**Small Changes Have Big Effects:**
Genetic profiling to predict pathogenicity

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**Abstract**
Dengue virus (DENV) and Zika virus (ZIKV) are mosquito-borne viruses that belong to the Flavivirus genus of the Flaviviridae family. Both DENV and ZIKV have dramatically increased their geographic distribution in recent years with much of the tropical and subtropical world is now hyperendemic for these viruses. In light of with increasing global population growth, urbanization and international transportation of people and goods, these viruses are likely to continue their rapid expansion for the foreseeable future. Despite aggressive mosquito control and public awareness campaigns, Singapore is continues to battle year-round transmission of all four DENV serotypes and more recently suffered its first autochthonous ZIKV outbreak.

While drug and vaccine development efforts are underway for these viruses, there are concerns that resistant strains will rapidly emerge. Indeed, the rapid spread of these viruses has greatly increased overall viral genetic diversity, some of which appears to be associated with increased epidemic potential. The mechanisms underlying viral fitness in epidemiological settings however, remain poorly defined. To address these deficiencies, we are employing a number of novel methodologies to examine both the viral and host determinants of pathogenesis. Our findings provide fresh insights into antiviral targets for these pathogens and could potentially serve as a template for the rapid identification of evolutionarily constrained regions for therapeutic targeting in other RNA viruses.

**Selected Publications for Reference**
3. Fernandez-Garcia et al 2009, Cell Host and Microbe (PMID: 19380111)