NIAID Modeling Activities

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DAIT/ NIAID

NIAID - Mission

- The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases.

Modeling Immunity for Biodefense

Initiative: RFP-NIH-NIAID-DAIT-BAA-05-10
Modeling Immunity for Biodefense

Goals:

- Establish highly interactive, multi-disciplinary teams to develop innovative mathematical models of immunity to vaccines/therapeutics or infection with a focus on NIAID Category A, B, C Priority Pathogens.

- Develop “user-friendly: mathematical tools for high (whole organism or system), intermediate (tissue or organ), or fine (single cell) resolution modeling of host immune responses to infection and vaccines/therapeutics against NIAID Category A-C priority pathogens.

Objectives

- Centers conduct basic research for new mathematical model development or the improvement of existing models, accompanied by validation and model refinement through laboratory experimentation.
- Minimally the teams would consist of immunologists, bioinformaticians, and scientists with expertise in mathematical modeling. Additional expertise in statistics, infectious diseases, microbiology, and epidemiology could also be included as dictated by the proposal.

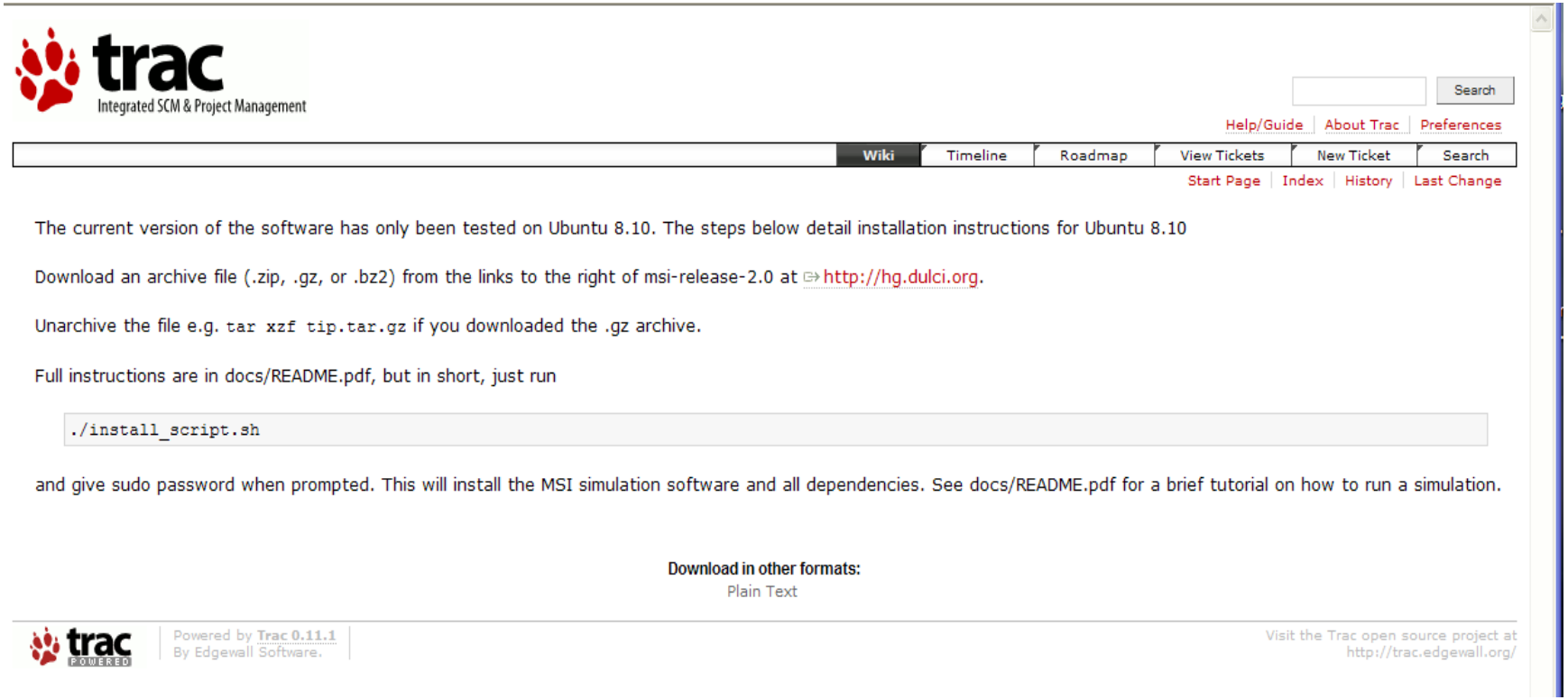
Immune Modeling Centers

- Four (4) contracts were awarded in 2005
- Duke University – DULCI
  - Duke University Laboratory for Computational Immunology
    - https://dulci.org/
- Mount Sinai School of Medicine – PRIME
  - Program for Research on Immune Modeling and Experimentation
    - http://tsb.mssm.edu/primeportal/
- University of Pittsburgh – CMPI
  - Center for Modeling Pulmonary Immunity
    - http://cmpi.cs.pitt.edu/
- University of Rochester – URCBIM
  - University of Rochester Center for Biodefense Immune Modeling
    - https://cbim.urmc.rochester.edu/

Duke University - DULCI

- The main goal of this program is to develop computational tools to aid in the design of vaccine adjuvants. In order to achieve this goal, the contractor is characterizing dendritic cell, B cell, and T cell function in response to various adjuvant/antigen combinations, with a focus on activation of innate immune receptors (TLRs).
- Immune cells will be examined at the site of injection, draining lymph nodes, and spleen at early times points after inoculation with anthrax recombinant Protective Antigen (rPA) mixed with one of three adjuvants (shistosome egg antigen (SEA), Alum, or LPS).
- Developing ODE-based models of the cellular population dynamics of the humoral response to rPA. The model accounts for DC activation as well as migration and has been fit to extensive flow-cytometric data. Developing a user-interface to make this model available to the immunology community.

