

CRACK IT

Crack-IT Challenges from an Industry Perspective

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Towards Virtual Laboratories

- Virtual Infectious Disease Research Challenge

“develop a virtual platform that models infection and the host response to pathogen assault for basic research and enhances new target development in infectious diseases”

CRACK IT



National Centre
for the Replacement
Refinement & Reduction
of Animals in Research

Consortium



UNIVERSITY
of York



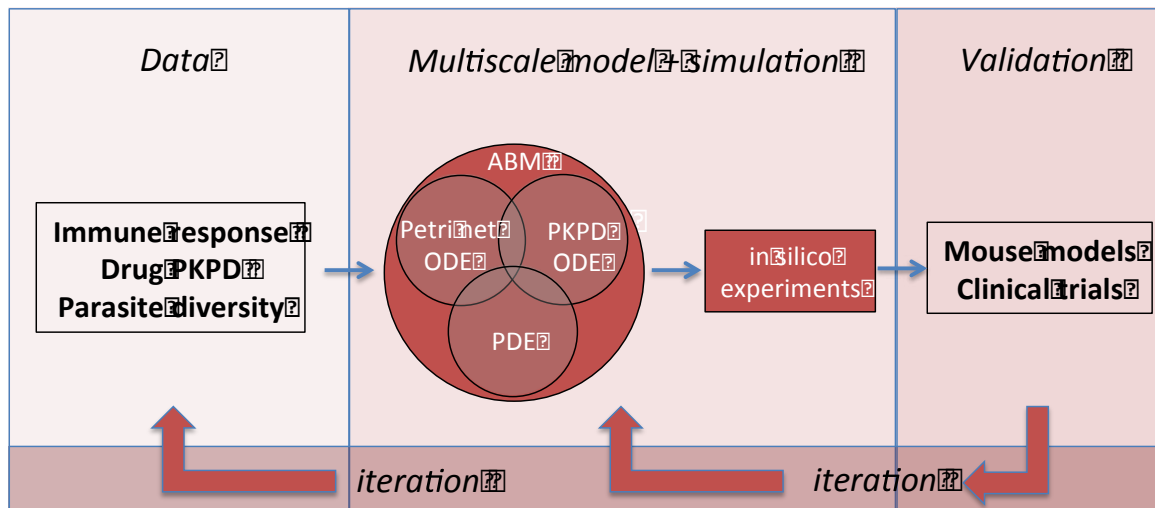
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The Challenge of Leishmaniasis Drug Development



Existing approaches = *30,000 animals at LSHTM / York in 10 years*
~40,000 animals per year globally



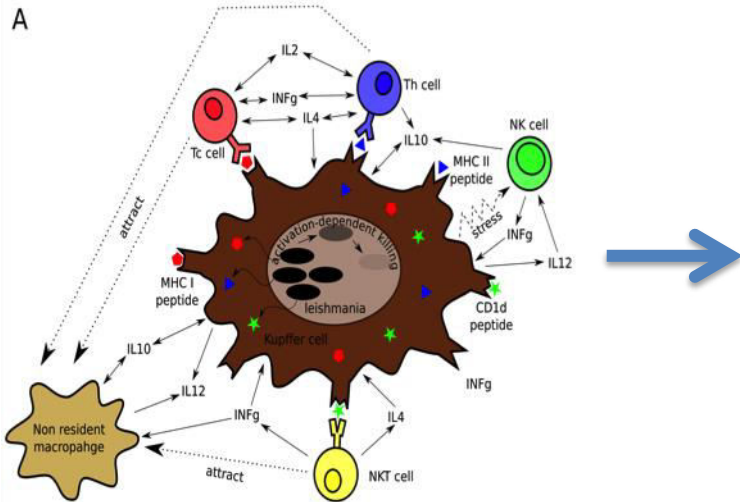
Goal of Virtual Lab

- Allows exploration of the drugable space
- Provides new mechanistic understanding
- Addresses unmet clinical needs
- Has broad application to infectious disease
- Is evidenced and free to use
 - *delivers maximum 3Rs impact*

Models are not the real system: For Immunologists this includes mice (it does not matter how you dress it up)

