**Is net charge a good indicator of receptor binding avidity change?**

Hsiang-Yu Yuan

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In total, 59 single substitutions in HA (58 from H1N1 and 1 from H3N2) which have receptor binding avidity data are collected from literatures. I classify their binding avidity into 3 groups: increased (+1), neutral (0), and decreased (-1) binding. Net charge changes of each virus from wild type to mutant are calculated. First I use Fisher’s exact test on contingency table to check whether net charge distribute differently with binding avidity.

Fisher’s Exact Test on contingency table

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | **Binding** |  |
| **Net charge** | Decreased(-1) | Neutral(0) | Increased(+1) |
| <0 | 4 | 4 | 2 |
| >0 | 0 | 6 | 18 |
| p = 0.00098 |  |  |  |
|  |  |  |  |
|  |  |  |  |

If I merge negative and neutral net charge into one group, and decreased and neutral binding avidity into one group, then we can test on 2 x 2 table.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | | **Binding** | |  |  |
| **Net charge** | | Decreased or Neutral(-1 or 0) | | Increased(+1) |  |
| <=0 | | 23 | | 12 |  |
| >0 | | 6 | | 18 |  |
|  |  | |
| p = 0.00333 | |  | |  |  |

Either way, p value is less than 0.01, which is significant.

To evaluate whether positive correlation exists between binding and net charge, ordinal logistic regression was use to evaluate whether binding avidity is positive correlated to net charge change.

**Null hypothesis H0**: Binding avidity is not positive correlated to net charge change.

**Alternative hypothesis H1**: Binding avidity is positive correlated to net charge change.

Using ordinal logistic regression to test the association, I got p value:

P = 9.920866e-04

The result shows that the alternative hypothesis that positive net charge change would lead to increased binding avidity is significantly supported.

I further calculate the binding score 58 substitutions (I exclude one substitution belong to H3) and test the association of receptor binding avidity level and computational binding score. The scatter plot is shown in the figure. Using one-tailed test for ordinal logistic regression, p value 0.039488814 (0.045 for one-tailed test for simple linear regression), which is weakly significant. The regression result supports that computational binding score would positive correlate to experimental binding avidity level.

Conclusion:

Both net charge changes and computational binding score are good indicator (in terms of statistical view) for predicting binding avidity level. However, the index of net charge shows even stronger significant than binding score using computational approach.