Obesity and social network influence in inflammatory biomarkers in a general youth population

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1 Abstract

1.1 Methods

The Fit Futures 1 study collected interview data on social contact among 1038 first level students in the same high school district in Norway. In this context, we also collected blood samples (n = 937), OLINK inflamatory proteomic data (n = 936) and did antropomorphic measurements (n = 1034). Social networks were constructed from self-reported social contact between participants.

All statistics summary things goes here.

1.2 Findings

There is an association between lifestyle factors, diseases, vitamim D levels and social interaction with several biomarkers.

1.3 Interpretation

We found results that might suggest that people in your social network may influence your inflammatory response.

1.4 Funding

The Northern Norway regional Health Authorities (grant number HNF1457-19) funded this study.

2 Introduction

Obesity is a condition associated with several health problems including the number one cause of death in almost every socio-economic group, cardiovascular diseases, as well as many types of cancers and other complications.

While there are genetic conditions associated with it, the most common causes of obesity are excessive food consumption or a lack of exercise. In simple terms your amount of body fat is simply the difference between your energy intake and energy output. These two factors are heavily influenced by your lifestyle, which in term are impacted by your friends. Obesity, despite not been caused by a viral, bacterial, or parasitic agent, is nevertheless contagious among close group of friends [1]. Even though it is impossible for an individual to perform lipogenesis with what somebody else eats, people tend to behave in the same way to their peers, and end up eating and exercising similarly as their direct contact network.

Obesity is associated with the inflammatory response of your immune system. While the exact mechanism is unclear, it might be due that a poor immune response that otherwise would have curled the infiltration of opportunistic bacteria, thus causing an unwelcome inflammatory response. In this study we explore the possibility that people in the same social network can influence your influence response, as well as how much these biomarkers are expressed with respect to your anthropometric variables. Answering two fundamental questions:

- Does the spread of levels of obesity also spread the biomarkers levels?
- How does the average proteomic profile compare between different categories of obesity?

3 Methods

3.1 Population and study design

The Tromsø Study Fit Futures 1 (TFF1) is a health survey conducted from 2010 to 2011 in the duration of 8 months. All first-year high school students in the municipalities of Tromsø and Balsfjord, Norway were invited. TFF1 included students from eight schools consecutively. A total of 1117 youths were invited and 93% attended, 508 girls and 530 boys.

Participants had a one-day visit at The Clinical Research Unit at the University Hospital of North Norway (UNN), including clinical examinations, microbiological samples, blood samples, a web-based general questionnaire, and an interview [2]. All procedures were performed by trained research nurses.

3.2 Host risk factors

Height and weight were measured on an electronic scale with participants wearing light clothing and no footwear. BMI was calculated as weight (kg) divided by the squared height (m^2). From the web-based questionnaire we got information about lifestyle including, sex, age, type of studies and recreational physical activity.

3.3 Olink Target 96 Inflammation

The 92 bioarkers were analyzed at the Clinical Biomarkers Facility, SciLifeLab, (Uppsala, Sweden), using the Target 96 Inflammation panel from OLINK Holding AB (Uppsala, Sweden) [3] . From these 92 biomarkers we have two different values. The LOD (Limit of Detection) value, and the NDL (I still don't know what NDL actually means) value. The LOD level is the lowest value that can be detected, so any number lower than that is censored to the left. The NDL is the real value measured by the machine and can be under the LOD level. When this happens, it cannot be guaranteed that the value is correct.

All the biomarkers detailed information, can be found in **??** on page 7.

3.4 Social network analysis

The social network was constructed based on the following question in the interview: "Which students have you had most contact with the last week? Name up to 5 students at your own school or other schools in Tromsø and Balsfjord.". Reciprocity in the nomination was not mandatory. For each of the nominations, five "yes/no" questions assessed the type of contact they had with their nominations: "Do you have physical contact?", "Are you together at school?", "Are you together at sports?", "Are you together at home?", "Are you together at other places?". This resulted in five social networks: Physical Network, School Network, Sport Network, Home Network, and Other Network (Supplementary Figure 2). Adding all the relationships together formed a sixth network that was called the Overall Network. To evaluate if the friends mentioned were representative for the participants´ social network, the following question was asked: "To what degree does this table of friends give an overview of your social network? Please indicate on a scale from 0 (small degree) to 10 (high degree)." Nominated friends that did not participate in TFF1 were excluded from the analysis (n=134). Each student is represented by one node in the network. Each relationship is represented by an undirected edge, i.e., line, in the network.

