

Correlation between Autoimmune Disease Frequency and IL-2 Expression Due to Treg Cells

Author: Yugyung Oh

Korean Minjok Leadership Academy

euniceoh04@gmail.com

ABSTRACT

In some circumstances, immune cells attack their normal cells. CD4+ helper T lymphocytes are mainly in charge of removing some lymphocytes that contain receptors with self-antigens to develop self-tolerance, and regulatory T cells (Treg) are in charge of additional potential risk. Treg cells suppress immune responses by consuming IL-2 cytokines, essential for T cell responses. IL-2 molecules activate naive CD4+ T cells into CD4+ Treg cells through the STAT5s signaling process and positive feedback of CD25 production with the FoxP3 transcription factor. Therefore, IL-2 cytokines are responsible for two opposite roles: activating immune responses through T cell proliferation and inhibiting immune responses by binding to regulatory T cells instead of proliferating T cells. Due to IL-2's precise ability to control immune responses, IL-2 expression showed a relatively high correlation with autoimmune disease frequency compared to other interleukin substances. The IL-2 expression amount and autoimmune disease prevalence in five tissues showed a relatively high negative coefficient of determination, indicating a tissue with low IL-2 expression would have a high percentage of the autoimmune disease occurring and less likely to occur in tissue with high IL-2 expression. However, as the control of immune responses is very important, many alternative routes can substitute when one is blocked that turned up as exceptions. Nevertheless, the IL-2 expression was found to have a stronger relationship with autoimmune disease occurrence than other interleukins, except IL-10, which is a product of IL-2 functioning.

Keywords: Interleukin-2, Treg cells, regulatory T cells, autoimmune disease frequency, coefficient of determination

1. INTRODUCTION

Immunity plays a vital role in defending our bodies from diverse external materials, therefore preventing infections. However, there is a common bias that immunity will always protect our body. There are also some circumstances where immune cells attack our normal cells, which are the causes of Autoimmune Lymphoproliferative Syndrome, Psoriasis, Rheumatoid Arthritis, Systemic Lupus Erythematosus, Type I Diabetes, etc. However, we do not suffer from all those syndromes because there is a self-tolerance system in the body that distinguishes self cells from non-self cells so that we do not attack our own cells. Some lymphocytes containing receptors that react with self-antigens are removed or inhibited, and this process is mainly focused on CD4+ helper T lymphocytes, which participate in both cell-mediated and humoral immune responses. However, for some situations where this process isn't sufficient, regulatory T cells (Treg) are in charge of additional potential risk.

Regulatory T cells suppress immune responses through several mechanisms. First, Tregs produce CTLA-4, which removes or blocks B7 molecules, which are produced by APC(antigen-presenting cell) and prevents APC from providing costimulation through CD28 and activating T cells. Also, Treg suppresses immune responses by consuming IL-2 cytokines which are essential for T cell responses. When a naive CD4+ T cell