Duke University - DULCI

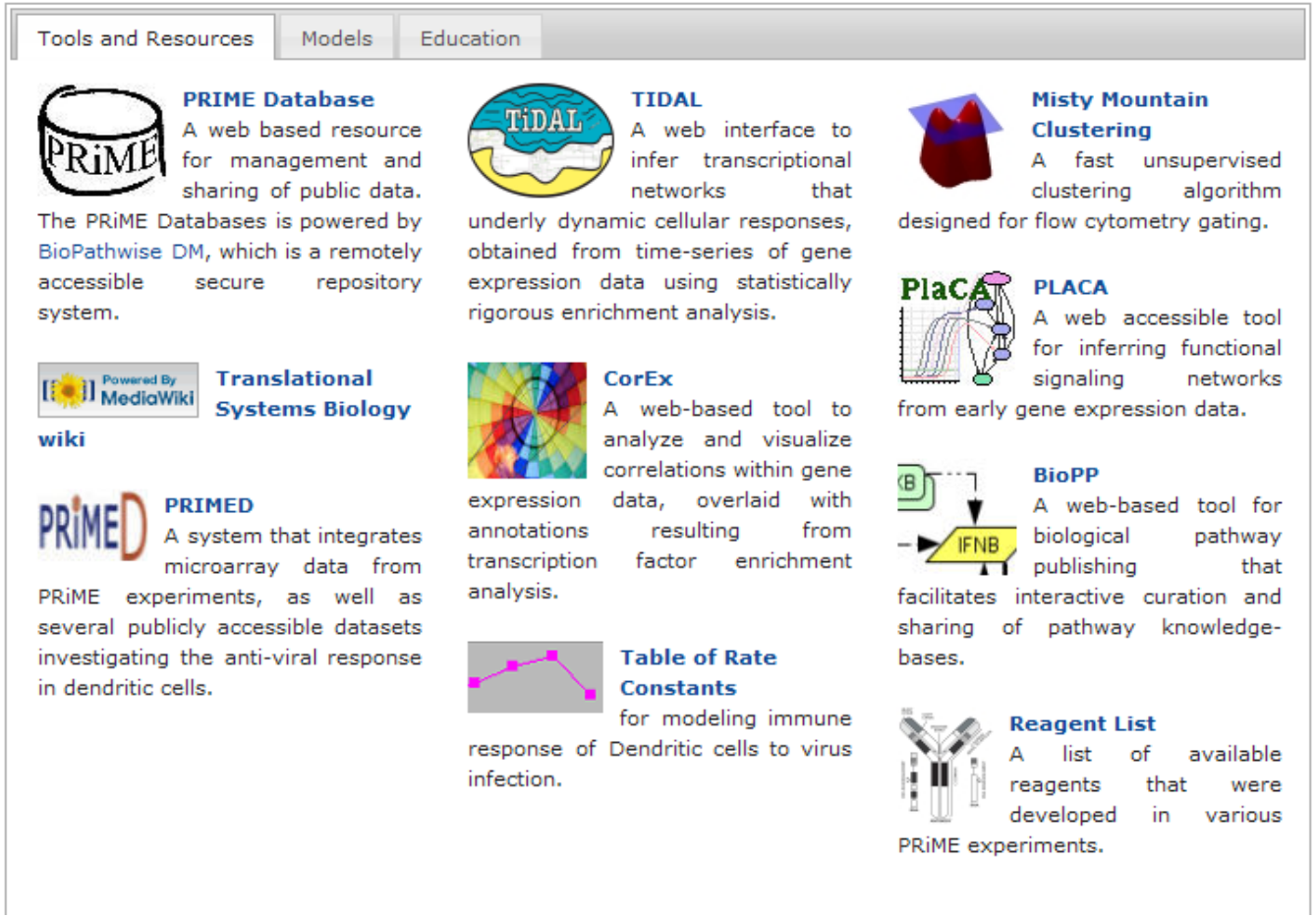


https://galen.dulci.duhs.duke.edu/msi/wiki/Software
http://hg.dulci.org

Mt. Sinai School of Medicine - PRIME

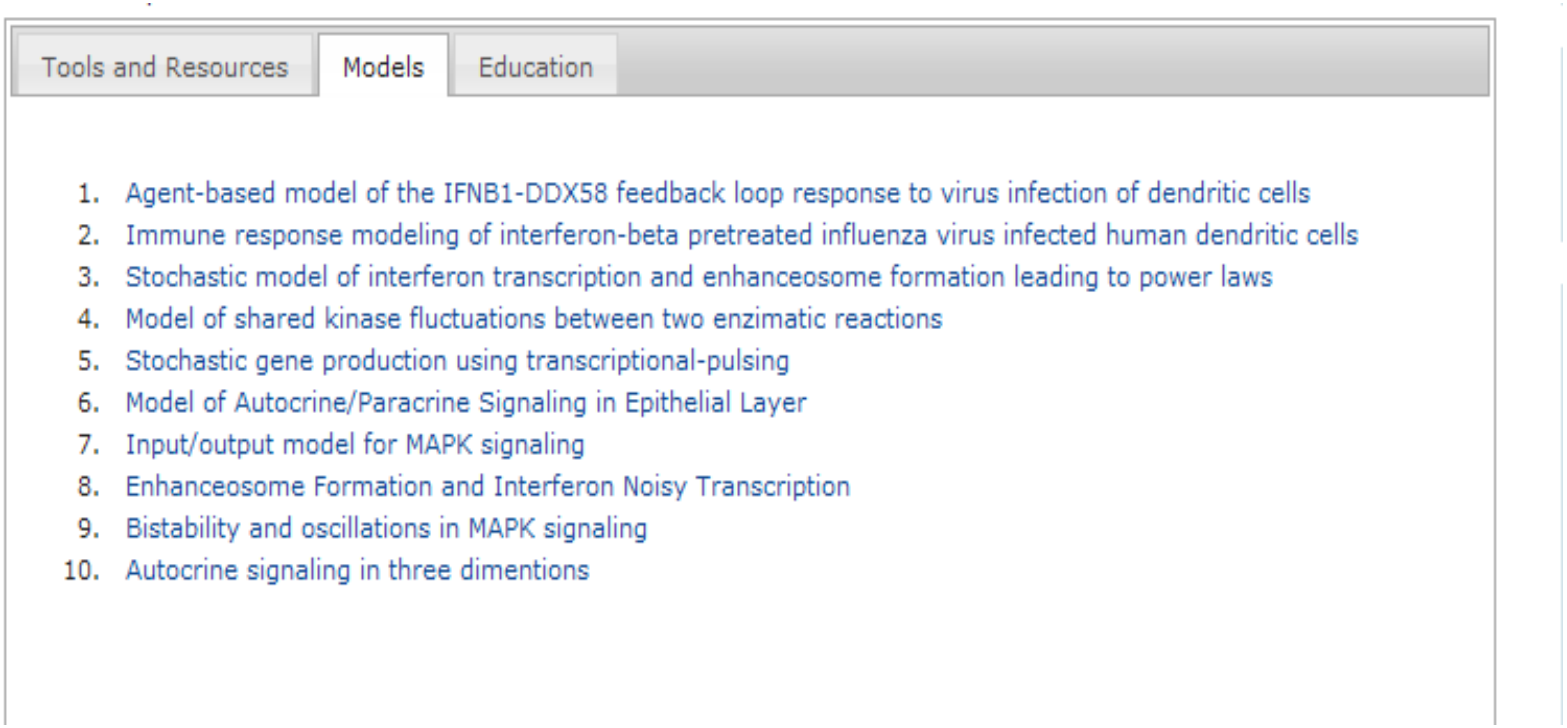
- The goal of this Immune Modeling Center is to develop predictive, experimentally-validated, cellular resolution models of human dendritic cell responses to category A-C viruses. Specific viral components from Influenza (NS1), Ebola (VP35), vaccinia (E3L), and Nipah (P, V, and W proteins), which alter various pathways in the interferon signaling cascade, will be evaluated for their effects on human dendritic cell function and innate immune responses.
- The contractor will attempt to identify the mechanisms of action of viral antagonists, identifying and simulating potential therapeutic strategies to overcome viral antagonism.

