Mathematical Statistics
Stockholm University
Master Thesis **2017:12**
http://www.math.su.se

My Adventures with ELISPOT Assays: Design and Analysis of Experiments in Vaccine Development

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December 2017

Abstract

The ELISPOT assay is a method for testing the human immune system's response to infection, and has become an important component in the development of vaccines for pathogens such as HIV and influenza. Testing the efficacy of these vaccines using ELISPOT requires testing hundreds of peptides associated with a pathogen. But performing such large assays is associated with considerable resource costs and time commitments, and becomes very inefficient when one factors in that only a small percentage of these peptides turn out to give positive responses. For this reason, peptides are often pooled and tested together rather than individually. This reduces the resource requirements, but makes it more difficult to distinguish the individual peptides. If a pool gives a positive response, which peptide(s) in that pool generated the response? The need for smart ways of designing these peptide pools is apparent.

In this thesis we present a generalization of the standard method of pooling, motivated by a newly introduced idea ofpeptide overlapẆe then implement the Expectation Maximization algorithm as a tool to directly estimate individual peptide responses among hundreds using only a single ELISPOT microtiter plate. A new criterion for distinguishing a responding pool from inherent background noise is also introduced and compared to current alternatives. These three components come together to provide an accurate and cost-efficient method for designing and analyzing ELISPOT assays. These tools are made available through a free web application, putting them directly into the hands of immunologists using an easy-to-use interface.

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