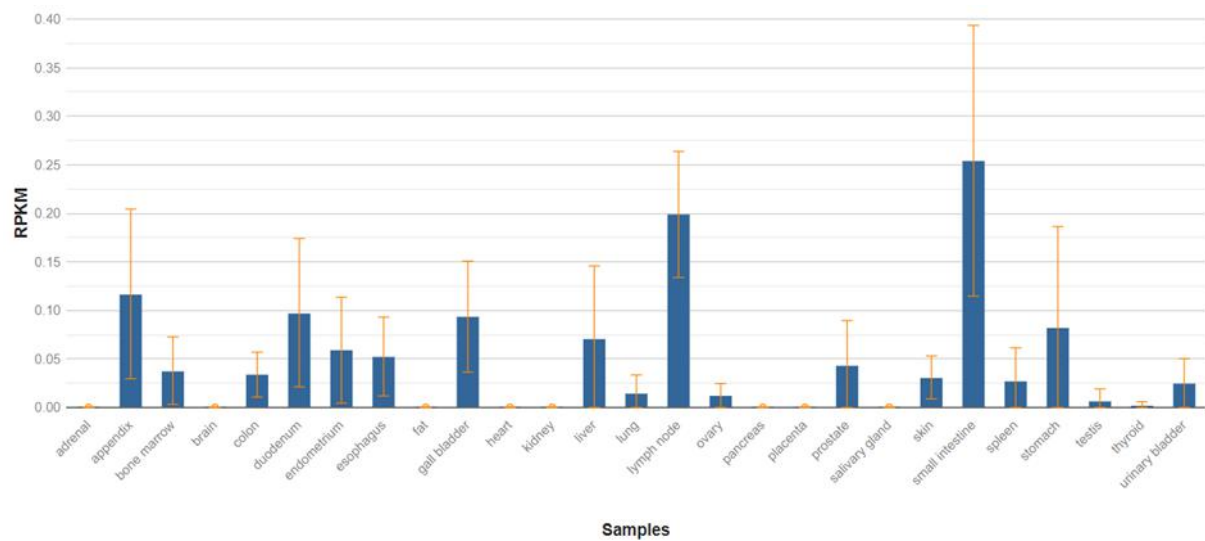


Figure 1. IL-2 expression in 27 different human tissues

This figure compares the average IL-2 expression amount in 27 different human tissue.

transiently expresses CD25 on its surface, the CD4+ cell becomes able to recognize the IL-2 molecule and activates the STAT5s signaling process. Throughout the STAT5s process, CD25 is permanently expressed on the cell surface, inducing positive feedback in CD25 production with the FoxP3 transcription factor. By the successive upregulation done by CD25, the CD4+ T cells evolve into mature CD4+ Tregs and then into activated CD4+ Tregs. (Similar process is also done in CD8+ Treg production.) Then, these activated CD4+ Tregs control the local inflammation of effector CD4+ T cells, autoantibody production in B cells, and T cell-mediated autoimmunity in effector CD8+ T cells. Lastly, regulatory T cells can inhibit the activations of lymphocytes, dendritic cells, and macrophages by secreting cytokines such as IL-10 or TFG-β. IL-10 is a multifunctional cytokine that is an important anti-inflammatory and immunosuppressive molecule. Its expression is selectively promoted by IL-2 through the synergistic activation from the STAT5 [1], and it enhances the peripheral tolerance of Treg. Therefore, IL-2 cytokines are responsible for two opposite roles: activating immune responses through T cell proliferation and inhibiting immune responses by binding to regulatory T cells instead of proliferating T cells. With this precise ability to control immune responses, IL-2 is one of the core molecules that are deeply involved in rejection and inflammation in autoimmune diseases. As the control of immune responses is such an important process, there are

many alternative routes that can substitute when one route is blocked. Nevertheless, there seems to be a strong correlation between IL-2 gene expression amount and autoimmune disease frequency or occurrence probability, when compared to other interleukin substances.

2. Interleukin Molecules Expression and Autoimmune Disease Prevalence

2.1 Tissue-Specific Expression of Interleukin Molecules

IL-2 genes are relatively expressed less in tissues that are involved in more frequently occurring autoimmune diseases. In contrast, in other tissues that are involved in rare autoimmune diseases, significantly more IL-2 genes are expressed.

First, like other genes, IL-2 gene expression is different from tissue to tissue (Figure 1). As all the human cells are started from the same cell, they will contain the same DNA set. However, the function and shape of each cell are different, and this is due to the mechanism in which each gene is expressed differently in each cell. This tissue-specific mechanism generates differentiated phenotypes among tissues. IL-2, IL-6, IL-10, and IL-12 genes are also expressed in different amounts, depending on the tissue, and the below chart, from the data obtained from NCBI, shows the tissue-specific IL-2, IL-6, IL-10, and IL-12A gene expression (Table 1). These interleukin molecules were found to be responsible for the control of immune responses. Cytokine IL-10 inhibits the natural killer cells, Th1

cells secretion of IL-1, IL-3, IL-6, IL-12, and other inflammatory cytokines. IL-12 has a distinctive characteristic of chain-pairing, which provides diverse functions in IL-12 immune regulatory. The dimerization of an alpha chain with IL-12p40 activates the IL-12 cytokines to promote inflammatory responses and the development of chronic inflammatory diseases. In contrast, the dimerization of IL-12 with Ebi3 suppresses

inflammation and mitigates autoimmune diseases [2]. The tissue-specific IL-2, IL-6, IL-10, and IL-12A expression results in the incidence of autoimmune disease.

