



Collaborative Virtual Organisation & Infrastructure for Anti-Malarial Drug Design

Barry Hardy PhD

Director of Communities & Research Activities

Douglas Connect, Switzerland

BioIT World Conference & Expo, Boston, USA

12-14 April 2011

Community of Practice starting point



We started with community development interactions, both virtual and face-to-face...

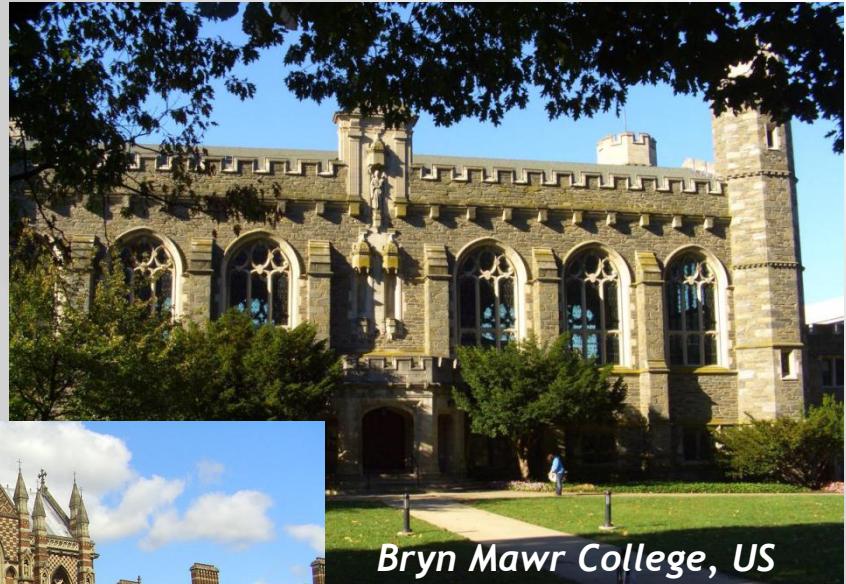


Knowledge Cafe Discussions

Community of Practice starting point



...and continued by holding
workshops and InterAction Meetings
in US and Europe



Bryn Mawr College, US



Oxford University, UK

Community of Practice starting point



Community of Practice for
Drug Discovery & Development

**Interactive pragmatic workshops
with leading experts and industry
practitioners...**

- ▶ Protein Target & Ligand Modelling
- ▶ Virtual Screening & Docking
- ▶ Structure-based Drug Design
- ▶ Pharmacophore Models
- ▶ Focused Library Design
- ▶ ADME, QSAR & Predictive Toxicology

Latest Advances in Drug Discovery & Planning Methods

Advanced Training Workshop

Oxford University, June 25-29, 2007



**Study problems in detail using leading-edge
Software & Databases**

Community of Practice starting point

Community and workshop interactions created a valuable environment and network from which to build collaborations



Caprivi Delta, Namibia

While on a start-up conservation field trip in a remote region of Namibia, we visited many local villages -- meet your 'future patients' for malaria treatment.

Malaria is a common infection in this region which has many wetlands and a strong wet season.



Caprivi Delta, Namibia

Families and village communities form a critical part of the social fabric in this region.

Unfortunately a high HIV infection rate is having devastating impact on such communities.

Infections go untreated and many children lose their parents.



Caprivi Delta, Namibia

Educational context:
visiting a local school

Education requires healthy families and children



Caprivi Delta, Namibia

The next
generation of a
community...
who grow up
with malaria
and little
medical care



Caprivi Delta, Namibia

A family we interviewed with proudly showed us their material possessions.

The current cost of our anti-malarials for just two weeks would exceed their entire annual income.



Health, Conservation and Sustainable Development

We can work on biodiversity conservation (rhino rescue work shown).

But we need a healthy, educated community involvement for it to be sustainable.

Criminal groups exploit these communities and region for poaching.



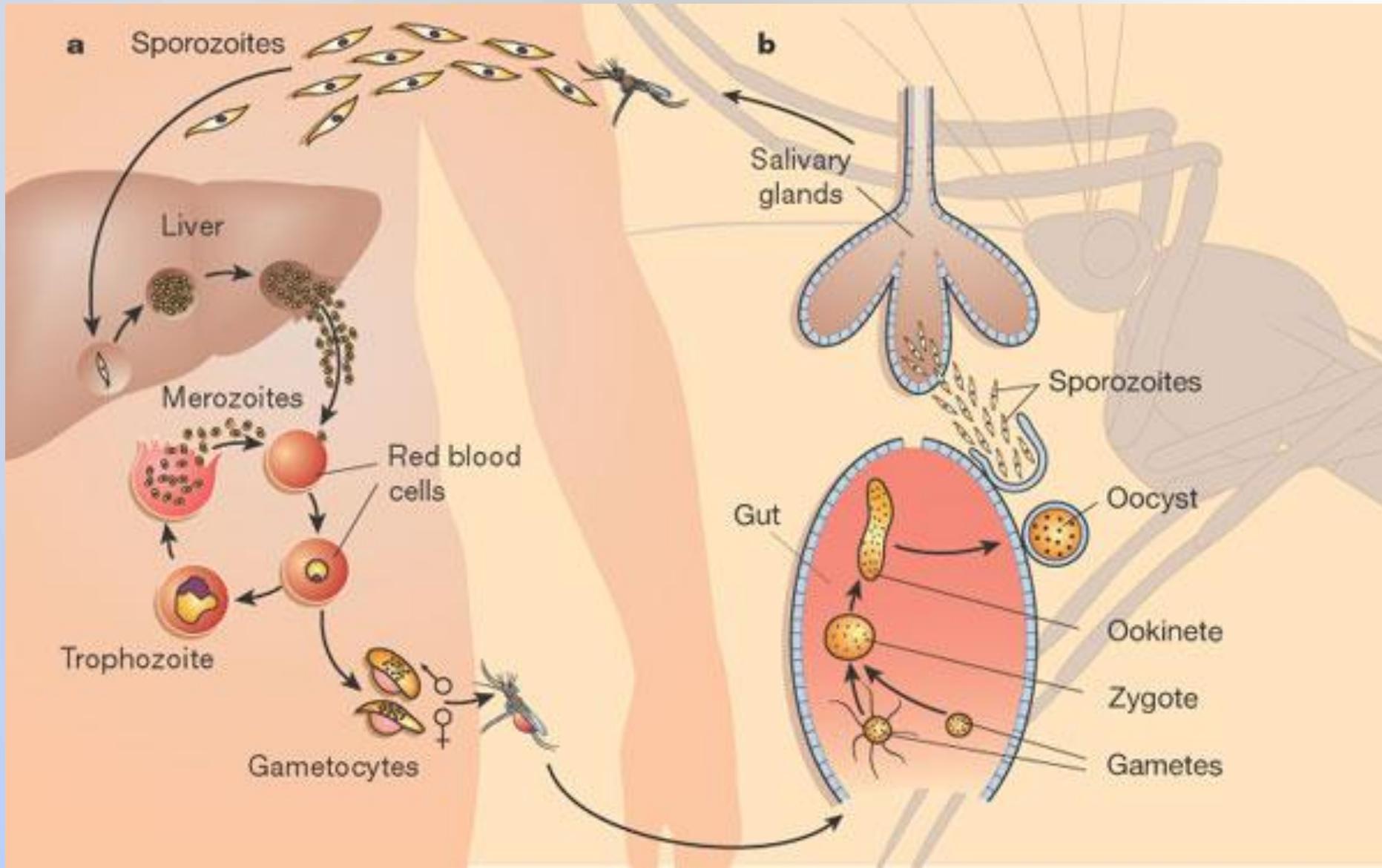
Health, Conservation and Sustainable Development

