

B-Cell Analysis in Type 1 Diabetes

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October 21, 2024

Project Overview



This project focuses on understanding how B-cells, a crucial part of the immune system, differ between individuals with type 1 diabetes and healthy individuals.



We aim to explore differences in **clone size**, **mutation rates**, and **V-gene usage** between the two groups to better understand immune response changes associated with type 1 diabetes.

Key Research Questions

1. Is there a correlation between B-cell clone size and mutation rate?

2. How consistent is V-gene usage across different individuals?

3. How does type 1 diabetes impact the overall clonal repertoire of B-cells?

4. Compare B-cell characteristics between healthy individuals and those with type 1 diabetes.

Data Summary

The dataset consists of B-cell clonotype information from 6 individuals: 3 healthy donors and 3 donors with type 1 diabetes.

Analyzed:

**Clone
size** (number of
copies),

**V-gene
usage** (types of
B-cells),

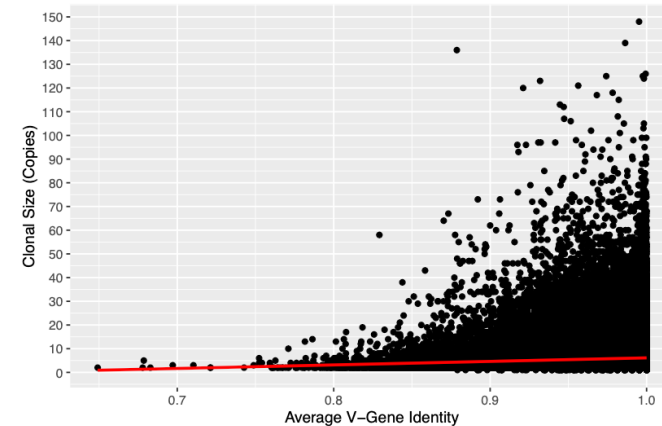
**Mutation
rate** (average V-
gene identity).

Q1. Correlation Between Clone Size and Mutation

- **Objective:** Determine if there is a correlation between B-cell clone size and mutation rate.
- **Findings:**
 - Larger B-cell clones show a slight increase in mutation rate, but the correlation is weak.
 - There is a significant relationship between copies and avg_v_identity.
 - **P-value:** A p-value of $< 2.2e-16$ indicates high significance.
 - **Rejecting the Null Hypothesis:** The very small p-value ($< 2.2e-16$) gives us confidence that the relationship is relevant, not due to chance.

Key Insight: Although the relationship is statistically significant, the effect is small.

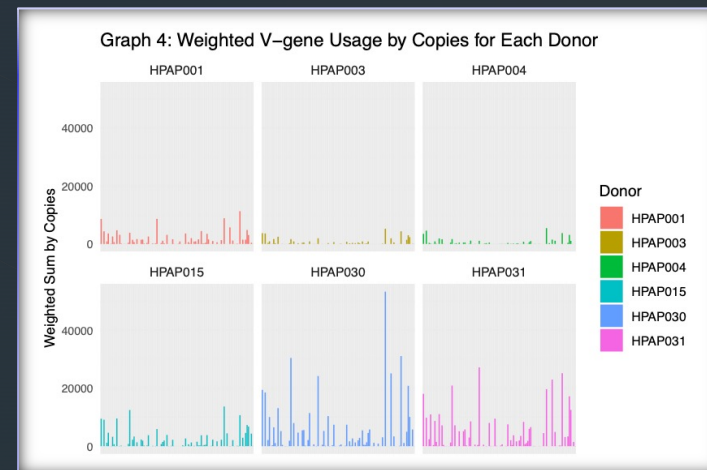
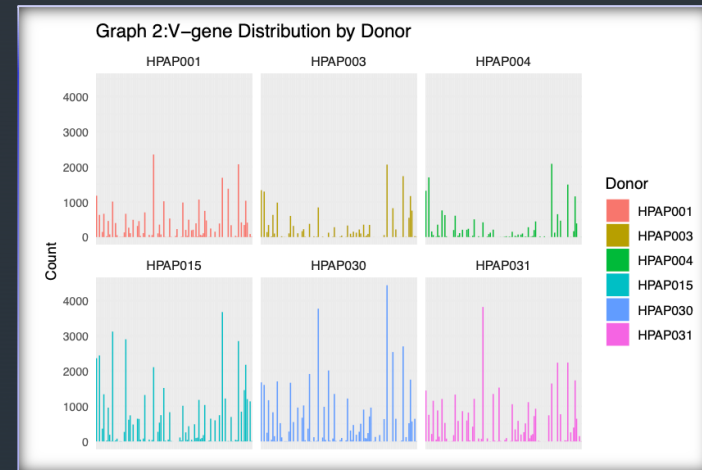
Graph 1: Relationship Between Average V-Gene Identity and Clonal Size

