Difference in Immunity Systems Of Mice From Two TCR Groups

Somak Dutta, Wooseok Ha, Yuefeng Liang, and Shailee Mehta

Clients: Benjamin McDonald & Albert Bendelac, Pathology.

University of Chicago

April 22, 2014

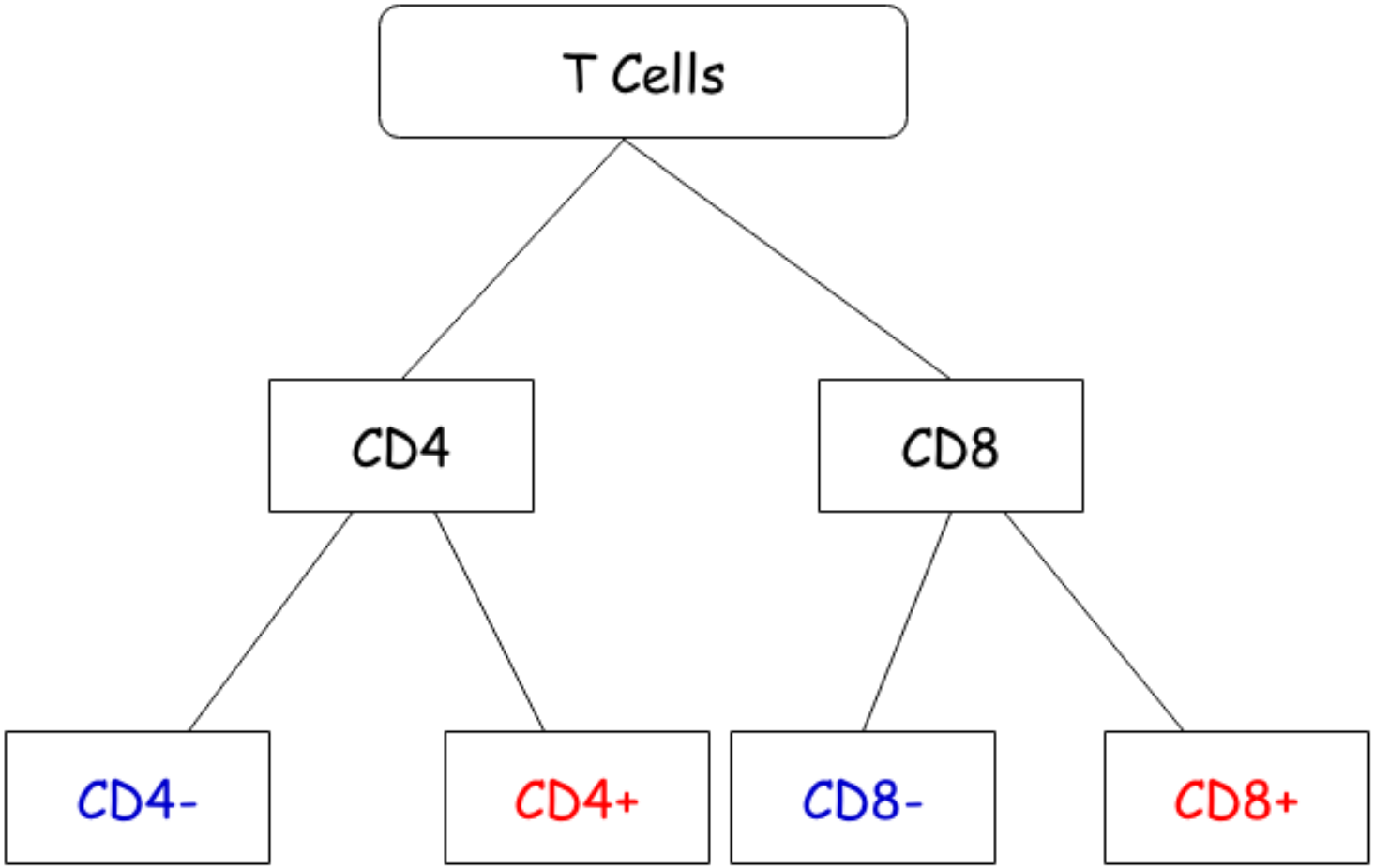
Raised hands?

The client is interested in studying the development of a population of immune system cells (T cells) located in three glands: spleen, thymus and the intraepithelial lymphocyte (IEL). To this end, the client has bred a total of 39 mice broadly categorized into two groups (C & U) by their TCR, which in turn have 5 and 3 subcategories respectively based on the TCR subtypes. For each mice and each gland, the client obtained the ratio of two types of cell counts. The cell-count ratio is the variable that is used to test for any significant differences between the TCR development in the two categories of mice. **THIS SENTENCE IS AN EXPERIMENT TO SEE IF PEOPLE ACTUALLY READ THE WHOLE ABSTRACT; PLEASE RESPOND BY RAISING A HAND DURING THE PRESENTATION**. Our main contribution is to account for the within subtype correlation and thus making more sensible inference out of the data. We will also discuss issues like imbalance in the design created by the cost of the experiment.