2.2 Autoimmune Disease Prevalence

The information on IL-2, IL-6, IL-10, and IL-12 expression in each tissue were compared with the frequency of autoimmune diseases. According to the

Table 1. IL-2, IL-6, IL-10, and IL-12 expression in 27 different human tissue

RNA-sequencing was performed in samples collected from 27 different tissues of 95 human individuals and the tissue-specificity expression amount of IL-2, IL-6, IL-10, and IL-12 are shown in the table. Their units are RPKM(reads per kilobase per million reads placed). [3], [4], [5]

sample	RPKM (IL-2)	RPKM (IL-6)	RPKM (IL-10)	RPKM(IL-12)
adrenal	0 ± 0	2.688 ± 1.793	1.065 ± 0.946	0.163 ± 0.047
appendix	0.117 ± 0.087	6.776 ± 4.4	3.722 ± 2.324	0.384 ± 0.1
bone marrow	0.038 ± 0.035	4.933 ± 4.67	1.033 ± 0.641	0.78 ± 0.433
brain	0 ± 0	0.47 ± 0.431	0.242 ± 0.27	0.8665 ± 0.413
colon	0.034 ± 0.023	0.32 ± 0.168	0.309 ± 0.166	0.23 ± 0.12
duodenum	0.098 ± 0.076	0.333 ± 0.24	0.405 ± 0.045	0.26 ± 0.099
endometrium	0.059 ± 0.055	0.934 ± 1.28	0.092 ± 0.076	0.124 ± 0.135
esophagus	0.053 ± 0.041	5.313 ± 3.739	0.279 ± 0.112	2.215 ± 0.55
fat	0 ± 0	1.864 ± 2.409	0.435 ± 0.169	0.156 ± 0.184
gall bladder	0.094 ± 0.057	7.816 ± 2.068	1.776 ± 0.642	0.143 ± 0.041
heart	0 ± 0	0.925 ± 1.222	0.253 ± 0.191	0.192 ± 0.053
kidney	0 ± 0	0.279 ± 0.319	0.038 ± 0.024	0.145 ± 0.095
liver	0.072 ± 0.074	1.438 ± 1.022	0.161 ± 0.099	0.016 ± 0.023
lung	0.015 ± 0.019	4.32 ± 3.875	0.341 ± 0.147	1.388 ± 0.287
lymph node	0.199 ± 0.065	1.426 ± 0.709	2.445 ± 1.414	0.556 ± 0.158
ovary	0.012 ± 0.012	0.039 ± 0.03	0.056 ± 0.011	0.379 ± 0.083
pancreas	0 ± 0	0.631 ± 0.423	0 ± 0	0.051 ± 0.01
placenta	0 ± 0	1.495 ± 0.184	0.566 ± 0.125	0.07 ± 0.043

prostate	0.043 ± 0.046	2.425 ± 2.1	0.075 ± 0.065	0.198 ± 0.148
salivary gland	0 ± 0	0.02 ± 0.015	0.03 ± 0.03	0.039 ± 0.01
skin	0.031 ± 0.022	0.008 ± 0.006	0.053 ± 0.034	0.014 ± 0.02
small intestine	0.254 ± 0.139	0.24 ± 0.116	0.389 ± 0.302	0.241 ± 0.093
spleen	0.028 ± 0.034	0.796 ± 0.359	0.709 ± 0.264	0.834 ± 0.306
stomach	0.083 ± 0.103	0.178 ± 0.135	0.478 ± 0.228	0.197 ± 0.102
testis	0.007 ± 0.012	0.189 ± 0.298	0.371 ± 0.11	0.222 ± 0.066
thyroid	0.002 ± 0.004	0.243 ± 0.15	0.074 ± 0.056	0.082 ± 0.056
urinary bladder	0.025 ± 0.025	10.69 ± 9.449	1.38 ± 0.021	0.205 ± 0.065

Table 2. Autoimmune diseases and their prevalence per 10⁵

The table shows the prevalence per 10⁵ of each frequently occurring autoimmune disease.

