

Insights into Pre-existing T-cell Immunity to Influenza Infection from a Population-based Cohort Study in Singapore

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Background/Objective

T-cell responses mediate viral clearance during an influenza infection, but their protective role is unclear. We investigated if baseline T-cell response to influenza A/Singapore/CDC204/2012(H3N2) strain protected against subsequent H3N2 infection(s) after accounting for potential confounding factors by HI titers and demographic variables.

Method

Rolling recruitment for a community cohort started in February 2012, with follow-ups every six months till December 2013. A maximum of four blood samples with accompanying questionnaires were contributed by each participant. Influenza-specific antibody response was tested by Haemagglutination inhibition (HI) assay against three H3N2 strains: A/Singapore/CDC204/2012, A/Perth/16/2009 and A/Victoria/361/2011 while pre-existing T-cell response (SFU) was tested by ELISPOT assay against A/Singapore/CDC204/2012(H3N2). We investigated associations between geometric mean titers(GMT) and SFU with demographic factors using linear regression, GMT and SFU on seroconversion to any H3N2 strains as the outcome (with person-interval as the unit of analysis) using logistic regression.

Result

Increasing trend in population immunity against A/Perth/16/2009(H3N2) and decreasing trend for A/Victoria/361/2011 were observed when A/Victoria/361/2011(H3N2) was the circulating strain. A higher GMT was observed to be associated with age ≤ 20 and vaccination within one year before the study. Female was associated with a lower SFU, but no difference in GMT. Pearson's correlation indicates a strong association between A/Singapore/CDC204/2012(H3N2) and A/Victoria/361/2011(H3N2) (OR=0.87, $p < 0.001$); weak associations observed in T-cell with GMTs (with A/Singapore/CDC204/2012: OR=0.06, $p = 0.004$; with A/Perth/16/2009: OR=0.12, $p < 0.001$; with A/Victoria/361/2011: OR=0.08, $p < 0.001$). By multivariate logistic regression, T-cell and most recent HI titer to A/Victoria/361/2011(H3N2) are observed to associate strongly with seroconversion (T-cell: OR=0.83, $p = 0.009$; most recent HI titer to A/Victoria/361/2011(H3N2): OR=0.42, $p < 0.001$), association was only observed at lower HI titer ($p = 0.01$) upon stratification.

Conclusion

Weak but significant correlation observed between T-cell response and antibody profile; strongest association observed in A/Perth/16/2009(H3N2). Most recent HI titer predicts protection better than baseline GMT. T-cell confers protection against influenza infection and is independent of GMT.