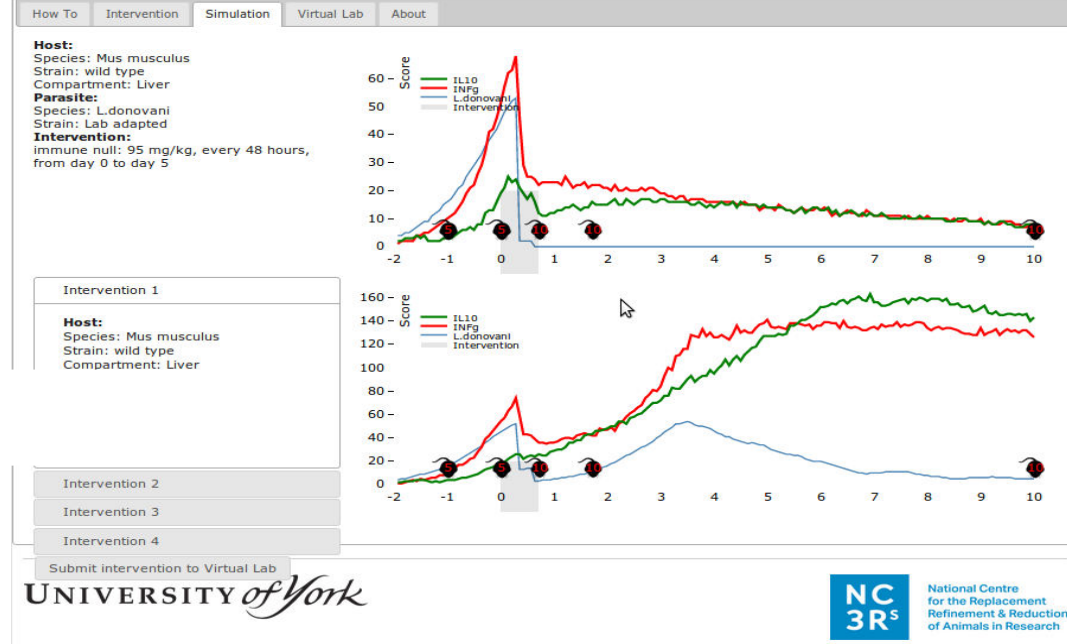


Phase 1: From academic model to prototype R&D tool



LeishSim 1.1

Virtual Lab powered by SimOmics

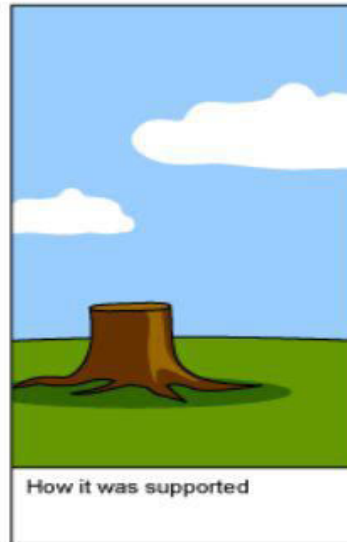
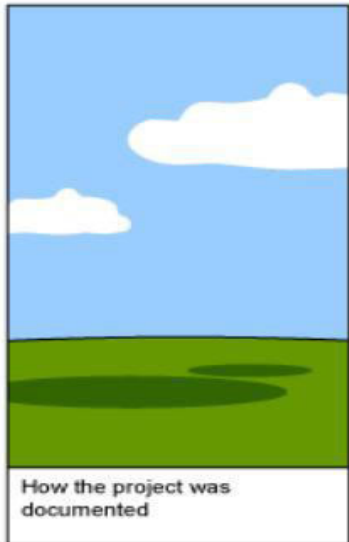
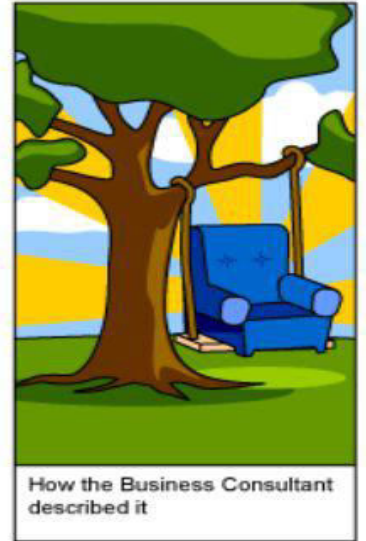