A breeding and
reintroduction
project fleeing the
chaos in
Zimbabwe.

And another
neglected disease:
Bovine TB, is
threatening lions'
genetic strength and
survival (e.g., prides
in Southern Kruger
Park).

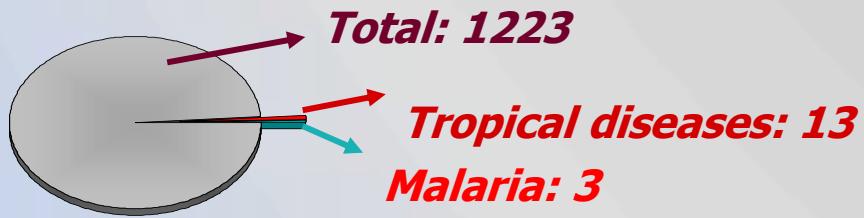


The (complicated) Plasmodium Life Cycle



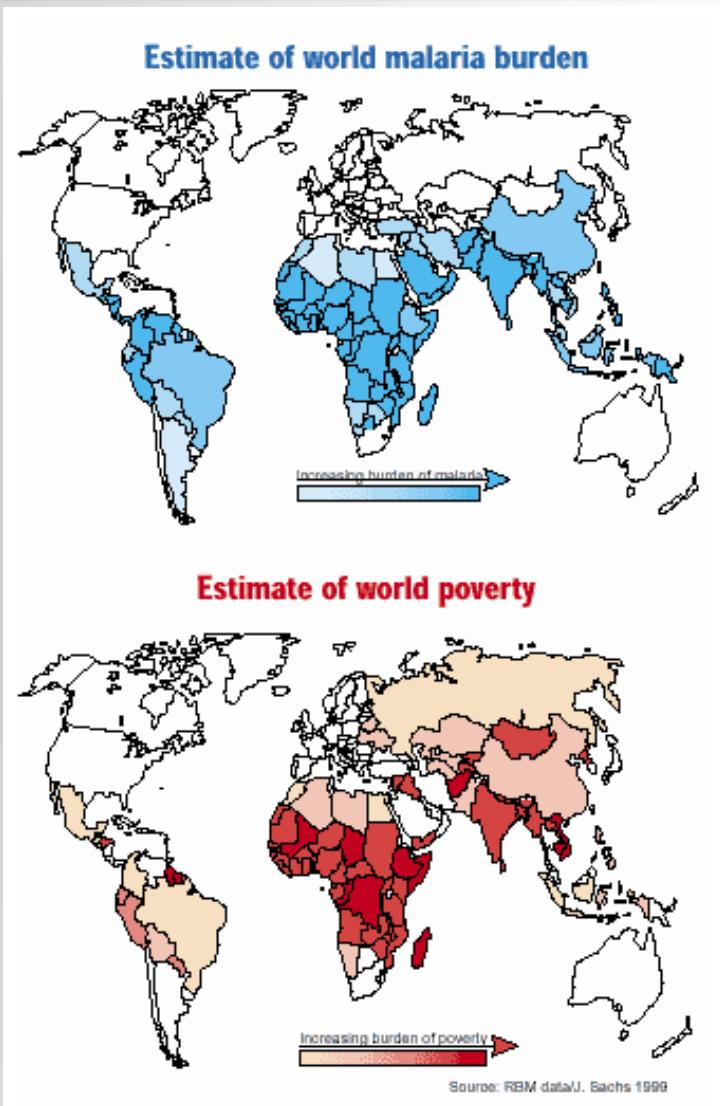
Malaria Treatment: Lack of Investment

- 2.5 billion people at risk
- 500 M cases yearly
- 1-3 M deaths yearly
- Many child fatalities
- Brain Damage, Impaired Development
- Few drugs, no vaccine
- Impact on Education, Community, Income, Conservation, Sustainability

