

# The Tropical Disease Initiative

*An open source approach to drug development*

[www.tropicaldisease.org](http://www.tropicaldisease.org)

[www.thesynapticleap.org/malaria/](http://www.thesynapticleap.org/malaria/)



**Marc A. Marti-Renom**

<http://salilab.org/~marcius>

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California Institute for Quantitative Biomedical Research  
University of California at San Francisco

not quite a scientific talk ;-)



# Some time back...

**14 Mar 2005**

I think TDI is a unique and very interesting project. I would like so much to make something for it...

**So, where are we going? What's happening? What can we do?**

I still trust in open source drug discovery. :-))

Luca Brivio

**t, if any, the bottlenecks are?**  
g ideas and potential avenues to explore,  
**n Action Plan!**

**9 Mar 2005**

I'm a programmer, not  
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**If someone will tell me when  
begin on, I'd be grateful.**

disease for underserved popu:  
however, confused.  
Regards,  
Jacob Lester

**GNU started with RM**  
**Linux started with Lin**  
Thank you kindly,  
Adam Huber

**You need someone g**  
**people start sending patches...**

I know this is chicken-egg, but someone needs to point this out, since I haven't seen this brought up in the papers or the website.

And you might consider merging into the bios.net effort mentioned already. Together, you just might reach the critical mass for things to take off. Consider this like when people jumped off the HURD project to come together and make linux work.

Daniel Amelang

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Stephen Mark Maurer

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**So, where are we going? What's happening?**

I still trust in open source drug discovery. :-))

Luca Brivio

16 Feb 2005

Hi,

**It would be interesting to know what, if any, the bottlenecks are?**

The Wiki site contains many interesting ideas and potential avenues to explore, but from what I can see it is **lacking an Action Plan!**

Regards,  
Jacob Lester

9 Mar 2005

I'm a programmer, not a biologist. I'd like to do something to keep the disease for underserved populations, however, confused. **If someone will tell me where to begin on, I'd be grateful.**

**GNU started with RM**  
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So, where are we?

I still trust in open source.

Luca Brivio

16 Feb 2005

Hi,

10 Feb 2005

Hello,

My name is Adam Huber and I am a medical student at UNSW in Sydney Australia. I am interested in beginning research focused on tropical and infectious disease for underserved populations (A mission that seemingly matches TDI). I am, however, confused.

**If someone will tell me where to sign up and give me some research topics to begin on, I'd be grateful.**

Thank you kindly,

Adam Huber

9 Mar 2005

I'm a programmer, not a researcher. I'd like to do something to keep the project alive.

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Daniel Amelang

What are the bottlenecks are?

What are the initial avenues to explore,

**It's not so mystic that the**

Stephen Mark Maurer

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**GNU started with RMS. He gave us programming/administration tools to play with.**

**Linux started with Linus. He released an operating system for us to play with.**

**You need someone great in the field to release something for everyone to 'play with'. Then people start sending patches...**