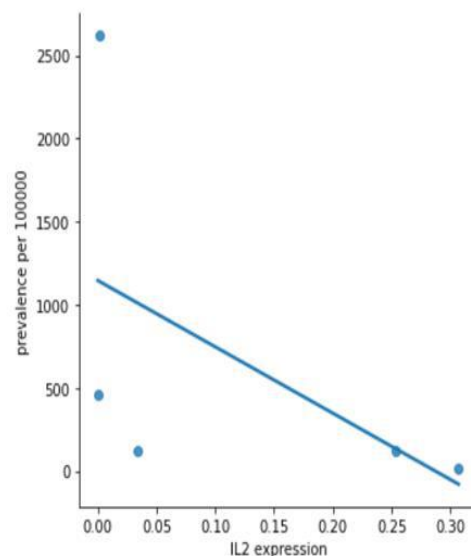
	prevalence per 10⁵
autoimmune thyroiditis	2619
type 1 diabetes	464
ulcerative colitis	124
celiac disease	124
Sjogren's syndrome	31
Crohn's disease	15

Autoimmune thyroiditis, also called Hashimoto's disease, is an autoimmune disease that attacks the thyroid cells [6]. Type 1 diabetes mostly occurs in the pancreas, destroying insulin-producing β -cells due to insulin deficiency [7]. Ulcerative colitis is a relatively long-term condition in which the immune system inflames the colon and rectum [8]. Next, Celiac disease damages the small intestine when eating gluten, reducing its ability to absorb virtually all nutrients [9]. Sjogren's syndrome attacks the lachrymal gland in the eye and the salivary gland in the mouth, causing dry eyes and mouth. Chron's disease is caused in the colon and the last part of the small intestine [10]. Lastly, while ulcerative colitis affects only the colon, Chron's disease involves both the small and large intestines [11].

```
A.raw_data_IL2 = {'IL2 expression' : [0.002, 0, 0.034, 0.254, 0.307],
                  'prevalence per 100000' : [2619, 464, 124, 124, 15]}
AutoimmuneDisease = ['autoimmune thyroiditis', 'type1 diabetes', 'ulcerative colitis',
                     'celiac disease', 'Crohn disease']
AD_data_IL2 = DataFrame(raw_data_IL2, index=AutoimmuneDisease)
print(AD_data_IL2)
```

	IL2 expression	prevalence per 100000
autoimmune thyroiditis	0.002	2619
type1 diabetes	0.000	464
ulcerative colitis	0.034	124
celiac disease	0.254	124
Crohn disease	0.307	15

```
B. ax = sns.lmplot(x="IL2 expression", y="prevalence per 100000", data=AD_data_IL2, ci=None)
```



```
C. # Data Conversion into Matrix
IL2_expression = np.array(AD_data_IL2.loc[:, 'IL2 expression']).reshape((-1,1))
prevalence_per_100000 = np.array(AD_data_IL2.loc[:, 'prevalence per 100000']).reshape((-1,1))

# Linear Regression
model = LinearRegression()
model.fit(IL2_expression, prevalence_per_100000)
r_sq = model.score(IL2_expression, prevalence_per_100000)
print('IL2 expression - coefficient of determination is ', r_sq)
```

IL2 expression - coefficient of determination is 0.2904413917016426

Figure 2. IL-2 expression and autoimmune disease prevalence

A. ‘raw_data_IL_2’, the data about autoimmune disease frequency and IL-2 expression was organized into a data frame named ‘AD_data_IL_2’.

B. ‘AD_data_IL_2’ was plotted into a graph on the coordinate plane.

C. ‘AD_data_IL_2’ data was converted into the matrix. Then, its linear regression was modeled and the coefficient of determination was calculated as 0.2904413917016426.

“Research Gate,” the most prevalent autoimmune disease is autoimmune thyroiditis, which has 2619 prevalence per 100000 (Table 2). The next was type 1 diabetes, multiple sclerosis, ulcerative colitis, celiac disease, Sjogren’s syndrome, and Crohn’s disease; their prevalence per 100000 were 464, 224, 124, 124, 31, and 15 sequentially.

3. Coefficient of Determination of Autoimmune Diseases and Interleukin Molecules

3.1 IL-2 Expression and Autoimmune Disease Prevalence

By comparing the affected tissues in each disease and the expressed IL-2 amount from Tables 1 and 2, two more columns were added to the above chart (Table 3), and this was drawn into scatter plots through python coding (Figure 2). Here, Sjogren’s syndrome, which has a Treg-independent upregulation of Th17 generation, was excluded in this analysis, as it lacks the IL-2 mediated suppression and was controlled by a novel mechanism [12].

