Singaporean Society for Immunology

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SgSI Seminar Series: Infectious Diseases

Date & Time: 10 July 2014 (Thursday), 4.30 - 5.45pm

*Venue: Aspiration, Matrix Level 2M, Biopolis

Host: Dr. Katja Fink, SIgN

Registration is based on first-come first-served.
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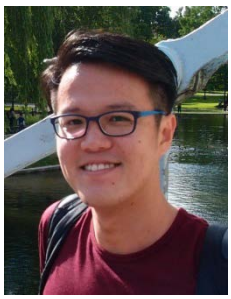


Dr. Yie Hou Lee

Research Scientist
SMART

Secondary dengue and DENV2 as molecular prognostication indicators for Dengue Fever sequelae?

Early, effective triage of patients likely to develop severe dengue sequelae has been challenging because of late presentation of heterogeneous clinical symptoms. Molecular evidence stemming from serum immunomodulatory proteins, hematologic and virologic parameters may provide consistent and deeper mechanistic insights, thereby complementing existing clinical definitions for early prognosis of severe dengue hemorrhagic fever (DHF) from milder dengue fever (DF). Through a stacked generalization-based machine learning technique that combines multiple tunable binary classification methods on two clinical cohorts (n = 204) of clinically confirmed DF and DHF individuals in Singapore and a combined dataset of 38 serum molecular features, accurately predicted patients who developed DHF [area under curve (AUC) = 0.88]. Models generated based on primary or secondary dengue infection status, and DENV1 or DENV2 revealed the importance of secondary, heterotypic dengue infection (AUC = 0.88) and DENV2 (AUC = 0.89) in progressing toward DHF. Secondary dengue-infection induced molecular features that regulate a Th2 response switch (up-regulation of IL-10 and repression of IL-12 and IL-1β) and DENV2 demonstrated a dampened viral clearance (down-regulation of IFNγ and IP-10 and high viral titers). Model construction using one clinical cohort data and cross-validating with the other cohort data further demonstrated the generalizability of the high-level learner (AUC = 0.66 & 0.71). Thus, molecular data validates the inferences derived from epidemiologic data, and suggests a clinically complementary framework to improve triage of dengue-affected patients.