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Daniel Amelang

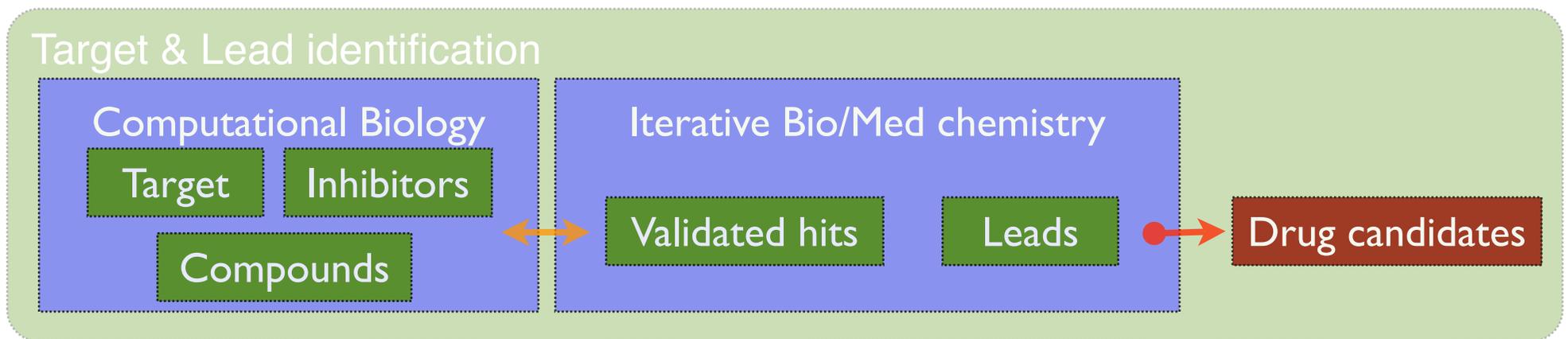
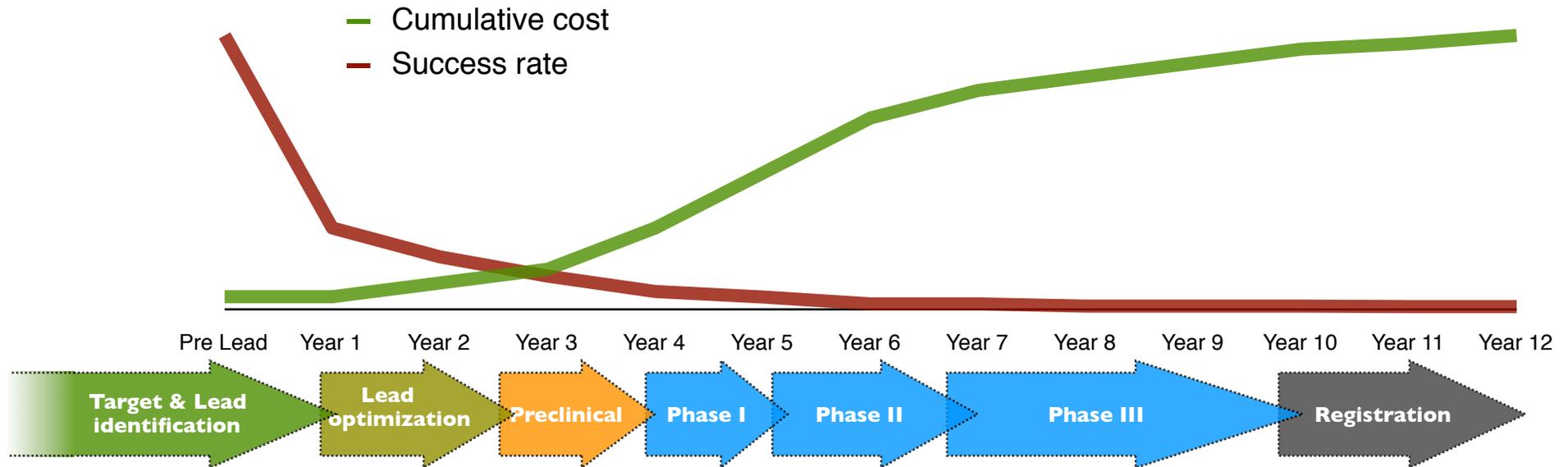
19 Jan 2005

