Applied Microbiology Research

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Towards a system understanding of immune responses, personalized vaccination strategies, and pathogen transmission

Hosts and pathogens share complex interactions across scales from molecules to populations. The Applied Microbiology Research group aims to understand these various levels of interactions by the identification of key factors involved using a systems biological approach (Fig. 1). We want to translate our understanding of the complex host-pathogen interactions into clinical applications, such as novel adjuvant development targeting specific signaling pathways or preventive measurements on a population level. As a main model to explore the host-pathogen interaction, we use influenza vaccination and epidemic transmission.

Vaccine response to influenza

Influenza infection is associated with significant morbidity and mortality in immunosuppressed hosts, such as patients after allogeneic stem cell transplantation. Although vaccination is *the* preventive strategy, many vaccinated patients fail to mount a protective humoral immunity. Along with transplant related factors such as time after transplantation, immune reconstitution and graft-versus-host diseases, the genetic background of each patient also plays a crucial role in modulating and building seroprotection against influenza (and every other pathogen).
Currently, we are exploring the impact of genetic polymorphisms (single nucleotide polymorphisms, SNPs) on the interferon signaling pathway to influenza-specific humoral vaccine responses in a multi-center vaccine trial. SNPs in the Interferon (IFN)-lambda pathway may influence the way B-cells encounter vaccine antigens. Alternative variants of IFN-lambda (IFN lambda 1-3) show different binding affinities to the receptor (Fig. 2A). This is mainly dependent on a few amino acid differences at the binding interaction site (Fig. 2B). B-cells show a significant response to members of the IFN-lambda family (IFNL1-3) (Fig. 2C). Influenza vaccine recipients might therefore, based on their genetic background in the Interferon lambda genes show important variability in the vaccine responsiveness. The immunological data is computationally modeled in collaboration with the D-BSSE (ETHZ, Prof. Stelling). This may allow the development of personalized vaccine strategies.
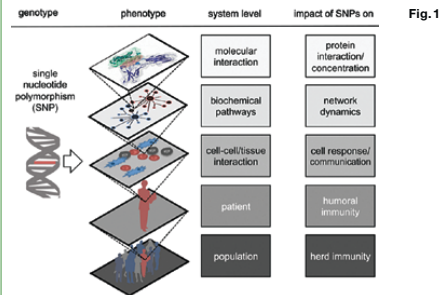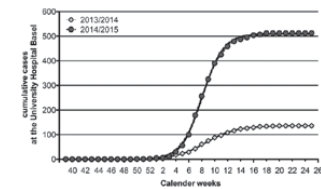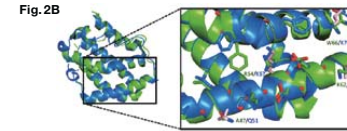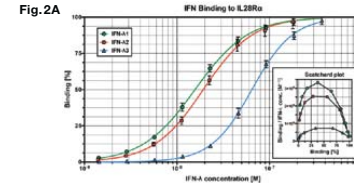

Fig. 1

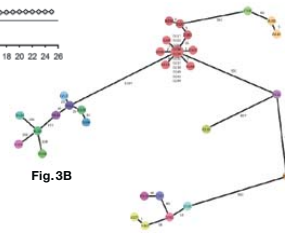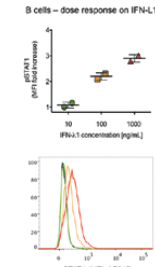### Influenza transmission in an urban population

Influenza transmission is highly complex and dependent on multiple factors such as population density, age distributions, and individual and herd immunity. Although the severity of a flu season can be described with the basic reproduction number (R0, Fig. 3A), which serves as a surrogate for transmission efficacy, it remains unclear where and in what context influenza transmission actually happens. In an interdisciplinary and inter-institutional collaboration with the Human Geography and Center for Primary Health Care (both University of Basel), Infectious Diseases and Hospital Epidemiology and Emergency Medicine (both University Hospital Basel), Pediatric Infectious Diseases and Emergency Medicine (both Children's Hospital University of Basel) and the Computational Evolution Research Group (Department of Biosystems Science and Engineering, ETH Zurich), we aim to explore the influenza transmission in the City of Basel.
Using whole genome sequencing, a technology which has been established for a broad series of pathogens (Fig. 3B), we will determine phylogenetic relationships of influenza samples and transmission pathways. The whole genome data will be used to develop a model to identify where and in what context influenza transmission is most efficient. Besides influenza, such models can be adapted to other infectious diseases. This will provide important information to identify and develop novel preventive counter measurements.

Fig. 2A
Fig. 2C
Fig. 2B

Fig. 3A
Fig. 3B

Selected Publications

Syedbasha M, Linnik J, Santer D, O'Shea D, Barakat K, Joyce M, Khanna N, Tyrrell DL, Houghton M, Egli A. An ELISA Based Binding and Competition Method to Rapidly Determine Ligand-receptor Interactions. J Vis Exp. 2016 Mar 14;(109). doi: 10.3791/53575

Linnik JE, Egli A. Impact of host genetic polymorphisms on vaccine induced antibody response. Hum Vaccin Immunother. 2016 Apr 2;12(4):907–15. doi: 10.1080/21645515.2015.1119345. Epub 2016 Jan 25

Egli A, Santer DM, O'Shea D, Tyrrell DL, Houghton M. The impact of the interferon-lambda family on the innate and adaptive immune response to viral infections. Emerg Microbes Infect. 2014 Jul;3(7):e51. doi: 10.1038/emi.2014.51. Epub 2014 Jul 16. Review

Egli A, Humar A, Widmer LA, Lisboa LF, Santer DM, Mueller T, Stelling J, Baluch A, O'Shea D, Houghton M, Kumar D. Effect of Immunosuppression on T-Helper 2 and B-Cell Responses to Influenza Vaccination. J Infect Dis. 2015 Jul 1;212(1):137–46. doi: 10.1093/infdis/jiv015. Epub 2015 Jan 14

Egli A, Santer DM, O'Shea D, Barakat K, Syedbasha M, Vollmer M, Baluch A, Bhat R, Groenendyk J, Joyce MA, Lisboa LF, Thomas BS, Battegay M, Khanna N, Mueller T, Tyrrell DL, Houghton M, Humar A, Kumar D. IL-28B is a key regulator of B- and T-cell vaccine responses against influenza. PLoS Pathog. 2014 Dec 11;10(12):e1004556. doi: 10.1371/journal.ppat.1004556. eCollection 2014 Dec