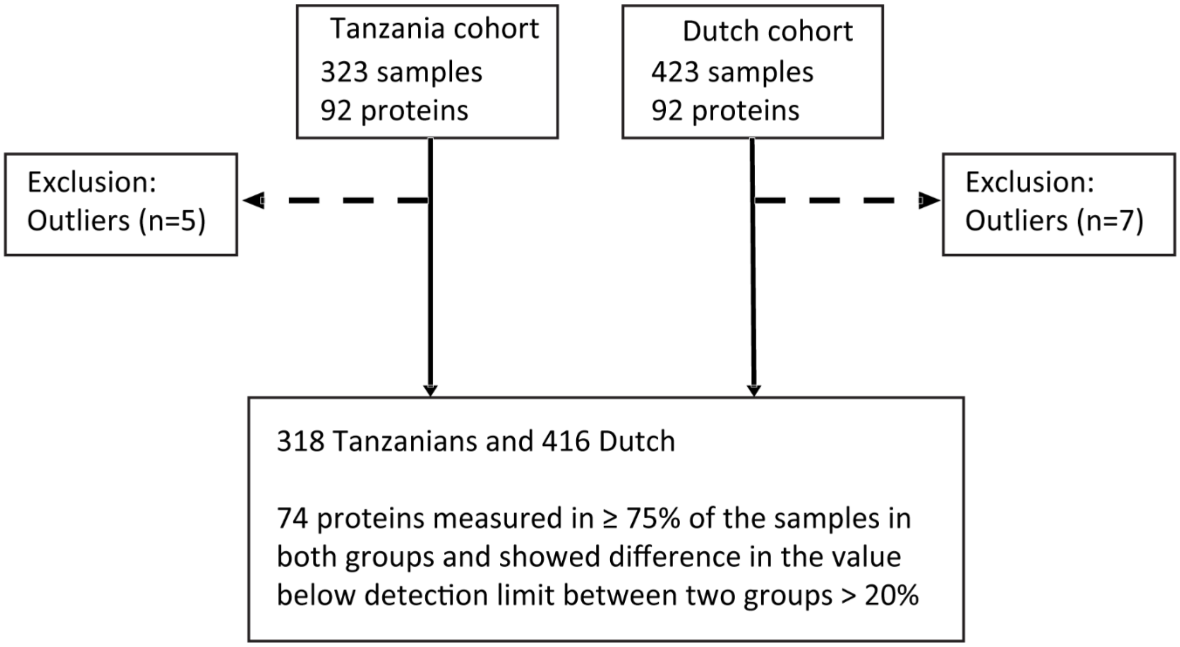
Supplemental Figures and Tables

Supplemental Figure 1



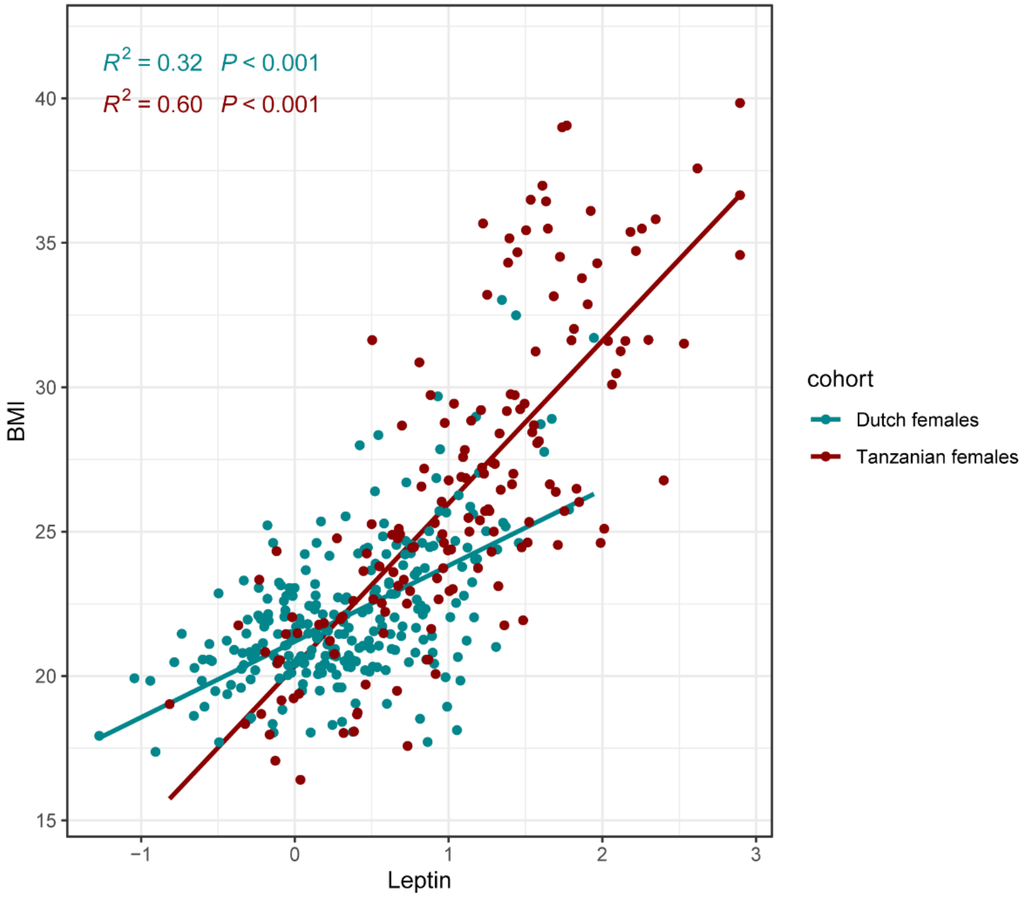
Supplemental Fig. 1: Histograms and pie charts showing the distribution of cohorts characteristics comparing Tanzanian and Dutch samples. Histograms **A)** and **B)** show the age and BMI distributions of Tanzanians and Dutch subjects, respectively**)** A pie chart comparing the gender distributions of Tanzanians and the Dutch cohort.

Supplemental Figure 2.



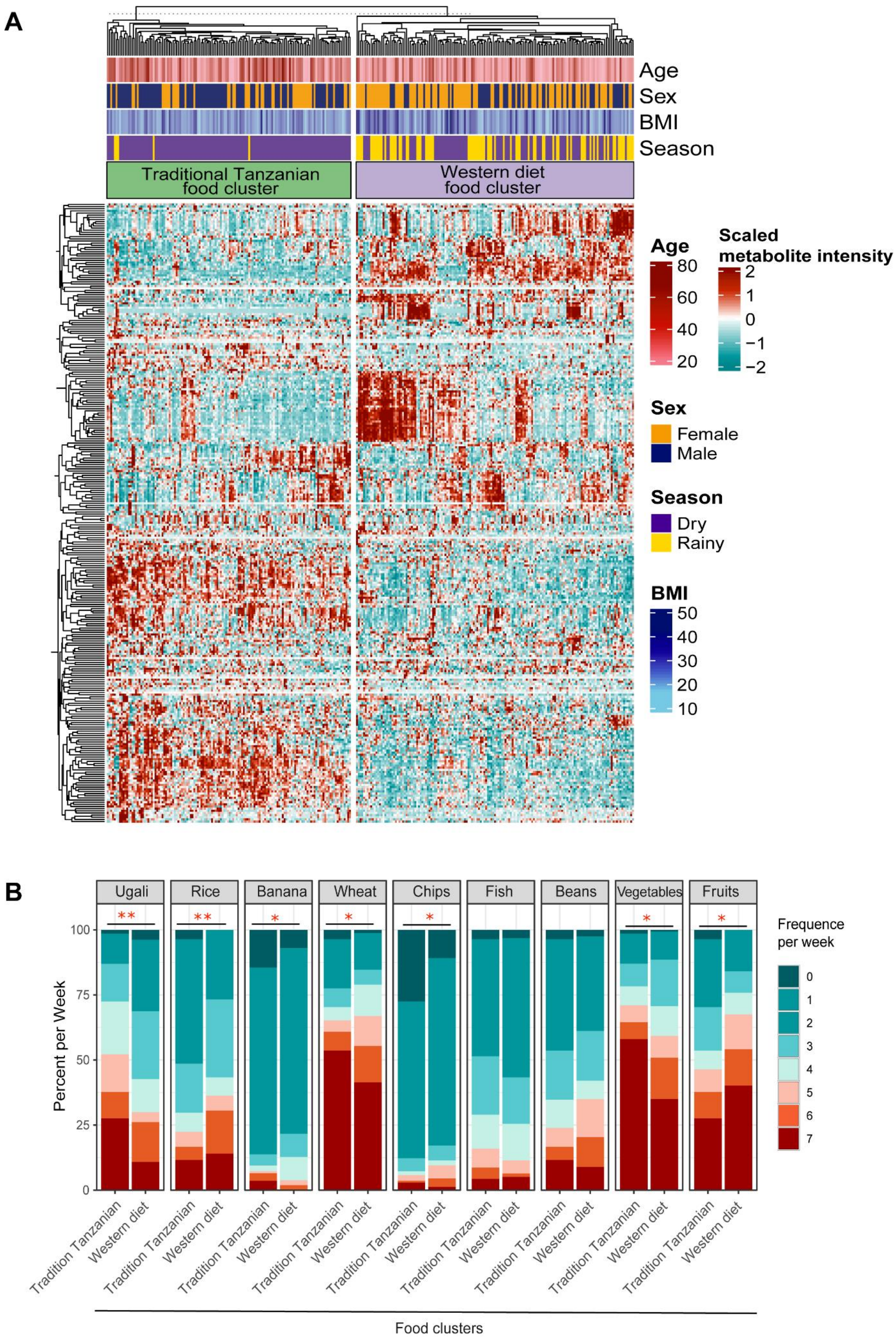
Supplemental Fig. 2: Schematic diagram showing the sample preprocessing according to the measured inflammatory protein in both cohorts

Supplemental Figure 3



Supplemental Fig. 3: Scatter plot showing the association of plasma concentration of leptin with BMI in Tanzanian females compared to Dutch females. The comparison was performed using linear regression (unadjusted) on the inversed ranked based values of leptin concentration.

Supplemental Figure 4



Supplemental Fig. 4: Food-metabolome clusters and their associations with weekly food consumption within the Tanzanian cohort. A) Heat map displaying unsupervised k-means clustering of individuals from the Tanzanian cohort (N = 318) based on food-derived metabolites (N = 298 food-derived metabolites). Food-derived metabolites from the untargeted plasma metabolome were clustered, which yielded two clusters (traditional Tanzanian food cluster and Western diet food cluster). Red and blue colors indicate higher and lower metabolite intensity, respectively. Presented are annotations for age, sex, BMI, and seasonality. **B)** Weekly food consumption of various foods across both metabolic clusters. Differences in food consumption frequency categories were tested using the chi-squared test. The colors red and blue represent higher and lower weekly consumption frequencies of specific foods, respectively; p-values 0.05 (*), 0.005 (**), and 0.0001 (***).BMI stands for body mass index.

Table S1. Differential expression analysis 300TZ vs 500FG cohort

Proteins	av_expr	Log2FC (Tanzanian/Dutch)	pvalue	fdr
4E-BP1	6,596	1,875	1,06587E-61	1,31458E-60
ADA	5,153	0,528	2,7438E-52	2,90059E-51
AXIN1	3,036	-0,728	2,19745E-18	6,50445E-18
CASP-8	3,036	-0,432	1,09865E-19	3,53478E-19
CCL11	5,900	0,679	2,95603E-64	7,29154E-63
CCL19	8,580	-0,039	0,47982057	0,514590176
CCL20	6,296	0,477	8,82426E-13	1,92058E-12
CCL23	10,041	-0,328	3,98093E-18	1,09107E-17
CCL25	5,662	0,309	1,83527E-13	4,11546E-13
CCL28	1,718	0,396	2,19671E-39	1,62556E-38
CCL3	3,380	0,557	2,92987E-10	5,55924E-10
CCL4	4,986	0,358	1,34199E-15	3,4244E-15
CD244	7,036	0,021	0,45012628	0,489843304
CD40	10,998	-0,212	2,66298E-12	5,63031E-12
CD5	5,084	0,282	1,45729E-31	8,29532E-31
CD6	5,026	0,351	1,22626E-21	4,53716E-21
CD8A	10,299	0,568	2,10053E-15	5,18131E-15
CDCP1	1,268	0,732	9,84134E-63	1,82065E-61
CSF-1	9,623	0,024	0,177665233	0,212052052
CST5	5,228	0,484	6,25405E-34	3,85666E-33
CX3CL1	5,801	-0,015	0,622772179	0,640071406
CXCL1	8,300	-0,412	2,29827E-05	3,61855E-05
CXCL10	8,337	-0,236	4,33405E-05	6,68165E-05
CXCL11	7,016	-0,042	0,557401936	0,580954131
CXCL5	9,100	-0,548	1,0954E-05	1,76217E-05
CXCL6	8,019	-0,554	2,24875E-14	5,20022E-14
CXCL9	6,578	0,111	0,076518212	0,097626684
DNER	9,268	0,398	1,34737E-82	9,97056E-81
EN-RAGE	1,757	0,380	1,86908E-14	4,46166E-14
FGF-19	8,168	0,195	0,005867961	0,008350561
FGF-21	4,470	1,325	2,38017E-31	1,25809E-30
FGF-23	2,035	0,052	0,366680053	0,408915624
Flt3L	8,594	-0,120	7,99968E-05	0,000120811
HGF	7,444	0,246	2,92717E-18	8,33117E-18
IFN-gamma	5,931	-0,053	0,531423753	0,561790825
IL-10RA	1,202	0,064	0,286528227	0,326201366
IL-10RB	5,717	0,033	0,137157208	0,166387433
IL-12B	4,981	-0,074	0,092338531	0,113884188
IL-12B	4,981	-0,074	0,092338531	0,113884188
IL-15RA	1,106	-0,107	3,12389E-08	5,63824E-08
IL-17A	1,749	0,709	1,43118E-34	9,62792E-34

IL-17C	1,177	0,713	3,0894E-76	1,14308E-74
IL-18R1	7,612	-0,011	0,722011984	0,731902559
IL10	3,493	0,397	4,32004E-12	8,88009E-12
IL18	7,416	0,396	1,84574E-18	5,69104E-18
IL6	1,390	0,193	0,001294948	0,001916523
IL7	2,779	-0,368	7,9284E-11	1,54395E-10
IL8	4,203	-0,289	1,48778E-06	2,50218E-06
LAP.TGF-beta-1	7,126	-0,199	1,82213E-07	3,21042E-07
LIF-R	3,759	0,357	3,62208E-62	5,36068E-61
MCP-1	10,375	-0,445	1,36861E-30	6,75183E-30
MCP-2	7,256	0,499	2,15356E-23	8,38757E-23
MCP-3	0,573	0,609	8,98684E-43	7,38918E-42
MCP-4	11,402	-0,100	0,064788541	0,084111439
MMP-1	8,996	-0,372	1,89878E-06	3,12243E-06
MMP-10	8,567	0,235	1,26357E-06	2,17451E-06
NT-3	3,061	-0,098	0,009930266	0,0138649
OSM	2,845	0,613	3,46374E-21	1,22056E-20
PD-L1	6,595	-0,078	0,003293161	0,004778312
SCF	9,155	0,185	5,6904E-10	1,05272E-09
SIRT2	4,459	-0,198	0,031175292	0,041944939
SLAMF1	1,389	0,278	2,015E-27	9,31936E-27
ST1A1	4,094	-0,772	8,21151E-17	2,17019E-16
STAMBP	5,359	-0,143	0,023265062	0,031881751
TGF-alpha	2,925	0,383	5,93976E-52	5,49428E-51
TNF	2,646	0,479	8,21195E-20	2,7622E-19
TNFB	4,819	0,044	0,201404932	0,236570872
TNFRSF9	6,993	0,036	0,223880475	0,258861799
TNFSF14	3,132	0,063	0,087857702	0,110194406
TRAIL	7,429	0,266	9,26858E-26	4,03456E-25
TRANCE	4,783	-0,046	0,370234416	0,408915624
TWEAK	9,311	0,294	2,99206E-25	1,23007E-24
uPA	9,893	0,218	5,83238E-11	1,16648E-10
VEGFA	9,554	-0,007	0,759842371	0,759842371

Table S2. Multivariate linear regression analysis for factors affecting protein expression in Tanzanian cohort

Proteins	Covariate	Estimate	Std.Error	t value	pvalue	fdr
4E-BP1	Age	-0,0110	0,0045	-2,4367	0,0154	0,0670
4E-BP1	Female	-0,3651	0,0919	-3,9715	0,0001	0,0012
4E-BP1	BMI	0,0185	0,0101	1,8282	0,0685	0,1964
4E-BP1	Residency_AreaUrban	0,0551	0,1120	0,4921	0,6230	0,7841
4E-BP1	Seasonality_Rainy	0,1432	0,0950	1,5080	0,1326	0,3170
ADA	Age	-0,0055	0,0028	-1,9776	0,0489	0,1588
ADA	Female	-0,2835	0,0570	-4,9718	0,0000	0,0000
ADA	BMI	0,0174	0,0063	2,7777	0,0058	0,0330
ADA	Residency_AreaUrban	-0,1337	0,0695	-1,9248	0,0552	0,1709
ADA	Seasonality_Rainy	-0,0336	0,0589	-0,5711	0,5683	0,7605
AXIN1	Age	-0,0083	0,0062	-1,3467	0,1791	0,3743
AXIN1	Female	-0,3679	0,1264	-2,9113	0,0039	0,0267
AXIN1	BMI	0,0305	0,0139	2,1910	0,0292	0,1080
AXIN1	Residency_AreaUrban	-0,2318	0,1539	-1,5062	0,1330	0,3170
AXIN1	Seasonality_Rainy	-0,0027	0,1305	-0,0204	0,9837	0,9918
CASP-8	Age	-0,0046	0,0036	-1,2783	0,2021	0,4086
CASP-8	Female	-0,3861	0,0739	-5,2241	0,0000	0,0000
CASP-8	BMI	0,0215	0,0081	2,6435	0,0086	0,0449
CASP-8	Residency_AreaUrban	-0,0502	0,0900	-0,5573	0,5777	0,7641
CASP-8	Seasonality_Rainy	-0,0569	0,0764	-0,7457	0,4564	0,6701
CCL11	Age	0,0203	0,0026	7,7792	0,0000	0,0000
CCL11	Female	-0,1850	0,0532	-3,4780	0,0006	0,0058
CCL11	BMI	-0,0111	0,0059	-1,8880	0,0600	0,1808
CCL11	Residency_AreaUrban	-0,0119	0,0648	-0,1830	0,8549	0,9390
CCL11	Seasonality_Rainy	0,1023	0,0550	1,8616	0,0636	0,1868
CCL19	Age	-0,0025	0,0043	-0,5715	0,5681	0,7605
CCL19	Female	-0,0078	0,0877	-0,0885	0,9295	0,9688
CCL19	BMI	0,0053	0,0097	0,5525	0,5810	0,7641
CCL19	Residency_AreaUrban	0,0965	0,1068	0,9031	0,3672	0,5830
CCL19	Seasonality_Rainy	-0,0631	0,0906	-0,6969	0,4864	0,7003
CCL20	Age	-0,0076	0,0051	-1,5084	0,1325	0,3170
CCL20	Female	-0,0159	0,1034	-0,1542	0,8775	0,9487
CCL20	BMI	-0,0021	0,0114	-0,1887	0,8504	0,9390
CCL20	Residency_AreaUrban	-0,3156	0,1259	-2,5068	0,0127	0,0584
CCL20	Seasonality_Rainy	0,1651	0,1068	1,5463	0,1230	0,2995
CCL23	Age	0,0035	0,0029	1,2000	0,2311	0,4453
CCL23	Female	-0,1330	0,0594	-2,2398	0,0258	0,0984
CCL23	BMI	0,0047	0,0065	0,7207	0,4717	0,6844
CCL23	Residency_AreaUrban	-0,0826	0,0723	-1,1420	0,2543	0,4674
CCL23	Seasonality_Rainy	-0,0856	0,0613	-1,3948	0,1641	0,3571
CCL25	Age	0,0176	0,0029	6,0714	0,0000	0,0000
CCL25	Female	-0,2490	0,0593	-4,2006	0,0000	0,0006
CCL25	BMI	-0,0113	0,0065	-1,7294	0,0847	0,2239
CCL25	Residency_AreaUrban	-0,0393	0,0722	-0,5438	0,5870	0,7641
CCL25	Seasonality_Rainy	-0,0320	0,0612	-0,5227	0,6015	0,7728
CCL28	Age	0,0099	0,0023	4,3804	0,0000	0,0003
CCL28	Female	0,2375	0,0463	5,1300	0,0000	0,0000
CCL28	BMI	-0,0137	0,0051	-2,6886	0,0076	0,0411
CCL28	Residency_AreaUrban	0,0027	0,0564	0,0474	0,9622	0,9835
CCL28	Seasonality_Rainy	0,0225	0,0478	0,4704	0,6384	0,7900
CCL3	Age	-0,0014	0,0093	-0,1473	0,8830	0,9487
CCL3	Female	0,0722	0,1899	0,3801	0,7041	0,8377
CCL3	BMI	0,0290	0,0209	1,3885	0,1660	0,3575