What are we talking about?

- T–cells are a type of lymphocyte that play a central role in cell-mediated immunity. T cells are GOOD CELLS.
- A T cell receptor or TCR is a molecule that is found on T–cells.
- TCR recognizes antigens.
- Thus TCR is linked with the immunity system of a mammal (contrary to the T–virus which create zombies).

Types of T–cells



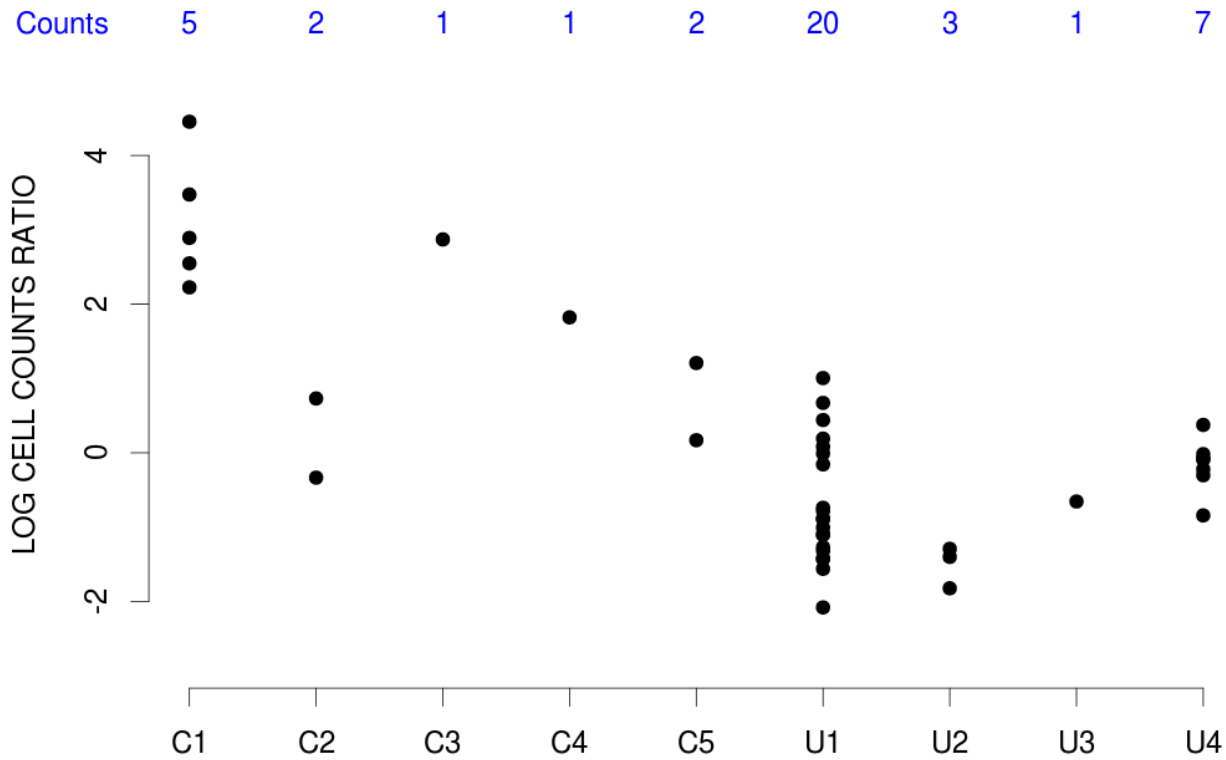
Two types of TCR: C and U

Q: Type C and U – which one increases immunity?

- Response: $\log \frac{\#\text{T CELL} +}{\#\text{T CELL} -}$.
- Cells from three glands: Thymus, Spleen and intraepithelial lymphocyte (IEL)
- Each TCR has subtypes:
  1. TCR C has 5 subtypes: C1,. . . ,C5.
  2. TCR U has 4 subtypes: U1,. . . ,U4.