Mt. Sinai School of Medicine - PRIME



http://tsb.mssm.edu/primeportal/

Mt. Sinai School of Medicine - PRIME



http://tsb.mssm.edu/primeportal/

University of Pittsburgh - CMPI

- The main goal of this program is to develop and validate mathematical models of pulmonary innate immune responses in mice and non-human primates to three pathogens administered by the inhalation route: Influenza, Mycobacterium tuberculosis, and Francescella tularensis.
- Biological information (e.g., cytokine expression patterns) is used to train and validate the models. The majority of this biological data is obtained through analysis of innate immune responses *ex vivo* and *in vivo* in mouse and non-human primate models.
- Selected studies also will be validated through *ex vivo* analysis of human antigen presenting cell responses to influenza in cells obtained from bronchoaveolar lavage.

University of Pittsburgh - CMPI

Software Tools

by Alexandros Labrinidis — last modified 2009-10-22 12:57

List of software developed by group members:

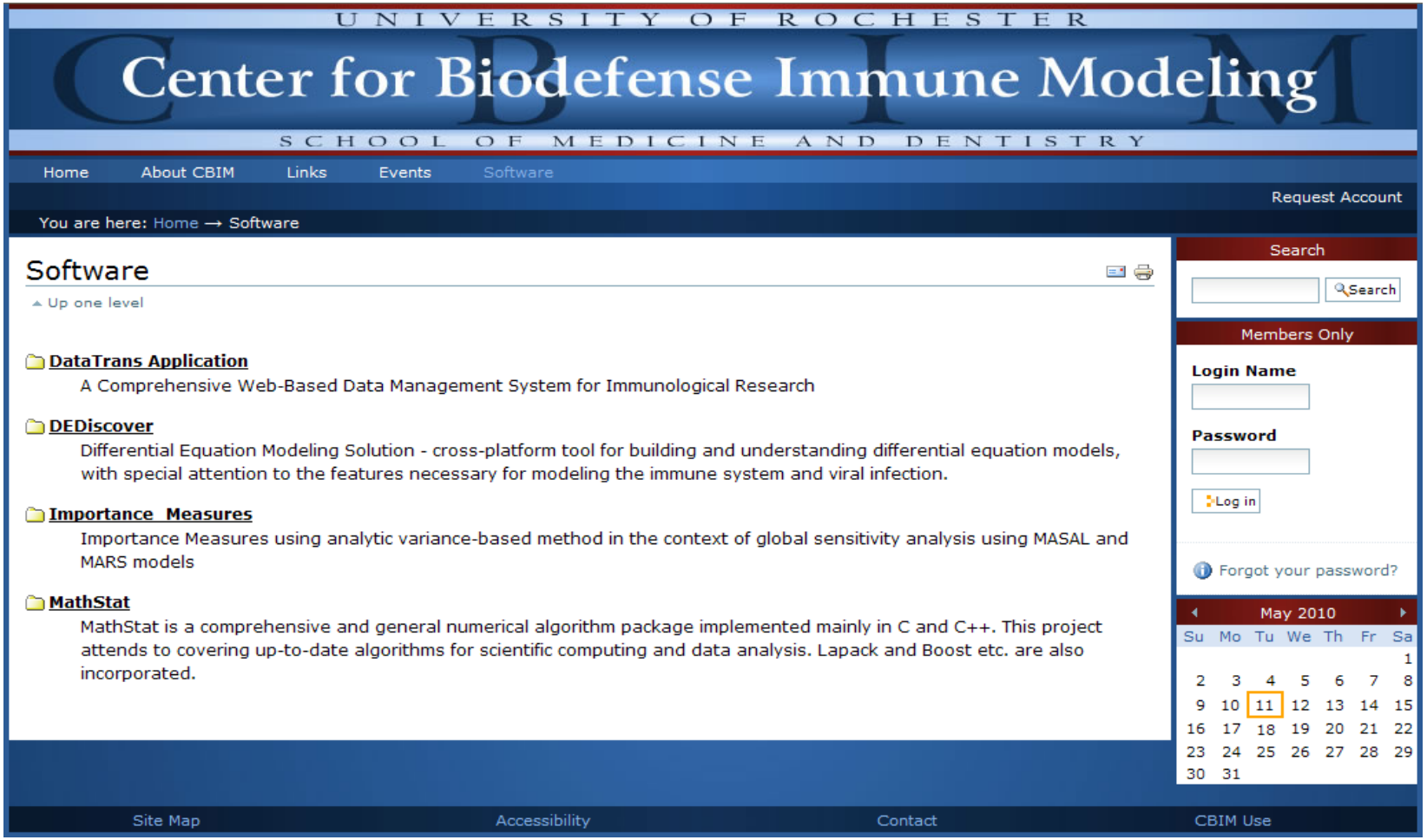
- **Alignment, Similarity, & Database Matching for DNA Motifs (STAMP)**
  - Shaun Mahony and Takis Benos (University of Pittsburgh)
- **Short Time-series Expression Miner (STEM)**
  - Jason Ernst, Ziv Bar-Joseph (Carnegie Mellon University)