3.5 Statistical analysis

3.5.1 Software

Statistical analyses was performed by using R version 3.6.3 and R Studio 1.3.1093. Noticeable libraries were "igraph" [4] "statnet" (sna, egrm) [5] for linear autocorrelation and EGRM analysis, and "ggraph" [6] for display of results.

3.5.2 Host factors

For the evaluation of host risk factors for S. aureus carriage, univariable associations by t-test and Xi-square test, with Yates's correction for 2x2 tables and Fisher correction were performed, when applicable. In all cases, all the assumptions for the Xi-square test applied.

3.5.3 Social influence

The connection between nodes was analyzed using ERGM or Additive and Multiplicative Effects models (Supplementary Table 1 and Supplementary Figure 5). Patterns of connections (non-carriers connected to non-carriers, non-carriers connected to carriers, carriers connected to carriers) were analyzed by using Simulation Investigation for Empirical Network Analysis, an autocorrelation model [28] (Table 5). Further analysis was done with bootstrapping simulated networks against the observed network (Tables 2, 3 and Supplementary Table 2), descriptive analysis (Supplementary Table 3), and logistic regression (Supplementary Table 4, Figure 4). The mathematical background for the statistical methods is described in the supplementary material.

3.5.4 Ethics

A declaration of consent was signed by each participant in TFF1, participants younger than 16 years of age had to bring written consent from a parent or guardian. TFF1 was approved by The Regional Committee of Medical and Health Research Ethics (REK) and the Norwegian Data Protection Authority. The present study was approved by REK North, reference 2018/1975/REK Nord.

4 Results

4.1 Summary statistics

4.1.1 Sex differences

Men and women have different biological processes that affect the biomarkers levels, regardless of their social network or their current health status. This is appreciated in figure [?] and supplementary table [?] where we provide an overview of all biomarkers with respect sex. Since the difference is so prominent, we stratified all our results with respect sex.

4.1.2 LOD

In figure [?] we see an overview of all biomarkers levels. Since most of the collected values are well above the LOD, we decided to run all the analysis usind the NDL values. However, please notice that for biomarkers with very high proportion of Under LOD values, the result of the analysis is not guaranteed.

4.1.3 Categories

5 Discussion

6 Toy section

This is just to test where the floating images fall in the text. Go wild and do whatever you want here.

In hac habitasse [7] platea dictumst. [8] , Vivamus eu finibus leo. Donec malesuada dui non sagittis auctor.

We should delete this section eventually

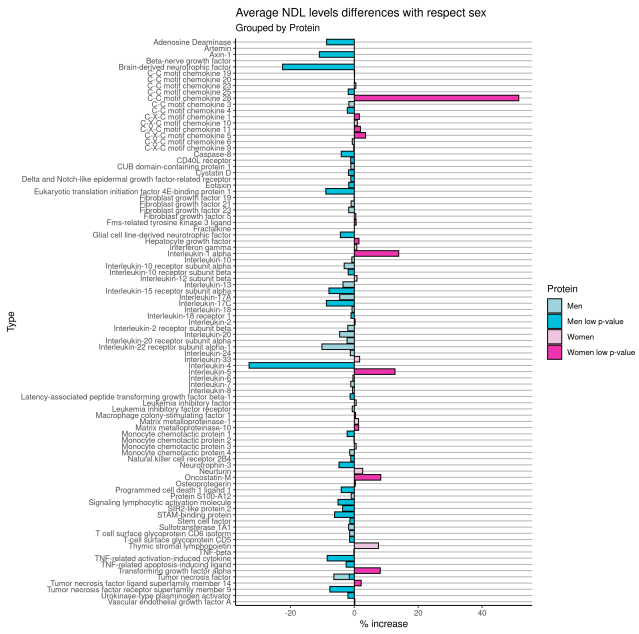

Figure 1: *Overview of all biomarkers diferences with respect sex. In many cases there is a significant difference between men and women (p<0.05). Due biological reasons.*

Figure 2: *A majestic grizzly bear*

Table 1: *Example table*

Name		
First Name	Last Name	Grade
John	Doe	7.5
Richard	Miles	5

Aenean condimentum eros metus. Nunc tempus id velit ut tempus. Quisque fermentum, nisl sit amet consectetur ornare. This sentence requires multiple citations to imply that it is better supported. Finally, when conducting an appeal to authority, it can be useful to cite a reference in-text, much like do quite a bit. Oh, and make sure to check out the bear in Figure 2.