**If we do the science well, I'm optimistic that the rest of TDI will fall into place.**

Stephen Mark Maurer

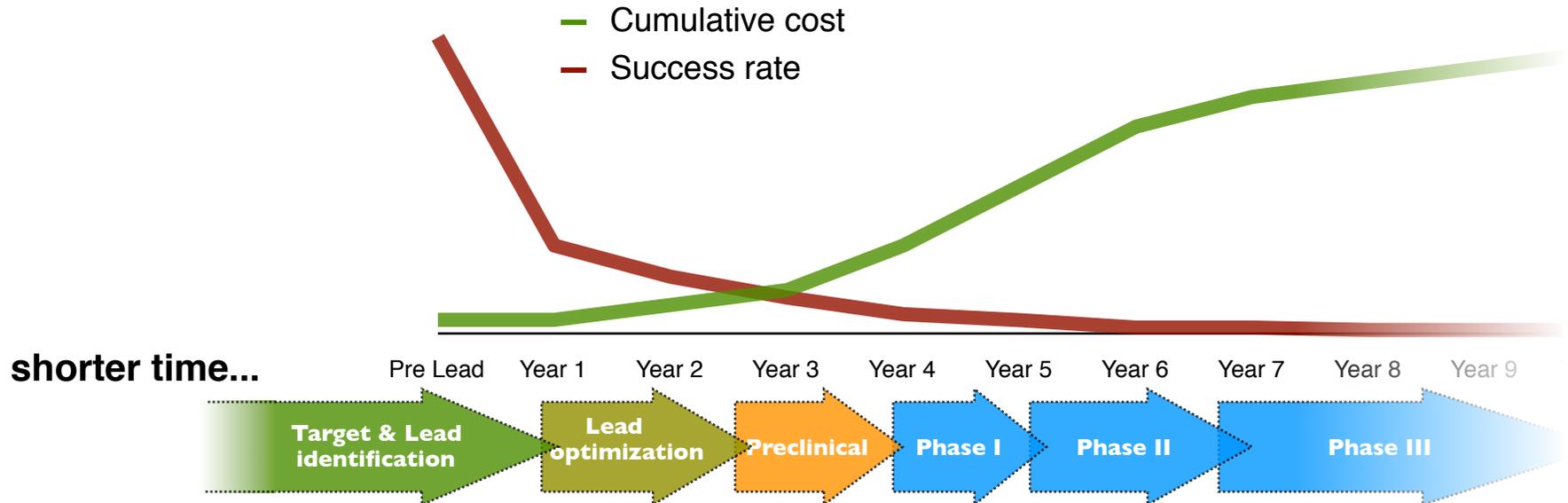
# Action plan @ Tropical Disease Initiative

# Drug Discovery pipeline



Adapted from: - Nwaka & Ridley. (2003) *Nature Reviews. Drug Discovery*. 2:919  
 - Austin, Brady, Insel & collins. (2004) *Science*. 306:1138

# Drug Discovery pipeline



- + Completeness of genome projects (Malaria)
- + New and more complete biological databases
- + New software and computers (cheaper and faster)
- + Internet == more people == less cost

- Computational Biology **alone** is not enough
- TDI needs chemistry and biology! (**How?**)

# TDI projects

PROJECT I

**Gene Cards**

PROJECT II

**Structure Prediction**

PROJECT III

**Target Selection for Structural Genomics**

PROJECT IV

**Gene Annotation**

PROJECT V

**Gene Basket**

# Gene Cards

## collecting gene information



As of September 2005, the Malaria genome had 5,270 ORFs.

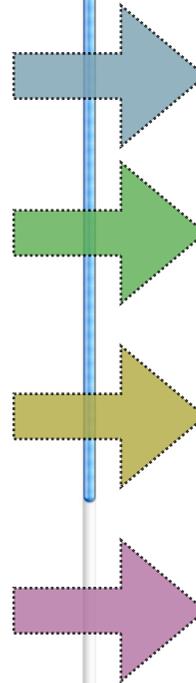
- NCBI at <http://www.ncbi.nlm.nih.gov/>
- BioMart at <http://www.biomart.org/>
- ModBase at <http://www.salilab.org/modbase>

Literature

Annotation

Structure

Function



**Development Site**  
Link to Malaria Site

**User login**  
Username:   
Password:

**Navigation**  

- search
- resource links
- projects
- discussion forums
- create content
- blogs
- news feeds
- CiteULike
- Connotea
- Malaria Journal
- Technorati
- categories