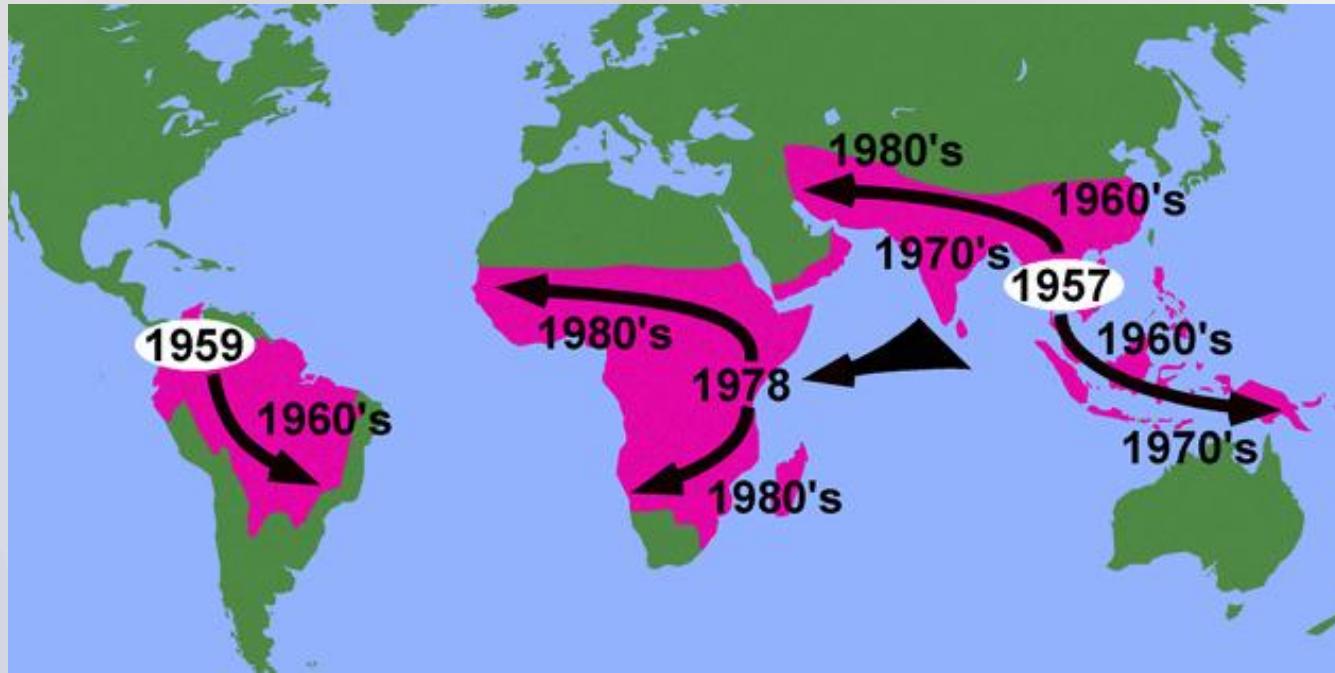


*Drug development outcome,
last quarter of the XXth century*

Greenwood & Mutabingwa, Nature 415:670-672



Drug Resistance is a challenge



Emergence and spread of chloroquine resistance

Malaria, Death, Children

malaria death children

Search SafeSearch moderate ▾

About 821,000 results (0.16 seconds)