I don't like this part

$$A = \begin{bmatrix} A_{11} & A_{21} \\ A_{21} & A_{22} \end{bmatrix} \tag{1}$$

Some random text here

1. First numbered item in a list
2. Second numbered item in a list
3. Third numbered item in a list

Pellentesque ac nisi dolor. Pellentesque maximus est arcu, eu scelerisque est rutrum vitae. Mauris ullamcorper vulputate vehicula. Praesent fermentum leo ac velit accumsan consectetur. Aliquam eleifend ex eros, ut lacinia tellus volutpat non. Pellentesque sit amet cursus diam. Maecenas elementum mattis est, in tincidunt ex pretium ac. Integer ultrices nunc rutrum, pretium sapien vitae, lobortis velit.

First This is the first item
Last This is the last item

Donec nec nibh sagittis, finibus mauris quis, laoreet augue. Maecenas aliquam sem nunc, vel semper urna hendrerit nec. Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas. Maecenas pellentesque dolor lacus, sit amet pretium felis vestibulum finibus. Duis tincidunt sapien faucibus nisi vehicula tincidunt. Donec euismod suscipit ligula a tempor. Aenean a nulla sit amet magna ullamcorper condimentum. Fusce eu velit vitae libero varius condimentum at sed dui.

Aliquam elementum nulla at arcu finibus aliquet. Praesent congue ultrices nisl pretium posuere. Nunc vel nulla hendrerit, ultrices justo ut, ultrices sapien. Duis ut arcu at nunc pellentesque consectetur. Vestibulum eget nisl porta, ultricies orci eget.

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7 Document Version control

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Table 2: *Solved issues*

Date	Original	Solved
2022.02.01	Write something!	Abstract and
2022.02.02	Definition of obesity is not included	Added defin

References

[1] A. C. Nicholas and H. F. James, "The spread of obesity in a large social network over 32 years," *The New England Journal of Medicine*, 2007. https://www.nejm.org/doi/full/10.1056/NEJMsa066082.

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[8] J. Doe", ""title"," "*Journal*", "2017".