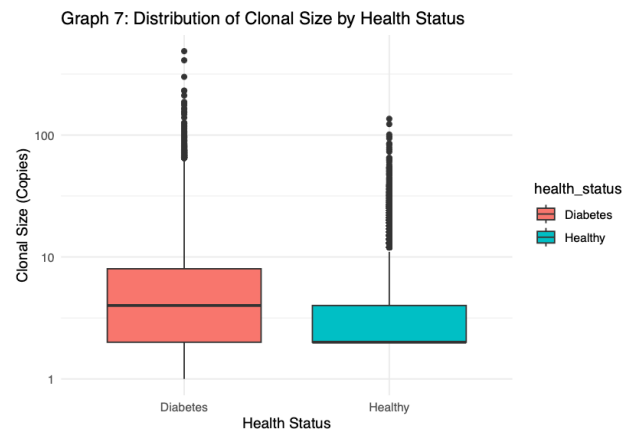
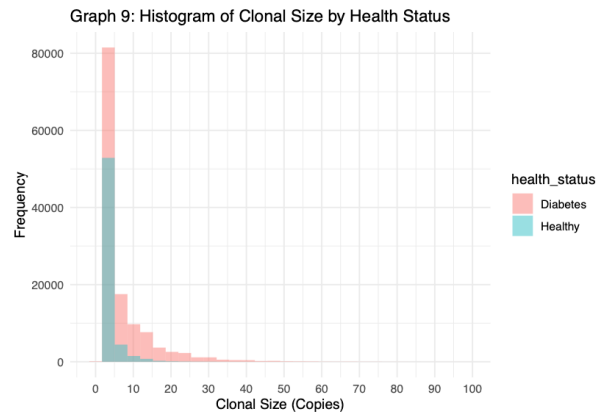


```
##  
## Call:  
## lm(formula = avg_v_identity ~ copies, data = hpap_cleaned)  
##  
## Residuals:  
##      Min       1Q   Median       3Q      Max   
## -0.32691 -0.01682  0.01657  0.02370  0.02428   
##  
## Coefficients:  
##              Estimate Std. Error t value Pr(>|t|)      
## (Intercept)  9.754e-01  9.434e-05 10339.23  <2e-16 ***  
## copies       2.873e-04  1.014e-05   28.35  <2e-16 ***  
## ---  
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1  
##  
## Residual standard error: 0.03211 on 189813 degrees of freedom  
## Multiple R-squared:  0.004216,    Adjusted R-squared:  0.004211  
## F-statistic: 803.6 on 1 and 189813 DF,  p-value: < 2.2e-16
```

Q2: V-gene distribution among donors

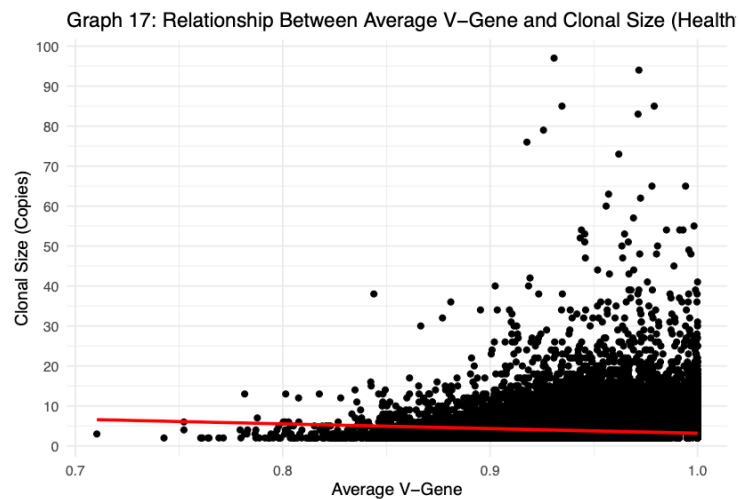
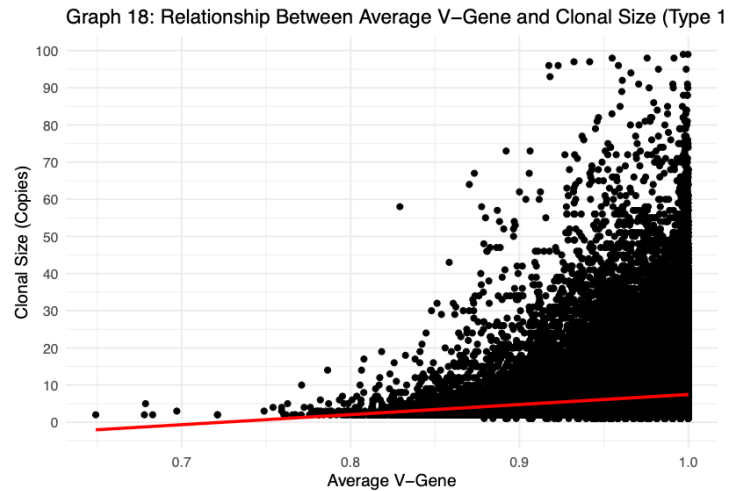
- **Objective:** Investigate whether V-gene usage is consistent across individuals.
- **Finding:** V-gene usage shows variation between donors.
- **Key Insight:** Diabetic donors tend to rely more heavily on certain V-genes.





Q3: Impact of Disease on Clonal Repertoire

- **Objective:** Assess how type 1 diabetes affects the overall clonal repertoire of B-cells, with a focus on clone size.
- **Finding:** Individuals with type 1 diabetes have larger B-cell clones compared to healthy individuals.
- **Key Insight:** The expansion of larger clones in diabetic individuals suggests a heightened response compared to healthy individuals.



Q4. Healthy vs. Diabetic Clonal Behavior

- **Objective:** Explore how clonal behavior (size and mutation) differs between healthy and diabetic individuals.
- **Finding:** In healthy individuals, larger clones tend to have fewer mutations. In diabetic individuals, larger clones exhibit more mutations.
- **Key Insight:** The opposite mutation patterns in healthy vs. diabetic individuals suggest that these patterns could help predict outcomes in diabetic patients.

Key Takeaways

- There is a weak but statistically significant correlation between B-cell clone size and mutation rate.
- V-gene usage varies between individuals, with notable differences between healthy and diabetic donors.
- Type 1 diabetes is associated with larger and more diverse B-cell clones, potentially reflecting an overactive immune response.

Conclusion

- The analysis highlights clear differences in B-cell behavior between healthy and diabetic individuals, particularly in terms of clonal size, mutation rates, and V-gene usage.
- These findings provide insight into how the immune system may be altered in type 1 diabetes.