CCL3	Residency_AreaUrban	-0,3653	0,2312	-1,5797	0,1152	0,2900
CCL3	Seasonality_Rainy	-0,0086	0,1961	-0,0441	0,9649	0,9835
CCL4	Age	-0,0016	0,0034	-0,4818	0,6303	0,7852
CCL4	Female	-0,2893	0,0695	-4,1659	0,0000	0,0007
CCL4	BMI	0,0220	0,0076	2,8746	0,0043	0,0282
CCL4	Residency_AreaUrban	-0,0643	0,0846	-0,7600	0,4479	0,6602
CCL4	Seasonality_Rainy	0,1761	0,0717	2,4538	0,0147	0,0647
CD244	Age	0,0000	0,0021	-0,0016	0,9987	0,9987
CD244	Female	-0,1125	0,0430	-2,6167	0,0093	0,0472
CD244	BMI	0,0027	0,0047	0,5605	0,5756	0,7641
CD244	Residency_AreaUrban	-0,0125	0,0524	-0,2379	0,8121	0,9189
CD244	Seasonality_Rainy	-0,0607	0,0444	-1,3676	0,1724	0,3625
CD40	Age	0,0059	0,0019	3,0564	0,0024	0,0196
CD40	Female	-0,1119	0,0398	-2,8146	0,0052	0,0310
CD40	BMI	0,0104	0,0044	2,3809	0,0179	0,0727
CD40	Residency_AreaUrban	-0,0510	0,0484	-1,0538	0,2928	0,5039
CD40	Seasonality_Rainy	-0,1233	0,0411	-3,0016	0,0029	0,0219
CD5	Age	-0,0047	0,0017	-2,6736	0,0079	0,0417
CD5	Female	0,0154	0,0356	0,4344	0,6643	0,8085
CD5	BMI	0,0042	0,0039	1,0804	0,2808	0,4901
CD5	Residency_AreaUrban	0,0156	0,0433	0,3596	0,7194	0,8531
CD5	Seasonality_Rainy	-0,0286	0,0367	-0,7795	0,4362	0,6509
CD6	Age	0,0014	0,0024	0,5776	0,5639	0,7605
CD6	Female	-0,0736	0,0497	-1,4801	0,1399	0,3255
CD6	BMI	0,0036	0,0055	0,6617	0,5086	0,7240
CD6	Residency_AreaUrban	0,0486	0,0605	0,8036	0,4223	0,6429
CD6	Seasonality_Rainy	-0,0261	0,0513	-0,5093	0,6109	0,7767
CD8A	Age	-0,0023	0,0050	-0,4563	0,6485	0,7954
CD8A	Female	0,0612	0,1016	0,6021	0,5476	0,7531
CD8A	BMI	-0,0162	0,0112	-1,4494	0,1482	0,3304
CD8A	Residency_AreaUrban	0,1924	0,1237	1,5558	0,1208	0,2993
CD8A	Seasonality_Rainy	-0,0362	0,1049	-0,3446	0,7306	0,8637
CDCP1	Age	0,0285	0,0034	8,4002	0,0000	0,0000
CDCP1	Female	-0,2371	0,0693	-3,4227	0,0007	0,0067
CDCP1	BMI	0,0176	0,0076	2,3073	0,0217	0,0863
CDCP1	Residency_AreaUrban	-0,0066	0,0844	-0,0778	0,9381	0,9743
CDCP1	Seasonality_Rainy	-0,1726	0,0716	-2,4118	0,0165	0,0684
CSF-1	Age	0,0004	0,0013	0,3111	0,7559	0,8854
CSF-1	Female	0,0542	0,0259	2,0891	0,0375	0,1285
CSF-1	BMI	0,0098	0,0029	3,4312	0,0007	0,0066
CSF-1	Residency_AreaUrban	0,0090	0,0316	0,2841	0,7766	0,8955
CSF-1	Seasonality_Rainy	-0,0116	0,0268	-0,4312	0,6666	0,8087
CST5	Age	0,0093	0,0032	2,9078	0,0039	0,0267
CST5	Female	-0,2641	0,0655	-4,0298	0,0001	0,0010
CST5	BMI	-0,0114	0,0072	-1,5844	0,1141	0,2892
CST5	Residency_AreaUrban	-0,0863	0,0798	-1,0808	0,2806	0,4901
CST5	Seasonality_Rainy	-0,1205	0,0677	-1,7791	0,0762	0,2108
CX3CL1	Age	0,0026	0,0022	1,1725	0,2419	0,4566
CX3CL1	Female	0,0283	0,0456	0,6213	0,5348	0,7468
CX3CL1	BMI	-0,0092	0,0050	-1,8422	0,0664	0,1929
CX3CL1	Residency_AreaUrban	-0,0810	0,0556	-1,4575	0,1460	0,3274
CX3CL1	Seasonality_Rainy	0,0238	0,0471	0,5042	0,6145	0,7767
CXCL1	Age	-0,0093	0,0085	-1,0903	0,2764	0,4871
CXCL1	Female	-0,0879	0,1746	-0,5034	0,6151	0,7767
CXCL1	BMI	0,0239	0,0192	1,2432	0,2147	0,4295
CXCL1	Residency_AreaUrban	-0,2043	0,2126	-0,9610	0,3373	0,5481

CXCL1	Seasonality_Rainy	0,5050	0,1803	2,8002	0,0054	0,0314
CXCL10	Age	0,0008	0,0042	0,1875	0,8514	0,9390
CXCL10	Female	0,0228	0,0858	0,2654	0,7909	0,9039
CXCL10	BMI	0,0189	0,0094	1,9994	0,0464	0,1534
CXCL10	Residency_AreaUrban	-0,0012	0,1045	-0,0111	0,9912	0,9943
CXCL10	Seasonality_Rainy	0,1698	0,0887	1,9147	0,0564	0,1726
CXCL11	Age	0,0017	0,0061	0,2834	0,7770	0,8955
CXCL11	Female	0,2232	0,1253	1,7819	0,0757	0,2108
CXCL11	BMI	0,0100	0,0138	0,7286	0,4668	0,6800
CXCL11	Residency_AreaUrban	0,0176	0,1526	0,1155	0,9081	0,9600
CXCL11	Seasonality_Rainy	0,2707	0,1294	2,0915	0,0373	0,1285
CXCL5	Age	-0,0124	0,0108	-1,1512	0,2505	0,4661
CXCL5	Female	0,2685	0,2200	1,2202	0,2233	0,4395
CXCL5	BMI	0,0466	0,0242	1,9228	0,0554	0,1709
CXCL5	Residency_AreaUrban	-0,5563	0,2680	-2,0759	0,0387	0,1314
CXCL5	Seasonality_Rainy	0,7667	0,2273	3,3730	0,0008	0,0076
CXCL6	Age	-0,0081	0,0067	-1,2108	0,2269	0,4418
CXCL6	Female	-0,1400	0,1360	-1,0293	0,3041	0,5162
CXCL6	BMI	0,0169	0,0150	1,1303	0,2592	0,4725
CXCL6	Residency_AreaUrban	-0,2162	0,1657	-1,3050	0,1928	0,3963
CXCL6	Seasonality_Rainy	0,4643	0,1405	3,3045	0,0011	0,0094
CXCL9	Age	0,0155	0,0048	3,2124	0,0015	0,0120
CXCL9	Female	-0,2947	0,0986	-2,9879	0,0030	0,0224
CXCL9	BMI	-0,0062	0,0109	-0,5708	0,5685	0,7605
CXCL9	Residency_AreaUrban	0,0154	0,1201	0,1285	0,8978	0,9570
CXCL9	Seasonality_Rainy	0,0627	0,1019	0,6154	0,5387	0,7482
DNER	Age	0,0015	0,0013	1,2154	0,2251	0,4408
DNER	Female	-0,1608	0,0258	-6,2290	0,0000	0,0000
DNER	BMI	-0,0055	0,0028	-1,9256	0,0551	0,1709
DNER	Residency_AreaUrban	-0,0294	0,0314	-0,9363	0,3499	0,5653
DNER	Seasonality_Rainy	-0,1048	0,0267	-3,9307	0,0001	0,0013
EN-RAge	Age	-0,0103	0,0036	-2,8670	0,0044	0,0282
EN-RAge	Female	-0,2638	0,0731	-3,6076	0,0004	0,0039
EN-RAge	BMI	0,0216	0,0080	2,6783	0,0078	0,0417
EN-RAge	Residency_AreaUrban	0,0577	0,0891	0,6474	0,5179	0,7335
EN-RAge	Seasonality_Rainy	-0,1919	0,0755	-2,5406	0,0116	0,0562
FGF-19	Age	0,0189	0,0051	3,6715	0,0003	0,0033
FGF-19	Female	-0,2616	0,1050	-2,4907	0,0133	0,0599
FGF-19	BMI	-0,0194	0,0116	-1,6768	0,0946	0,2430
FGF-19	Residency_AreaUrban	0,0508	0,1279	0,3968	0,6918	0,8257
FGF-19	Seasonality_Rainy	0,0057	0,1085	0,0527	0,9580	0,9819
FGF-21	Age	0,0239	0,0084	2,8518	0,0046	0,0291
FGF-21	Female	-0,2658	0,1714	-1,5511	0,1219	0,2993
FGF-21	BMI	-0,0182	0,0189	-0,9668	0,3344	0,5475
FGF-21	Residency_AreaUrban	-0,2726	0,2087	-1,3063	0,1924	0,3963
FGF-21	Seasonality_Rainy	-0,1074	0,1770	-0,6070	0,5443	0,7515
FGF-23	Age	0,0016	0,0055	0,2870	0,7743	0,8955
FGF-23	Female	0,5069	0,1131	4,4807	0,0000	0,0002
FGF-23	BMI	-0,0013	0,0125	-0,1063	0,9154	0,9644
FGF-23	Residency_AreaUrban	0,1908	0,1378	1,3847	0,1671	0,3575
FGF-23	Seasonality_Rainy	-0,0788	0,1169	-0,6744	0,5005	0,7178
Flt3L	Age	0,0086	0,0024	3,6254	0,0003	0,0038
Flt3L	Female	0,1054	0,0487	2,1626	0,0313	0,1136
Flt3L	BMI	0,0064	0,0054	1,1871	0,2361	0,4479
Flt3L	Residency_AreaUrban	-0,0166	0,0593	-0,2804	0,7794	0,8955
Flt3L	Seasonality_Rainy	-0,0270	0,0503	-0,5364	0,5921	0,7659

HGF	Age	0,0009	0,0019	0,4862	0,6271	0,7852
HGF	Female	-0,0367	0,0378	-0,9696	0,3330	0,5475
HGF	BMI	0,0200	0,0042	4,8000	0,0000	0,0001
HGF	Residency_AreaUrban	-0,0305	0,0461	-0,6615	0,5088	0,7240
HGF	Seasonality_Rainy	0,0662	0,0391	1,6936	0,0913	0,2363
IFN-gamma	Age	-0,0054	0,0071	-0,7716	0,4409	0,6527
IFN-gamma	Female	0,0768	0,1443	0,5326	0,5947	0,7667
IFN-gamma	BMI	0,0223	0,0159	1,4069	0,1604	0,3534
IFN-gamma	Residency_AreaUrban	0,1390	0,1757	0,7913	0,4294	0,6442
IFN-gamma	Seasonality_Rainy	0,1238	0,1490	0,8306	0,4069	0,6272
IL-10RA	Age	-0,0049	0,0046	-1,0700	0,2854	0,4958
IL-10RA	Female	-0,0216	0,0930	-0,2325	0,8163	0,9193
IL-10RA	BMI	-0,0018	0,0102	-0,1751	0,8611	0,9390
IL-10RA	Residency_AreaUrban	0,0205	0,1133	0,1811	0,8564	0,9390
IL-10RA	Seasonality_Rainy	0,1430	0,0961	1,4875	0,1379	0,3229
IL-10RB	Age	0,0011	0,0017	0,6331	0,5271	0,7388
IL-10RB	Female	-0,0999	0,0352	-2,8425	0,0048	0,0294
IL-10RB	BMI	0,0067	0,0039	1,7396	0,0829	0,2207
IL-10RB	Residency_AreaUrban	-0,0174	0,0428	-0,4064	0,6847	0,8226
IL-10RB	Seasonality_Rainy	-0,0910	0,0363	-2,5047	0,0128	0,0584
IL-12B	Age	-0,0037	0,0033	-1,1400	0,2552	0,4674
IL-12B	Female	0,3557	0,0672	5,2958	0,0000	0,0000
IL-12B	BMI	0,0155	0,0074	2,0982	0,0367	0,1281
IL-12B	Residency_AreaUrban	0,0806	0,0818	0,9853	0,3253	0,5397
IL-12B	Seasonality_Rainy	-0,0512	0,0694	-0,7374	0,4614	0,6748
IL-15RA	Age	0,0019	0,0015	1,3218	0,1872	0,3891
IL-15RA	Female	-0,0979	0,0301	-3,2508	0,0013	0,0110
IL-15RA	BMI	0,0026	0,0033	0,7959	0,4267	0,6442
IL-15RA	Residency_AreaUrban	-0,0023	0,0367	-0,0630	0,9498	0,9789
IL-15RA	Seasonality_Rainy	0,0012	0,0311	0,0379	0,9698	0,9845
IL-17A	Age	0,0068	0,0050	1,3697	0,1718	0,3625
IL-17A	Female	0,2469	0,1015	2,4317	0,0156	0,0671
IL-17A	BMI	-0,0164	0,0112	-1,4672	0,1433	0,3273
IL-17A	Residency_AreaUrban	-0,0506	0,1237	-0,4089	0,6829	0,8226
IL-17A	Seasonality_Rainy	-0,0598	0,1049	-0,5696	0,5693	0,7605
IL-17C	Age	0,0032	0,0030	1,0371	0,3005	0,5123
IL-17C	Female	-0,0690	0,0623	-1,1075	0,2689	0,4845
IL-17C	BMI	0,0007	0,0069	0,0971	0,9227	0,9644
IL-17C	Residency_AreaUrban	-0,0705	0,0759	-0,9293	0,3535	0,5686
IL-17C	Seasonality_Rainy	-0,0671	0,0644	-1,0434	0,2976	0,5097
IL-18R1	Age	-0,0009	0,0022	-0,4153	0,6782	0,8201
IL-18R1	Female	-0,0382	0,0452	-0,8455	0,3985	0,6169
IL-18R1	BMI	0,0217	0,0050	4,3724	0,0000	0,0003
IL-18R1	Residency_AreaUrban	0,0014	0,0550	0,0254	0,9798	0,9905
IL-18R1	Seasonality_Rainy	-0,0689	0,0467	-1,4768	0,1407	0,3255
IL10	Age	0,0086	0,0046	1,8718	0,0622	0,1840
IL10	Female	-0,1605	0,0934	-1,7185	0,0867	0,2275
IL10	BMI	-0,0056	0,0103	-0,5415	0,5886	0,7641
IL10	Residency_AreaUrban	0,1248	0,1137	1,0971	0,2734	0,4863
IL10	Seasonality_Rainy	0,0300	0,0965	0,3107	0,7562	0,8854
IL18	Age	0,0045	0,0037	1,2065	0,2285	0,4427
IL18	Female	-0,3011	0,0756	-3,9832	0,0001	0,0012
IL18	BMI	0,0179	0,0083	2,1557	0,0319	0,1136
IL18	Residency_AreaUrban	-0,0710	0,0921	-0,7715	0,4410	0,6527
IL18	Seasonality_Rainy	-0,1734	0,0781	-2,2200	0,0271	0,1014
IL6	Age	0,0056	0,0051	1,1056	0,2698	0,4845

IL6	Female	-0,4481	0,1038	-4,3173	0,0000	0,0004
IL6	BMI	0,0403	0,0114	3,5241	0,0005	0,0050
IL6	Residency_AreaUrban	-0,0381	0,1264	-0,3011	0,7636	0,8894
IL6	Seasonality_Rainy	0,0551	0,1072	0,5141	0,6075	0,7767
IL7	Age	-0,0020	0,0044	-0,4553	0,6492	0,7954
IL7	Female	-0,0650	0,0908	-0,7159	0,4746	0,6859
IL7	BMI	0,0115	0,0100	1,1473	0,2521	0,4664
IL7	Residency_AreaUrban	0,0903	0,1105	0,8166	0,4148	0,6368
IL7	Seasonality_Rainy	0,0066	0,0937	0,0702	0,9441	0,9757
IL8	Age	0,0007	0,0061	0,1228	0,9024	0,9570
IL8	Female	-0,1259	0,1237	-1,0182	0,3094	0,5196
IL8	BMI	0,0025	0,0136	0,1802	0,8571	0,9390
IL8	Residency_AreaUrban	-0,2836	0,1506	-1,8833	0,0606	0,1808
IL8	Seasonality_Rainy	0,1179	0,1277	0,9227	0,3569	0,5716
LAP.TGF-beta-1	Age	0,0011	0,0026	0,4405	0,6599	0,8058
LAP.TGF-beta-1	Female	0,0078	0,0521	0,1489	0,8817	0,9487
LAP.TGF-beta-1	BMI	0,0068	0,0057	1,1921	0,2341	0,4465
LAP.TGF-beta-1	Residency_AreaUrban	-0,0372	0,0635	-0,5858	0,5584	0,7605
LAP.TGF-beta-1	Seasonality_Rainy	0,0701	0,0538	1,3020	0,1939	0,3963
LIF-R	Age	0,0027	0,0014	2,0277	0,0434	0,1461
LIF-R	Female	-0,0244	0,0277	-0,8836	0,3776	0,5927
LIF-R	BMI	-0,0084	0,0030	-2,7507	0,0063	0,0353
LIF-R	Residency_AreaUrban	-0,0285	0,0337	-0,8461	0,3981	0,6169
LIF-R	Seasonality_Rainy	-0,0693	0,0286	-2,4268	0,0158	0,0672
MCP-1	Age	0,0080	0,0030	2,6224	0,0092	0,0471
MCP-1	Female	-0,1336	0,0620	-2,1550	0,0319	0,1136
MCP-1	BMI	0,0161	0,0068	2,3651	0,0186	0,0750
MCP-1	Residency_AreaUrban	-0,0174	0,0755	-0,2310	0,8174	0,9193
MCP-1	Seasonality_Rainy	0,3085	0,0641	4,8153	0,0000	0,0001
MCP-2	Age	0,0020	0,0035	0,5716	0,5680	0,7605
MCP-2	Female	-0,1400	0,0713	-1,9639	0,0504	0,1622
MCP-2	BMI	0,0282	0,0078	3,5886	0,0004	0,0041
MCP-2	Residency_AreaUrban	-0,0223	0,0868	-0,2570	0,7974	0,9071
MCP-2	Seasonality_Rainy	0,1685	0,0736	2,2881	0,0228	0,0897
MCP-3	Age	0,0062	0,0035	1,7708	0,0776	0,2108
MCP-3	Female	-0,0565	0,0715	-0,7902	0,4300	0,6442
MCP-3	BMI	0,0298	0,0079	3,7882	0,0002	0,0022
MCP-3	Residency_AreaUrban	0,0975	0,0871	1,1194	0,2638	0,4785
MCP-3	Seasonality_Rainy	-0,0152	0,0739	-0,2059	0,8370	0,9385
MCP-4	Age	0,0091	0,0046	1,9544	0,0515	0,1644
MCP-4	Female	0,0169	0,0949	0,1783	0,8586	0,9390
MCP-4	BMI	0,0266	0,0104	2,5476	0,0113	0,0559
MCP-4	Residency_AreaUrban	0,0463	0,1156	0,4002	0,6893	0,8254
MCP-4	Seasonality_Rainy	0,5117	0,0981	5,2188	0,0000	0,0000
MMP-1	Age	0,0113	0,0064	1,7701	0,0777	0,2108
MMP-1	Female	-0,3555	0,1309	-2,7153	0,0070	0,0386
MMP-1	BMI	0,0253	0,0144	1,7572	0,0799	0,2141
MMP-1	Residency_AreaUrban	0,0195	0,1595	0,1224	0,9026	0,9570
MMP-1	Seasonality_Rainy	0,3948	0,1353	2,9190	0,0038	0,0267
MMP-10	Age	0,0104	0,0037	2,8036	0,0054	0,0314
MMP-10	Female	0,0117	0,0757	0,1546	0,8772	0,9487
MMP-10	BMI	-0,0247	0,0083	-2,9664	0,0032	0,0235
MMP-10	Residency_AreaUrban	0,0235	0,0922	0,2546	0,7992	0,9071
MMP-10	Seasonality_Rainy	-0,1383	0,0782	-1,7678	0,0781	0,2108
NT-3	Age	-0,0024	0,0028	-0,8508	0,3955	0,6169
NT-3	Female	-0,0565	0,0582	-0,9710	0,3323	0,5475