8 Suplementary material

In this section, we present some useful extra information

Acronym	Protein	UniProt	LOD_Batch_20160383	LOD_Batch_20160977	Uniprt_Web	Wiki_Web
ADA	Adenosine Deaminase	P00813	0.436494	1.584419	http://www.uniprot.org/uniprot/P00813	https://en.wikipedia.org/wiki/Adenosine_deaminase
ARTN	Artemin	Q5T4W7	0.031349	0.031349	http://www.uniprot.org/uniprot/Q5T4W7	https://en.wikipedia.org/wiki/Artemin
AXIN1	Axin-1	O15169	0.845030	0.576816	http://www.uniprot.org/uniprot/O15169	https://en.wikipedia.org/wiki/AXIN1
BDNF	Brain-derived neurotrophic factor	P23560	-0.380273	-0.045445	http://www.uniprot.org/uniprot/P23560	https://en.wikipedia.org/wiki/Brain-derived_neurotrophic_factor
BNGF	Beta-nerve growth factor	P01138	0.755167	0.631771	http://www.uniprot.org/uniprot/P01138	
CASP8	Caspase-8	Q14790	0.507711	0.151261	http://www.uniprot.org/uniprot/Q14790	https://en.wikipedia.org/wiki/Caspase_8
CCL11	Eotaxin	P51671	1.427776	0.950032	http://www.uniprot.org/uniprot/P51671	https://en.wikipedia.org/wiki/CCL11
CCL19	C-C motif chemokine 19	Q99731	0.988040	-0.038600	http://www.uniprot.org/uniprot/Q99731	https://en.wikipedia.org/wiki/CCL19
CCL20	C-C motif chemokine 20	P78556	1.276281	1.290873	http://www.uniprot.org/uniprot/P78556	https://en.wikipedia.org/wiki/CCL20
CCL23	C-C motif chemokine 23	P55773	0.780150	0.047888	http://www.uniprot.org/uniprot/P55773	https://en.wikipedia.org/wiki/CCL23
CCL25	C-C motif chemokine 25	O15444	1.083723	0.634603	http://www.uniprot.org/uniprot/O15444	https://en.wikipedia.org/wiki/CCL25
CCL28	C-C motif chemokine 28	Q9NRJ3	0.069990	-0.046866	http://www.uniprot.org/uniprot/Q9NRJ3	https://en.wikipedia.org/wiki/CCL28
CCL3	C-C motif chemokine 3	P10147	-0.077074	-0.524618	http://www.uniprot.org/uniprot/P10147	https://en.wikipedia.org/wiki/CCL3
CCL4	C-C motif chemokine 4	P13236	0.392063	-0.121811	http://www.uniprot.org/uniprot/P13236	https://en.wikipedia.org/wiki/CCL4
CD244	Natural killer cell receptor 2B4	Q9BZW8	1.658169	1.062742	http://www.uniprot.org/uniprot/Q9BZW8	https://en.wikipedia.org/wiki/CD244
CD40	CD40L receptor	P25942	0.757131	-0.447591	http://www.uniprot.org/uniprot/P25942	https://en.wikipedia.org/wiki/CD40_(protein)
CD5	T-cell surface glycoprotein CD5	P06127	-0.487334	-0.578852	http://www.uniprot.org/uniprot/P06127	https://en.wikipedia.org/wiki/CD5_(protein)
CD6	T cell surface glycoprotein CD6 isoform	Q8WWJ7	-0.194972	-0.146330	http://www.uniprot.org/uniprot/Q8WWJ7	https://en.wikipedia.org/wiki/CD6
CDCP1	CUB domain-containing protein 1	Q9H5V8	0.367527	0.038621	http://www.uniprot.org/uniprot/Q9H5V8	https://en.wikipedia.org/wiki/CDCP1
CSF1	Macrophage colony-stimulating factor 1	P09603	-0.003590	0.396328	http://www.uniprot.org/uniprot/P09603	https://en.wikipedia.org/wiki/Macrophage_colony-stimulating_factor
CST5	Cystatin D	P28325	0.046105	5.808007	http://www.uniprot.org/uniprot/P28325	https://en.wikipedia.org/wiki/CST5
CX3CL1	Fractalkine	P78423	1.875148	1.166002	http://www.uniprot.org/uniprot/P78423	https://en.wikipedia.org/wiki/CX3CL1
CXCL1	C-X-C motif chemokine 1	P09341	1.387787	0.758507	http://www.uniprot.org/uniprot/P09341	https://en.wikipedia.org/wiki/CXCL10