**Who's online**  
There are currently 0 users and 1 guest online.

**Poll**  
Which News Source is Better?  
CiteULike: 50%  
Connotea: 50%  
Let's Use Both: 0%  
Don't Know: 0%  
Total votes: 2  
[login or register to post comments](#) | [older polls](#)

**Home**

**Gene Card**  
**NP\_702320 - serine/threonine kinase-1.**

**Literature**  
There are 1 pubmed entries:  
**Genome sequence of the human malaria parasite *Plasmodium falciparum***  
Gardner, M.J., Hall, N., Fung, E., White, O., Bertman, M., Hyman, R.W., Carlton, J.M., Pain, A., Nelson, K.E., Bowman, S., Paulsen, I.T., James, K., Eisen, J.A., Rutherford, K., Salzberg, S.L., Craig, A., Kyte, S., Chan, M.-S., Nene, V., Shalim, S.J., Suh, B., Peterson, J., Angiuoli, S., Pertea, M., Allen, J., Selengku, J., Haft, D., Mather, M.W., Vaidya, A.B., Martin, D.M.A., Fairlamb, A.H., Fraunholz, M.J., Roos, D.S., Ralph, S.A., McFadden, G.I., Cummings, L.M., Subramanian, G.M., Mungall, C., Venter, J.C., Carucci, D.J., Hoffman, S.L., Newbold, C., Davis, R.W., Fraser, C.M. and Barrell, B. Nature 419 (6906), 498-511 (2002)

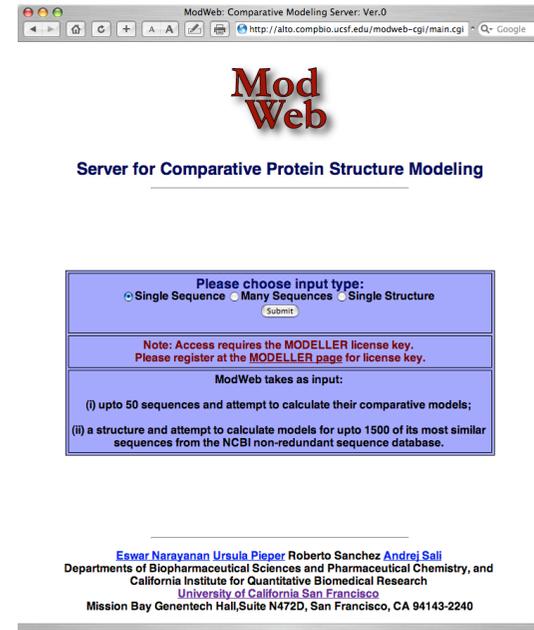
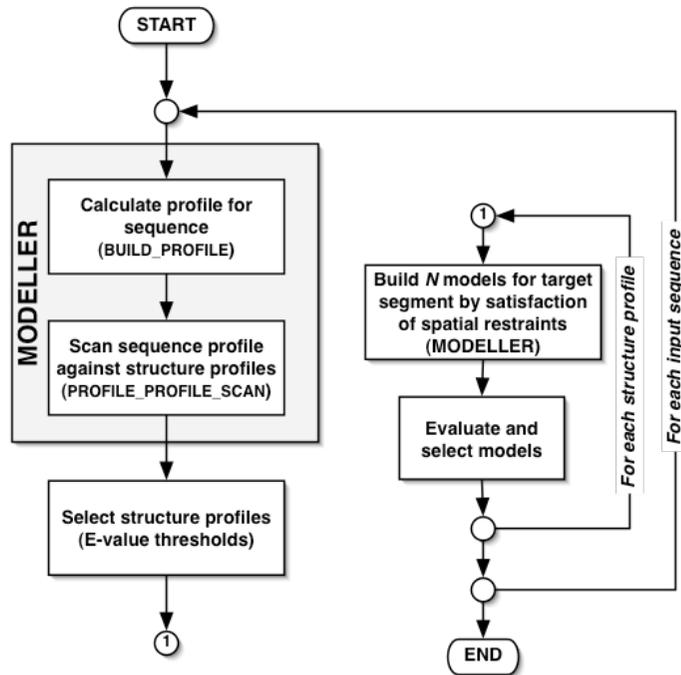
**Annotation**  
There are 8 external links:  
GenPept entry id: 23497502  
GenPept entry id: 23509653  
NCBI protein db entry id: AAN37044.1  
PlasmoDB entry id: chr14\_glm\_487  
PlasmoDB entry id: chr14\_phat\_425  
PlasmoDB entry id: PF14\_0431  
TrEMBL entry id: Q8IL19  
TrEMBL entry id: Q8IL19\_PLAF7