Table 3. Autoimmune diseases, their prevalence per 10⁵, and IL-2 expression in affected tissues

	prevalence per 10 ⁵	tissue	IL-2 expression
autoimmune thyroiditis	2426 ~ 2824	thyroid	0.002 ± 0.004
type 1 diabetes	384 ~ 554	pancreas	0 ± 0
ulcerative colitis	85 ~ 175	colon (rectum)	0.034 ± 0.023

celiac disease	85 ~ 175	small intestine	0.254 ± 0.139
Sjogren’s syndrome	13 ~ 61	salivary gland	0 ± 0 (exception)
Crohn’s disease	4~40	esophagus, small intestine	0.053 ± 0.041, 0.254 ± 0.139

```
import pandas as pd
import numpy as np
import matplotlib.pyplot as plt
import seaborn as sns
from pandas import Series, DataFrame
from sklearn.linear_model import LinearRegression
```

First, the data modules for NumPy, plotting graphs, datasets, and linear regression were imported. After several preprocessing of data, the linear regression of IL-2 expression and prevalence of autoimmune diseases was calculated, and the coefficient of determination(R²) was 0.29, a value close to 0.3. As the R² value between 0.3 and 0.7 indicates a moderate negative linear relationship, it can be concluded that there exists a linear relationship between IL-2 expression and autoimmune disease prevalence [13].

3.2 IL-6, IL-10, IL-12 Expression and Autoimmune Disease Prevalence

For comparison, the analyses of other interleukin molecules, related to autoimmune disease, were done similarly. The IL-6, IL-10, and IL-12A expressions were imported from NCBI and compared with the prevalence per 10⁵ of each autoimmune disease (Table 4, Figure 3, Figure 4, Figure 5).

The R² values of IL6, IL-10, and IL-2 expression and autoimmune disease prevalence were

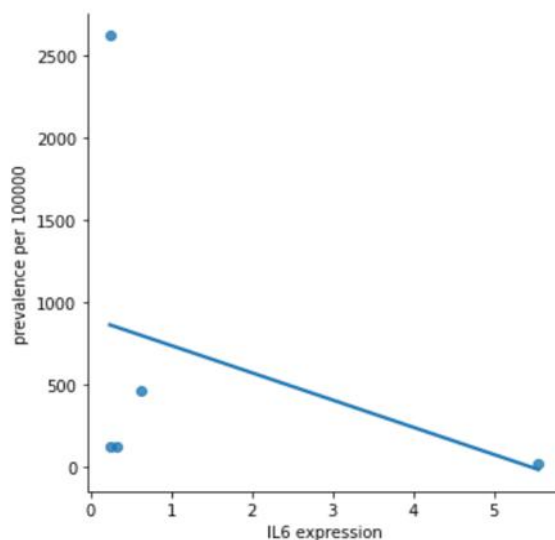
Table 4. Autoimmune disease and IL-6, and IL-12A expression

	prevalence per 10 ⁵	tissue	IL-6 expression (RPKM)	IL-10 expression (RPKM)	IL-12A expression (RPKM)
autoimmune thyroiditis	2426 ~ 2824	thyroid	0.243 ± 0.15	0.074 ± 0.056	0.082 ± 0.056
type 1 diabetes	384 ~ 554	pancreas	0.631 ± 0.423	0 ± 0	0.051 ± 0.01
ulcerative colitis	85 ~ 175	colon (rectum)	0.32 ± 0.168	0.309 ± 0.166	0.23 ± 0.12
celiac disease	85 ~ 175	small intestine	0.24 ± 0.116	0.389 ± 0.302	0.241 ± 0.093
Crohn's disease	4~40	esophagus, small intestine	5.313 ± 3.739 0.24 ± 0.116	0.279 ± 0.112 0.389 ± 0.302	2.215 ± 0.55 0.241 ± 0.093

```
A raw_data_IL6 = {'IL6 expression' : [0.243, 0.631, 0.32, 0.24, 5.553],
                  'prevalence per 100000' : [2619, 464, 124, 124, 15]}
AutoimmuneDisease = ['autoimmune thyroiditis', 'type1 diabetes', 'ulcerative colitis',
                      'celiac disease', 'Crohn disease']
AD_data_IL6 = DataFrame(raw_data_IL6, index=AutoimmuneDisease)
print(AD_data_IL6)
```