A stochastic Petri net model of anti-leishmanial immunity

Albergante et al *PLoS Comp. Biol* 2013

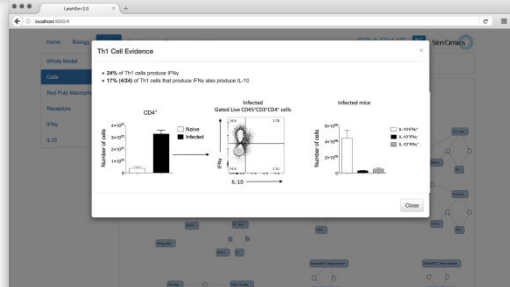
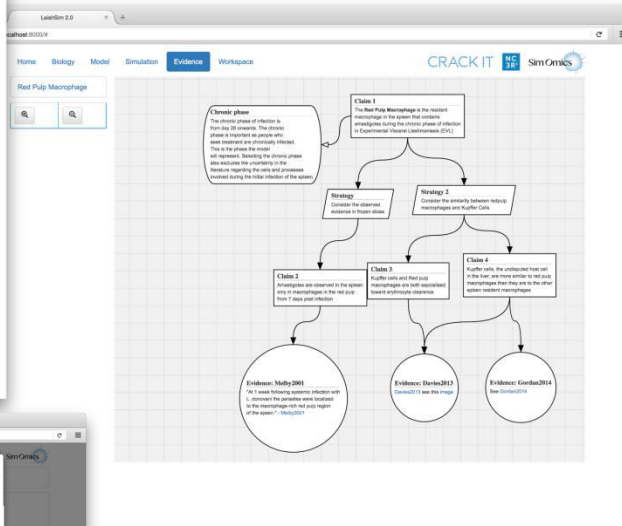
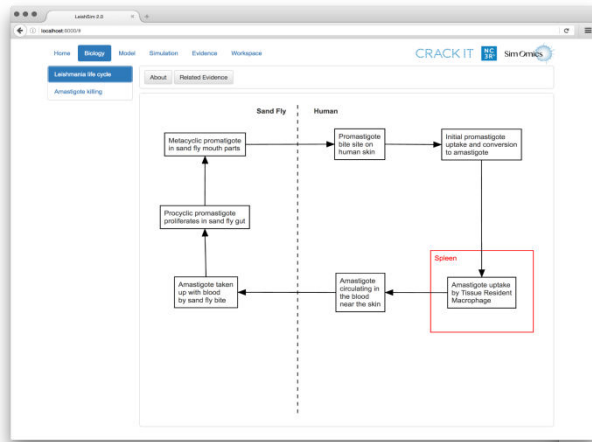
LeishSim v1.1 - The first virtual laboratory for leishmaniasis drug development

Good engineering is important



Version 2: Leishsim Virtual Lab

- Combines **model, simulation, results, analysis, evidencing and arguments** into a single web-based tool



```
#on surface reaction
IFNg around redpulp_macrophage binds IFNg_receptor on redpulp_macrophage modifier IFNg_on <=> IFNg_bound under redpulp_macrophage modifier IFNg_off
IL-4 around redpulp_macrophage binds IL-4_receptor on redpulp_macrophage modifier IL-4_on <=> IL-4_bound under redpulp_macrophage modifier IL-4_off
IL-6 around redpulp_macrophage binds IL-6_receptor on redpulp_macrophage modifier IL-6_on <=> IL-6_bound under redpulp_macrophage modifier IL-6_off
IL-10 around redpulp_macrophage binds IL-10_receptor on redpulp_macrophage modifier IL-10_on <=> IL-10_bound under redpulp_macrophage modifier IL-10_off
IL-1 around redpulp_macrophage binds IL-1_receptor on redpulp_macrophage modifier IL-1_on <=> IL-1_bound under redpulp_macrophage modifier IL-1_off
TNFa around redpulp_macrophage binds TNFa_receptor on redpulp_macrophage modifier TNFa_on <=> TNFa_bound under redpulp_macrophage modifier TNFa_off
LPS around redpulp_macrophage binds LPS_receptor on redpulp_macrophage modifier LPS_on <=> LPS_bound under redpulp_macrophage modifier LPS_off #LPS_
TGFb around redpulp_macrophage binds TGFb_receptor on redpulp_macrophage modifier TGFb_on <=> TGFb_bound under redpulp_macrophage modifier TGFb_off
```

What has Crack-IT enabled?

- Industry and academia to collaborate on a challenging problem
- Driven by 3Rs requirements
- Allowed SME's to develop new technology
- Developed into a series of technology to support 3Rs for wider impact:
 - Virtual Laboratory infrastructure
 - Argumentation diagramming tools
- Successful development of an SME

Summary

- Leishmania is a global problem
- Taking basic academic research into deployable tools for the wider community
- Make use of different modelling approaches
- Academic and SME partnership

Engineering a robust, and useful, virtual laboratory

Acknowledgements

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