**Structure**  
Sorry, no PDB entries for this target..  
There are 8 models in ModBase for this target:  
Summary for the highest sequence identity model in ModBase  
  
Sequence Identity: 34.00%  
IPSI-Blast e-value: 4e-62  
Model Coverage: 38.3%  
Model Score: 1.00

**Function**  
There are 27 GO terms associated to this target.  
GO Molecular Function terms:  
GO:000166 nucleotide binding  
GO:0003824 catalytic activity  
GO:0004672 protein kinase activity  
GO:0004674 protein serine/threonine kinase activity  
GO:0005488 binding  
GO:0005524 ATP binding  
GO:0016301 kinase activity  
GO:0016740 transferase activity  
GO:0016772 transferase activity, transferring phosphorus-containing groups  
GO:0016773 phosphotransferase activity, alcohol group as acceptor  
GO:0017076 purine nucleotide binding  
GO:0030954 adenylyl nucleotide binding

# Protein Structure Modeling

structure my genes!



<http://www.salilab.org/modweb/>

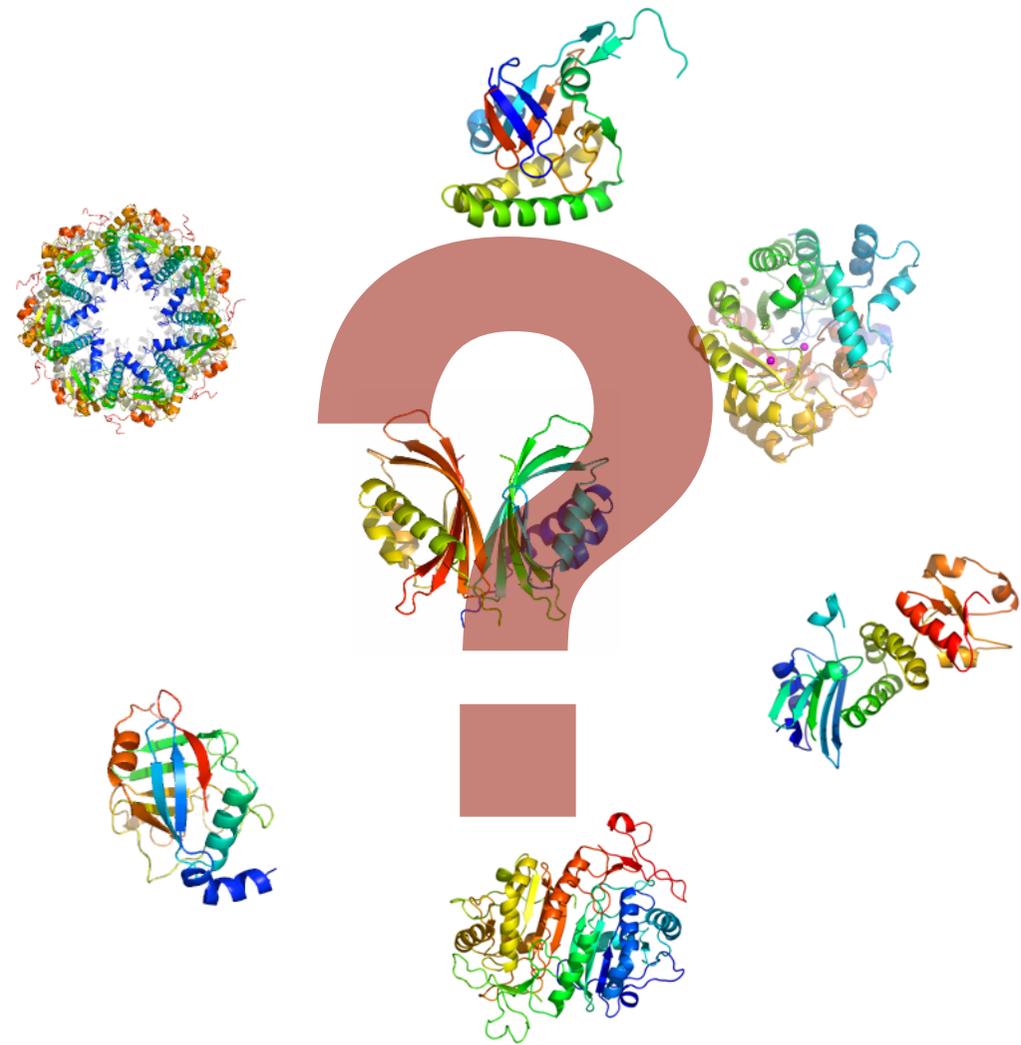
*Eswar et al., (2003) Nucl.Acids.Res. 31(13)*

