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Modeling original antigenic sin in dengue viral infection

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Modeling original antigenic sin in dengue viral infection

Ryan Nikin-Beers

Cross-reactive T cell responses induced by a primary dengue virus infection may contribute to increased disease severity following heterologous infections with a different virus serotype in a phenomenon known as the original antigenic sin. In this study, we developed and analyzed in-host models of T cell responses to primary and secondary dengue virus infections that considered the effect of T cell cross-reactivity in disease enhancement. We fit the models to published patient data and showed that the overall infected cell killing is similar in dengue heterologous infections, resulting in dengue fever and dengue hemorrhagic fever. The contribution to overall killing, however, is dominated by non-specific T cell responses during the majority of secondary dengue hemorrhagic fever cases. By contrast, more than half of secondary dengue fever cases have predominant strain-specific T cell responses with high avidity. These results support the hypothesis that cross-reactive T cell responses occur mainly during severe disease cases of heterologous dengue virus infections.