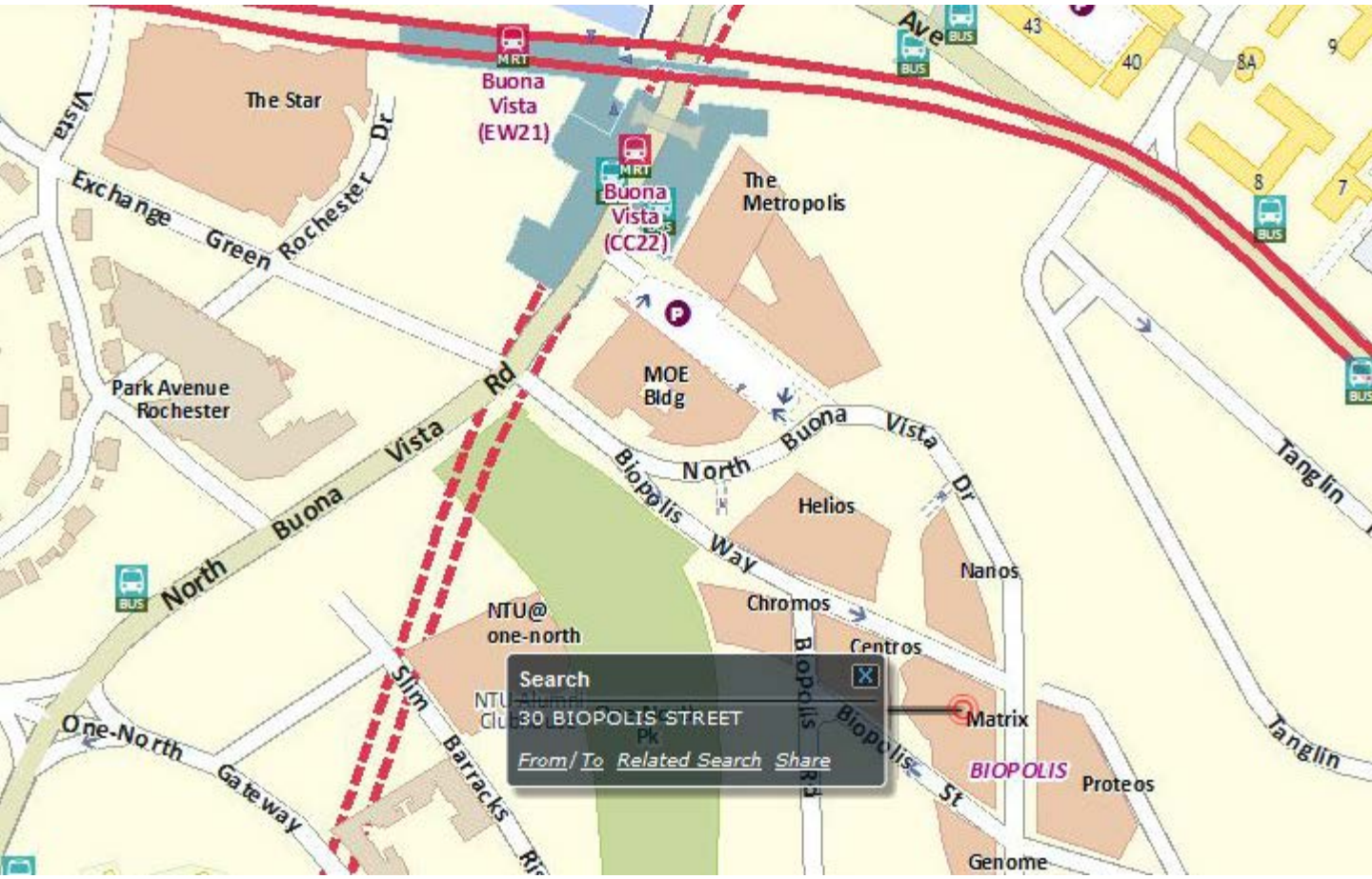
Dr. Martin Gengenbacher

Head of TB Lab
NUS

How to improve an aging tuberculosis vaccine

The only tuberculosis (TB) vaccine in use today, bacillus Calmette-Guérin (BCG), only protects during childhood and can cause adverse events in immunocompromised individuals, such as BCGosis in HIV(+) newborns. The recombinant vaccine candidate BCG Δ*ureC*::*hly*, which secretes the pore-forming protein listeriolysin O of *Listeria monocytogenes,* showed better preclinical safety and efficacy than canonical BCG. While BCG Δ*ureC*::*hly* progresses through the clinical development pipeline, we followed several strategies for further improvement. vitamin B6 synthase rendered the vaccine auxotrophic Deletion of *pdx1*, which encodes the for this essential cofactor in a concentration-dependent manner, as was its survival *in vivo*. BCG Δ*ureC*::*hly* Δ*pdx1* showed markedly restricted dissemination in mice, which was ameliorated by dietary supplementation with vitamin B6. The construct was safer in SCID mice than the parental BCG Δ*ureC*::*hly*. A prompt innate immune response to vaccination remained independent of vitamin B6 administration, while acquired immunity, notably stimulation of antigen-specific CD4 T cells, B cells, and memory T cells, was contingent on vitamin B6 administration. Prime-boost vaccination increased protection against the canonical *M. tuberculosis* H37Rv laboratory strain and a clinical isolate of the Beijing/W lineage. The principle to modulate vaccine efficacy by administration of small molecules such as vitamin B6 might foster the development of safer vaccines required for immunocompromised individuals.

*Address: 30 Biopolis Street, Singapore 138671
Nearest Bus Stop: Buses 91, 92, 95, 74, 191, 196, 198, 200 (walk 5 min)
Nearest MRT Station: Buona Vista CC22/EW21 (walk 5 min)



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