Sequences	5,270
Modeled sequences	3,321
Models	10,743

# Target Selection for structural genomics

The aim of the project is to generate a list of target proteins, which structure may help the advance of drug discovery for malaria.

We intend to do so by allowing the community of researchers to collectively determine such a priority list.



Dr. Raymond Hui  
University of Toronto and SGC

# Target Annotation

## what do you know about this gene?

The aim of the project is to provide tools to registered users to manually annotate malaria genes.

The screenshot shows a web browser window with the URL [http://dev.thesynapticleap.org/malaria/?q=genecard&target=NP\\_702320](http://dev.thesynapticleap.org/malaria/?q=genecard&target=NP_702320). The page is titled "Gene Card | Development Site" and "Development Site | Link to Malaria Site". It features a user login section, a navigation menu, and a main content area for the gene card. The gene card is for "NP\_702320 - serine/threonine kinase-1" and includes sections for Literature, Annotation, Structure, and Function. A large blue arrow points from the gene card towards the right side of the slide.

**Home**

**Gene Card**

**NP\_702320 - serine/threonine kinase-1.**

**Literature**

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**Genome sequence of the human malaria parasite *Plasmodium falciparum***  
Gardner, M.J., Hall, N., Fung, E., White, O., Berriman, M., Hyman, R.W., Carlton, J.M., Pain, A., Nelson, K.E., Bowman, S., Paulsen, J.T., James, K., Eisen, J.A., Rutherford, K., Salzberg, S.L., Craig, A., Kyes, S., Chan, M.-S., Nene, V., Shallom, S.J., Suh, B., Peterson, J., Angiuoli, S., Perera, M., Allen, J., Selengut, J., Haft, D., Mather, M.W., Veidya, A.B., Martin, D.M.A., Fairlamb, A.H., Fraunholz, M.J., Roos, D.S., Ralph, S.A., McFadden, G.I., Cummings, L.M., Subramanian, G.M., Mangill, C., Venter, J.C., Carucci, D.J., Hoffman, S.L., Newbold, C., Davis, R.W., Fraser, C.M. and Barrell, B. Nature 419 (6906), 498-511 (2002)

**Annotation**

There are 8 external links:

GenPept entry id: 23497502  
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PlasmoDB entry id: PF14\_0431  
TrEMBL entry id: Q8IL19  
TrEMBL entry id: Q8IL19\_PLAF7

**Structure**

Sorry, no PDB entries for this target...