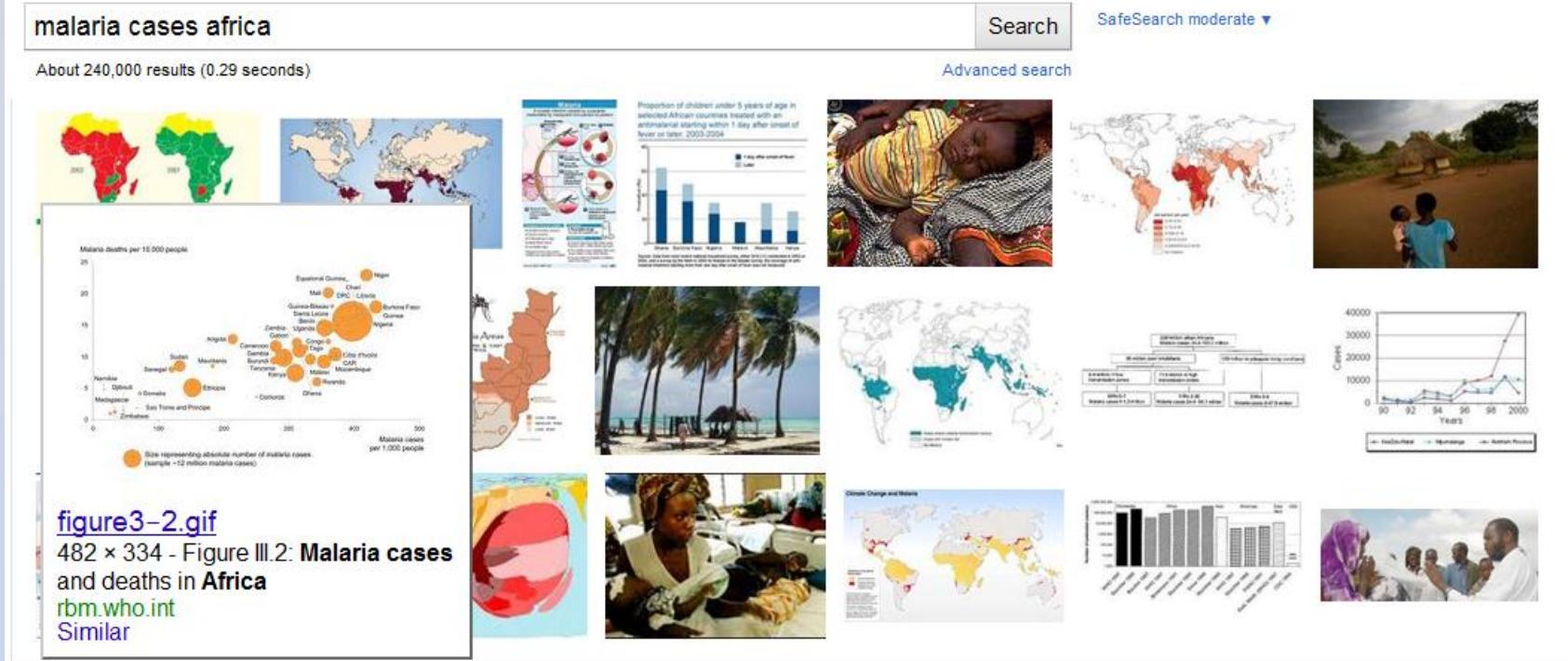
Advanced search

The search results page displays a grid of images and a central chart. The images include: a child in a hospital bed; a child lying down; a close-up of a child's face with a text overlay stating 'Globally, malaria kills more than one million people each year.'; a woman working at a loom; a woman holding a child; a world map with a red ribbon and the word 'MALARIA'; a pie chart showing causes of death in children under 5; a group of children standing together; a close-up of a mosquito; a child looking directly at the camera; a group of children sitting together; a child sitting on the ground; a close-up of hands; and two children sleeping in beds.

pic094.gif
510 × 331 - Children less than 5 years of age have a higher mortality rate from conflict.lshtm.ac.uk

[Similar](#)

Malaria, Cases, Africa



Pharmaceutical, News

pharmaceutical news

Search SafeSearch moderate ▾

About 17,800,000 results (0.25 seconds)

Advanced search

INDIAN PHARMA INDUSTRY NEWS

OUNTERTHINK
IF BIG PHARMA TOOK OVER THE CHURCH

FORGIVE ME FATHER FOR I HAVE SINNED.

WE HAVE A DRUG FOR THAT!

CONCEPT-MIKE ADAMS, ART-DAN BERGERE www.burnettnews.com

[pharma-news.jpg](#)
600 × 628 - **Pharma News**:
No news is good news
thegoutkiller.com
Similar – More sizes

Pharmaceutical, Drug

pharmaceutical drug

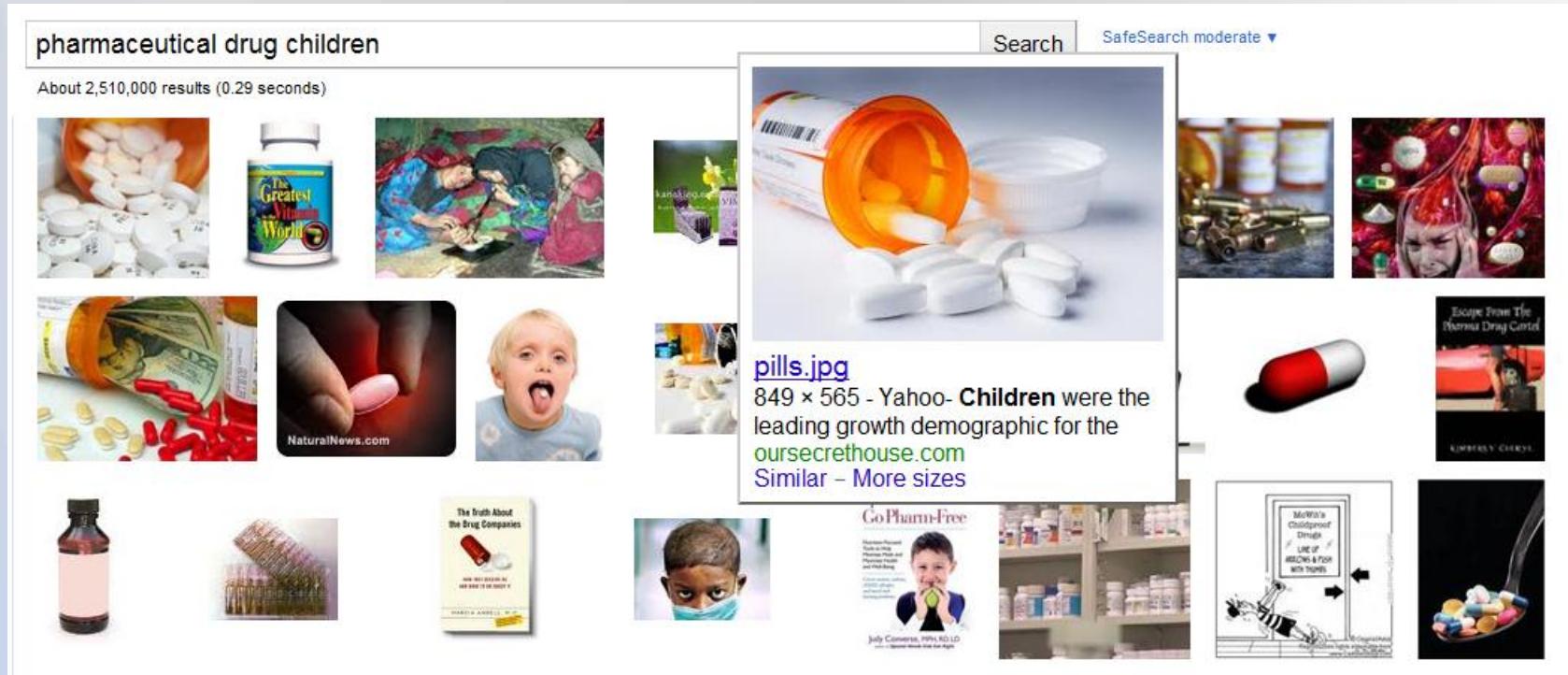
Search SafeSearch moderate ▾

About 8,010,000 results (0.29 seconds)

Advanced search

[pillwave.jpg](#)
396 × 386 - Pharmaceutical
Research ...
institute-shot.com
Similar – More sizes

Pharmaceutical, Drug, Children



Scientists, Collaboration, Malaria

scientists collaboration malaria

Search SafeSearch moderate ▾

About 87,000 results (0.05 seconds)