CXCL10	C-X-C motif chemokine 10	P02778	1.534295	1.358654	http://www.uniprot.org/uniprot/P02778	https://en.wikipedia.org/wiki/CXCL10
CXCL11	C-X-C motif chemokine 11	O14625	1.471448	0.111323	http://www.uniprot.org/uniprot/O14625	https://en.wikipedia.org/wiki/CXCL11
CXCL5	C-X-C motif chemokine 5	P42830	1.184377	1.639521	http://www.uniprot.org/uniprot/P42830	https://en.wikipedia.org/wiki/CXCL5
CXCL6	C-X-C motif chemokine 6	P80162	0.843005	0.398682	http://www.uniprot.org/uniprot/P80162	https://en.wikipedia.org/wiki/CXCL6
CXCL9	C-X-C motif chemokine 9	Q07325	1.559012	1.430370	http://www.uniprot.org/uniprot/Q07325	https://en.wikipedia.org/wiki/CXCL9
DNER	Delta and Notch-like epidermal growth factor-related receptor	Q8NFT8	-0.127219	-0.730436	http://www.uniprot.org/uniprot/Q8NFT8	https://en.wikipedia.org/wiki/DNER
EIF4EBP1	Eukaryotic translation initiation factor 4E-binding protein 1	Q13541	0.893928	0.969980	http://www.uniprot.org/uniprot/Q13541	https://en.wikipedia.org/wiki/EIF4EBP1
ENRAGE	Protein S100-A12	P80511	0.313350	0.996331	http://www.uniprot.org/uniprot/P80511	https://en.wikipedia.org/wiki/S100A12
FGF19	Fibroblast growth factor 19	O95750	0.662450	0.255022	http://www.uniprot.org/uniprot/O95750	https://en.wikipedia.org/wiki/FGF19
FGF21	Fibroblast growth factor 21	Q9NSA1	0.844435	-0.310457	http://www.uniprot.org/uniprot/Q9NSA1	https://en.wikipedia.org/wiki/FGF21
FGF23	Fibroblast growth factor 23	Q9GZV9	1.039348	1.108382	http://www.uniprot.org/uniprot/Q9GZV9	https://en.wikipedia.org/wiki/FGF23
FGF5	Fibroblast growth factor 5	Q8NF90	1.142597	0.876939	http://www.uniprot.org/uniprot/Q8NF90	https://en.wikipedia.org/wiki/FGF5
FLT3L	Fms-related tyrosine kinase 3 ligand	P49771	1.866726	1.119030	http://www.uniprot.org/uniprot/P49771	https://en.wikipedia.org/wiki/FLT3LG
GDNF	Glial cell line-derived neurotrophic factor	P39905	1.331378	1.648532	http://www.uniprot.org/uniprot/P39905	https://en.wikipedia.org/wiki/Glial_cell_line-derived_neurotrophic_factor
HGF	Hepatocyte growth factor	P14210	1.146276	0.395915	http://www.uniprot.org/uniprot/P14210	https://en.wikipedia.org/wiki/Hepatocyte_growth_factor
IFNG	Interferon gamma	P01579	0.992133	0.992133	http://www.uniprot.org/uniprot/P01579	https://en.wikipedia.org/wiki/Interferon_gamma
IL10	Interleukin-10	P22301	1.839415	2.432488	http://www.uniprot.org/uniprot/P22301	https://en.wikipedia.org/wiki/Interleukin_10
IL10RA	Interleukin-10 receptor subunit alpha	Q13651	0.996689	0.662247	http://www.uniprot.org/uniprot/Q13651	https://en.wikipedia.org/wiki/Interleukin_10_receptor,_alpha_subunit
IL10RB	Interleukin-10 receptor subunit beta	Q08334	1.425411	1.405083	http://www.uniprot.org/uniprot/Q08334	https://en.wikipedia.org/wiki/Interleukin_10_receptor,_beta_subunit
IL12B	Interleukin-12 subunit beta	P29460	-0.338237	-0.143724	http://www.uniprot.org/uniprot/P29460	https://en.wikipedia.org/wiki/Interleukin_12_receptor,_beta_1_subunit
IL13	Interleukin-13	P35225	1.537823	1.537823	http://www.uniprot.org/uniprot/P35225	https://en.wikipedia.org/wiki/Interleukin_13
IL15RA	Interleukin-15 receptor subunit alpha	Q13261	0.783341	0.595480	http://www.uniprot.org/uniprot/Q13261	https://en.wikipedia.org/wiki/Interleukin_15_receptor,_alpha_subunit