There are 8 models in ModBase for this target:

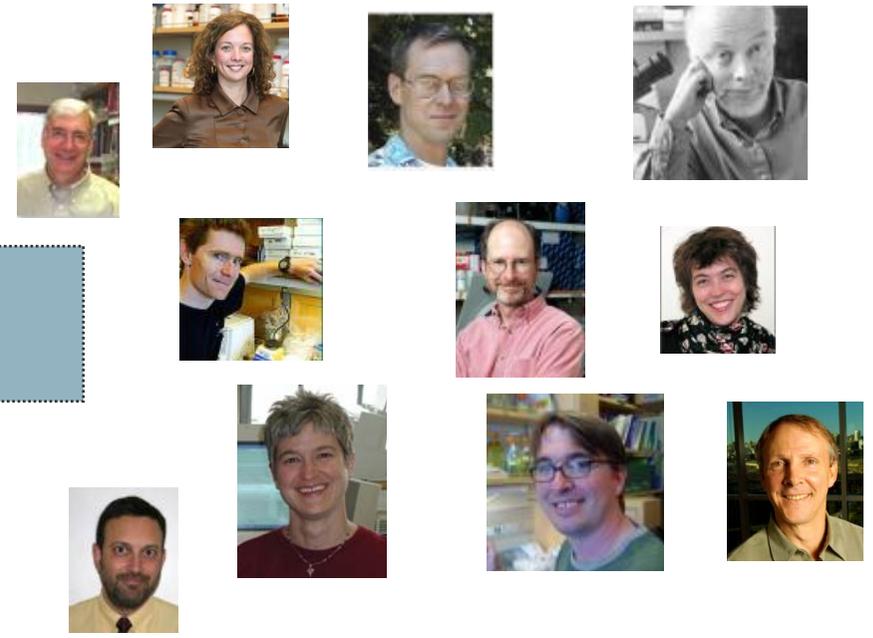
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**Function**

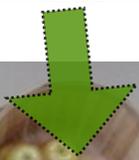
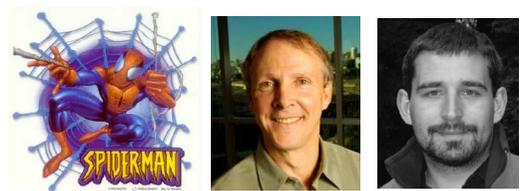
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GO:0005488 binding  
GO:0005524 ATP binding  
GO:0016301 kinase activity  
GO:0016740 transferase activity  
GO:0016772 transferase activity, transferring phosphorus-containing groups  
GO:0016773 phosphotransferase activity, alcohol group as acceptor  
GO:0017076 purine nucleotide binding  
GO:0030554 adenyly nucleotide binding



# Gene Basket

add content to your genes... add genes to your content



TSL registered users will be able to save *gene cards* in their baskets and associate pieces of information to entries in the basket.