Advanced search

4. OpenTox computes toxicity predictions

EUN

Synergy

OpenTox

Molecular Initiative on Malaria

SAM

UGA

CDC

Microsoft-tycoon-Bill-Gates

610 x 472 - ... to Liverpool

scientists researching against luxury.cm

Similar

Scientists, Collaboration, Malaria

scientists collaboration malaria

About 87,000 results (0.05 seconds)

Search SafeSearch moderate ▾ Advanced search

4. OpenTox computes toxicity predictions
ELISA Synergy OpenTox
Multilateral Initiative on Malaria
OpenTox

SAM Scientists Against Malaria

6a00d8342054ce53ef014e5fb863ad970c-800wi
800 × 174 - Scientists Against Malaria - our first step to creating a Collaborative ...
barryhardy.blogs.com
Similar

Barriers to research in the Malaria Institute for Tropical Diseases (MITD) in Singapore. (Source: Malaria Institute for Tropical Diseases)



Drug, Design, Malaria

Drug Design, Informatics, Malaria

Malaria, Vaccine

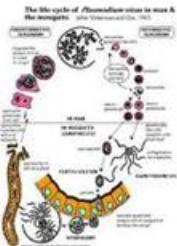
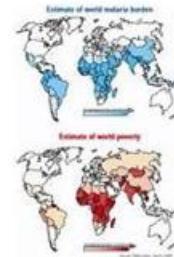
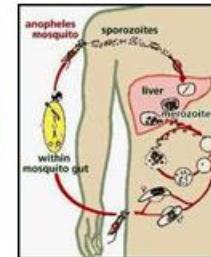
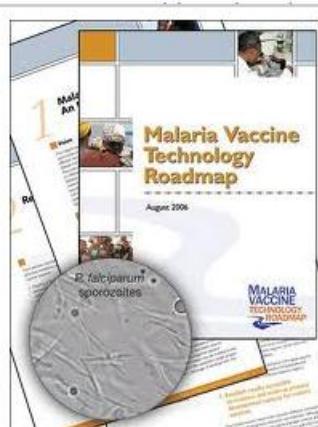
malaria vaccine

Search

SafeSearch moderate ▾

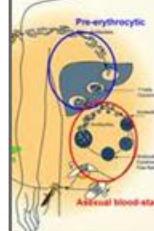
About 77,400 results (0.05 seconds)

Related searches: [malaria life cycle](#) [malaria mosquito](#) [malaria map](#)