	IL6 expression	prevalence per 100000
autoimmune thyroiditis	0.243	2619
type1 diabetes	0.631	464
ulcerative colitis	0.320	124
celiac disease	0.240	124
Crohn disease	5.553	15

```
B ax = sns.lmplot(x="IL6 expression", y='prevalence per 100000', data=AD_data_IL6, ci=None)
```



```
C # Data Conversion into Matrix
IL6_expression = np.array(AD_data_IL6.loc[:, 'IL6 expression']).reshape((-1,1))
prevalence_per_100000 = np.array(AD_data_IL6.loc[:, 'prevalence per 100000']).reshape((-1,1))

# Linear Regression
model = LinearRegression()
model.fit(IL6_expression, prevalence_per_100000)
r_sq = model.score(IL6_expression, prevalence_per_100000)
print('IL6 expression - coefficient of determination is ', r_sq)

IL6 expression - coefficient of determination is 0.12236406743133765
```

Figure 3. IL-6 expression and autoimmune disease prevalence

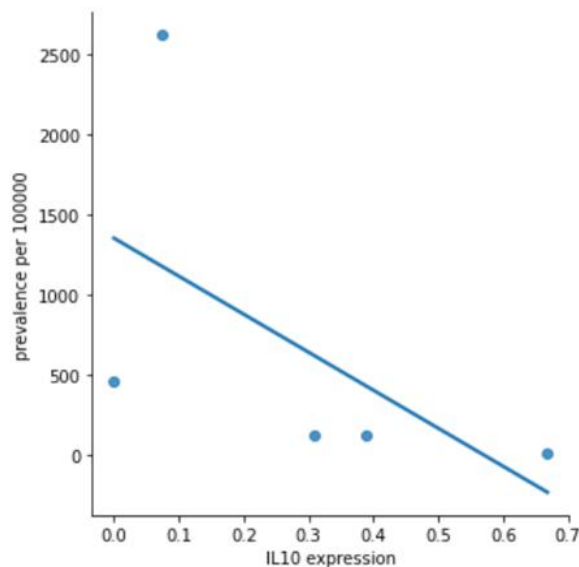
A. 'raw_data_IL_6', the data about autoimmune disease frequency and IL-6 expression was organized into a data frame named 'AD_data_IL_6'.

R 'AD_data_IL_6' was plotted into a graph on the coordinate plane

```
C. 'A] A.raw_data_IL10 = {'IL10 expression' : [0.074, 0, 0.309, 0.3890, 0.668],
                        'prevalence per 100000' : [2619, 464, 124, 124, 15]}
AutoimmuneDisease = ['autoimmune thyroiditis','type1 diabetes','ulcerative colitis',
                      'celiac disease','Crohn disease']
AD_data_IL10 = DataFrame(raw_data_IL10, index=AutoimmuneDisease)
print(AD_data_IL10)
```

	IL10 expression	prevalence per 100000
autoimmune thyroiditis	0.074	2619
type1 diabetes	0.000	464
ulcerative colitis	0.309	124
celiac disease	0.389	124
Crohn disease	0.668	15

```
B. ax = sns.lmplot(x="IL10 expression", y='prevalence per 100000', data=AD_data_IL10, ci=None)
```



```
C.# Data Conversion into Matrix
IL10_expression = np.array(AD_data_IL10.loc[:, 'IL10 expression']).reshape((-1,1))
prevalence_per_100000 = np.array(AD_data_IL10.loc[:, 'prevalence per 100000']).reshape((-1,1))

# Linear Regression
model = LinearRegression()
model.fit(IL6_expression, prevalence_per_100000)
r_sq = model.score(IL6_expression, prevalence_per_100000)
print('IL6 expression - coefficient of determination is ', r_sq)

IL6 expression - coefficient of determination is 0.12236406743133765
```