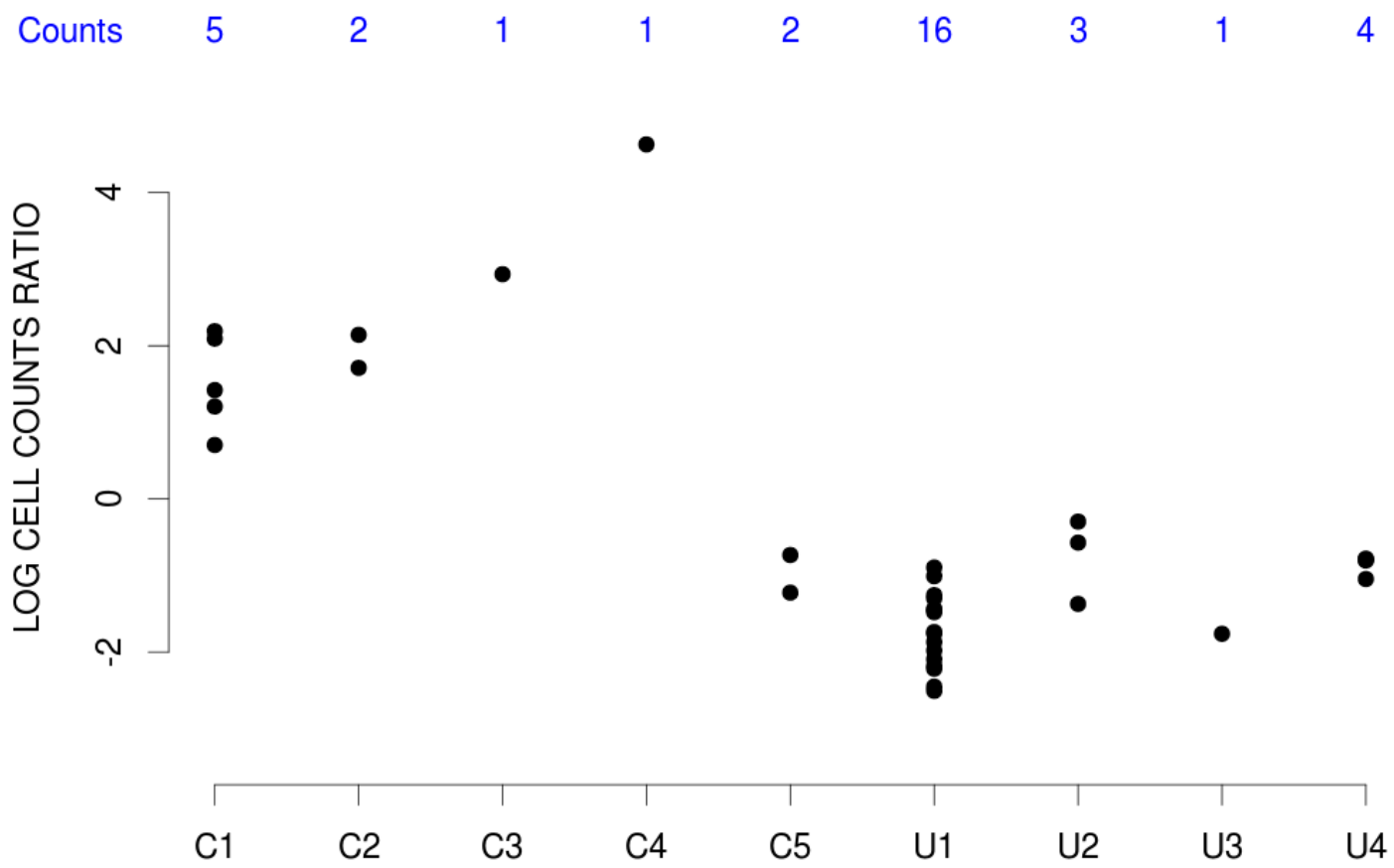
Plot of the data for thymus.

Two sample t-statistic: 7.61 on 40 d.f., p-value ≈ 0.