- **Analysis of Short Time-series using Rank Order preservation (ASTRO)**
  - Alain B.Tchagang, Thomas McGinnis, David Corcoran, Panayiotis V. Benos (University of Pittsburgh)
- **Energy normalized LOGOs (enoLOGOS)**
  - Workman CT, Yin Y, Corcoran DL, Ideker T, Stormo GD, Benos PV (University of Pittsburgh)
- **Energy normalized LOGOs of the C2H2 protein family (enoLOGOS-C2H2)**
  - Workman CT, Yin Y, Corcoran DL, Ideker T, Stormo GD, Benos PV (University of Pittsburgh)
- **Footer image: finding mammalian transcription factor binding sites using phylogentic footprinting (Footer)**
  - Corcoran David et al. (University of Pittsburgh)

http://cmpi.cs.pitt.edu/software

University of Rochester -URCBIM

- The project objectives are to: develop mathematical/computational models to simulate immune responses to influenza A virus; design and conduct *in vitro*, *ex vivo*, and *in vivo* experiments to identify, measure and validate the immune models; develop statistical methods and user-friendly statistical packages for immunology data analysis, model identifications and predictions; develop a web-based database and software system for modeling and simulating immune responses to influenza A virus.
- Investigate the feasibility to extend and modify influenza mathematical/computational models to vaccinia virus for immune response simulations.