IL17A	Interleukin-17A	Q16552	0.532945	0.371852	http://www.uniprot.org/uniprot/Q16552	https://en.wikipedia.org/wiki/IL17A
IL17C	Interleukin-17C	Q9P0M4	1.371362	1.358013	http://www.uniprot.org/uniprot/Q9P0M4	
IL18	Interleukin-18	Q14116	-0.188372	0.365590	http://www.uniprot.org/uniprot/Q14116	https://en.wikipedia.org/wiki/Interleukin_18
IL18R1	Interleukin-18 receptor 1	Q13478	0.933131	0.638867	http://www.uniprot.org/uniprot/Q13478	https://en.wikipedia.org/wiki/Interleukin-18_receptor
IL1A	Interleukin-1 alpha	P01583	0.336995	1.802489	http://www.uniprot.org/uniprot/P01583	https://en.wikipedia.org/wiki/IL1A
IL2	Interleukin-2	P60568	1.223237	1.223237	http://www.uniprot.org/uniprot/P60568	https://en.wikipedia.org/wiki/Interleukin_2
IL20	Interleukin-20	Q9NYY1	0.728374	0.813528	http://www.uniprot.org/uniprot/Q9NYY1	https://en.wikipedia.org/wiki/Interleukin_20
IL20RA	Interleukin-20 receptor subunit alpha	Q9UHF4	0.877718	0.881812	http://www.uniprot.org/uniprot/Q9UHF4	
IL22RA1	Interleukin-22 receptor subunit alpha-1	Q8N6P7	2.260242	2.260242	http://www.uniprot.org/uniprot/Q8N6P7	
IL24	Interleukin-24	Q13007	1.336190	1.336190	http://www.uniprot.org/uniprot/Q13007	https://en.wikipedia.org/wiki/Interleukin_24
IL2RB	Interleukin-2 receptor subunit beta	P14784	0.845790	0.845790	http://www.uniprot.org/uniprot/P14784	https://en.wikipedia.org/wiki/IL2RB
IL33	Interleukin-33	O95760	1.425509	1.425509	http://www.uniprot.org/uniprot/O95760	https://en.wikipedia.org/wiki/Interleukin_33
IL4	Interleukin-4	P05112	1.184842	0.958605	http://www.uniprot.org/uniprot/P05112	https://en.wikipedia.org/wiki/Interleukin_4
IL5	Interleukin-5	P05113	1.725314	1.647055	http://www.uniprot.org/uniprot/P05113	https://en.wikipedia.org/wiki/Interleukin_5
IL6	Interleukin-6	P05231	0.824445	2.415735	http://www.uniprot.org/uniprot/P05231	https://en.wikipedia.org/wiki/Interleukin_6
IL7	Interleukin-7	P13232	1.021735	1.336047	http://www.uniprot.org/uniprot/P13232	https://en.wikipedia.org/wiki/Interleukin_7
IL8	Interleukin-8	P10145	1.162271	2.227435	http://www.uniprot.org/uniprot/P10145	https://en.wikipedia.org/wiki/Interleukin_8
LIF	Leukemia inhibitory factor	P15018	0.800844	0.800844	http://www.uniprot.org/uniprot/P15018	https://en.wikipedia.org/wiki/Leukemia_inhibitory_factor
LIFR	Leukemia inhibitory factor receptor	P42702	1.665534	-0.265929	http://www.uniprot.org/uniprot/P42702	https://en.wikipedia.org/wiki/LIFR
MCP1	Monocyte chemotactic protein 1	P13500	0.358877	-0.161967	http://www.uniprot.org/uniprot/P13500	https://en.wikipedia.org/wiki/Monocyte_chemoattractant_protein_1
MCP2	Monocyte chemotactic protein 2	P80075	1.385177	1.823898	http://www.uniprot.org/uniprot/P80075	
MCP3	Monocyte chemotactic protein 3	P80098	1.493173	1.699734	http://www.uniprot.org/uniprot/P80098	
MCP4	Monocyte chemotactic protein 4	Q99616	-0.265469	-0.298464	http://www.uniprot.org/uniprot/Q99616	
MMP1	Matrix metalloproteinase-1	P03956	-0.024189	-6.622735	http://www.uniprot.org/uniprot/P03956	https://en.wikipedia.org/wiki/Matrix_metalloproteinase
MMP10	Matrix metalloproteinase-10	P09238	1.379258	3.725904	http://www.uniprot.org/uniprot/P09238	https://en.wikipedia.org/wiki/Matrix_metalloproteinase