NT-3	BMI	-0,0065	0,0064	-1,0206	0,3082	0,5196
NT-3	Residency_AreaUrban	-0,0123	0,0709	-0,1729	0,8629	0,9390
NT-3	Seasonality_Rainy	-0,0696	0,0601	-1,1577	0,2479	0,4655
OPG	Age	0,0033	0,0027	1,2266	0,2209	0,4371
OPG	Female	0,0655	0,0548	1,1951	0,2329	0,4465
OPG	BMI	-0,0003	0,0060	-0,0555	0,9558	0,9819
OPG	Residency_AreaUrban	-0,1601	0,0667	-2,3982	0,0171	0,0701
OPG	Seasonality_Rainy	0,0620	0,0566	1,0942	0,2747	0,4863
OSM	Age	-0,0131	0,0046	-2,8258	0,0050	0,0304
OSM	Female	-0,0609	0,0949	-0,6419	0,5214	0,7335
OSM	BMI	0,0316	0,0104	3,0233	0,0027	0,0209
OSM	Residency_AreaUrban	-0,0230	0,1156	-0,1989	0,8425	0,9390
OSM	Seasonality_Rainy	0,1431	0,0981	1,4590	0,1456	0,3274
PD-L1	Age	-0,0024	0,0021	-1,1508	0,2507	0,4661
PD-L1	Female	-0,1755	0,0433	-4,0532	0,0001	0,0009
PD-L1	BMI	0,0028	0,0048	0,5913	0,5547	0,7602
PD-L1	Residency_AreaUrban	-0,0466	0,0527	-0,8827	0,3781	0,5927
PD-L1	Seasonality_Rainy	-0,0808	0,0447	-1,8055	0,0720	0,2048
SCF	Age	-0,0019	0,0019	-1,0161	0,3104	0,5196
SCF	Female	0,1305	0,0386	3,3764	0,0008	0,0076
SCF	BMI	-0,0129	0,0043	-3,0420	0,0025	0,0201
SCF	Residency_AreaUrban	-0,0888	0,0471	-1,8867	0,0601	0,1808
SCF	Seasonality_Rainy	-0,0594	0,0399	-1,4890	0,1375	0,3229
SIRT2	Age	-0,0154	0,0069	-2,2255	0,0268	0,1010
SIRT2	Female	-0,3578	0,1418	-2,5241	0,0121	0,0574
SIRT2	BMI	0,0385	0,0156	2,4665	0,0142	0,0632
SIRT2	Residency_AreaUrban	-0,0948	0,1727	-0,5489	0,5835	0,7641
SIRT2	Seasonality_Rainy	0,1293	0,1465	0,8830	0,3779	0,5927
SLAMF1	Age	0,0071	0,0017	4,1522	0,0000	0,0007
SLAMF1	Female	-0,0880	0,0348	-2,5278	0,0120	0,0574
SLAMF1	BMI	-0,0053	0,0038	-1,3847	0,1671	0,3575
SLAMF1	Residency_AreaUrban	0,0452	0,0424	1,0656	0,2874	0,4970
SLAMF1	Seasonality_Rainy	0,0013	0,0360	0,0361	0,9712	0,9845
ST1A1	Age	-0,0136	0,0069	-1,9771	0,0489	0,1588
ST1A1	Female	-0,3389	0,1401	-2,4198	0,0161	0,0677
ST1A1	BMI	0,0284	0,0154	1,8399	0,0667	0,1929
ST1A1	Residency_AreaUrban	-0,1876	0,1706	-1,0999	0,2722	0,4863
ST1A1	Seasonality_Rainy	0,0383	0,1447	0,2646	0,7915	0,9039
STAMBP	Age	-0,0102	0,0048	-2,1209	0,0347	0,1223
STAMBP	Female	-0,4075	0,0980	-4,1579	0,0000	0,0007
STAMBP	BMI	0,0243	0,0108	2,2493	0,0252	0,0971
STAMBP	Residency_AreaUrban	-0,0945	0,1194	-0,7921	0,4289	0,6442
STAMBP	Seasonality_Rainy	0,0817	0,1012	0,8068	0,4204	0,6427
TGF-alpha	Age	-0,0021	0,0022	-0,9601	0,3377	0,5481
TGF-alpha	Female	-0,0647	0,0440	-1,4698	0,1426	0,3273
TGF-alpha	BMI	0,0076	0,0048	1,5753	0,1162	0,2905
TGF-alpha	Residency_AreaUrban	0,0172	0,0536	0,3209	0,7485	0,8820
TGF-alpha	Seasonality_Rainy	0,0449	0,0455	0,9869	0,3245	0,5397
TNF	Age	-0,0004	0,0043	-0,0973	0,9226	0,9644
TNF	Female	-0,0418	0,0879	-0,4755	0,6348	0,7882
TNF	BMI	0,0088	0,0097	0,9072	0,3650	0,5821
TNF	Residency_AreaUrban	-0,1320	0,1071	-1,2325	0,2187	0,4351
TNF	Seasonality_Rainy	0,0438	0,0908	0,4824	0,6298	0,7852
TNFB	Age	-0,0087	0,0021	-4,2230	0,0000	0,0006
TNFB	Female	0,2140	0,0420	5,1003	0,0000	0,0000
TNFB	BMI	0,0069	0,0046	1,5037	0,1337	0,3170

TNFB	Residency_AreaUrban	-0,0745	0,0511	-1,4584	0,1457	0,3274
TNFB	Seasonality_Rainy	-0,0672	0,0433	-1,5501	0,1221	0,2993
TNFRSF9	Age	-0,0034	0,0024	-1,4342	0,1525	0,3379
TNFRSF9	Female	-0,0943	0,0487	-1,9355	0,0538	0,1703
TNFRSF9	BMI	0,0004	0,0054	0,0752	0,9401	0,9743
TNFRSF9	Residency_AreaUrban	-0,0766	0,0593	-1,2912	0,1976	0,4017
TNFRSF9	Seasonality_Rainy	-0,0828	0,0503	-1,6456	0,1009	0,2573
TNFSF14	Age	-0,0047	0,0028	-1,7100	0,0883	0,2300
TNFSF14	Female	-0,0364	0,0567	-0,6421	0,5213	0,7335
TNFSF14	BMI	0,0282	0,0062	4,5176	0,0000	0,0002
TNFSF14	Residency_AreaUrban	-0,0098	0,0691	-0,1415	0,8875	0,9491
TNFSF14	Seasonality_Rainy	0,0319	0,0586	0,5451	0,5861	0,7641
TRAIL	Age	-0,0047	0,0016	-2,8672	0,0044	0,0282
TRAIL	Female	-0,1547	0,0334	-4,6272	0,0000	0,0001
TRAIL	BMI	0,0083	0,0037	2,2536	0,0249	0,0970
TRAIL	Residency_AreaUrban	-0,0221	0,0407	-0,5424	0,5879	0,7641
TRAIL	Seasonality_Rainy	-0,0050	0,0345	-0,1453	0,8846	0,9487
TRANCE	Age	-0,0185	0,0036	-5,0800	0,0000	0,0000
TRANCE	Female	-0,0457	0,0745	-0,6136	0,5400	0,7482
TRANCE	BMI	0,0265	0,0082	3,2283	0,0014	0,0116
TRANCE	Residency_AreaUrban	0,0415	0,0907	0,4576	0,6476	0,7954
TRANCE	Seasonality_Rainy	-0,2216	0,0769	-2,8808	0,0042	0,0282
TWEAK	Age	-0,0048	0,0019	-2,5039	0,0128	0,0584
TWEAK	Female	-0,0843	0,0391	-2,1566	0,0318	0,1136
TWEAK	BMI	0,0008	0,0043	0,1837	0,8543	0,9390
TWEAK	Residency_AreaUrban	-0,0850	0,0476	-1,7840	0,0754	0,2108
TWEAK	Seasonality_Rainy	-0,0204	0,0404	-0,5038	0,6148	0,7767
uPA	Age	-0,0047	0,0027	-1,7723	0,0773	0,2108
uPA	Female	-0,0761	0,0545	-1,3960	0,1637	0,3571
uPA	BMI	0,0076	0,0060	1,2719	0,2044	0,4109
uPA	Residency_AreaUrban	-0,1732	0,0664	-2,6079	0,0095	0,0477
uPA	Seasonality_Rainy	-0,0058	0,0563	-0,1023	0,9186	0,9644
VEGFA	Age	0,0036	0,0018	2,0031	0,0460	0,1534
VEGFA	Female	0,0004	0,0363	0,0105	0,9917	0,9943
VEGFA	BMI	0,0153	0,0040	3,8210	0,0002	0,0020
VEGFA	Residency_AreaUrban	-0,0610	0,0442	-1,3804	0,1684	0,3582
VEGFA	Seasonality_Rainy	0,0112	0,0375	0,2999	0,7644	0,8894

Table S3: Comparison of inflammatory clusters analysis

Parameters		Lower expression inflammatory cluster (N = 167)	Higher expression inflammatory cluster (N = 124)		Statistics
age	Median	29,63	32,75	0.010605	Mann-Whitney
	IQR	16,52	17,14		
	Quantile1	18,13	17,76		
	Quantile2	22,25	25,24		
	Quantile3	29,63	32,75		
	Quantile4	38,77	42,38		
	Quantile5	66,43	59,53		
BMI	Median	23,45	24,40	0.1362899	Mann-Whitney
	IQR	5,50	6,89		
	Quantile1	16,41	17,04		
	Quantile2	21,33	21,79		
	Quantile3	23,45	24,40		
	Quantile4	26,83	28,69		
	Quantile5	41,91	39,84		
Gender	Female	89/167 (53.3%)	57/124 (46.0%)	0.2638188	Chi-square
	Male	78/167 (46.7%)	67/124 (54.0%)		
Residency_Area	Rural	33/167 (19.8%)	30/124 (24.2%)	0.4448202	Chi-square
	Urban	134/167 (80.2%)	94/124 (75.8%)		
Seasonality	Dry	127/167 (76.0%)	85/124 (68.5%)	0.1973038	Chi-square
	Rainy	40/167 (24.0%)	39/124 (31.5%)		
Food Cluster	Healthier food cluster	89/167 (53.3%)	46/124 (37.1%)	0.008769825	Chi-square
	Less healthy food cluster	78/167 (46.7%)	78/124 (62.9%)	0.0005506364	Log regression model corrected for age

Table S4. Multivariate linear regression analysis between plasma metabolites and inflammation-related proteins in Tanzanian cohort