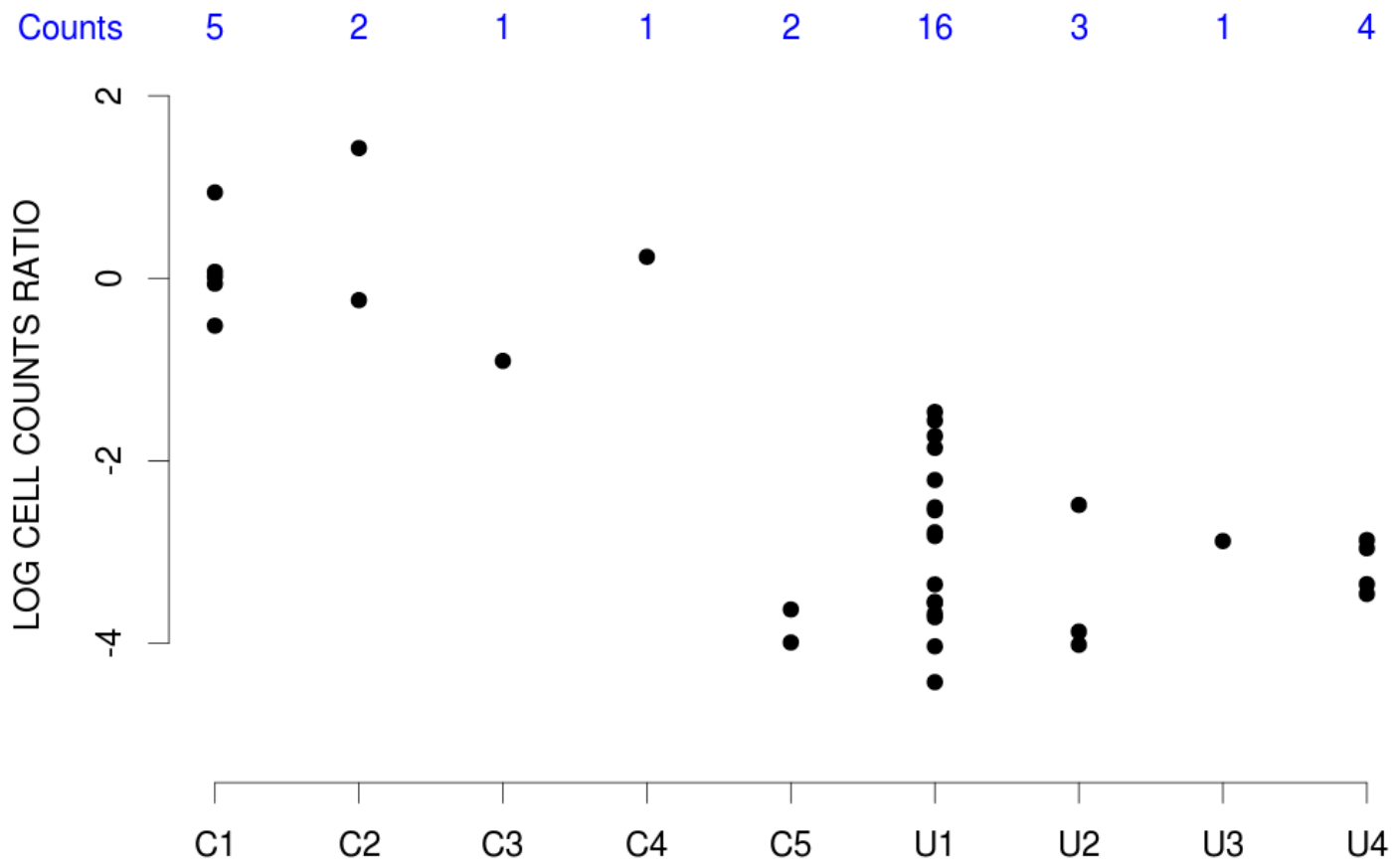
Plot of the data for spleen.

Two sample t-statistic = 5.98 on 11.32 d.f., p-value = 0.0001.



Plot of the data for IEL.

Two sample t-statistic = 4.39 on 12.2 d.f., p-value = 0.0008.



MODEL FOR EACH GLAND

Gaussian model for the log-response: For ith and jth mice, $i \neq j$

$$
\begin{aligned}
\text{log ratio} &\sim \mathcal{N}(\boldsymbol{\mu}, \Sigma) \\
\mu_i &= \alpha + \beta_{type(i)} \qquad type(i) \in \{C, U\} \\
\Sigma_{ii} &= \sigma^2 + \sigma^2_{st}, \qquad \textit{marginal variance}. \\
\Sigma_{i,j} &= \begin{cases} \sigma^2_{st}, & \text{if } i \neq j \text{ have same TCR subtype.} \\ 0 & \text{otherwise} \end{cases}
\end{aligned}
$$

Person of interest: $\beta_C - \beta_U$

Estimates using REML: $\beta_C - \beta_U$

$$\mu_i = \alpha + \beta_{type(i)} \qquad type(i) \in \{C, U\}$$

Gland	Estimate	s.e.	t-ratio	p-value
Thymus	2.46	0.71	3.49	0.010
Spleen	3.24	1.05	3.08	0.018
IEL	2.33	0.91	2.55	0.038

Estimates using REML: Variance components

$$\Sigma_{ii} = \sigma^2 + \sigma^2_{st}, \qquad \textit{marginal variance.}$$

$$\Sigma_{i,j} = \begin{cases} \sigma^2_{st}, & \text{if } i \neq j \text{ have same TCR subtype.} \\ 0 & \text{otherwise} \end{cases}$$

Gland	Parameter	Estimate (s.e.)	Parameter	Estimate (s.e.)
Thymus	σ^2	0.551 (0.135)	σ^2_{st}	0.871 (0.604)
Spleen	σ^2	0.234 (0.065)	σ^2_{st}	2.334 (1.313)
IEL	σ^2	0.663 (0.184)	σ^2_{st}	1.536 (1.000)

Comments

1. Imbalance in design caused by cost of breeding mice of certain subtypes.
2. The mixed linear models fit the data better (higher log-likelihood values).
3. Client happy with higher (but still significant) p-values.

Thank You