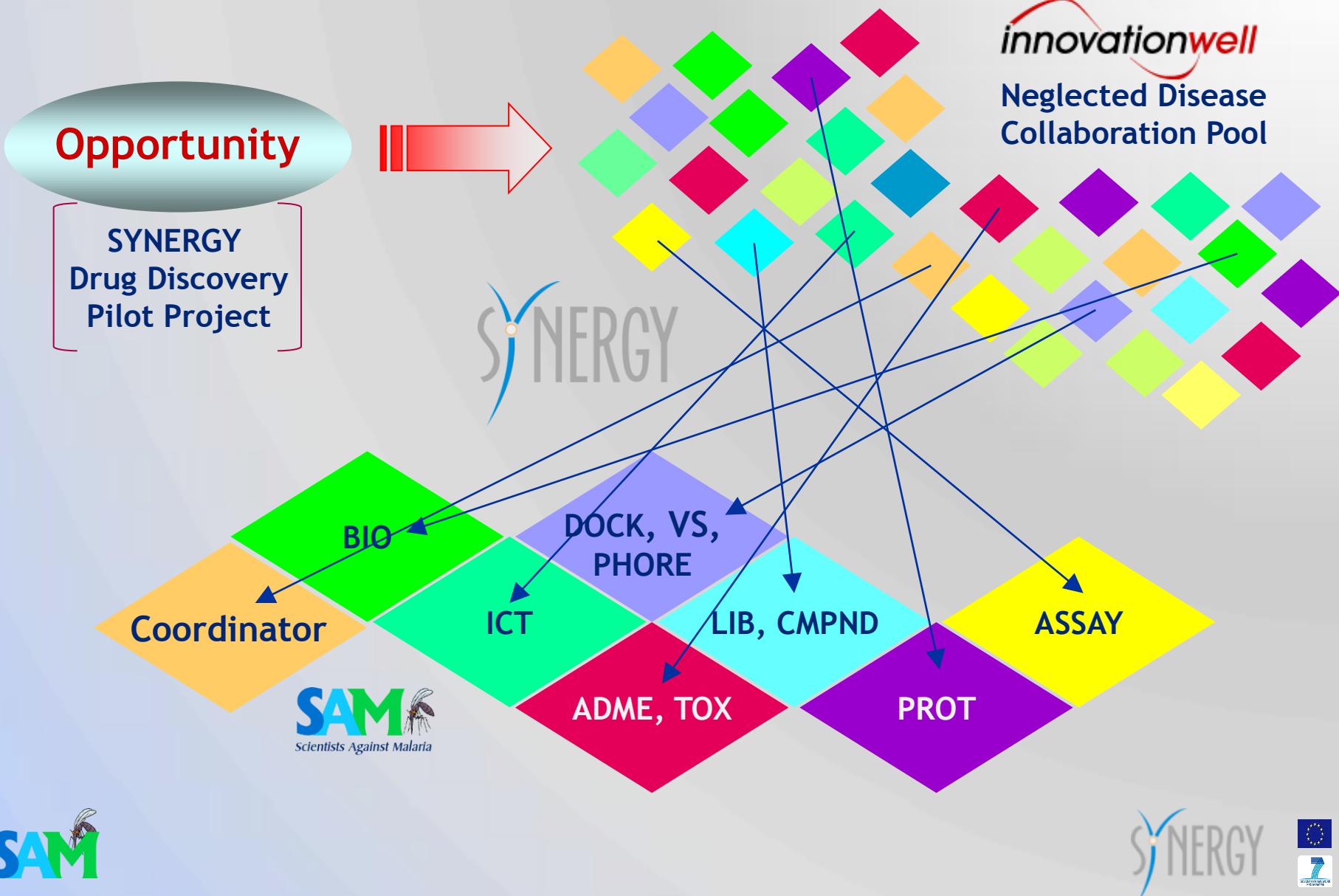


graphic-1.jpg

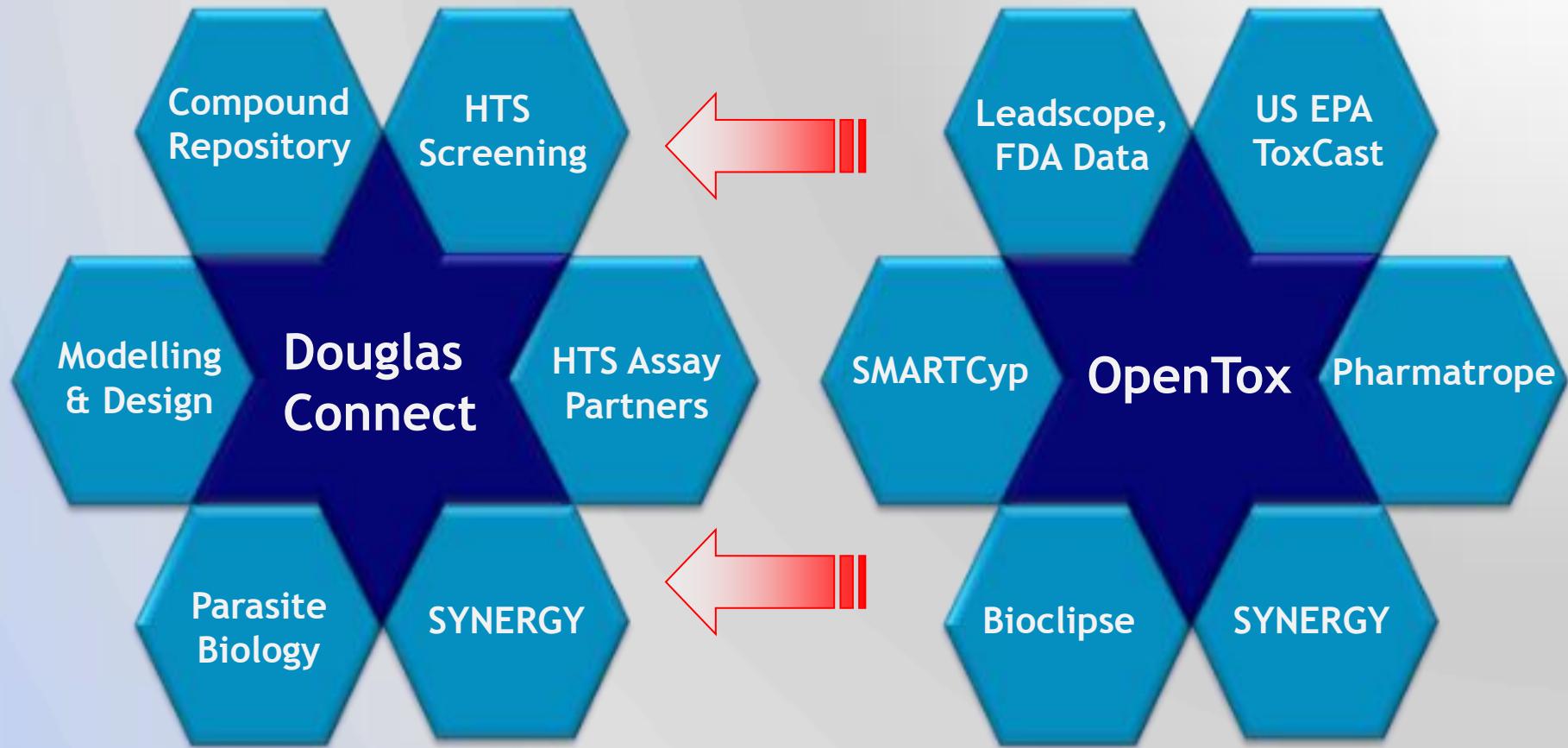
400 × 530 - (Photo credit:
Malaria Vaccine Funders
jama.ama-assn.org
Similar – More sizes