Proteins	Covariate	Estimate	Std. Error	t value	pvalue	fdr	class	sub class
SIRT2	Resveratrol 4''-(6-galloylglucoside)	3,835	0,228	16,794	6,36282E-45	1,35604E-40	Prenol lipids	Sesterterpenoids
AXIN1	Resveratrol 4''-(6-galloylglucoside)	3,414	0,204	16,708	1,33007E-44	1,41732E-40	Prenol lipids	Sesterterpenoids
STAMBP	Resveratrol 4''-(6-galloylglucoside)	2,620	0,160	16,358	2,72255E-43	1,9341E-39	Prenol lipids	Sesterterpenoids
CASP-8	Resveratrol 4''-(6-galloylglucoside)	1,853	0,128	14,518	1,96975E-36	1,04948E-32	Prenol lipids	Sesterterpenoids
ST1A1	Resveratrol 4''-(6-galloylglucoside)	3,459	0,239	14,469	2,97312E-36	1,26726E-32	Prenol lipids	Sesterterpenoids
CXCL1	Resveratrol 4''-(6-galloylglucoside)	4,094	0,311	13,169	1,73244E-31	6,15363E-28	Prenol lipids	Sesterterpenoids
CXCL6	Resveratrol 4''-(6-galloylglucoside)	3,064	0,251	12,218	4,51705E-28	1,37525E-24	Prenol lipids	Sesterterpenoids
SIRT2	Triose	5,097	0,452	11,270	9,45593E-25	2,51906E-21	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CXCL5	Resveratrol 4''-(6-galloylglucoside)	4,749	0,424	11,210	1,51909E-24	3,5972E-21	Prenol lipids	Sesterterpenoids
STAMBP	Triose	3,494	0,315	11,107	3,43988E-24	7,33107E-21	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
IL7	Resveratrol 4''-(6-galloylglucoside)	1,840	0,170	10,832	2,99397E-23	5,80069E-20	Prenol lipids	Sesterterpenoids
AXIN1	Triose	4,351	0,411	10,587	2,01044E-22	3,57055E-19	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CASP-8	Triose	2,405	0,246	9,779	9,41559E-20	1,54358E-16	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
ST1A1	Triose	4,412	0,463	9,529	5,99653E-19	9,12843E-16	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CXCL1	Triose	5,471	0,582	9,398	1,57738E-18	2,24113E-15	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-4	Resveratrol 4''-(6-galloylglucoside)	1,834	0,198	9,265	4,14392E-18	5,5197E-15	Prenol lipids	Sesterterpenoids
CXCL6	Triose	4,222	0,460	9,182	7,54757E-18	9,46199E-15	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CXCL5	Triose	6,752	0,761	8,868	7,15038E-17	8,46605E-14	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-4	Triose	2,840	0,343	8,274	4,46793E-15	5,01161E-12	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
FGF-21	Ethyl beta-D-glucopyranoside	1,381	0,168	8,210	6,88359E-15	7,33516E-12	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
TNFSF14	Resveratrol 4''-(6-galloylglucoside)	0,970	0,119	8,156	9,91782E-15	1,00652E-11	Prenol lipids	Sesterterpenoids
IL7	Triose	2,501	0,307	8,138	1,1273E-14	1,09205E-11	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
AXIN1	Aminobutanoic acid (ABA)/3-Aminobutanoic acid	8,204	1,021	8,037	2,21383E-14	2,05136E-11	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CASP-8	Aminobutanoic acid (ABA)/3-Aminobutanoic acid	4,577	0,605	7,571	4,72883E-13	4,1992E-10	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
ST1A1	Aminobutanoic acid (ABA)/3-Aminobutanoic acid	8,527	1,132	7,534	6,01893E-13	5,13101E-10	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-4	Heptadecanoic acid	1,596	0,224	7,133	7,56414E-12	6,20027E-09	Fatty Acyls	Fatty acids and conjugates
4E-BP1	Resveratrol 4''-(6-galloylglucoside)	1,372	0,193	7,104	9,05951E-12	7,15098E-09	Prenol lipids	Sesterterpenoids
SIRT2	Aminobutanoic acid (ABA)/3-Aminobutanoic acid	8,258	1,167	7,073	1,09484E-11	8,3333E-09	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-4	Gallic acid	-2,176	0,311	-6,993	1,79949E-11	1,32244E-08	Benzene and substituted derivatives	Benzoic acids and derivatives
CD40	Resveratrol 4''-(6-galloylglucoside)	0,586	0,084	6,984	1,89791E-11	1,34827E-08	Prenol lipids	Sesterterpenoids
MCP-4	Brassinin	-1,216	0,175	-6,945	2,39824E-11	1,64875E-08	Indoles and derivatives	Indoles
STAMBP	Aminobutanoic acid (ABA)/3-Aminobutanoic acid	5,619	0,811	6,929	2,65785E-11	1,77013E-08	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
LAP.TGF-beta-1	Resveratrol 4''-(6-galloylglucoside)	0,730	0,109	6,700	1,04989E-10	6,78041E-08	Prenol lipids	Sesterterpenoids
MCP-4	Mangostenone B	2,330	0,354	6,590	2,01043E-10	1,26018E-07	Benzopyrans	1-benzopyrans
MCP-4	Feruloylcholine	0,902	0,139	6,482	3,7873E-10	2,30614E-07	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
MCP-4	Apigenin	-1,539	0,242	-6,365	7,40391E-10	4,38311E-07	Flavonoids	Flavones
TNFSF14	Triose	1,321	0,209	6,309	1,02297E-09	5,89231E-07	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CXCL11	Resveratrol 4''-(6-galloylglucoside)	1,618	0,261	6,189	2,01319E-09	1,12908E-06	Prenol lipids	Sesterterpenoids
MCP-2	Gallic acid	-1,409	0,228	-6,183	2,0817E-09	1,13757E-06	Benzene and substituted derivatives	Benzoic acids and derivatives
CD40	Triose	0,886	0,145	6,128	2,83683E-09	1,51146E-06	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MMP-1	Resveratrol 4''-(6-galloylglucoside)	1,685	0,277	6,074	3,82459E-09	1,98804E-06	Prenol lipids	Sesterterpenoids
FGF-21	Samin	2,775	0,461	6,021	5,13745E-09	2,60689E-06	Benzodioxoles	NOT AVAILABLE
4E-BP1	Triose	1,993	0,334	5,960	7,15289E-09	3,54517E-06	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-1	5''''-(4-Hydroxy-(E)-cinnamoyl) alpha-L-arabinofuranosyl-(1->3)-be	0,554	0,094	5,918	9,00816E-09	4,26627E-06	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-4	5''''-(4-Hydroxy-(E)-cinnamoyl) alpha-L-arabinofuranosyl-(1->3)-be	0,890	0,150	5,920	8,92383E-09	4,26627E-06	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CXCL11	Triose	2,624	0,445	5,895	1,01998E-08	4,72559E-06	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-4	(-)-Dioxibrassinin	-2,356	0,402	-5,855	1,26452E-08	5,73391E-06	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-4	4'',5,6-Trimethylscutellarein 7-glucoside	2,111	0,361	5,846	1,32698E-08	5,89181E-06	Anthracenes	Anthraquinones
MCP-4	1-(5Z,8Z,11Z,14Z-eicosatetraenoyl)-sn-glycero-3-phosphate	-1,584	0,272	-5,828	1,4669E-08	6,38013E-06	Glycerophospholipids	Glycerophosphates
4E-BP1	Artonin D	1,612	0,279	5,783	1,86062E-08	7,93071E-06	Linear 1,3-diarylpropanoids	Chalcones and dihydrochalcones
MCP-4	1-(11Z-eicosenoyl)-glycero-3-phosphate	-1,822	0,315	-5,778	1,90861E-08	7,97576E-06	Glycerophospholipids	Glycerophosphates
MCP-4	1,6-Dihydroxy-3,7-dimethoxy-2-(3-methyl-2-butenyl)-8-(3-hydroxy	1,096	0,191	5,737	2,38096E-08	9,75829E-06	Benzopyrans	1-benzopyrans
MCP-4	Sorgoleone 358	1,425	0,249	5,733	2,43008E-08	9,77166E-06	Organooxygen compounds	Carbonyl compounds
CXCL5	Aminobutanoic acid (ABA)/3-Aminobutanoic acid	10,743	1,900	5,654	3,68587E-08	1,45469E-05	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-1	Feruloylcholine	0,496	0,088	5,639	3,99757E-08	1,54902E-05	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
FGF-21	Syndesine	2,045	0,365	5,607	4,7242E-08	1,7979E-05	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CXCL6	Gallic acid	-2,427	0,438	-5,547	6,44364E-08	2,3677E-05	Benzene and substituted derivatives	Benzoic acids and derivatives
MCP-2	Resveratrol 4''-(6-galloylglucoside)	0,855	0,154	5,548	6,41684E-08	2,3677E-05	Prenol lipids	Sesterterpenoids
MCP-4	Murrayanol	1,495	0,273	5,481	9,07238E-08	3,27713E-05	Indoles and derivatives	Carbazoles
MCP-4	1-O-Galloylglycerol	-1,701	0,312	-5,451	1,05457E-07	3,74582E-05	Benzene and substituted derivatives	Benzoic acids and derivatives
MCP-1	4'',5,6-Trimethylscutellarein 7-glucoside	1,229	0,226	5,430	1,17721E-07	4,1129E-05	Anthracenes	Anthraquinones
LAP.TGF-beta-1	Triose	1,024	0,189	5,422	1,22454E-07	4,20925E-05	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-4	Oxobutanoic acid	-4,991	0,925	-5,398	1,38624E-07	4,54516E-05	Keto acids and derivatives	Short-chain keto acids and derivatives
MCP-4	2-O-(Z-p-Hydroxycinnamoyl)-(x)-glyceric acid	-2,305	0,427	-5,398	1,38478E-07	4,54516E-05	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
MCP-2	Triose	1,414	0,262	5,402	1,35556E-07	4,54516E-05	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-4	KB 2	1,105	0,206	5,370	1,59243E-07	5,14209E-05	Flavonoids	Flavones
MCP-4	3-Methylcyclopentadecanone	1,050	0,196	5,357	1,69883E-07	5,4038E-05	Organooxygen compounds	Carbonyl compounds
MCP-4	LysoPE(0:0/20:0)	-1,275	0,239	-5,334	1,91446E-07	6,00016E-05	Glycerophospholipids	Glycerophosphoethanolamines
MCP-4	2-Methoxynaphthalene	-1,401	0,263	-5,328	1,9663E-07	6,07329E-05	Naphthalenes	NOT AVAILABLE
MCP-1	Brassinin	-0,598	0,112	-5,324	2,01048E-07	6,12106E-05	Indoles and derivatives	Indoles
MCP-4	Lyciumin A	-1,279	0,243	-5,272	2,60968E-07	7,83345E-05	2-arylbenzofuran flavonoids	NOT AVAILABLE
MCP-2	Oxobutanoic acid	-3,515	0,668	-5,264	2,71412E-07	7,95104E-05	Keto acids and derivatives	Short-chain keto acids and derivatives
MCP-4	[6]-Gingerdiol 3,5-diacetate	0,903	0,172	5,263	2,72347E-07	7,95104E-05	Fatty Acyls	Fatty alcohol esters
CXCL1	Gallic acid	-2,937	0,560	-5,246	2,96418E-07	8,53684E-05	Benzene and substituted derivatives	Benzoic acids and derivatives
CX3CL1	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-0,776	0,149	-5,200	3,72436E-07	0,000104793	Flavonoids	Flavonoid glycosides
MCP-4	1-Phenyl-1,3-heptadecanedione	1,178	0,226	5,199	3,73699E-07	0,000104793	Organooxygen compounds	Carbonyl compounds
MCP-4	Curcumin	-1,848	0,358	-5,159	4,55473E-07	0,000126066	Diarylheptanoids	Linear diarylheptanoids
MCP-4	3-hydroxynonanoyl carnitine	0,634	0,123	5,150	4,74984E-07	0,00012978	Fatty Acyls	Fatty acid esters
MCP-1	(-)-Dioxibrassinin	-1,303	0,254	-5,137	5,06314E-07	0,000136589	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-1	Lyciumin A	-0,771	0,152	-5,091	6,33709E-07	0,000167425	2-arylbenzofuran flavonoids	NOT AVAILABLE
MCP-2	1-Phenyl-1,3-heptadecanedione	0,832	0,163	5,090	6,36327E-07	0,000167425	Organooxygen compounds	Carbonyl compounds
CXCL1	Aminobutanoic acid (ABA)/3-Aminobutanoic acid	7,530	1,486	5,068	7,08843E-07	0,00018423	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
SCF	LysoPE(0:0/20:2(11Z,14Z))	0,373	0,074	5,049	7,76E-07	0,000199254	Glycerophospholipids	Glycerophosphoethanolamines
MCP-4	Alpha-Linolenic acid	0,620	0,124	5,016	9,12143E-07	0,00022937	Fatty Acyls	Lineolic acids and derivatives
MCP-2	Murrayanol	0,993	0,198	5,015	9,14809E-07	0,00022937	Indoles and derivatives	Carbazoles
MCP-4	(S)-[8]-Gingerol	0,458	0,092	4,996	1,00104E-06	0,000248072	Phenols	Methoxyphenols
MCP-4	Myricanol 5-glucoside	-1,480	0,296	-4,993	1,01583E-06	0,000248749	Lactones	Gamma butyrolactones
MCP-2	3-hydroxynonanoyl carnitine	0,444	0,089	4,991	1,02712E-06	0,000248749	Fatty Acyls	Fatty acid esters
MCP-1	1-O-Galloylglycerol	-0,975	0,196	-4,979	1,08903E-06	0,000260366	Benzene and substituted derivatives	Benzoic acids and derivatives
MCP-2	Heptadecanoic acid	0,834	0,168	4,977	1,09952E-06	0,000260366	Fatty Acyls	Fatty acids and conjugates
MCP-4	Kanzonol F	1,119	0,225	4,972	1,12346E-06	0,000263112	Isoflavonoids	Furanoisoflavonoids
CCL4	Gallic acid	-1,136	0,229	-4,957	1,20718E-06	0,000279645	Benzene and substituted derivatives	Benzoic acids and derivatives
MCP-2	[6]-Gingerdiol 3,5-diacetate	0,614	0,124	4,945	1,2788E-06	0,000289934	Fatty Acyls	Fatty alcohol esters
MCP-4	Albanin B	1,231	0,249	4,947	1,26574E-06	0,000289934	Flavonoids	Flavones
MCP-1	Ethyl cinnamate	1,691	0,343	4,935	1,33827E-06	0,000300222	Cinnamic acids and derivatives	Cinnamic acid esters
MCP-1	14,16-Nonacosanedione	0,769	0,156	4,926	1,40119E-06	0,000311063	Organooxygen compounds	Carbonyl compounds
MMP-1	LysoPE(0:0/20:0)	-1,549	0,315	-4,919	1,44673E-06	0,000317862	Glycerophospholipids	Glycerophosphoethanolamines
LAP.TGF-beta-1	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-0,842	0,171	-4,917	1,46194E-06	0,000317928	Flavonoids	Flavonoid glycosides
MCP-4	FAHFA(18:0/9-O-18:0)	0,642	0,131	4,904	1,55016E-06	0,000333707	Fatty Acyls	Fatty acids and conjugates
CCL4	Resveratrol 4''-(6-galloylglucoside)	0,752	0,153	4,902	1,56687E-06	0,000333932	Prenol lipids	Sesterterpenoids
MMP-1	Oxobutanoic acid	-5,970	1,220	-4,894	1,62606E-06	0,000340028	Keto acids and derivatives	Short-chain keto acids and derivatives
MCP-4	3-Hydroxymugineic acid	0,216	0,044	4,894	1,62738E-06	0,000340028	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-4	Marcanine A	-2,506	0,512	-4,891	1,64822E-06	0,000341038	Quinolines and derivatives	Benzoquinolines
MCP-4	(2S,4S)-Monatin	-1,039	0,214	-4,849	2,00763E-06	0,00041141	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-4	Methylpicraquassioside A	0,961	0,199	4,835	2,1434E-06	0,000435049	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MMP-1	1-Propenyl 1-(1-propenylthio)propyl disulfide	-1,944	0,405	-4,803	2,48537E-06	0,000499699	Thioethers	Thioenol ethers
CXCL6	Brassinin	-1,195	0,249	-4,798	2,53963E-06	0,000505838	Indoles and derivatives	Indoles
MCP-2	Lyciumin A	-0,843	0,176	-4,787	2,68208E-06	0,000529263	2-arylbenzofuran flavonoids	NOT AVAILABLE
MCP-4	3-hydroxyundecanoyl carnitine	0,600	0,125	4,783	2,72463E-06	0,000532727	Fatty Acyls	Fatty acid esters
MCP-4	6-Prenylnaringenin	0,280	0,059	4,779	2,77922E-06	0,00053846	Flavonoids	Flavans
MMP-1	3-Hydroxymyristate	1,934	0,405	4,772	2,87005E-06	0,000551049	Fatty Acyls	Fatty acids and conjugates
MCP-2	Brassinin	-0,625	0,131	-4,762	3,00685E-06	0,00057216	Indoles and derivatives	Indoles
CXCL6	(-)-Dioxibrassinin	-2,661	0,561	-4,745	3,25675E-06	0,000611388	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-2	Sorgoleone 358	0,863	0,182	4,744	3,27038E-06	0,000611388	Organooxygen compounds	Carbonyl compounds
MCP-2	Shoyuflavone C	-4,792	1,011	-4,740	3,32921E-06	0,000611656	Isoflavonoids	Isoflav-2-enes
HGF	Somniferine	-0,338	0,071	-4,740	3,31955E-06	0,000611656	Morphinans	NOT AVAILABLE
MCP-4	Distichonic acid A	-1,133	0,239	-4,735	3,4E-06	0,000619322	Carboxylic acids and derivatives	Amino acids, peptides, and analogues

MCP-1	Myricanol 5-glucoside	-0,876	0,185	-4,732	3,45228E-06	0,000623518	Lactones	Gamma butyrolactones
MCP-2	Methylpicraquassioside A	0,678	0,143	4,729	3,49766E-06	0,000626405	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CXCL5	Gallic acid	-3,440	0,729	-4,721	3,62797E-06	0,000636776	Benzene and substituted derivatives	Benzoic acids and derivatives
MMP-1	1-(11Z-eicosenoyl)-glycero-3-phosphate	-1,079	[illegible]	-4,716	3,70497E-06	0,000636776	Glycerophospholipids	Glycerophosphates
MCP-4	LysoPE(0:0/20:1(11Z))	-1,062	0,225	-4,717	3,68783E-06	0,000636776	Glycerophospholipids	Glycerophosphoethanolamines
MCP-2	1-Propenyl 1-(1-propenylthio)propyl disulfide	-1,054	0,223	-4,723	3,59146E-06	0,000636776	Thioethers	Thioenol ethers
MMP-1	Triose	2,268	0,481	4,718	3,66879E-06	0,000636776	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-1	3,4-Dimethyl-5-pentyl-2-furantridecanoic acid	0,778	0,165	4,713	3,75909E-06	0,00064091	Fatty Acyls	Fatty acids and conjugates
MCP-2	(S)-[8]-Gingerol	0,312	0,066	4,701	3,97246E-06	0,000671914	Phenols	Methoxyphenols
MCP-1	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-0,966	0,206	-4,695	4,07778E-06	0,000684297	Flavonoids	Flavonoid glycosides
MCP-1	Apigenin	-0,727	0,155	-4,692	4,13816E-06	0,000689004	Flavonoids	Flavones
MCP-4	3-Hydroxymyristate	1,454	0,310	4,689	4,18936E-06	0,000692121	Fatty Acyls	Fatty acids and conjugates
MCP-4	14,16-Nonacosanedione	1,174	0,252	4,666	4,6548E-06	0,0007631	Organooxygen compounds	Carbonyl compounds
CX3CL1	Hv-NCC-1	-0,808	0,174	-4,656	4,87933E-06	0,000793804	Tetrapyrroles and derivatives	NOT AVAILABLE
MCP-2	Feruloylcholine	0,481	0,103	4,644	5,15099E-06	0,00083165	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
CXCL11	Gallic acid	-1,861	0,401	-4,642	5,19023E-06	0,000831686	Benzene and substituted derivatives	Benzoic acids and derivatives
MMP-1	Shoyuflavone C	-8,529	1,839	-4,638	5,29555E-06	0,00084223	Isoflavonoids	Isoflav-2-enes
CXCL6	Myricanol 5-glucoside	-1,889	0,408	-4,633	5,4121E-06	0,00085439	Lactones	Gamma butyrolactones
MCP-4	Histidine	0,813	0,176	4,620	5,73382E-06	0,000891964	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-4	Phenylethyl primeveroside	1,318	0,285	4,622	5,69403E-06	0,000891964	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-4	Naringenin	-0,865	0,187	-4,615	5,873E-06	0,000906996	Flavonoids	Flavans
LIF-R	Erucic acid	-0,266	0,058	-4,594	6,43398E-06	0,000986482	Fatty Acyls	Fatty acids and conjugates
MCP-2	Alpha-Linolenic acid	0,412	0,090	4,593	6,48202E-06	0,000986749	Fatty Acyls	Lineolic acids and derivatives
LIF-R	Heptadecanoic acid	-0,302	0,066	-4,586	6,67333E-06	0,001008667	Fatty Acyls	Fatty acids and conjugates
MCP-4	Torvanol A	0,546	0,119	4,580	6,86645E-06	0,001030548	Isoflavonoids	O-methylated isoflavonoids
MCP-2	Marcanine A	-1,696	0,371	-4,574	7,05772E-06	0,001051847	Quinolines and derivatives	Benzoquinolines
OSM	Protogonyautoxin I	-1,686	0,369	-4,567	7,27114E-06	0,001074428	Saxitoxins, gonyautoxins, and derivatives	NOT AVAILABLE
SCF	Syndesine	-0,383	0,084	-4,564	7,36095E-06	0,001074428	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-1	Torvanol A	0,339	0,074	4,565	7,33038E-06	0,001074428	Isoflavonoids	O-methylated isoflavonoids
TNFSF14	C24:6	0,536	0,117	4,562	7,44374E-06	0,001074428	Fatty Acyls	Fatty acyl thioesters
MCP-2	1,6-Dihydroxy-3,7-dimethoxy-2-(3-methyl-2-butenyl)-8-(3-hydroxy	0,640	0,140	4,561	7,4613E-06	0,001074428	Benzopyrans	1-benzopyrans
MMP-1	Gallic acid	-1,935	0,425	-4,552	7,76339E-06	0,001103023	Benzene and substituted derivatives	Benzoic acids and derivatives
FGF-21	Phenylethyl alcohol	3,866	0,849	4,553	7,72418E-06	0,001103023	Benzene and substituted derivatives	NOT AVAILABLE
CXCL6	1-(11Z-eicosenoyl)-glycero-3-phosphate	-2,002	0,440	-4,549	7,8599E-06	0,001109338	Glycerophospholipids	Glycerophosphates
MCP-1	Oxobutanoic acid	-2,649	0,583	-4,540	8,19896E-06	0,001149478	Keto acids and derivatives	Short-chain keto acids and derivatives
MCP-4	7-Hydroxy-5-(4-hydroxy-2-oxopentyl)-2-methylchromone 7-glucos	0,490	0,108	4,538	8,25216E-06	0,001149478	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CXCL5	Heptadecanoic acid	2,385	0,527	4,527	8,67876E-06	0,00120105	Fatty Acyls	Fatty acids and conjugates
MCP-2	1-(2-Thienyl)-1,2-propanedione	-3,563	0,789	-4,518	9,01319E-06	0,001239284	Organooxygen compounds	Carbonyl compounds
FGF-21	7-Methoxy-2-methylisoflavone	2,015	0,447	4,509	9,40844E-06	0,001285337	Isoflavonoids	O-methylated isoflavonoids
MCP-4	1-(2-Thienyl)-1,2-propanedione	-4,933	1,095	-4,506	9,51322E-06	0,001291374	Organooxygen compounds	Carbonyl compounds
CXCL1	2-Methoxynaphthalene	-2,086	0,464	-4,497	9,89388E-06	0,001317865	Naphthalenes	NOT AVAILABLE
MCP-2	(-)-Dioxibrassinin	-1,333	0,296	-4,497	9,8917E-06	0,001317865	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
LAP.TGF-beta-1	Gallic acid	-0,760	0,169	-4,498	9,84813E-06	0,001317865	Benzene and substituted derivatives	Benzoic acids and derivatives
MCP-1	Hv-NCC-1	-1,064	0,238	-4,474	1,0971E-05	0,001452261	Tetrapyrroles and derivatives	NOT AVAILABLE
MMP-1	L-1,2,3,4-Tetrahydro-beta-carboline-3-carboxylic acid	-1,460	0,327	-4,471	1,11142E-05	0,001462128	Indoles and derivatives	Pyridoindoles
MCP-1	Pectenotoxin 2	-1,028	0,230	-4,467	1,13025E-05	0,001468773	Macrolides and analogues	Pectenotoxins and derivatives
SCF	1-(8Z,11Z,14Z-eicosatrienoyl)-glycero-3-phosphate	0,457	0,102	4,467	1,12904E-05	0,001468773	Glycerophospholipids	Glycerophospholipids
MCP-2	Neferine	-0,884	0,198	-4,455	1,19136E-05	0,001538804	Isoquinolines and derivatives	Benzylisoquinolines
HGF	Protogonyautoxin I	-0,675	0,152	-4,447	1,23282E-05	0,001561676	Saxitoxins, gonyautoxins, and derivatives	NOT AVAILABLE
VEGFA	Somniferine	-0,298	0,067	-4,446	1,24077E-05	0,001561676	Morphinans	NOT AVAILABLE
CSF-1	LysoPE(0:0/20:0)	-0,277	0,062	-4,447	1,23489E-05	0,001561676	Glycerophospholipids	Glycerophosphoethanolamines
CCL4	Triose	1,164	0,262	4,445	1,24571E-05	0,001561676	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CXCL5	Sorgoleone 358	2,537	0,571	4,446	1,24123E-05	0,001561676	Organooxygen compounds	Carbonyl compounds
TNFSF14	Gallic acid	-0,843	0,191	-4,423	1,36861E-05	0,001705715	Benzene and substituted derivatives	Benzoic acids and derivatives
MMP-1	(-)-Dioxibrassinin	-2,382	0,539	-4,421	1,38338E-05	0,001714106	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-2	1-O-Galloylglycerol	-1,007	0,228	-4,409	1,45487E-05	0,001780011	Benzene and substituted derivatives	Benzoic acids and derivatives
MCP-4	C24:6	0,886	0,201	4,409	1,45512E-05	0,001780011	Fatty Acyls	Fatty acyl thioesters
MCP-4	2'',4,4''-Trihydroxy-6''-methoxy-3'',5''-diprenylchalcone	1,636	0,371	4,408	1,46163E-05	0,001780011	Linear 1,3-diarylpropanoids	Chalcones and dihydrochalcones
MCP-4	Shoyuflavone C	-6,210	1,410	-4,404	1,48573E-05	0,001780897	Isoflavonoids	Isoflav-2-enes
MCP-2	7-Hydroxy-5-(4-hydroxy-2-oxopentyl)-2-methylchromone 7-glucos	0,343	0,078	4,404	1,48742E-05	0,001780897	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-1	3-Hydroxymyristate	0,854	0,194	4,405	1,47899E-05	0,001780897	Fatty Acyls	Fatty acids and conjugates
TNFSF14	LysoPE(0:0/20:2(11Z,14Z))	-0,491	0,112	-4,389	1,5877E-05	0,001890343	Glycerophospholipids	Glycerophosphoethanolamines
HGF	Gallic acid	-0,556	0,127	-4,369	1,73136E-05	0,00204993	Benzene and substituted derivatives	Benzoic acids and derivatives
MCP-4	Hydrocortamate	1,370	0,315	4,356	1,83184E-05	0,002156915	Steroids and steroid derivatives	Pregnane steroids
MCP-2	4'',5,6-Trimethylscutellarein 7-glucoside	1,156	0,266	4,338	1,97528E-05	0,002313029	Anthracenes	Anthraquinones
FGF-21	Diacetoxyscirpenol	3,065	0,707	4,335	1,99865E-05	0,00232761	Prenol lipids	Sesquiterpenoids
MCP-1	D-erythro-L-galacto-Nonulose	-0,347	0,080	-4,333	2,0193E-05	0,002338874	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CXCL6	Lyciumin A	-1,455	0,337	-4,318	2,15198E-05	0,002479082	2-arylbenzofuran flavonoids	NOT AVAILABLE
DNER	Feruloylcholine	-0,164	0,038	-4,301	2,30745E-05	0,00264389	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
CCL4	(-)-Dioxibrassinin	-1,259	0,293	-4,297	2,34655E-05	0,002671011	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-2	N-Hexadecanoylpyrrolidine	0,692	0,161	4,297	2,35618E-05	0,002671011	Pyrrolidines	N-acylpyrrolidines
MCP-2	L-1,2,3,4-Tetrahydro-beta-carboline-3-carboxylic acid	-0,774	0,180	-4,294	2,38402E-05	0,00268827	Indoles and derivatives	Pyridoindoles
CXCL11	LysoPE(0:0/20:0)	-1,285	0,300	-4,281	2,51373E-05	0,002819609	Glycerophospholipids	Glycerophosphoethanolamines
EN-RAGE	1-Arachidonoylglycerophosphoinositol	0,779	0,182	4,279	2,53392E-05	0,00282738	Glycerophospholipids	Glycerophosphates
CXCL6	2-Methoxynaphthalene	-1,562	0,366	-4,272	2,61266E-05	0,002900055	Naphthalenes	NOT AVAILABLE
LIF-R	1-heptadecanoyl-glycero-3-phosphate	-0,332	0,078	-4,258	2,77247E-05	0,003053456	Glycerophospholipids	Glycerophosphates
LIF-R	3-hydroxyundecanoyl carnitine	-0,151	0,036	-4,256	2,79129E-05	0,003053456	Fatty Acyls	Fatty acid esters
CXCL5	[6]-Gingerdiol 3,5-diacetate	1,667	0,392	4,256	2,79384E-05	0,003053456	Fatty Acyls	Fatty alcohol esters
CXCL10	Murrayanol	1,021	0,240	4,248	2,88632E-05	0,003138431	Indoles and derivatives	Carbazoles
CXCL6	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-1,927	0,455	-4,234	3,06552E-05	0,003316363	Flavonoids	Flavonoid glycosides
CXCL10	Gallic acid	-1,194	0,282	-4,230	3,11318E-05	0,003350918	Benzene and substituted derivatives	Benzoic acids and derivatives
MCP-4	Theogallin	-2,134	0,505	-4,224	3,20479E-05	0,00341613	Organooxygen compounds	Alcohols and polyols
IL18	Glycine	-0,816	0,193	-4,223	3,20583E-05	0,00341613	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-4	Hv-NCC-1	-1,617	0,384	-4,215	3,3175E-05	0,003504472	Tetrapyrroles and derivatives	NOT AVAILABLE
CXCL6	Feruloylcholine	0,833	0,198	4,215	3,32162E-05	0,003504472	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
MCP-4	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-1,400	0,333	-4,208	3,42147E-05	0,00353973	Flavonoids	Flavonoid glycosides
TNFSF14	(-)-Dioxibrassinin	-1,018	0,242	-4,209	3,4057E-05	0,00353973	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-2	(2S,4S)-Monatin	-0,656	0,156	-4,210	3,39622E-05	0,00353973	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-2	C24:6	0,611	0,145	4,211	3,38219E-05	0,00353973	Fatty Acyls	Fatty acyl thioesters
CXCL10	Licoagrodin	-1,463	0,348	-4,201	3,51894E-05	0,003622979	Flavonoids	Flavans
CXCL11	Oxobutanoic acid	-4,883	1,163	-4,197	3,58056E-05	0,003660599	Keto acids and derivatives	Short-chain keto acids and derivatives
CXCL10	Methylpicraquassioside A	0,728	0,173	4,195	3,60701E-05	0,003660599	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CXCL11	4'',5,6-Trimethylscutellarein 7-glucoside	1,921	0,458	4,196	3,59724E-05	0,003660599	Anthracenes	Anthraquinones
CCL4	Feruloylcholine	0,429	0,103	4,178	3,87825E-05	0,003917218	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
IL6	LysoPE(0:0/20:2(11Z,14Z))	-0,848	0,203	-4,176	3,91402E-05	0,003934694	Glycerophospholipids	Glycerophosphoethanolamines
MCP-2	1-(8Z,11Z,14Z-eicosatrienoyl)-glycero-3-phosphate	-0,793	0,190	-4,172	3,96861E-05	0,003970851	Glycerophospholipids	Glycerophospholipids
EN-RAGE	Glycine	-0,805	0,193	-4,170	4,00457E-05	0,0039881	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CXCL11	Myricanol 5-glucoside	-1,543	0,371	-4,165	4,09305E-05	0,004038473	Lactones	Gamma butyrolactones
MCP-2	3-hydroxyundecanoyl carnitine	0,380	0,091	4,166	4,0755E-05	0,004038473	Fatty Acyls	Fatty acid esters
MCP-2	Theogallin	-1,516	0,364	-4,160	4,1719E-05	0,004097309	Organooxygen compounds	Alcohols and polyols
MCP-1	LysoPE(0:0/20:0)	-0,630	0,151	-4,159	4,19642E-05	0,004102478	Glycerophospholipids	Glycerophosphoethanolamines
TNFSF14	L-1,2,3,4-Tetrahydro-beta-carboline-3-carboxylic acid	-0,609	0,147	-4,149	4,37126E-05	0,004234559	Indoles and derivatives	Pyridoindoles
CX3CL1	Lyciumin A	-0,466	0,112	-4,150	4,35664E-05	0,004234559	2-arylbenzofuran flavonoids	NOT AVAILABLE
IL7	Aminobutanoic acid (ABA)/3-Aminobutanoic acid	3,193	0,772	4,137	4,58163E-05	0,004418269	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
VEGFA	Divanillyltetrahydrofuran ferulate	-0,541	0,131	-4,134	4,64333E-05	0,004457599	Furanoid lignans	Tetrahydrofuran lignans
DNER	Mangostenone B	-0,402	0,097	-4,133	4,6645E-05	0,004457842	Benzopyrans	1-benzopyrans
CSF-1	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-0,353	0,086	-4,130	4,72602E-05	0,004496469	Flavonoids	Flavonoid glycosides
TNFSF14	1-Propenyl 1-(1-propenylthio)propyl disulfide	-0,754	0,183	-4,124	4,84777E-05	0,004591805	Thioethers	Thioenol ethers
CXCL6	Oxobutanoic acid	-5,313	1,290	-4,119	4,94719E-05	0,004665245	Keto acids and derivatives	Short-chain keto acids and derivatives
MCP-4	N-Hexadecanoylpyrrolidine	0,922	0,224	4,115	5,0186E-05	0,004711738	Pyrrolidines	N-acylpyrrolidines
MCP-4	Erucic acid	0,850	0,207	4,112	5,08039E-05	0,004748832	Fatty Acyls	Fatty acids and conjugates
MCP-1	Naringenin	-0,483	0,117	-4,111	5,11589E-05	0,004761126	Flavonoids	Flavans
CSF-1	Dicyclohexyl disulfide	0,200	0,049	4,107	5,19875E-05	0,004816204	Organic disulfides	Dialkyldisulfides
CXCL1	C24:6	1,443	0,352	4,106	5,22027E-05	0,004816204	Fatty Acyls	Fatty acyl thioesters
CX3CL1	LysoPE(0:0/20:0)	-0,455	0,111	-4,101	5,32023E-05	0,004887277	Glycerophospholipids	Glycerophosphoethanolamines
CXCL6	LysoPE(0:0/20:0)	-1,365	0,333	-4,095	5,44267E-05	0,004978294	Glycerophospholipids	Glycerophosphoethanolamines
FGF-21	(Iso)Leucine	-2,761	0,675	-4,093	5,50431E-05	0,005013152	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CXCL11	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-1,684	0,412	-4,090	5,56167E-05	0,005040886	Flavonoids	Flavonoid glycosides
TNFSF14	Protogonyautoxin I	-0,934	0,229	-4,089	5,58206E-05	0,005040886	Saxitoxins, gonyautoxins, and derivatives	NOT AVAILABLE