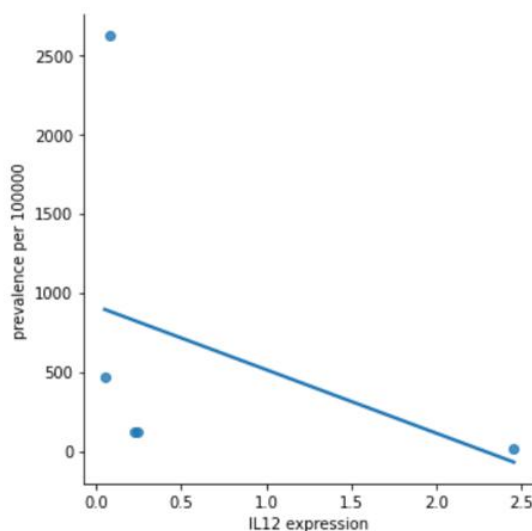
Figure 4. IL-10 expression and autoimmune disease prevalence

- A. 'raw_data_IL_10', the data about autoimmune disease frequency and IL-10 expression was organized into a data frame named 'AD_data_IL_10'.
- B. 'AD_data_IL_10' was plotted into a graph on the coordinate plane.
- C. 'AD_data_IL_10' data was converted into the matrix. Then, its linear regression was modeled, and the coefficient of determination was calculated as 0.3282431136030811.

```
A.raw_data_IL12 = {'IL12 expression' : [0.082, 0.051, 0.23, 0.241, 2.456],
                  'prevalence per 100000' : [2619, 464, 124, 124, 15]}
AutoimmuneDisease = ['autoimmune thyroiditis', 'type1 diabetes', 'ulcerative colitis',
                    'celiac disease', 'Crohn disease']
AD_data_IL12 = DataFrame(raw_data_IL12, index=AutoimmuneDisease)
print(AD_data_IL12)
```

	IL12 expression	prevalence per 100000
autoimmune thyroiditis	0.082	2619
type1 diabetes	0.051	464
ulcerative colitis	0.230	124
celiac disease	0.241	124
Crohn disease	2.456	15

```
B.ax = sns.lmplot(x="IL12 expression", y='prevalence per 100000', data=AD_data_IL12, ci=None)
```



```
C.# Data Conversion into Matrix
IL12_expression = np.array(AD_data_IL12.loc[:, 'IL12 expression']).reshape((-1,1))
prevalence_per_100000 = np.array(AD_data_IL12.loc[:, 'prevalence per 100000']).reshape((-1,1))
```

```
# Linear Regression
```

Figure 5. IL-12A expression and autoimmune disease prevalence

- A. 'raw_data_IL12', the data about IL-12 expression was organized into a data frame named 'AD_data_IL12'.
- B. 'AD_data_IL12' was plotted into a graph on the coordinate plane.
- C. 'AD_data_IL12' data was converted into the matrix. Then, its linear regression was modeled, and the coefficient of determination was calculated as 0.14108209310742847.

0.12236406743133765, 0.3282431136030811, and 0.14108209310742847. An R^2 value of IL-10 expression was the highest among the three interleukin cytokines, and its 0.33 proves the negative linear correlation between the two factors. In contrast, the R^2 value of IL-6 and IL-12 expression was only 0.12 and 0.14, showing the

relatively high R^2 value of IL-2 and IL-10 and the strong relationship with autoimmune disease frequency. These statistics prove the importance of IL-2 and IL-10 in autoimmune disease regulation. This tendency of high R^2 value is due to the characteristic of IL-10, which is one of the molecules that IL-2 secretes during immune

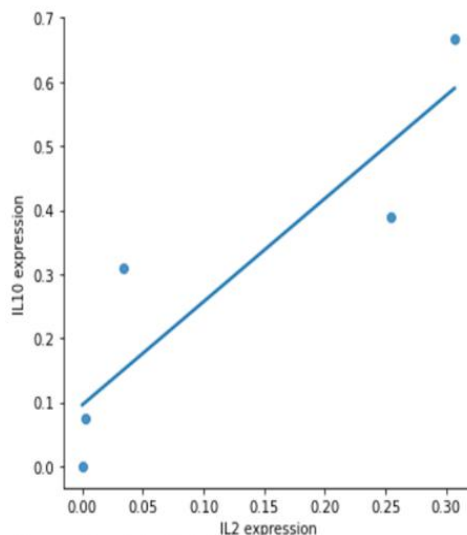
response suppression with the regulatory T cells. As the IL-10 secretion from Treg cells is selectively stimulated by IL-2, there exists a positive correlation between the expression of IL-2