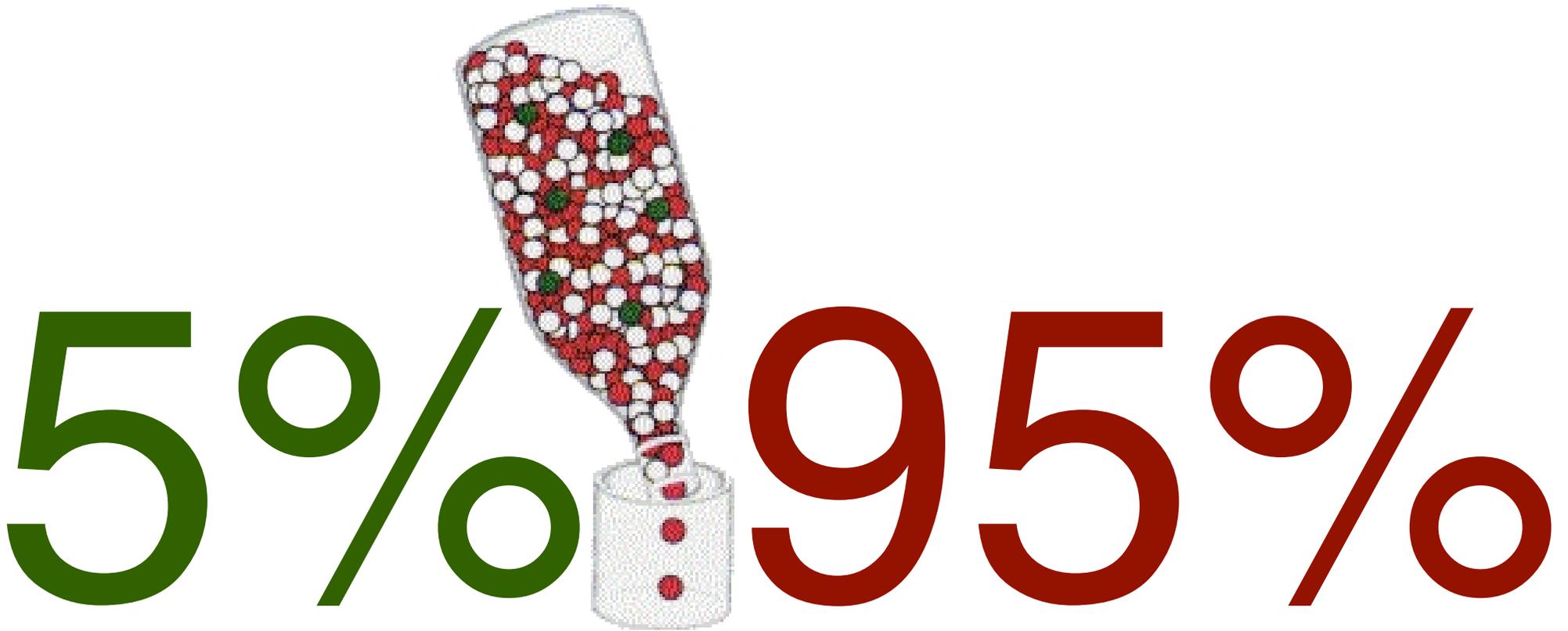
For example, a user may be browsing the literature at PubMed and find an interesting article, with just one click the system should be able to propose and association between the article and any of the genes in his/her basket.

As seen on: **YAHOO!** flickr<sup>BETA</sup>



**YOURS!**  
send us suggestions

[tdi@tropicaldisease.org](mailto:tdi@tropicaldisease.org)



# What is in it for the 95%?

**you**

- to be a part of **innovative** new approaches for research - "**the power of us**"
- to connect, work with other scientists interested in the same disease - **worldwide...**
- to access to **new** research tools
- **free** collaborative site

# Acknowledgments

## Read more @

- PLoS Medicine, Dec. 2004. Vol 1(3) e56
- The Economist (June 10, 2004)

**“At its best, academia is a market of ideas. But many scientists are reluctant to embrace the latest web tools that would allow them to communicate their ideas in new ways.”**

Declan Butler (Nature, vol 438, p548)

**“Put a description of your paper on a weblog, and something very different happens. People who are very far afield from your usual circle start thinking about the subject . They bring up interesting perspectives. ”**

Paul Meyers (Nature, vol 438, p549)

<http://www.tropicaldisease.org/>

## The Sali Lab

Andrej Sali  
Eswar Narayanan  
Ursula Pieper

## Tropical Disease Initiative

Stephen Maurer  
Arti Rai  
Andrej Sali  
Thomas Kepler

## The Synaptic Leap

Ginger Taylor  
Randy Akl  
Chris Heller  
Rich Manalang  
Ken Pugsley

## Wiki site at NPG

Timo Hannay  
Declan Butler