MCP-2	gamma-Glutamyl-beta-(isoxazolin-5-on-2-yl)alanine	-0,788	0,193	-4,087	5,63306E-05	0,00506548	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CXCL6	1-(5Z,8Z,11Z,14Z-eicosatetraenoyl)-sn-glycero-3-phosphate	-1,560	0,382	-4,083	5,716E-05	0,005075806	Glycerophospholipids	Glycerophosphates
TNFSF14	Neferine	-0,662	0,162	-4,084	5,71118E-05	0,005075806	Isoquinolines and derivatives	Benzylisoquinolines
MMP-1	4'',5,6-Trimethylscutellarein 7-glucoside	-1,083	0,265	-4,085	5,68575E-05	0,005075806	Anthracenes	Anthraquinones
LAP.TGF-beta-1	Divanillyltetrahydrofuran ferulate	-0,759	0,186	-4,075	5,91535E-05	0,005216096	Furanoid lignans	Tetrahydrofuran lignans
EN-RAGE	1-Oleoylglycerophosphoinositol	0,669	0,164	4,075	5,92293E-05	0,005216096	Glycerophospholipids	Glycerophosphoinositols
OSM	Threonine	-0,900	0,221	-4,073	5,97555E-05	0,005229876	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CSF-1	1-[(2,5-Dimethylphenyl)azo]-2-naphthalenol	0,113	0,028	4,072	5,98766E-05	0,005229876	Naphthalenes	Naphthols and derivatives
OSM	Glycine	-1,014	0,249	-4,066	6,12383E-05	0,005282371	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MMP-1	Somniferine	-0,980	0,241	-4,067	6,11765E-05	0,005282371	Morphinans	NOT AVAILABLE
MCP-1	(2S,4S)-Monatin	-0,548	0,135	-4,066	6,14213E-05	0,005282371	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
LIF-R	1,6-Dihydroxy-3,7-dimethoxy-2-(3-methyl-2-butenyl)-8-(3-hydroxy	-0,224	0,055	-4,066	6,1469E-05	0,005282371	Benzopyrans	1-benzopyrans
CCL4	Marcanine A	-1,495	0,368	-4,062	6,22827E-05	0,005330799	Quinolines and derivatives	Benzoquinolines
MCP-1	Distichonic acid A	-0,610	0,150	-4,059	6,3182E-05	0,005386141	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
HGF	4'',5,6-Trimethylscutellarein 7-glucoside	0,588	0,145	4,054	6,43014E-05	0,005459724	Anthracenes	Anthraquinones
LAP.TGF-beta-1	Neferine	-0,584	0,144	-4,052	6,48669E-05	0,005485887	Isoquinolines and derivatives	Benzylisoquinolines
CXCL6	Heptadecanoic acid	1,306	0,323	4,048	6,60531E-05	0,005564126	Fatty Acyls	Fatty acids and conjugates
CXCL11	1-(11Z-eicosenoyl)-glycero-3-phosphate	-1,618	0,400	-4,045	6,6711E-05	0,00559742	Glycerophospholipids	Glycerophosphates
MCP-1	Cuminaldehyde	0,970	0,240	4,043	6,73181E-05	0,005626213	Prenol lipids	Monoterpenoids
TNFSF14	1-(8Z,11Z,14Z-eicosatrienoyl)-glycero-3-phosphate	-0,624	0,155	-4,034	6,99797E-05	0,005825809	Glycerophospholipids	Glycerophospholipids
CXCL6	Apigenin	-1,385	0,344	-4,031	7,05702E-05	0,005852112	Flavonoids	Flavones
LIF-R	Kanzonol F	-0,258	0,064	-4,022	7,32037E-05	0,006064964	Isoflavonoids	Furanoisoflavonoids
CXCL5	3-hydroxynonanoyl carnitine	1,132	0,281	4,021	7,36711E-05	0,006062078	Fatty Acyls	Fatty acid esters
CSF-1	N-(1-Deoxy-1-fructosyl)valine	0,303	0,075	4,016	7,51931E-05	0,006163517	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
4E-BP1	(-)-Dioxibrassinin	-1,543	0,385	-4,010	7,68639E-05	0,006273331	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
VEGFA	1-Propenyl 1-(1-propenylthio)propyl disulfide	-0,458	0,114	-4,009	7,71215E-05	0,006273331	Thioethers	Thioenol ethers
MCP-2	LysoPE(0:0/20:0)	-0,704	0,176	-4,007	7,79541E-05	0,006293467	Glycerophospholipids	Glycerophosphoethanolamines
MCP-2	LysoPE(0:0/20:1(11Z))	-0,656	0,164	-4,007	7,79596E-05	0,006293467	Glycerophospholipids	Glycerophosphoethanolamines
MCP-2	1-(11Z-eicosenoyl)-glycero-3-phosphate	-0,934	0,233	-4,004	7,89615E-05	0,006350291	Glycerophospholipids	Glycerophosphates
LAP.TGF-beta-1	LysoPE(0:0/20:0)	-0,507	0,127	-3,999	8,02799E-05	0,006432049	Glycerophospholipids	Glycerophosphoethanolamines
CCL4	Oxobutanoic acid	-2,677	0,670	-3,993	8,23583E-05	0,00657386	Keto acids and derivatives	Short-chain keto acids and derivatives
CXCL5	Brassinin	-1,651	0,414	-3,990	8,34898E-05	0,006639306	Indoles and derivatives	Indoles
MCP-2	FAHFA(18:0/9-O-18:0)	0,381	0,096	3,987	8,44819E-05	0,006693229	Fatty Acyls	Fatty acids and conjugates
MCP-4	Calystegin B2	-2,020	0,507	-3,982	8,58953E-05	0,006779999	Tropane alkaloids	NOT AVAILABLE
MCP-1	1-(5Z,8Z,11Z,14Z-eicosatetraenoyl)-sn-glycero-3-phosphate	-0,693	0,174	-3,979	8,71541E-05	0,006853977	Glycerophospholipids	Glycerophosphates
CXCL1	Brassinin	-1,274	0,321	-3,975	8,86392E-05	0,006945145	Indoles and derivatives	Indoles
MCP-1	Licoagrodin	-0,999	0,251	-3,973	8,92658E-05	0,006968618	Flavonoids	Flavans
CD8A	1-(11Z-eicosenoyl)-glycero-3-phosphate	-1,255	0,316	-3,970	9,02353E-05	0,007018591	Glycerophospholipids	Glycerophosphates
CCL28	Hv-NCC-1	-0,714	0,180	-3,967	9,12352E-05	0,007044942	Tetrapyrroles and derivatives	NOT AVAILABLE
CX3CL1	Myricanol 5-glucoside	-0,543	0,137	-3,967	9,12248E-05	0,007044942	Lactones	Gamma butyrolactones
CX3CL1	Aminobutanoic acid (ABA)/3-Aminobutanoic acid	-1,561	0,395	-3,956	9,54833E-05	0,007346351	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CXCL6	Marcanine A	-2,809	0,710	-3,954	9,61549E-05	0,007371412	Quinolines and derivatives	Benzoquinolines
CXCL6	Divanillyltetrahydrofuran ferulate	-1,941	0,491	-3,951	9,72053E-05	0,007425231	Furanoid lignans	Tetrahydrofuran lignans
CXCL5	Myricanol 5-glucoside	-2,672	0,676	-3,950	9,76486E-05	0,00742645	Lactones	Gamma butyrolactones
MMP-1	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-1,725	0,437	-3,949	9,82666E-05	0,00742645	Flavonoids	Flavonoid glycosides
MCP-4	trans-Ferulic acid	-1,147	0,290	-3,949	9,80011E-05	0,00742645	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-1	KB 2	0,516	0,131	3,947	9,88949E-05	0,007447519	Flavonoids	Flavones
VEGFA	Threonine	-0,335	0,085	-3,944	0,000100032	0,007506611	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CSF-1	Licoagrodin	-0,409	0,104	-3,937	0,000102932	0,007697183	Flavonoids	Flavans
MCP-4	Pectenotoxin 2	-1,463	0,372	-3,931	0,000105328	0,00780324	Macrolides and analogues	Pectenotoxins and derivatives
MCP-4	1-(8Z,11Z,14Z-eicosatrienoyl)-glycero-3-phosphate	-1,040	0,264	-3,932	0,000104893	0,00780324	Glycerophospholipids	Glycerophospholipids
VEGFA	Peonidin-3-galactoside	-0,381	0,097	-3,930	0,000105869	0,00780324	Flavonoids	Flavonoid glycosides
LIF-R	Garcimangosone C	-0,303	0,077	-3,930	0,000105689	0,00780324	Benzopyrans	1-benzopyrans
FGF-19	Decarbamoylneosaxitoxin	1,787	0,455	3,929	0,000106181	0,00780324	Saxitoxins, gonyautoxins, and derivatives	NOT AVAILABLE
MCP-1	Ximenoylacetone	0,435	0,111	3,925	0,000108115	0,007918032	Organooxygen compounds	Carbonyl compounds
LIF-R	(S)-[8]-Gingerol	-0,102	0,026	-3,909	0,000114884	0,008384961	Phenols	Methoxyphenols
CXCL1	Apigenin	-1,711	0,438	-3,906	0,000116125	0,008446629	Flavonoids	Flavones
MCP-4	Tamarixetin	-1,279	0,328	-3,902	0,000118057	0,008557946	Flavonoids	O-methylated flavonoids
VEGFA	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-0,476	0,122	-3,899	0,000119519	0,008576838	Flavonoids	Flavonoid glycosides
MCP-1	Histidine	0,431	0,111	3,898	0,000119928	0,008576838	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MMP-1	Ximenoylacetone	0,909	0,233	3,899	0,000119725	0,008576838	Organooxygen compounds	Carbonyl compounds
CXCL5	Feruloylcholine	1,273	0,326	3,900	0,000118868	0,008576838	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
FGF-21	[4]-Gingerdiol 3,5-diacetate	2,271	0,583	3,896	0,000121058	0,008628712	Phenols	Methoxyphenols
MCP-2	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-0,936	0,241	-3,891	0,0001236	0,008751356	Flavonoids	Flavonoid glycosides
CD40	Aminobutanoic acid (ABA)/3-Aminobutanoic acid	1,360	0,349	3,891	0,000123189	0,008751356	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
DNER	Naringenin	0,195	0,050	3,889	0,000124116	0,008758795	Flavonoids	Flavans
MCP-2	Licoagrodin	-1,133	0,291	-3,887	0,000125362	0,008798283	Flavonoids	Flavans
CXCL6	Sorgoleone 358	1,360	0,350	3,887	0,000125501	0,008798283	Organooxygen compounds	Carbonyl compounds
VEGFA	(-)-Dioxibrassinin	-0,589	0,152	-3,884	0,000126939	0,008869944	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
FGF-21	LysoPE(0:0/20:1(11Z))	1,524	0,393	3,881	0,000128508	0,008950202	Glycerophospholipids	Glycerophosphoethanolamines
CXCL6	Eriojaposide B	-2,028	0,523	-3,874	0,000131669	0,009139389	Fatty Acyls	Fatty acyl glycosides
SCF	Benzyl alcohol	0,129	0,033	3,874	0,000132082	0,009139389	Benzene and substituted derivatives	Benzyl alcohols
CSF-1	2-Amino-1,6-dimethylfuro[3,2-e]imidazo[4,5-b]pyridine	0,166	0,043	3,870	0,000133921	0,009236631	Imidazopyridines	NOT AVAILABLE
LIF-R	FAHFA(18:0/9-O-18:0)	-0,145	0,037	-3,868	0,000134893	0,009272986	Fatty Acyls	Fatty acids and conjugates
MMP-1	Feruloylcholine	0,734	0,190	3,867	0,000135753	0,009272986	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
FGF-23	Phthalate	3,124	0,808	3,867	0,00013571	0,009272986	Benzene and substituted derivatives	Benzoic acids and derivatives
CXCL1	(-)-Dioxibrassinin	-2,792	0,722	-3,865	0,000136808	0,009315188	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
SCF	C24:6	-0,305	0,079	-3,862	0,000137911	0,00936035	Fatty Acyls	Fatty acyl thioesters
MMP-1	KB 2	1,061	0,275	3,855	0,000141863	0,009598057	Flavonoids	Flavones
CXCL11	Lyciumin A	-1,179	0,306	-3,854	0,000142573	0,009615562	2-arylbenzofuran flavonoids	NOT AVAILABLE
CXCL6	Histidine	0,937	0,243	3,850	0,000144823	0,009736519	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CXCL6	1-O-Galloylglycerol	-1,683	0,437	-3,849	0,000145411	0,009737769	Benzene and substituted derivatives	Benzoic acids and derivatives
MCP-1	Mangostenone B	0,885	0,230	3,848	0,000145756	0,009737769	Benzopyrans	1-benzopyrans
MCP-2	Apigenin	-0,697	0,181	-3,846	0,000146783	0,009745295	Flavonoids	Flavones
MCP-4	3,4-Dimethyl-5-pentyl-2-furantridecanoic acid	1,032	0,268	3,847	0,000146732	0,009745295	Fatty Acyls	Fatty acids and conjugates
ADA	Resveratrol 4''-(6-galloylglucoside)	0,490	0,127	3,841	0,000149632	0,009903599	Prenol lipids	Sesterterpenoids
CXCL11	Apigenin	-1,194	0,311	-3,839	0,000151098	0,009952185	Flavonoids	Flavones
CST5	Methyl 3,4-dihydroxy-5-prenylbenzoate 3-glucoside	-0,454	0,118	-3,839	0,0001513	0,009952185	Prenol lipids	Terpene glycosides
MCP-4	Eriojaposide B	-1,464	0,383	-3,825	0,000159719	0,010473615	Fatty Acyls	Fatty acyl glycosides
LIF-R	Rutin	-0,434	0,113	-3,822	0,000161675	0,010569377	Flavonoids	Flavonoid glycosides
MCP-1	Octadecyl fumarate	0,377	0,099	3,819	0,000163233	0,010638587	Fatty Acyls	Fatty acid esters
DNER	5''''-(4-Hydroxy-(E)-cinnamoyl) alpha-L-arabinofuranosyl-(1->3)-be	-0,157	0,041	-3,814	0,000166362	0,010809471	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CXCL1	Marcanine A	-3,451	0,906	-3,810	0,000169086	0,010821515	Quinolines and derivatives	Benzoquinolines
MCP-4	Erinapyrone C	-3,438	0,902	-3,811	0,000168233	0,010821515	Pyrans	Pyranones and derivatives
TNFSF14	Divanillyltetrahydrofuran ferulate	-0,803	0,211	-3,813	0,000167083	0,010821515	Furanoid lignans	Tetrahydrofuran lignans
SCF	Neferine	0,413	0,108	3,811	0,000168392	0,010821515	Isoquinolines and derivatives	Benzylisoquinolines
FGF-21	5-Hydroxypentanoic acid	0,846	0,222	3,811	0,000168637	0,010821515	Fatty Acyls	Fatty acids and conjugates
CXCL6	4'',5,6-Trimethylscutellarein 7-glucoside	1,939	0,509	3,806	0,000171911	0,010969336	Anthracenes	Anthraquinones
MCP-4	N-(1-Deoxy-1-fructosyl)leucine	-1,482	0,389	-3,805	0,000172515	0,01097507	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
SCF	Diacetoxyscirpenol	-0,610	0,161	-3,793	0,000180681	0,011460331	Prenol lipids	Sesquiterpenoids
MCP-2	Kanzonol F	0,625	0,165	3,790	0,000182794	0,011559945	Isoflavonoids	Furanoisoflavonoids
DNER	LysoPE(0:0/20:2(11Z,14Z))	0,193	0,051	3,788	0,000183964	0,011599534	Glycerophospholipids	Glycerophosphoethanolamines
CCL28	(-)-Epigallocatechin 3,5-di-gallate	-0,648	0,171	-3,786	0,000185065	0,01163453	Flavonoids	Flavans
DNER	Heptadecanoic acid	-0,237	0,063	-3,782	0,00018793	0,011779876	Fatty Acyls	Fatty acids and conjugates
CCL4	Brassinin	-0,495	0,131	-3,781	0,000189289	0,01183026	Indoles and derivatives	Indoles
CXCL5	Kanzonol F	1,946	0,515	3,779	0,000190192	0,011851971	Isoflavonoids	Furanoisoflavonoids
LAP.TGF-beta-1	1-(11Z-eicosenoyl)-glycero-3-phosphate	-0,637	0,169	-3,773	0,000194514	0,012085981	Glycerophospholipids	Glycerophosphates
MCP-1	1-(11Z-eicosenoyl)-glycero-3-phosphate	-0,763	0,202	-3,772	0,000195214	0,012094207	Glycerophospholipids	Glycerophosphates
CXCL5	Somniferine	-1,568	0,416	-3,770	0,000197211	0,012182468	Morphinans	NOT AVAILABLE
MCP-2	N-(1-Deoxy-1-fructosyl)phenylalanine	-0,629	0,167	-3,768	0,000198727	0,012240691	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
EN-RAGE	Somniferine	-0,514	0,137	-3,766	0,00020035	0,01227426	Morphinans	NOT AVAILABLE
LIF-R	1-Phenyl-1,3-heptadecanedione	-0,245	0,065	-3,766	0,000200424	0,01227426	Organooxygen compounds	Carbonyl compounds
TNFSF14	7-Acetoxy-6-methoxycoumarin	-0,376	0,100	-3,764	0,000201781	0,01232195	Coumarins and derivatives	NOT AVAILABLE
CSF-1	1-(11Z-eicosenoyl)-glycero-3-phosphate	-0,314	0,083	-3,761	0,000203752	0,01240673	Glycerophospholipids	Glycerophosphates
CCL4	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-0,893	0,238	-3,757	0,000207171	0,012578995	Flavonoids	Flavonoid glycosides
IL-18R1	Protogonyautoxin I	-0,682	0,182	-3,744	0,000217451	0,013155318	Saxitoxins, gonyautoxins, and derivatives	NOT AVAILABLE
TRAIL	Tragopogonsaponin M	-0,330	0,088	-3,744	0,000217897	0,013155318	Isoflavonoids	O-methylated isoflavonoids
SIRT2	Eremopetasinorol	-2,573	0,688	-3,740	0,000220792	0,013292398	Organooxygen compounds	Alcohols and polyols
CXCL10	Lyciumin A	-0,802	0,215	-3,737	0,000223136	0,013395676	2-arylbenzofuran flavonoids	NOT AVAILABLE