Formation of VO from Collaboration Pool



Virtual Organization Operational Pilots



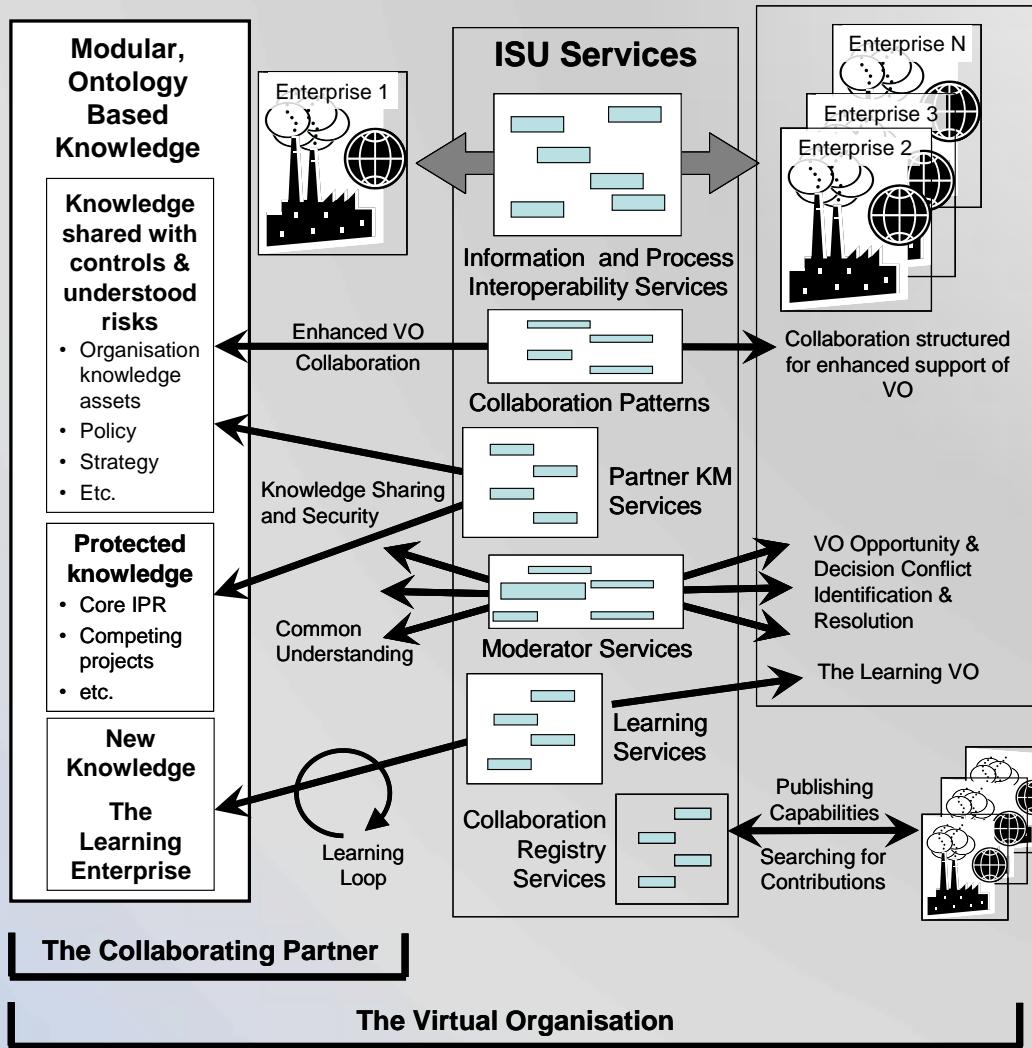
Scientists Against Malaria VO



Predictive Toxicology VO

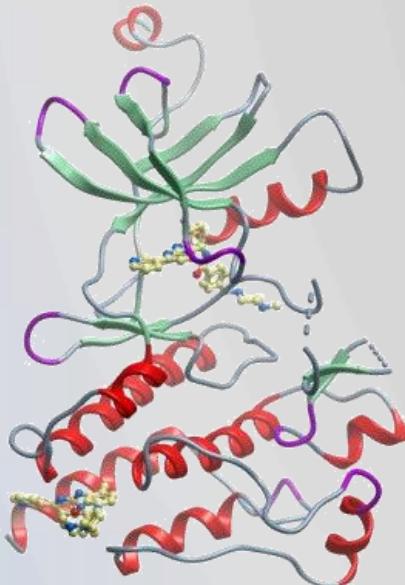


SYNERGY Collaboration Services



Operational Pilot 1 - Collaborative Drug Discovery

Target Protein Structure

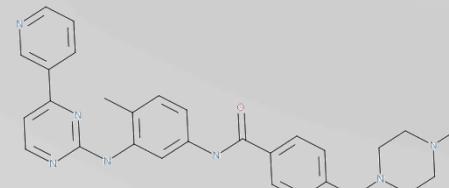


VO

- Drug Design Techniques
- Molecular Modelling
- Virtual Screening
- Biological Assays
- Synthesis or Acquisition
- Testing

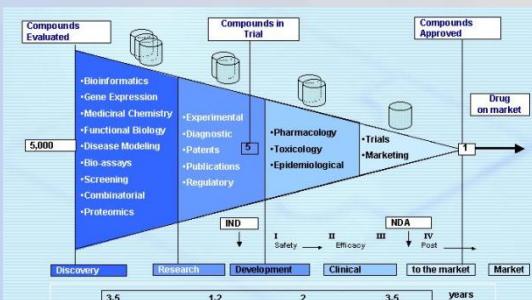
Output result

Drug Leads



Drivers

- Pharmaceutical Industry pressures on R&D environment
- Progressing innovation and discoveries for Neglected Diseases



Scientists Against Malaria Founding Partners



- **Barry Hardy & Roman Affentranger**
(Douglas Connect)
- **Alessandro Contini**
(University of Milan)
- **Hugo Gutierrez de Teran**
(Public Galician Foundation of
Genomic Medicine)
- **Jeffrey Wiseman & Matt Clark**
(Pharmatrophe)
- **Jeff Spitzner** (Rescentris)
- **Ruben Papoian, William Seibel &
Sandra Nelson** (Univ. of Cincinnati
Drug Discovery Center)
- **Sharon Bryant** (Inte:Ligand)
- **Andrew Wilks & Isabelle Lucet**
(Monash University)
- **Christian Doerig** Coordinator of the
FP7 MALSIG project on signalling in
Malarial parasites
- **Matteo Dal Peraro** (EPFL, Lausanne)

