U.S. FOOD & DRUG ADMINISTRATION

Session 1: In silico methods to assess binding affinity to MHC: Method validation and MHC selection

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FDA Workshop: Non-clinical Immunogenicity Assessment of Generic Peptide Products: Development, Validation, and Sampling
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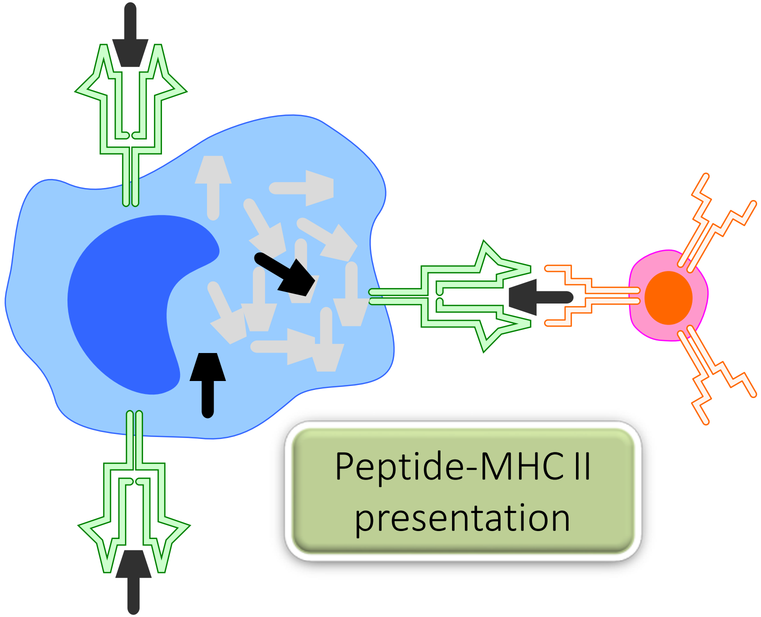
What do we want the in silico tool to do?

The most common in silico tool used are algorithms to predict peptide-MHC II binding affinity



Peptide-MHC II presentation

Should we consider other factors?

- Peptide processing
- Binding stability
- Peptide abundance
- Self-tolerance

How do we choose an in silico method to estimate peptide MHC binding affinities?

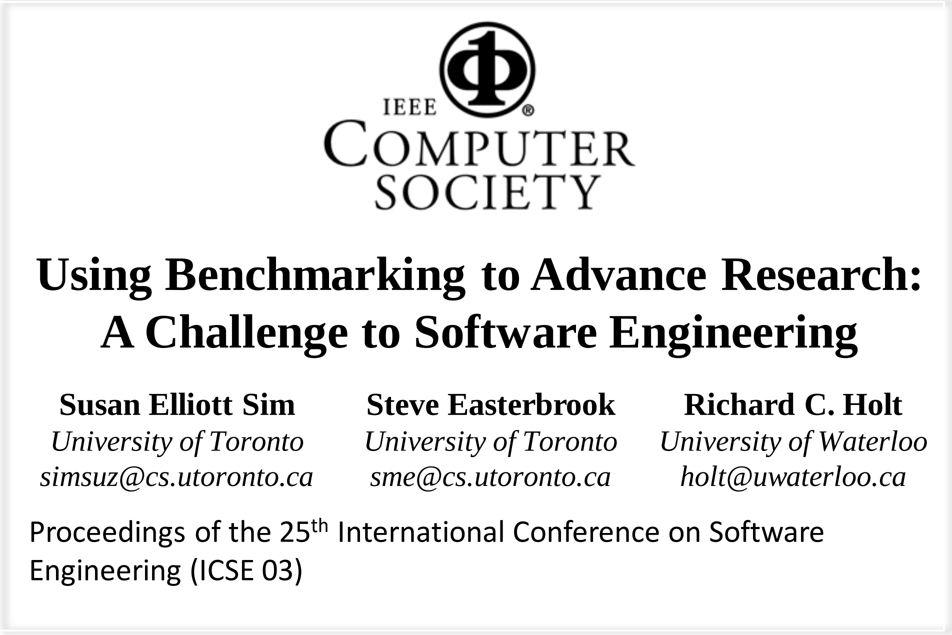
Methods in the public domain vs. commercially available tools

Methods based on sequence motifs and scoring matrices

Methods that use statistical learning algorithms

Methods that are based on structure vs. those base on sequence

In silico methods: Do we need benchmarking?