MMP-1	6-Methylquinoline	-1,406	0,377	-3,730	0,000229856	0,01374031	Quinolines and derivatives	NOT AVAILABLE
CXCL5	3-Methylcyclopentadecanone	1,683	0,451	3,729	0,000230166	0,01374031	Organooxygen compounds	Carbonyl compounds
CXCL11	Methylpicraquassioside A	0,929	0,249	3,727	0,000231702	0,01379341	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-1	Hydrocortamate	0,734	0,198	-3,719	0,000239354	0,014209229	Steroids and steroid derivatives	Pregnane steroids
IL6	Protogonyautoxin I	-1,544	0,415	-3,718	0,000240156	0,014217262	Saxitoxins, gonyautoxins, and derivatives	NOT AVAILABLE
MCP-2	Erucic acid	0,556	0,150	3,715	0,000242615	0,014322998	Fatty Acyls	Fatty acids and conjugates
CXCL6	2-O-(Z-p-Hydroxycinnamoyl)-(x)-glyceric acid	-2,223	0,599	-3,713	0,000244491	0,014354227	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
CX3CL1	LysoPE(0:0/22:4(7Z,10Z,13Z,16Z))	-0,375	0,101	-3,713	0,000244254	0,014354227	Glycerophospholipids	Glycerophosphoethanolamines
MCP-4	LysoPE(0:0/22:4(7Z,10Z,13Z,16Z))	-0,824	0,222	-3,712	0,000245415	0,014368924	Glycerophospholipids	Glycerophosphoethanolamines
4E-BP1	Divanillyltetrahydrofuran ferulate	-1,241	0,335	-3,710	0,00024756	0,014454788	Furanoid lignans	Tetrahydrofuran lignans
CCL4	Theogallin	-1,339	0,361	-3,707	0,000250415	0,014541826	Organooxygen compounds	Alcohols and polyols
DNER	4'',5,6-Trimethylscutellarein 7-glucoside	-0,366	0,099	-3,707	0,00024991	0,014541826	Anthracenes	Anthraquinones
MMP-1	(2S,4S)-Monatin	-1,053	0,285	-3,699	0,000258196	0,01486045	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
DNER	1-(8Z,11Z,14Z-eicosatrienoyl)-glycero-3-phosphate	0,260	0,070	3,699	0,000257896	0,01486045	Glycerophospholipids	Glycerophospholipids
CXCL5	Phenylethyl primeveroside	2,401	0,649	3,698	0,000258691	0,01486045	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
FGF-23	3-Furanmethanol glucoside	2,431	0,657	3,699	0,000258106	0,01486045	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
LIF-R	2-Phenylethyl beta-D-glucopyranoside	-0,535	0,145	-3,696	0,000261114	0,014959322	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CCL4	Apigenin	-0,660	0,179	-3,690	0,000267326	0,015274123	Flavonoids	Flavones
SCF	8-Propanoylneosolaniol	-0,396	0,107	-3,689	0,000268154	0,015280454	Isoquinolines and derivatives	Benzylisoquinolines
CCL28	Linoleamide	0,495	0,134	3,688	0,000268955	0,015285226	Fatty Acyls	Fatty amides
TNFSF14	Aminobutanoic acid (ABA)/3-Aminobutanoic acid	1,875	0,509	3,683	0,000274354	0,015550636	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CDCP1	7-Methoxy-2-methylisoflavone	0,672	0,183	3,680	0,000277316	0,015676811	Isoflavonoids	O-methylated isoflavonoids
CST5	1,6-Dihydroxy-3,7-dimethoxy-2-(3-methyl-2-butenyl)-8-(3-hydroxy	-0,477	0,130	-3,679	0,000278505	0,015702349	Benzopyrans	1-benzopyrans
MMP-1	Peonidin-3-galactoside	-1,280	0,348	-3,678	0,000279578	0,015721262	Flavonoids	Flavonoid glycosides
SIRT2	C24:6	1,058	0,288	3,673	0,000284699	0,015967142	Fatty Acyls	Fatty acyl thioesters
MCP-4	Neferine	-1,022	0,278	-3,671	0,000286924	0,016049666	Isoquinolines and derivatives	Benzylisoquinolines
MCP-1	3-Hydroxymugineic acid	0,102	0,028	3,667	0,000290939	0,016231652	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CCL4	1-Phenyl-1,3-heptadecanedione	0,602	0,164	3,665	0,000293582	0,016336317	Organooxygen compounds	Carbonyl compounds
CXCL5	Alpha-Linolenic acid	1,038	0,283	3,663	0,000295029	0,016374122	Fatty Acyls	Lineolic acids and derivatives
CXCL6	Dide-O-methylsimmondsin	-1,957	0,535	-3,659	0,000300122	0,016491367	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CXCL10	Marcanine A	-1,649	0,451	-3,659	0,000299235	0,016491367	Quinolines and derivatives	Benzoquinolines
MCP-1	N-(1-Deoxy-1-fructosyl)leucine	-0,888	0,243	-3,658	0,000300651	0,016491367	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MMP-1	Artonin D	1,481	0,405	3,658	0,000301011	0,016491367	Linear 1,3-diarylpropanoids	Chalcones and dihydrochalcones
CXCL5	Murrayanol	2,306	0,630	3,661	0,000297985	0,016491367	Indoles and derivatives	Carbazoles
MCP-4	7-Methoxy-6-methyl-2H-1-benzopyran-2-one	-1,266	0,346	-3,655	0,000304085	0,016505355	Coumarins and derivatives	NOT AVAILABLE
MCP-2	Distichonic acid A	-0,640	0,175	-3,656	0,000303063	0,016505355	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
VEGFA	Dicyclohexyl disulfide	0,254	0,070	3,654	0,000305138	0,016505355	Organic disulfides	Dialkyldisulfides
MCP-1	Murrayanol	0,637	0,174	3,655	0,000304581	0,016505355	Indoles and derivatives	Carbazoles
MMP-1	5''''-(4-Hydroxy-(E)-cinnamoyl) alpha-L-arabinofuranosyl-(1->3)-be	0,744	0,203	3,656	0,000303609	0,016505355	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-4	Divanillyltetrahydrofuran ferulate	-1,316	0,360	-3,653	0,000306775	0,016510087	Furanoid lignans	Tetrahydrofuran lignans
MCP-4	Ximenoylacetone	0,653	0,179	3,653	0,000306235	0,016510087	Organooxygen compounds	Carbonyl compounds
FGF-21	LysoPE(0:0/18:3(6Z,9Z,12Z))	1,398	0,383	3,652	0,000307825	0,016524832	Glycerophospholipids	Glycerophosphoethanolamines
CXCL11	Thymol	-2,293	0,629	-3,648	0,000311984	0,016706046	Prenol lipids	Monoterpenoids
TRANCE	Decarbamoylneosaxitoxin	-1,216	0,334	-3,642	0,000318963	0,017036931	Saxitoxins, gonyautoxins, and derivatives	NOT AVAILABLE
SCF	Acesulfame	0,887	0,244	3,639	0,000322765	0,017196898	Organic sulfuric acids and derivatives	NOT AVAILABLE
MCP-4	Artonin D	1,126	0,309	3,638	0,000324106	0,017225293	Linear 1,3-diarylpropanoids	Chalcones and dihydrochalcones
MCP-1	Eriojaposide B	-0,867	0,239	-3,629	0,000335364	0,017758431	Fatty Acyls	Fatty acyl glycosides
CXCL10	LysoPE(0:0/20:1(11Z))	-0,717	0,198	-3,628	0,000335804	0,017758431	Glycerophospholipids	Glycerophosphoethanolamines
IL6	LysoPE(0:0/18:2(9Z,12Z))	-0,578	0,159	-3,626	0,000338658	0,017838321	Glycerophospholipids	Glycerophosphoethanolamines
SCF	Ethyl beta-D-glucopyranoside	-0,149	0,041	-3,626	0,000339097	0,017838321	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
LAP.TGF-beta-1	Feruloylcholine	0,274	0,076	3,625	0,000339825	0,017838321	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
CXCL6	C24:6	1,006	0,278	3,623	0,000342998	0,017960614	Fatty Acyls	Fatty acyl thioesters
MCP-4	Hesperetin	-1,366	0,377	-3,620	0,000346682	0,018064748	Flavonoids	O-methylated flavonoids
CCL4	Torvanol A	0,310	0,086	3,620	0,000346189	0,018064748	Isoflavonoids	O-methylated isoflavonoids
CXCL11	2-Methoxynaphthalene	-1,204	0,333	-3,618	0,000349425	0,018163295	Naphthalenes	NOT AVAILABLE
CCL4	Lyciumin A	-0,637	0,176	-3,614	0,000353644	0,018337861	2-arylbenzofuran flavonoids	NOT AVAILABLE
CXCL6	1-(2-Thienyl)-1,2-propanedione	-5,475	1,516	-3,612	0,000356296	0,018430538	Organooxygen compounds	Carbonyl compounds
CXCL6	Hydrocortamate	1,569	0,435	3,610	0,00035952	0,018552284	Steroids and steroid derivatives	Pregnane steroids
MCP-2	1-(5Z,8Z,11Z,14Z-eicosatetraenoyl)-sn-glycero-3-phosphate	-0,730	0,202	-3,609	0,000361266	0,018597367	Glycerophospholipids	Glycerophosphates
IL6	1-(8Z,11Z,14Z-eicosatrienoyl)-glycero-3-phosphate	-1,014	0,281	-3,607	0,000362903	0,018636616	Glycerophospholipids	Glycerophospholipids
FGF-21	LysoPE(0:0/18:1(11Z))	0,965	0,267	3,606	0,000364283	0,018662477	Glycerophospholipids	Glycerophosphoethanolamines
CXCL11	(-)-Dioxibrassinin	-1,852	0,514	-3,602	0,000370066	0,018913303	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CD8A	LysoPE(0:0/20:0)	-0,860	0,239	-3,599	0,000373673	0,018915944	Glycerophospholipids	Glycerophosphoethanolamines
Flt3L	Protogonyautoxin I	-0,674	0,187	-3,599	0,000374431	0,018915944	Saxitoxins, gonyautoxins, and derivatives	NOT AVAILABLE
MCP-1	5-Hydroxypentanoic acid	-0,289	0,080	-3,599	0,000374556	0,018915944	Fatty Acyls	Fatty acids and conjugates
HGF	Feruloylcholine	0,205	0,057	3,601	0,000371438	0,018915944	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
TNF	Triose	1,186	0,329	3,600	0,000373138	0,018915944	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CX3CL1	Ovalicin	0,554	0,154	3,596	0,000378617	0,019075839	Organooxygen compounds	Alcohols and polyols
MMP-1	FAHFA(16:0/9-O-18:0)	0,533	0,148	3,593	0,000382638	0,019232984	Fatty Acyls	Fatty acids and conjugates
MMP-1	Brassinin	-0,869	0,242	-3,592	0,000383592	0,019235547	Indoles and derivatives	Indoles
CASP-8	Madlongiside C	-0,594	0,166	-3,587	0,000391865	0,019558382	Prenol lipids	Triterpenoids
TWEAK	Syndesine	-0,307	0,086	-3,587	0,000391597	0,019558382	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
OSM	1-Arachidonoylglycerophosphoinositol	0,848	0,237	3,584	0,000395717	0,019704472	Glycerophospholipids	Glycerophosphates
CCL28	(Iso)Leucine	-0,659	0,184	-3,581	0,00039974	0,019831128	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
IL6	3-hydroxyundecanoyl carnitine	0,483	0,135	3,581	0,000400121	0,019831128	Fatty Acyls	Fatty acid esters
SIRT2	L-1,2,3,4-Tetrahydro-beta-carboline-3-carboxylic acid	-1,283	0,358	-3,579	0,000403122	0,019844629	Indoles and derivatives	Pyridoindoles
MCP-4	Riboflavin	-0,668	0,187	-3,580	0,000401336	0,019844629	Pteridines and derivatives	Alloxazines and isoalloxazines
MCP-1	Ovalicin	0,754	0,211	3,579	0,000403187	0,019844629	Organooxygen compounds	Alcohols and polyols
CCL4	2-Methoxynaphthalene	-0,683	0,191	-3,571	0,000415625	0,020362769	Naphthalenes	NOT AVAILABLE
CCL4	Riboflavin	-0,473	0,133	-3,571	0,000415175	0,020362769	Pteridines and derivatives	Alloxazines and isoalloxazines
CXCL1	Thymol	-3,163	0,887	-3,567	0,000421309	0,020449879	Prenol lipids	Monoterpenoids
SIRT2	Gallic acid	-1,665	0,467	-3,566	0,000423161	0,020449879	Benzene and substituted derivatives	Benzoic acids and derivatives
VEGFA	1-[(2,5-Dimethylphenyl)azo]-2-naphthalenol	0,142	0,040	3,567	0,00042023	0,020449879	Naphthalenes	Naphthols and derivatives
CCL25	LysoPE(0:0/18:1(11Z))	0,322	0,090	3,569	0,000418381	0,020449879	Glycerophospholipids	Glycerophosphoethanolamines
MCP-2	3-Methylcyclopentadecanone	0,517	0,145	3,566	0,000422443	0,020449879	Organooxygen compounds	Carbonyl compounds
CXCL6	Murrayanol	1,368	0,384	3,566	0,00042269	0,020449879	Indoles and derivatives	Carbazoles
IL6	1,6-Dihydroxy-3,7-dimethoxy-2-(3-methyl-2-butenyl)-8-(3-hydroxy	0,744	0,209	3,563	0,00042702	0,020589701	Benzopyrans	1-benzopyrans
OPG	1-Oleoylglycerophosphoinositol	0,440	0,124	3,560	0,000432439	0,02080391	Glycerophospholipids	Glycerophosphoinositols
CXCL6	1-(8Z,11Z,14Z-eicosatrienoyl)-glycero-3-phosphate	-1,294	0,364	-3,559	0,000434064	0,020835061	Glycerophospholipids	Glycerophospholipids
CCL25	1-Oleoylglycerophosphoinositol	0,462	0,130	3,558	0,000435634	0,020863438	Glycerophospholipids	Glycerophosphoinositols
SIRT2	(-)-Dioxibrassinin	-2,102	0,591	-3,557	0,000436939	0,02087904	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CXCL5	PA(20:1(11Z)/15:0)	-2,051	0,577	-3,556	0,000438902	0,020925921	Glycerophospholipids	Glycerophosphates
CXCL1	Oxobutanoic acid	-5,876	1,653	-3,554	0,000441042	0,020981002	Keto acids and derivatives	Short-chain keto acids and derivatives
CXCL6	Hv-NCC-1	-1,880	0,529	-3,553	0,00044304	0,020982376	Tetrapyrroles and derivatives	NOT AVAILABLE
CXCL6	Aminobutanoic acid (ABA)/3-Aminobutanoic acid/3-Aminobutanoi	4,234	1,192	3,553	0,000442468	0,020982376	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
IL6	Neferine	-1,046	0,295	-3,542	0,000460514	0,02171344	Isoquinolines and derivatives	Benzylisoquinolines
TRAIL	N-Methylcalystegine B2	0,587	0,166	3,542	0,000460423	0,02171344	Tropane alkaloids	NOT AVAILABLE
LIF-R	3-hydroxynonanoyl carnitine	-0,126	0,035	-3,541	0,000463309	0,021797005	Fatty Acyls	Fatty acid esters
CXCL11	Alpha-Linolenic acid	0,551	0,156	3,537	0,000469296	0,022030034	Fatty Acyls	Lineolic acids and derivatives
MCP-2	Curcumin	-0,932	0,264	-3,533	0,000476735	0,022232314	Diarylheptanoids	Linear diarylheptanoids
LAP.TGF-beta-1	(-)-Dioxibrassinin	-0,765	0,217	-3,533	0,00047661	0,022232314	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CXCL11	Murrayanol	1,224	0,347	3,533	0,000475665	0,022232314	Indoles and derivatives	Carbazoles
FGF-19	2-Phenylethyl beta-D-glucopyranoside	-1,894	0,536	-3,531	0,00047995	0,022333398	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CST5	Methyl 4,6-di-O-galloyl-beta-D-glucopyranoside	-0,485	0,137	-3,528	0,000484493	0,022446749	Tannins	NOT AVAILABLE
MCP-2	D-erythro-L-galacto-Nonulose	-0,330	0,094	-3,528	0,000484398	0,022446749	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
DNER	3,4-Dimethyl-5-pentyl-2-furantridecanoic acid	-0,251	0,071	-3,528	0,000485913	0,02244859	Fatty Acyls	Fatty acids and conjugates
MCP-2	Phenylethyl primeveroside	0,735	0,208	3,527	0,000486639	0,02244859	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CSF-1	N1-trans-Feruloylagmatine	0,173	0,049	3,525	0,000489777	0,022527284	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
CSF-1	Austrobailignan 7	0,190	0,054	3,525	0,000490804	0,022527284	Furanoid lignans	Tetrahydrofuran lignans
MCP-1	Heptadecanoic acid	0,521	0,148	3,524	0,000491516	0,022527284	Fatty Acyls	Fatty acids and conjugates
STAMBP	Eremopetasinorol	-1,681	0,478	-3,518	0,000503802	0,023040816	Organooxygen compounds	Alcohols and polyols
OSM	Divanillyltetrahydrofuran ferulate	-1,208	0,344	-3,516	0,000507557	0,023145122	Furanoid lignans	Tetrahydrofuran lignans
Flt3L	(-)-Dioxibrassinin	-0,699	0,199	-3,515	0,000508254	0,023145122	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-1	Salvianolic acid L	-0,783	0,223	-3,511	0,000515375	0,023419365	Naphthalenes	Phenylnaphthalenes
MCP-2	(±)-2-Butylthiazolidine	-0,706	0,201	-3,511	0,000516709	0,023429995	Azolidines	Thiazolidines
CXCL6	Peonidin-3-galactoside	-1,280	0,365	-3,508	0,000522196	0,023628522	Flavonoids	Flavonoid glycosides
CXCL5	1,6-Dihydroxy-3,7-dimethoxy-2-(3-methyl-2-butenyl)-8-(3-hydroxy	1,556	0,444	3,504	0,000529311	0,023899744	Benzopyrans	1-benzopyrans
LAP.TGF-beta-1	Lyciumin A	-0,453	0,129	-3,502	0,000533151	0,024022221	2-arylbenzofuran flavonoids	NOT AVAILABLE
4E-BP1	1-Isothiocyanato-7-(methylsulfinyl)heptane	-1,272	0,363	-3,499	0,000539421	0,024253479	Sulfoxides	NOT AVAILABLE