and IL-10. Their coefficient of determination was calculated as above, and its result was 0.81, which strongly proves the positive relationship between IL-2 and IL-10 (Figure 6).

```
A.raw_data_IL2_IL10 = {'IL2 expression' : [0.002, 0, 0.034, 0.254, 0.307],
                        'IL10 expression' : [0.074, 0, 0.309, 0.3890, 0.668]}
AutoimmuneDisease = ['autoimmune thyroiditis','type1 diabetes','ulcerative colitis',
                      'celiac disease','Crohn disease']
AD_data_IL2_IL10 = DataFrame(raw_data_IL2_IL10, index=AutoimmuneDisease)
print(AD_data_IL2_IL10)

B.ax = sns.lmplot(x="IL2 expression", y="IL10 expression", data=AD_data_IL2_IL10, ci=None)
```

	IL2 expression	IL10 expression
autoimmune thyroiditis	0.002	0.074
type1 diabetes	0.000	0.000
ulcerative colitis	0.034	0.309
celiac disease	0.254	0.389
Crohn disease	0.307	0.668



```
C.# Data Conversion into Matrix
IL10_expression = np.array(AD_data_IL10.loc[:, 'IL10 expression']).reshape((-1,1))
prevalence_per_100000 = np.array(AD_data_IL10.loc[:, 'prevalence per 100000']).reshape((-1,1))

# Linear Regression
model = LinearRegression()
model.fit(IL2_expression, IL10_expression)
r_sq = model.score(IL2_expression, IL10_expression)
print('IL2&IL10 expression - coefficient of determination is ', r_sq)

IL2&IL10 expression - coefficient of determination is 0.8083673802754133
```

Figure 6. IL-2 expression and IL-12 expression

- A. 'raw_data_IL2_IL10', the data about IL-2 expression and IL-10 expression was organized into a data frame named 'AD_data_IL2_IL10'.
- B. 'AD_data_IL2_IL10' was plotted into a graph on the coordinate plane.
- C. 'AD_data_IL2_IL10' data was converted into the matrix. Then, its linear regression was modeled, and the coefficient of determination was calculated as 0.8083678802754133.

4. Conclusion

Immune system is known to protect one's body from invading outside substances such as bacteria, viruses,

fungi, and toxins, but not own normal cells. Thus, self-tolerance is designed in the immune system not to attack one's body. However, in some cases, self-

tolerance is lost, and several lymphocytes attack healthy cells. In this case, the regulatory T cells suppress the immune responses and minimize the damage.

Interleukin molecules are secreted by leukocytes (white blood cells) and other cells. Their primary function is to modulate growth, differentiation, and activation during inflammatory and immune responses. Specifically, several interleukin molecules, IL-2, IL-6, IL-10, and IL-12, were found to be related to the control of autoimmune diseases. Their expression amount from each tissue was analyzed and compared with the prevalence of autoimmune disease through python. The data were drawn in a coordinate plane, and the coefficient of determinations (R^2) was calculated. As a result, IL-2 and IL-10 had the highest coefficient of determination. This is due to the IL-10-specific stimulation of IL-2. Regulatory T cells are mainly in charge of the control of immune responses. Other cells, such as CD4+ helper T cells, are usually involved in eliminating self-attacking lymphocytes, and the regulatory T cells are there to assist in the suppression of immune responses. Treg cells consume IL-2 in this suppression process, which makes the IL-2 molecules crucial in the immune response control, preventing autoimmune diseases. Subsequently, IL-10 is also a molecule aroused by IL-2, and this relationship between IL-2 and IL-10 results in a similar tendency with their connection between tissue-specific expression and autoimmune disease prevalence.

Therefore, as the coefficient of determination of IL-2 and IL-10 were comparatively high, IL-2 and IL-10 seem to be more related to the control of autoimmune diseases. Especially, IL-2, which is even the cause of IL-10 production, is one of the essential molecules in charge of immune response controls.

5. References

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