University of Rochester -URCBIM



https://cbim.urmc.rochester.edu/software

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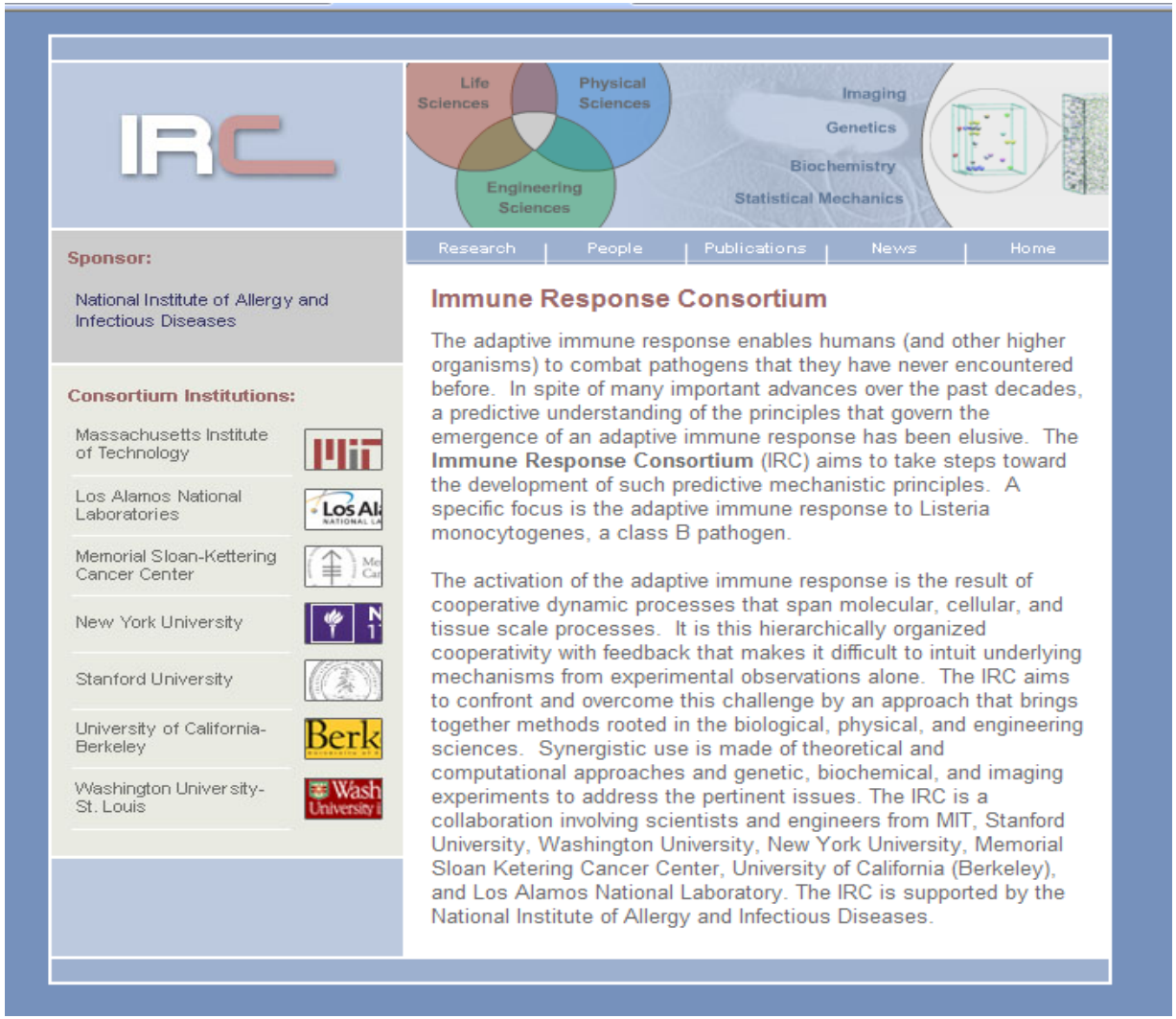
https://cbim.urmc.rochester.edu/software

Other Modeling Projects

- Program Project: **Immune Response Consortium: Integrated *In Silico*, *In Vitro*, and *In Vivo* Studies of the Immune Response to *Listeria Monocytogenes***
  - Principal Investigator: **Arup Chakraborty**
  - Institution: **Massachusetts Institute of Technology**
  - Project period: (06/15/2006 - 05/31/2011)
    - To understand how T cells detect antigen with high sensitivity and how T cell activation is regulated.
    - To develop an integrated, mechanistic understanding of how antigen presentation, T cell receptor (TCR) triggering, intracellular signaling, and migratory patterns of T cells influence the adaptive immune response to a pathogen.
    - Computational studies will be combined with in vitro and in vivo genetic and biochemical experiments to understand the adaptive immune response to *Listeria monocytogenes.* These computational studies could result in predictive algorithms that model the immune response.

Other Modeling Projects



http://web.mit.edu/irc/

Other Modeling Projects

http://web.mit.edu/irc/

Moving Forward

Reissued: BAA-NIAID-DAIT-NIHAI2009074
Modeling Immunity for Biodefense

Results:

- Reviewed in April 2010.
- Awards anticipated July-Aug 2010

Continue to accept and encourage individual and program project grants focused on mathematical and computational modeling of immune response and function.