NRTN	Neurturin	Q99748	1.124936	1.124936	http://www.uniprot.org/uniprot/Q99748	https://en.wikipedia.org/wiki/Neurturin
NT3	Neurotrophin-3	P20783	0.771270	0.918843	http://www.uniprot.org/uniprot/P20783	https://en.wikipedia.org/wiki/Neurotrophin-3
OPG	Osteoprotegerin	O00300	0.918419	0.590118	http://www.uniprot.org/uniprot/O00300	https://en.wikipedia.org/wiki/Osteoprotegerin
OSM	Oncostatin-M	P13725	-0.153103	-0.025163	http://www.uniprot.org/uniprot/P13725	https://en.wikipedia.org/wiki/Oncostatin_M
PDL1	Programmed cell death 1 ligand 1	Q9NZQ7	2.257393	2.092503	http://www.uniprot.org/uniprot/Q9NZQ7	https://en.wikipedia.org/wiki/PD-L1
SCF	Stem cell factor	P21583	0.922578	0.051798	http://www.uniprot.org/uniprot/P21583	https://en.wikipedia.org/wiki/Stem_cell_factor
SIRT2	SIR2-like protein 2	Q8IXJ6	1.402289	1.386472	http://www.uniprot.org/uniprot/Q8IXJ6	
SLAMF1	Signaling lymphocytic activation molecule	Q13291	1.849931	1.677337	http://www.uniprot.org/uniprot/Q13291	https://en.wikipedia.org/wiki/Signaling_lymphocytic_activation_molecule
ST1A1	Sulfotransferase 1A1	P50225	0.078597	0.568043	http://www.uniprot.org/uniprot/P50225	https://en.wikipedia.org/wiki/SULT1A1
STAMBP	STAM-binding protein	O95630	0.667136	0.627816	http://www.uniprot.org/uniprot/O95630	https://en.wikipedia.org/wiki/STAMBP
TGFA	Transforming growth factor alpha	P01135	-1.214780	-1.869967	http://www.uniprot.org/uniprot/P01135	https://en.wikipedia.org/wiki/TGF_alpha
TGFB1	Latency-associated peptide transforming growth factor beta-1	P01137	1.034369	0.482168	http://www.uniprot.org/uniprot/P01137	https://en.wikipedia.org/wiki/TGF_beta_1
TNF	Tumor necrosis factor	P01375	0.831819	0.837656	http://www.uniprot.org/uniprot/P01375	https://en.wikipedia.org/wiki/Tumor_necrosis_factor
TNFB	TNF-beta	P01374	0.605630	0.200990	http://www.uniprot.org/uniprot/P01374	https://en.wikipedia.org/wiki/Lymphotoxin_alpha
TNFRSF9	Tumor necrosis factor receptor superfamily member 9	Q07011	1.599546	1.466786	http://www.uniprot.org/uniprot/Q07011	https://en.wikipedia.org/wiki/4-1BB_ligand
TNFSF14	Tumor necrosis factor ligand superfamily member 14	O43557	0.210933	-0.170624	http://www.uniprot.org/uniprot/O43557	https://en.wikipedia.org/wiki/LIGHT_(protein)
TRAIL	TNF-related apoptosis-inducing ligand	P50591	0.651508	0.548601	http://www.uniprot.org/uniprot/P50591	https://en.wikipedia.org/wiki/TRAIL
TRANCE	TNF-related activation-induced cytokine	O14788	1.263670	1.118725	http://www.uniprot.org/uniprot/O14788	https://en.wikipedia.org/wiki/Receptor_activator_of_nuclear_factor_kappa-B_ligand
TSLP	Thymic stromal lymphopoietin	Q969D9	1.080835	1.080835	http://www.uniprot.org/uniprot/Q969D9	https://en.wikipedia.org/wiki/Thymic_stromal_lymphopoietin
TWEAK	Tumor necrosis factor	O43508	0.511139	0.439180	http://www.uniprot.org/uniprot/O43508	https://en.wikipedia.org/wiki/Tumor_necrosis_factor
UPA	Urokinase-type plasminogen activator	P00749	0.767444	0.691054	http://www.uniprot.org/uniprot/P00749	https://en.wikipedia.org/wiki/Urokinase
VEGFA	Vascular endothelial growth factor A	P15692	1.566666	1.233603	http://www.uniprot.org/uniprot/P15692	https://en.wikipedia.org/wiki/Vascular_endothelial_growth_factor