AXIN1	Dide-O-methylsimmondsin	-1,735	0,496	-3,497	0,000542887	0,024324997	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
LAP.TGF-beta-1	Somniferine	-0,337	0,096	-3,497	0,000543295	0,024324997	Morphinans	NOT AVAILABLE
DNER	14,16-Nonacosanedione	-0,236	0,068	-3,495	0,000546947	0,02443719	Organooxygen compounds	Carbonyl compounds
MCP-2	LysoPE(0:0/20:2(11Z,14Z))	-0,486	0,139	-3,492	0,000553418	0,024674577	Glycerophospholipids	Glycerophosphoethanolamines
DNER	Methylpicraquassioside A	-0,187	0,053	-3,490	0,000555646	0,024722188	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-1	Sorgoleone 358	0,558	0,160	3,489	0,000559149	0,024826223	Organooxygen compounds	Carbonyl compounds
IL6	(2S,4R)-4-(9H-Pyrido[3,4-b]indol-1-yl)-1,2,4-butanetriol	0,811	0,233	3,486	0,000564355	0,025005286	Harmala alkaloids	NOT AVAILABLE
CXCL11	Divanillyltetrahydrofuran ferulate	-1,554	0,446	-3,485	0,000566017	0,025018867	Furanoid lignans	Tetrahydrofuran lignans
CSF-1	Calystegine C1	0,403	0,116	3,485	0,00056701	0,025018867	Tropane alkaloids	NOT AVAILABLE
SIRT2	Divanillyltetrahydrofuran ferulate	-1,785	0,512	-3,483	0,000570633	0,025126715	Furanoid lignans	Tetrahydrofuran lignans
MCP-1	5-Phenylvaleric acid	1,369	0,393	3,481	0,000575235	0,025277118	Fatty Acyls	Fatty acids and conjugates
MCP-4	D-erythro-L-galacto-Nonulose	-0,452	0,130	-3,478	0,000580104	0,025411994	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-2	Mangostenone B	0,930	0,267	3,478	0,000580689	0,025411994	Benzopyrans	1-benzopyrans
FGF-19	LysoPE(0:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	-0,683	0,196	-3,477	0,000582923	0,025450865	Glycerophospholipids	Glycerophosphoethanolamines
CCL23	Butyl 3-O-caffeoylquinate	-0,511	0,147	-3,476	0,00058516	0,025450865	Organooxygen compounds	Alcohols and polyols
MCP-1	6-Prenylnaringenin	0,129	0,037	3,476	0,000584357	0,025450865	Flavonoids	Flavans
CXCL5	C24:6	1,589	0,457	3,474	0,000589419	0,025583895	Fatty Acyls	Fatty acyl thioesters
MCP-4	Licoagrodin	-1,410	0,406	-3,470	0,000598092	0,025907577	Flavonoids	Flavans
TNFSF14	Peonidin-3-galactoside	-0,541	0,156	-3,467	0,000604895	0,026096217	Flavonoids	Flavonoid glycosides
SCF	Murrayanol	-0,379	0,109	-3,467	0,000604851	0,026096217	Indoles and derivatives	Carbazoles
CCL4	4'',5,6-Trimethylscutellarein 7-glucoside	0,920	0,265	3,466	0,00060627	0,026102666	Anthracenes	Anthraquinones
FGF-19	Egonol glucoside	-0,928	0,268	-3,465	0,00060809	0,026128246	2-arylbenzofuran flavonoids	NOT AVAILABLE
LAP.TGF-beta-1	1-(8Z,11Z,14Z-eicosatrienoyl)-glycero-3-phosphate	-0,479	0,138	-3,462	0,000614155	0,026235248	Glycerophospholipids	Glycerophospholipids
LIF-R	Alpha-Linolenic acid	-0,123	0,036	-3,462	0,000614273	0,026235248	Fatty Acyls	Lineolic acids and derivatives
MCP-4	Crosatoside B	0,854	0,247	3,463	0,000612919	0,026235248	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
CCL28	Eriojaposide B	-0,622	0,180	-3,461	0,000616625	0,026283039	Fatty Acyls	Fatty acyl glycosides
CX3CL1	Licoagrodin	-0,640	0,185	-3,455	0,000629756	0,02678913	Flavonoids	Flavans
HGF	LysoPE(0:0/20:2(11Z,14Z))	-0,261	0,076	-3,453	0,000635954	0,026998916	Glycerophospholipids	Glycerophosphoethanolamines
CXCL10	3-hydroxynonanoyl carnitine	0,376	0,109	3,446	0,000651403	0,027599813	Fatty Acyls	Fatty acid esters
ST1A1	Dide-O-methylsimmondsin	-1,874	0,544	-3,443	0,000657826	0,02781197	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
TNFSF14	3-Methylcyclopentadecanone	0,406	0,118	3,442	0,000659681	0,02781197	Organooxygen compounds	Carbonyl compounds
CXCL1	Sorgoleone 358	1,541	0,448	3,442	0,000660325	0,02781197	Organooxygen compounds	Carbonyl compounds
CCL4	Myricanol 5-glucoside	-0,739	0,215	-3,439	0,000667878	0,028074608	Lactones	Gamma butyrolactones
VEGFA	Gallic acid	-0,414	0,120	-3,438	0,000671221	0,028134258	Benzene and substituted derivatives	Benzoic acids and derivatives
FGF-21	9-(4-Hydroxyphenyl)-2-methoxy-1H-phenalen-1-one	1,232	0,358	3,437	0,000671938	0,028134258	Naphthalenes	Phenylnaphthalenes
CXCL11	Licoagrodin	-1,726	0,502	-3,436	0,000675448	0,028225775	Flavonoids	Flavans
MMP-1	gamma-Glutamyl-beta-(isoxazolin-5-on-2-yl)alanine	-1,212	0,353	-3,433	0,000682803	0,028256589	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CXCL11	Neferine	-1,184	0,345	-3,433	0,000681414	0,028256589	Isoquinolines and derivatives	Benzylisoquinolines
DNER	Albanin B	-0,231	0,067	-3,434	0,000678473	0,028256589	Flavonoids	Flavones
VEGFA	S-3-oxodecanoyl cysteamine	0,447	0,130	3,433	0,000682815	0,028256589	Fatty Acyls	Fatty acyl thioesters
MMP-10	2-Methoxynaphthalene	0,705	0,205	3,433	0,000682099	0,028256589	Naphthalenes	NOT AVAILABLE
STAMBP	Divanillyltetrahydrofuran ferulate	-1,218	0,355	-3,431	0,000688106	0,028420367	Furanoid lignans	Tetrahydrofuran lignans
STAMBP	(-)-Dioxibrassinin	-1,404	0,410	-3,424	0,000704687	0,028921079	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-2	Myricanol 5-glucoside	-0,746	0,218	-3,423	0,000707401	0,028921079	Lactones	Gamma butyrolactones
HGF	Marcanine A	-0,699	0,204	-3,424	0,000703782	0,028921079	Quinolines and derivatives	Benzoquinolines
CCL28	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-0,538	0,157	-3,422	0,000708371	0,028921079	Flavonoids	Flavonoid glycosides
VEGFA	Hv-NCC-1	-0,485	0,142	-3,422	0,00070822	0,028921079	Tetrapyrroles and derivatives	NOT AVAILABLE
FGF-21	LysoPE(0:0/22:5(4Z,7Z,10Z,13Z,16Z))	1,428	0,417	3,424	0,000703667	0,028921079	Glycerophospholipids	Glycerophosphoethanolamines
CST5	Kanzonol F	-0,517	0,151	-3,419	0,000717703	0,029246037	Isoflavonoids	Furanoisoflavonoids
CX3CL1	1-(5Z,8Z,11Z,14Z-eicosatetraenoyl)-sn-glycero-3-phosphate	-0,438	0,128	-3,415	0,000725971	0,029470278	Glycerophospholipids	Glycerophosphates
LAP.TGF-beta-1	C24:6	0,361	0,106	3,416	0,000724719	0,029470278	Fatty Acyls	Fatty acyl thioesters
IL-10RB	Medicarpin 3-O-(6''-malonylglucoside)	-0,263	0,077	-3,413	0,000732254	0,029648992	Isoflavonoids	Furanoisoflavonoids
CXCL5	1-Phenyl-1,3-heptadecanedione	1,781	0,522	3,413	0,000733156	0,029648992	Organooxygen compounds	Carbonyl compounds
MMP-1	(-)-Epigallocatechin 3,5-di-gallate	-1,641	0,481	-3,412	0,000734626	0,029652188	Flavonoids	Flavans
VEGFA	1,2,4,5,7-Pentathiocane	-0,329	0,096	-3,411	0,000736621	0,029676516	Organic disulfides	NOT AVAILABLE
IL-18R1	1-Arachidonoylglycerophosphoinositol	0,395	0,116	3,410	0,000738764	0,02970668	Glycerophospholipids	Glycerophosphates
SCF	(S,E)-Zearalenone	-0,159	0,047	-3,410	0,000740874	0,029735431	Macrolides and analogues	Zearalenones
CXCL11	Brassinin	-0,780	0,229	-3,409	0,000743208	0,029773018	Indoles and derivatives	Indoles
CCL4	Shoyuflavone C	-3,454	1,014	-3,407	0,000749	0,029892693	Isoflavonoids	Isoflav-2-enes
CXCL6	LysoPE(0:0/20:1(11Z))	-1,068	0,313	-3,407	0,000747657	0,029892693	Glycerophospholipids	Glycerophosphoethanolamines
TNFSF14	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-0,670	0,197	-3,404	0,000756132	0,030064725	Flavonoids	Flavonoid glycosides
DNER	LysoPE(0:0/20:1(11Z))	0,206	0,061	3,404	0,000755189	0,030064725	Glycerophospholipids	Glycerophosphoethanolamines
CSF-1	Camelinin	0,338	0,099	3,402	0,000759738	0,030151834	Sulfoxides	NOT AVAILABLE
VEGFA	N-(1-Deoxy-1-fructosyl)valine	0,368	0,108	3,401	0,000763312	0,030203884	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CXCL1	Feruloylcholine	0,864	0,254	3,400	0,000765301	0,030203884	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
MMP-1	3,4-Dimethyl-5-pentyl-2-furantridecanoic acid	1,200	0,353	3,401	0,000764149	0,030203884	Fatty Acyls	Fatty acids and conjugates
4E-BP1	1-Propenyl 1-(1-propenylthio)propyl disulfide	-0,995	0,293	-3,398	0,000770755	0,030362906	Thioethers	Thioenol ethers
TNF	Methyl 4,6-di-O-galloyl-beta-D-glucopyranoside	0,627	0,185	3,397	0,000773548	0,030416701	Tannins	NOT AVAILABLE
CXCL11	Theogallin	-2,142	0,631	-3,396	0,00077593	0,03045418	Organooxygen compounds	Alcohols and polyols
CST5	(S)-[8]-Gingerol	-0,209	0,062	-3,394	0,000783725	0,030703582	Phenols	Methoxyphenols
DNER	LysoPE(0:0/18:2(9Z,12Z))	0,135	0,040	3,393	0,00078669	0,030763199	Glycerophospholipids	Glycerophosphoethanolamines
TNFB	Butyl 3-O-caffeoylquinate	-0,356	0,105	-3,391	0,000791741	0,030904006	Organooxygen compounds	Alcohols and polyols
CST5	Methylpicraquassioside A	-0,451	0,133	-3,385	0,000807666	0,031467973	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MMP-1	Protogonyautoxin I	-1,742	0,515	-3,383	0,000812878	0,031597104	Saxitoxins, gonyautoxins, and derivatives	NOT AVAILABLE
VEGFA	Resveratrol 4''-(6-galloylglucoside)	0,273	0,081	3,383	0,000813946	0,031597104	Prenol lipids	Sesterterpenoids
CXCL5	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-2,555	0,756	-3,380	0,000821953	0,031640356	Flavonoids	Flavonoid glycosides
AXIN1	Eremopetasinorol	-2,085	0,617	-3,381	0,000820458	0,031640356	Organooxygen compounds	Alcohols and polyols
MCP-1	Acesulfame	-1,320	0,391	-3,379	0,00082485	0,031640356	Organic sulfuric acids and derivatives	NOT AVAILABLE
OSM	Peonidin-3-galactoside	-0,859	0,254	-3,379	0,000825452	0,031640356	Flavonoids	Flavonoid glycosides
LAP.TGF-beta-1	Myricanol 5-glucoside	-0,532	0,157	-3,381	0,000820215	0,031640356	Lactones	Gamma butyrolactones
SLAMF1	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-0,396	0,117	-3,379	0,000823811	0,031640356	Flavonoids	Flavonoid glycosides
CSF-1	Hv-NCC-1	-0,336	0,100	-3,380	0,000822408	0,031640356	Tetrapyrroles and derivatives	NOT AVAILABLE
MCP-1	Indole-3-acetylglutamic acid	-0,861	0,255	-3,378	0,000827965	0,031679697	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-2	Riboflavin	-0,455	0,135	-3,377	0,000831881	0,031772501	Pteridines and derivatives	Alloxazines and isoalloxazines
MCP-1	1-Phenyl-1,3-heptadecanedione	0,487	0,145	3,372	0,000844152	0,032183496	Organooxygen compounds	Carbonyl compounds
MCP-4	Ethyl cinnamate	1,892	0,562	3,368	0,000858065	0,032655508	Cinnamic acids and derivatives	Cinnamic acid esters
MCP-2	Divanillyltetrahydrofuran ferulate	-0,876	0,260	-3,366	0,00086444	0,032839471	Furanoid lignans	Tetrahydrofuran lignans
IL6	Mangostenone B	1,324	0,394	3,365	0,000867592	0,032900586	Benzopyrans	1-benzopyrans
CCL4	Sorgoleone 358	0,614	0,183	3,363	0,00087337	0,033060855	Organooxygen compounds	Carbonyl compounds
MCP-1	LysoPE(0:0/20:1(11Z))	-0,480	0,143	-3,362	0,000876289	0,033112545	Glycerophospholipids	Glycerophosphoethanolamines
CCL4	(2S,4S)-Monatin	-0,521	0,155	-3,358	0,000887863	0,033490506	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CXCL5	4'',5,6-Trimethylscutellarein 7-glucoside	2,825	0,842	3,356	0,000895059	0,033702285	Anthracenes	Anthraquinones
HGF	Neferine	-0,366	0,109	-3,355	0,000898341	0,03370678	Isoquinolines and derivatives	Benzylisoquinolines
MMP-1	Hydrocortamate	1,399	0,417	3,355	0,000897314	0,03370678	Steroids and steroid derivatives	Pregnane steroids
4E-BP1	L-1,2,3,4-Tetrahydro-beta-carboline-3-carboxylic acid	-0,789	0,235	-3,354	0,000901476	0,033764938	Indoles and derivatives	Pyridoindoles
MMP-1	N-(1-Deoxy-1-fructosyl)leucine	-1,716	0,512	-3,351	0,00090985	0,034018825	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
ADA	Benzothiazole	-0,147	0,044	-3,349	0,000915797	0,034181214	Benzothiazoles	NOT AVAILABLE
CXCL11	Eriojaposide B	-1,591	0,475	-3,347	0,000923345	0,034374859	Fatty Acyls	Fatty acyl glycosides
CXCL10	Neferine	-0,808	0,242	-3,346	0,000924211	0,034374859	Isoquinolines and derivatives	Benzylisoquinolines
HGF	1-Propenyl 1-(1-propenylthio)propyl disulfide	-0,412	0,123	-3,343	0,0009344	0,034693269	Thioethers	Thioenol ethers
CXCL11	Marcanine A	-2,160	0,646	-3,343	0,00093637	0,034705927	Quinolines and derivatives	Benzoquinolines
MCP-4	2-Methoxystypandrone	-3,744	1,121	-3,341	0,000942476	0,034854275	Naphthalenes	Naphthoquinones
TNFSF14	1-Phenyl-1,3-heptadecanedione	0,454	0,136	3,340	0,000943643	0,034854275	Organooxygen compounds	Carbonyl compounds
CCL20	Hv-NCC-1	-1,343	0,403	-3,336	0,000957063	0,035106579	Tetrapyrroles and derivatives	NOT AVAILABLE
MCP-4	L-1,2,3,4-Tetrahydro-beta-carboline-3-carboxylic acid	-0,845	0,253	-3,337	0,000955559	0,035106579	Indoles and derivatives	Pyridoindoles
MCP-2	2'',4,4''-Trihydroxy-6''-methoxy-3'',5''-diprenylchalcone	0,905	0,271	3,338	0,000952913	0,035106579	Linear 1,3-diarylpropanoids	Chalcones and dihydrochalcones
CXCL5	Egonol glucoside	1,934	0,579	3,337	0,000955316	0,035106579	2-arylbenzofuran flavonoids	NOT AVAILABLE
DNER	KB 2	-0,187	0,056	-3,335	0,000961928	0,035224397	Flavonoids	Flavones
CCL4	Divanillyltetrahydrofuran ferulate	-0,856	0,257	-3,333	0,000968822	0,035355358	Furanoid lignans	Tetrahydrofuran lignans
MMP-1	Naringenin	-0,831	0,249	-3,333	0,000968598	0,035355358	Flavonoids	Flavans
VEGFA	N-(1-Deoxy-1-fructosyl)phenylalanine	-0,284	0,085	-3,332	0,000972448	0,035427013	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CXCL10	Oxobutanoic acid	-2,741	0,823	-3,331	0,000975038	0,035460763	Keto acids and derivatives	Short-chain keto acids and derivatives
TNFSF14	Marcanine A	-1,019	0,306	-3,329	0,000982669	0,035616745	Quinolines and derivatives	Benzoquinolines
CXCL11	Heptadecanoic acid	0,978	0,294	3,329	0,000981272	0,035616745	Fatty Acyls	Fatty acids and conjugates
MCP-2	Crosatoside B	0,592	0,178	3,328	0,000985017	0,035641239	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
EN-RAGE	1-(5Z,8Z,11Z,14Z-eicosatetraenoyl)-sn-glycero-3-phosphate	0,692	0,208	3,326	0,000991077	0,035799705	Glycerophospholipids	Glycerophosphates
MCP-4	1,2,4,5,7-Pentathiocane	-0,877	0,264	-3,324	0,000997326	0,035843188	Organic disulfides	NOT AVAILABLE
DNER	Histidine	-0,157	0,047	-3,325	0,00099436	0,035843188	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
FGF-21	1-Arachidonoylglycerophosphoinositol	1,429	0,430	3,325	0,000997194	0,035843188	Glycerophospholipids	Glycerophosphates