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Using Benchmarking to Advance Research: A Challenge to Software Engineering

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> "*Creating a benchmark requires a community to examine their understanding of the field, come to an agreement on what are the key problems, and encapsulate this knowledge in an evaluation.*"

Definition: A benchmark is a test or set of tests used to compare the performance of alternative tools or techniques.

Scope: Ideally benchmarking is a community effort. Benchmarks that are created by a single individual/ laboratory tend not to have the same impact on research results.

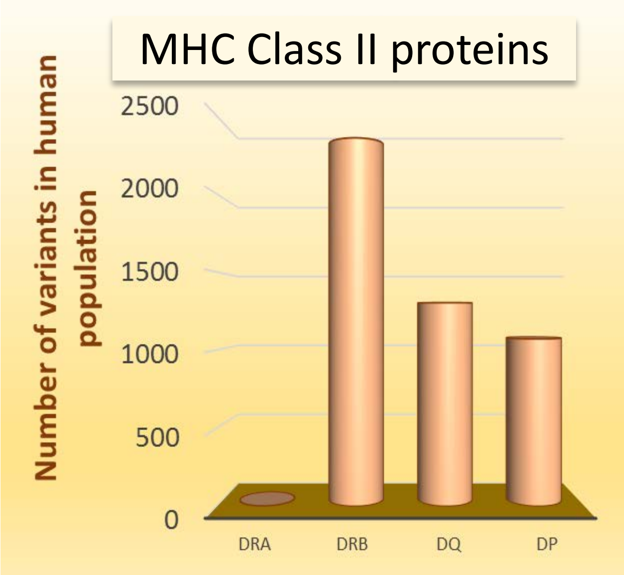
MHC diversity and immunogenicity assessments

The MHC is polygenic: every individual contains several MHC genes

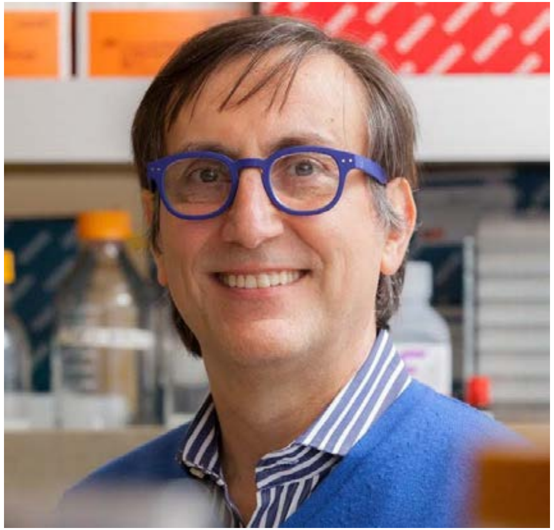
The MHC is polymorphic: The population has variants of each gene

The MHC genes are the most polymorphic genes in the human genome

Each MHC molecule binds different peptides with different affinities



The experts: Alessandro Sette



Dr. Alessandro Sette has made numerous (many of which were pioneering) contributions to enhancing our understanding of the immune response. One however stands out as a preeminent exemplar of scientific citizenship. His leadership in the design and curation of the national Immune Epitope Database (IEDB). This excellent bioinformatics resource is freely available and has been widely used to address some of the most urgent biomedical needs. We seek his insights in helping us address the complex issues raised in this workshop.

The experts: Annie de Groot

Annie De Groot’s extensive contributions in academia and industry are evidenced by over 200 peer reviewed publications and 46 patents. In her role as CEO and CSO of EpiVax she has led the development of *in silico* tools that are the subject of the discussions today. We hope to tap into Dr. de Groot’s intimate knowledge of the development of *in silico* tools for predicting immunogenicity.

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