Table 3: *Summary of all biomarkers*

Acronym	Protein	Significance	Men	Women
ADA	Adenosine Deaminase	****	5.16	4.75
ARTN	Artemin	ns	-0.21	-0.22
AXIN1	Axin-1	****	1.19	1.07
BDNF	Brain-derived neurotrophic factor	***	4.61	3.76
BNGF	Beta-nerve growth factor	ns	1.93	1.93
CASP8	Caspase-8	*	1.46	1.4
CCL11	Eotaxin	****	7.9	7.76
CCL19	C-C motif chemokine 19	ns	9.37	9.37
CCL20	C-C motif chemokine 20	ns	6.06	6.06
CCL23	C-C motif chemokine 23	ns	9.35	9.39
CCL25	C-C motif chemokine 25	**	6.17	6.05
CCL28	C-C motif chemokine 28	****	0.83	1.26
CCL3	C-C motif chemokine 3	ns	2.24	2.2
CCL4	C-C motif chemokine 4	****	6.58	6.44
CD244	Natural killer cell receptor 2B4	***	6.38	6.31
CD40	CD40L receptor	****	9.29	9.18
CD5	T-cell surface glycoprotein CD5	**	4.05	3.99
CD6	T cell surface glycoprotein CD6 isoform	ns	3.65	3.59
CDCP1	CUB domain-containing protein 1	ns	2.44	2.41
CSF1	Macrophage colony-stimulating factor 1	*	7.87	7.9
CST5	Cystatin D	****	6.87	6.75
CX3CL1	Fractalkine	ns	6.52	6.52
CXCL1	C-X-C motif chemokine 1	****	8.72	8.85
CXCL10	C-X-C motif chemokine 10	ns	9.51	9.6
CXCL11	C-X-C motif chemokine 11	**	7.1	7.24
CXCL5	C-X-C motif chemokine 5	****	12.1	12.53
CXCL6	C-X-C motif chemokine 6	ns	9.08	9.02
CXCL9	C-X-C motif chemokine 9	ns	7.29	7.28
DNER	Delta and Notch-like epidermal growth factor-related receptor	****	7.35	7.27
EIF4EBP1	Eukaryotic translation initiation factor 4E-binding protein 1	****	5.99	5.5
ENRAGE	Protein S100-A12	ns	5.16	5.11
FGF19	Fibroblast growth factor 19	ns	7.88	7.87
FGF21	Fibroblast growth factor 21	ns	3.16	3.13
FGF23	Fibroblast growth factor 23	ns	2.68	2.63
FGF5	Fibroblast growth factor 5	ns	1.42	1.43
FLT3L	Fms-related tyrosine kinase 3 ligand	*	8.78	8.83
GDNF	Glial cell line-derived neurotrophic factor	***	2.17	2.08
HGF	Hepatocyte growth factor	****	7.8	7.91
IFNG	Interferon gamma	ns	0.62	0.63
IL10	Interleukin-10	ns	4.14	4.11
IL10RA	Interleukin-10 receptor subunit alpha	ns	1.41	1.37
IL10RB	Interleukin-10 receptor subunit beta	****	7.61	7.47
IL12B	Interleukin-12 subunit beta	ns	4.81	4.85
IL13	Interleukin-13	ns	1.06	1.02
IL15RA	Interleukin-15 receptor subunit alpha	****	1.31	1.22
IL17A	Interleukin-17A	ns	0.83	0.8
IL17C	Interleukin-17C	****	1.72	1.58
IL18	Interleukin-18	ns	7.07	7.02
IL18R1	Interleukin-18 receptor 1	**	7.61	7.53
IL1A	Interleukin-1 alpha	***	1.04	1.18
IL2	Interleukin-2	ns	0.74	0.74
IL20	Interleukin-20	ns	0.54	0.52
IL20RA	Interleukin-20 receptor subunit alpha	ns	0.75	0.73
IL22RA1	Interleukin-22 receptor subunit alpha-1	ns	0.33	0.3
IL24	Interleukin-24	ns	0.73	0.72
IL2RB	Interleukin-2 receptor subunit beta	ns	0.52	0.51
IL33	Interleukin-33	ns	0.97	0.98
IL4	Interleukin-4	****	1.13	0.85
IL5	Interleukin-5	**	1.73	1.95
IL6	Interleukin-6	ns	2.85	2.84
IL7	Interleukin-7	ns	5.27	5.21
IL8	Interleukin-8	ns	7.56	7.52
LIF	Leukemia inhibitory factor	ns	0.46	0.46
LIFR	Leukemia inhibitory factor receptor	ns	3.4	3.38
MCP1	Monocyte chemotactic protein 1	****	10.01	9.79
MCP2	Monocyte chemotactic protein 2	ns	10.03	10.02
MCP3	Monocyte chemotactic protein 3	ns	2.23	2.25
MCP4	Monocyte chemotactic protein 4	ns	3.47	3.42
MMP1	Matrix metalloproteinase-1	ns	6.86	6.95
MMP10	Matrix metalloproteinase-10	**	8.83	8.95
NRTN	Neurturin	ns	0.91	0.94
NT3	Neurotrophin-3	**	2.19	2.09
OPG	Osteoprotegerin	ns	9.68	9.71
OSM	Oncostatin-M	****	4.42	4.79
PDL1	Programmed cell death 1 ligand 1	****	5.07	4.87
SCF	Stem cell factor	****	9.28	9.15
SIRT2	SIR2-like protein 2	**	3.01	2.9
SLAMF1	Signaling lymphocytic activation molecule	****	3.2	3.05
ST1A1	Sulfotransferase 1A1	ns	2.04	2
STAMBP	STAM-binding protein	****	2.74	2.58
TGFA	Transforming growth factor alpha	****	3.59	3.88
TGFB1	Latency-associated peptide transforming growth factor beta-1	****	8.1	7.99
TNF	Tumor necrosis factor	ns	0.47	0.45
TNFB	TNF-beta	ns	3.99	3.98
TNFRSF9	Tumor necrosis factor receptor superfamily member 9	****	7.19	6.68
TNFSF14	Tumor necrosis factor ligand superfamily member 14	**	4.62	4.71
TRAIL	TNF-related apoptosis-inducing ligand	****	8.39	8.18
TRANCE	TNF-related activation-induced cytokine	****	5.97	5.5
TSLP	Thymic stromal lymphopoietin	ns	0.42	0.46
TWEAK	Tumor necrosis factor	****	9.02	8.88
UPA	Urokinase-type plasminogen activator	****	10.07	9.87
VEGFA	Vascular endothelial growth factor A	ns	10.2	10.22

Table 4: *Sex differences for each biomarker*