CXCL5	Apigenin	-2,892	0,869	-3,324	0,000990171	0,035849052	Flavonoids	Flavones
IL18	Protogonyautoxin I	0,967	0,291	-3,320	0,001013872	0,036315358	Saxitoxins, gonyautoxins, and derivatives	NOT AVAILABLE
MMP-1	1-Isothiocyanato-7-(methylsulfinyl)heptane	-1,698	0,513	-3,311	0,001044004	0,037264341	Sulfoxides	NOT AVAILABLE
TNFRSF9	Marmesin	[illegible]	[illegible]	3,311	0,001045052	0,037264341	Coumarins and derivatives	Furanocoumarins
MCP-4	5-Phenylvaleric acid	2,096	0,633	3,311	0,001045612	0,037264341	Fatty Acyls	Fatty acids and conjugates
CXCL1	1-(2-Thienyl)-1,2-propanedione	-6,401	1,936	-3,307	0,001059322	0,037689932	Organooxygen compounds	Carbonyl compounds
MCP-1	Shoyuflavone C	-2,942	0,890	-3,306	0,0010626	0,03774357	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
TNFSF14	Murrayanol	0,544	0,165	3,304	0,001070691	0,03796767	Indoles and derivatives	Carbazoles
CXCL10	LysoPE(0:0/20:2(11Z,14Z))	-0,553	0,168	-3,301	0,001081169	0,038212057	Glycerophospholipids	Glycerophosphoethanolamines
MMP-1	Octadecyl fumarate	0,688	0,209	3,301	0,001079661	0,038212057	Fatty Acyls	Fatty acid esters
MCP-4	PA(20:1(11Z)/15:0)	-0,848	0,257	-3,300	0,001086399	0,038333339	Glycerophospholipids	Glycerophosphates
CXCL10	LysoPE(0:0/20:0)	-0,701	0,213	-3,299	0,001090542	0,038380845	Glycerophospholipids	Glycerophosphoethanolamines
IL6	Methylpicraquassioside A	0,708	0,215	3,298	0,001091347	0,038380845	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
MCP-1	Gallic acid	-0,677	0,205	-3,297	0,001094729	0,03843636	Benzene and substituted derivatives	Benzoic acids and derivatives
MCP-2	Eriojaposide B	-0,914	0,277	-3,294	0,001106648	0,038663739	Fatty Acyls	Fatty acyl glycosides
CSF-1	Aminobutanoic acid (ABA)/3-Aminobutanoic acid	-0,739	0,224	-3,295	0,001105333	0,038663739	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
NT-3	1-Propenyl 1-(1-propenylthio)propyl disulfide	-0,603	0,183	-3,295	0,001105497	0,038663739	Thioethers	Thioenol ethers
CXCL5	LysoPE(0:0/20:1(11Z))	-1,698	0,516	-3,291	0,001117352	0,038783387	Glycerophospholipids	Glycerophosphoethanolamines
PD-L1	Eriojaposide B	-0,549	0,167	-3,292	0,001115909	0,038783387	Fatty Acyls	Fatty acyl glycosides
CX3CL1	1-(11Z-eicosenoyl)-glycero-3-phosphate	-0,490	0,149	-3,291	0,001117326	0,038783387	Glycerophospholipids	Glycerophosphates
LAP.TGF-beta-1	Artonin D	0,532	0,162	3,292	0,001114679	0,038783387	Linear 1,3-diarylpropanoids	Chalcones and dihydrochalcones
FGF-19	Heptadecanoic acid	-0,814	0,248	-3,289	0,001128381	0,039059981	Fatty Acyls	Fatty acids and conjugates
MCP-2	3-Hydroxymyristate	0,748	0,227	3,288	0,001128986	0,039059981	Fatty Acyls	Fatty acids and conjugates
CCL28	Indole-3-acetylglutamic acid	-0,629	0,192	-3,283	0,001150404	0,039672179	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MMP-1	Ovalicin	1,459	0,444	3,283	0,001148734	0,039672179	Organooxygen compounds	Alcohols and polyols
NT-3	L-1,2,3,4-Tetrahydro-beta-carboline-3-carboxylic acid	-0,483	0,147	-3,282	0,001152582	0,039683092	Indoles and derivatives	Pyridoindoles
TNFSF14	4'',5,6-Trimethylscutellarein 7-glucoside	0,720	0,219	3,280	0,001160977	0,039907662	Anthracenes	Anthraquinones
MCP-4	Cuminaldehyde	1,275	0,389	3,278	0,001168308	0,040094967	Prenol lipids	Monoterpenoids
LIF-R	3-Methylcyclopentadecanone	-0,186	0,057	-3,277	0,001172685	0,040176461	Organooxygen compounds	Carbonyl compounds
TNF	3-hydroxynonanoyl carnitine	0,365	0,112	3,277	0,001174453	0,040176461	Fatty Acyls	Fatty acid esters
LAP.TGF-beta-1	Mangostenone B	0,633	0,193	3,275	0,001183772	0,04043037	Benzopyrans	1-benzopyrans
MMP-1	Thymol	-2,188	0,668	-3,274	0,001187876	0,040505637	Prenol lipids	Monoterpenoids
LAP.TGF-beta-1	Hv-NCC-1	-0,660	0,202	-3,271	0,001197346	0,040763309	Tetrapyrroles and derivatives	NOT AVAILABLE
MCP-2	Decenoic (C10:1)	0,293	0,090	3,271	0,001200042	0,040789945		
CXCL5	1-(5Z,8Z,11Z,14Z-eicosatetraenoyl)-sn-glycero-3-phosphate	-2,073	0,634	-3,269	0,001207418	0,040975315	Glycerophospholipids	Glycerophosphates
LAP.TGF-beta-1	Apigenin	-0,430	0,132	-3,268	0,001211118	0,041035525	Flavonoids	Flavones
CXCL10	[6]-Gingerdiol 3,5-diacetate	0,498	0,152	3,267	0,001215764	0,041127573	Fatty Acyls	Fatty alcohol esters
CST5	N-(1-Deoxy-1-fructosyl)threonine	-0,559	0,171	-3,266	0,001220591	0,041225396	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
DNER	1,6-Dihydroxy-3,7-dimethoxy-2-(3-methyl-2-butenyl)-8-(3-hydroxy	-0,171	0,052	-3,265	0,001222658	0,041229874	Benzopyrans	1-benzopyrans
MCP-2	Protogonyautoxin I	-0,926	0,284	-3,262	0,001236416	0,041627959	Saxitoxins, gonyautoxins, and derivatives	NOT AVAILABLE
CXCL11	1-Propenyl 1-(1-propenylthio)propyl disulfide	-1,271	0,390	-3,261	0,001239366	0,041661476	Thioethers	Thioenol ethers
4E-BP1	3,4-Dimethyl-5-pentyl-2-furantridecanoic acid	0,818	0,251	3,261	0,001241745	0,041675716	Fatty Acyls	Fatty acids and conjugates
CCL4	Heptadecanoic acid	0,551	0,169	3,259	0,001250211	0,041893868	Fatty Acyls	Fatty acids and conjugates
CXCL5	(-)-Dioxibrassinin	-3,059	0,939	-3,256	0,001261298	0,041977545	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CXCL5	2-Methoxynaphthalene	-1,980	0,608	-3,256	0,001262557	0,041977545	Naphthalenes	NOT AVAILABLE
TNFSF14	PS(18:4(6Z,9Z,12Z,15Z)/18:4(6Z,9Z,12Z,15Z))	-0,998	0,307	-3,257	0,001258712	0,041977545	Glycerophospholipids	Glycerophosphoserines
CSF-1	Lyciumin A	-0,209	0,064	-3,256	0,001259984	0,041977545	2-arylbenzofuran flavonoids	NOT AVAILABLE
MCP-1	3-Hydroxy-1-phenyl-1-heptadecanone	0,312	0,096	3,256	0,001259918	0,041977545	Fatty Acyls	Fatty alcohols
TNFSF14	Somniferine	-0,354	0,109	-3,255	0,001266927	0,042057243	Morphinans	NOT AVAILABLE
CXCL1	Murrayanol	1,593	0,490	3,250	0,001286777	0,042649757	Indoles and derivatives	Carbazoles
CASP-8	Eremopetasinorol	-1,175	0,362	-3,245	0,001309075	0,043321426	Organooxygen compounds	Alcohols and polyols
MMP-1	1-(2-Thienyl)-1,2-propanedione	-4,720	1,455	-3,244	0,001314333	0,043347455	Organooxygen compounds	Carbonyl compounds
MCP-1	Riboflavin	-0,378	0,117	-3,243	0,001315963	0,043347455	Pteridines and derivatives	Alloxazines and isoalloxazines
CXCL5	3-hydroxyundecanoyl carnitine	0,933	0,288	3,244	0,001314301	0,043347455	Fatty Acyls	Fatty acid esters
IL6	3-Methylcyclopentadecanone	0,693	0,214	3,241	0,001326011	0,043611026	Organooxygen compounds	Carbonyl compounds
CCL4	2-O-(Z-p-Hydroxycinnamoyl)-(x)-glyceric acid	-1,012	0,312	-3,239	0,001335725	0,043862819	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
CXCL1	Myricanol 5-glucoside	-1,710	0,528	-3,238	0,001340094	0,0439386	Lactones	Gamma butyrolactones
SLAMF1	(-)-cis-Rotenolone	-0,447	0,138	-3,236	0,00135173	0,044184144	Isoflavonoids	Rotenoids
FGF-19	5-Hydroxypentanoic acid	0,436	0,135	3,236	0,001351643	0,044184144	Fatty Acyls	Fatty acids and conjugates
CXCL5	3-Hydroxy-1-phenyl-1-eicosanone	-1,475	0,457	-3,232	0,001368599	0,044595228	Fatty Acyls	Fatty alcohols
DNER	Coumestrin	-0,277	0,086	-3,231	0,001370583	0,044595228	Isoflavonoids	Coumestans
MCP-2	Docosadienoate (22:2n6)	0,780	0,241	3,232	0,001368375	0,044595228	Fatty Acyls	Fatty acids and conjugates
MMP-1	Distichonic acid A	-1,031	0,319	-3,230	0,001375809	0,044632399	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
CD40	3-O-Methylglycyrol	-0,411	0,127	-3,230	0,001375914	0,044632399	Isoflavonoids	Coumestans
MCP-4	(±)-2-Butylthiazolidine	-0,902	0,280	-3,223	0,001408165	0,045300297	Azolidines	Thiazolidines
MCP-1	2-O-(Z-p-Hydroxycinnamoyl)-(x)-glyceric acid	-0,883	0,274	-3,225	0,0014018	0,045300297	Cinnamic acids and derivatives	Hydroxycinnamic acids and derivatives
CASP-8	Divanillyltetrahydrofuran ferulate	-0,867	0,269	-3,223	0,001409947	0,045300297	Furanoid lignans	Tetrahydrofuran lignans
MCP-1	Ternatin	-0,540	0,168	-3,223	0,001410929	0,045300297	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
HGF	1-(8Z,11Z,14Z-eicosatrienoyl)-glycero-3-phosphate	-0,336	0,104	-3,223	0,001411383	0,045300297	Glycerophospholipids	Glycerophospholipids
CXCL10	4'',5,6-Trimethylscutellarein 7-glucoside	1,046	0,324	3,225	0,001398662	0,045300297	Anthracenes	Anthraquinones
FGF-21	6-(2-Carboxyethyl)-7-hydroxy-2,2-dimethyl-4-chromanone glucosi	1,501	0,466	3,224	0,001407244	0,045300297	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
TNF	3-hydroxyundecanoyl carnitine	0,364	0,113	3,220	0,001424328	0,045647048	Fatty Acyls	Fatty acid esters
CCL20	Decenoic (C10:1)	0,416	0,129	3,219	0,001431661	0,045813137	Fatty Acyls	Fatty acids and conjugates
CXCL1	Cyanidin 3-(6-caffeoylglucoside) 5-glucoside	-1,885	0,586	-3,215	0,001448684	0,04601246	Flavonoids	Flavonoid glycosides
CSF-1	1-(8Z,11Z,14Z-eicosatrienoyl)-glycero-3-phosphate	-0,220	0,069	-3,217	0,001440277	0,04601246	Glycerophospholipids	Glycerophospholipids
MCP-2	Methyl 3,4-dihydroxy-5-prenylbenzoate 3-glucoside	0,419	0,130	3,216	0,00144458	0,04601246	Prenol lipids	Terpene glycosides
CX3CL1	Linoleamide	0,423	0,131	3,215	0,00144737	0,04601246	Fatty Acyls	Fatty amides
FGF-23	Madlongiside C	0,818	0,254	3,216	0,001444382	0,04601246	Prenol lipids	Triterpenoids
CXCL10	Theogallin	-1,421	0,442	-3,213	0,001458796	0,046264673	Organooxygen compounds	Alcohols and polyols
CX3CL1	(-)-Dioxibrassinin	-0,611	0,190	-3,212	0,001462126	0,046301377	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
LAP.TGF-beta-1	Marcanine A	-0,875	0,272	-3,212	0,001465208	0,046330152	Quinolines and derivatives	Benzoquinolines
CXCL6	Neferine	-1,229	0,383	-3,210	0,001472765	0,046409307	Isoquinolines and derivatives	Benzylisoquinolines
CSF-1	Peonidin-3-galactoside	-0,221	0,069	-3,210	0,0014712	0,046409307	Flavonoids	Flavonoid glycosides
IL6	(S)-[8]-Gingerol	0,319	0,099	3,210	0,001474245	0,046409307	Phenols	Methoxyphenols
MCP-4	Protogonyautoxin I	-1,264	0,394	-3,207	0,001488732	0,046658597	Saxitoxins, gonyautoxins, and derivatives	NOT AVAILABLE
Flt3L	Hv-NCC-1	-0,594	0,185	-3,207	0,001487638	0,046658597	Tetrapyrroles and derivatives	NOT AVAILABLE
CCL4	3-hydroxynonanoyl carnitine	0,288	0,090	3,207	0,00148604	0,046658597	Fatty Acyls	Fatty acid esters
CXCL10	Naringenin	-0,529	0,165	-3,205	0,001496345	0,046759673	Flavonoids	Flavans
DNER	Hydrocortamate	-0,271	0,084	-3,206	0,001494496	0,046759673	Steroids and steroid derivatives	Pregnane steroids
CCL20	Caffeine	1,111	0,347	3,205	0,001499449	0,046788074	Imidazopyrimidines	Purines and purine derivatives
MCP-4	Bis(2-furanylmethyl) sulfide	-0,718	0,224	-3,204	0,001504508	0,046877302	Heteroaromatic compounds	NOT AVAILABLE
CXCL11	1-(8Z,11Z,14Z-eicosatrienoyl)-glycero-3-phosphate	-1,055	0,330	-3,202	0,001513324	0,047083162	Glycerophospholipids	Glycerophospholipids
MCP-4	Ternatin	-0,861	0,269	-3,197	0,001539803	0,047837154	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
MCP-4	Egonol glucoside	0,824	0,258	3,194	0,00155319	0,048182788	2-arylbenzofuran flavonoids	NOT AVAILABLE
CXCL1	1-Phenyl-1,3-heptadecanedione	1,294	0,405	3,193	0,001559462	0,048307041	Organooxygen compounds	Carbonyl compounds
CCL28	Alpha-Tocopherol	0,271	0,085	3,193	0,001561918	0,048312907	Prenol lipids	Quinone and hydroquinone lipids
IL-18R1	Peonidin-3-galactoside	-0,397	0,124	-3,191	0,00157004	0,04849376	Flavonoids	Flavonoid glycosides
CXCL6	Thymol	-2,231	0,700	-3,189	0,001579103	0,048703099	Prenol lipids	Monoterpenoids
CXCL6	(-)-Epigallocatechin 3,5-di-gallate	-1,607	0,504	-3,187	0,001591754	0,048856353	Flavonoids	Flavans
MCP-4	PS(20:1(11Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	-0,809	0,254	-3,186	0,00159475	0,048856353	Glycerophospholipids	Glycerophosphoserines
CSF-1	Divanillyltetrahydrofuran ferulate	-0,296	0,093	-3,188	0,00158754	0,048856353	Furanoid lignans	Tetrahydrofuran lignans
IL18	Ethyl beta-D-glucopyranoside	0,250	0,079	3,186	0,001595534	0,048856353	Organooxygen compounds	Carbohydrates and carbohydrate conjugates
SCF	Protogonyautoxin I	0,490	0,154	3,187	0,001590252	0,048856353	Saxitoxins, gonyautoxins, and derivatives	NOT AVAILABLE
HGF	Resveratrol 4''-(6-galloylglucoside)	0,275	0,086	3,185	0,001600131	0,048926824	Prenol lipids	Sesterterpenoids
CXCL11	1-(5Z,8Z,11Z,14Z-eicosatetraenoyl)-sn-glycero-3-phosphate	-1,110	0,349	-3,185	0,001603297	0,048953394	Glycerophospholipids	Glycerophosphates
TRAIL	Secoisolariciresinol 9,9''-diglucoside	-0,402	0,126	-3,180	0,001628296	0,04964555	Lignan glycosides	NOT AVAILABLE
MCP-4	gamma-Glutamyl-beta-(isoxazolin-5-on-2-yl)alanine	-0,860	0,270	-3,179	0,001635051	0,049780309	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
LAP.TGF-beta-1	Histidine	0,296	0,093	3,178	0,001638832	0,049824239	Carboxylic acids and derivatives	Amino acids, peptides, and analogues
EN-RAGE	Madlongiside C	-0,526	0,165	-3,177	0,001644621	0,049857978	Prenol lipids	Triterpenoids
TNFSF14	Alpha-Linolenic acid	0,236	0,074	3,177	0,001642849	0,049857978	Fatty Acyls	Lineolic acids and derivatives