www.scientistsagainstmalaria.net



Plasmodium Life Cycle & Kinome

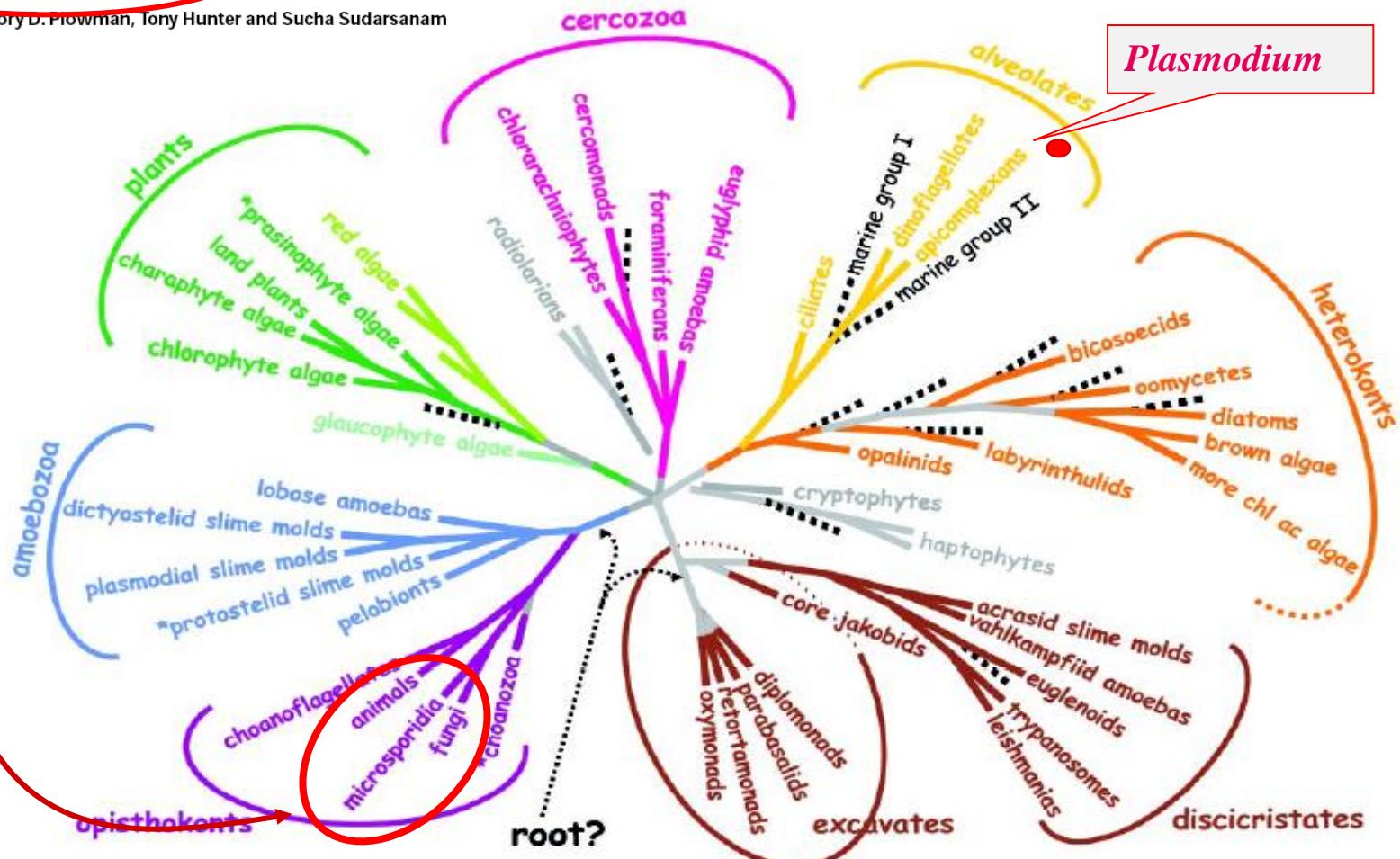
514

Review

TRENDS in Biochemical Sciences Vol.27 No.10 October 2002

Evolution of protein kinase signaling from yeast to man

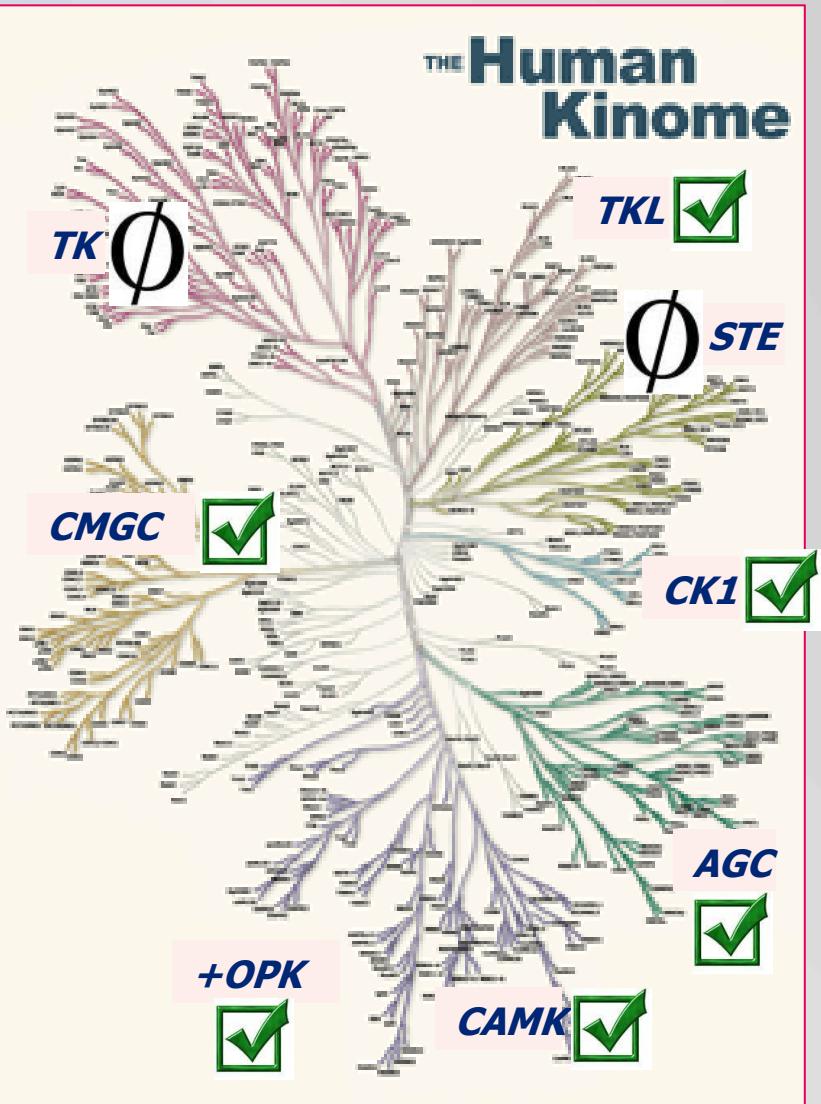
Gerard Manning, Gregory D. Piroozi, Tony Hunter and Sucha Sudarsanam



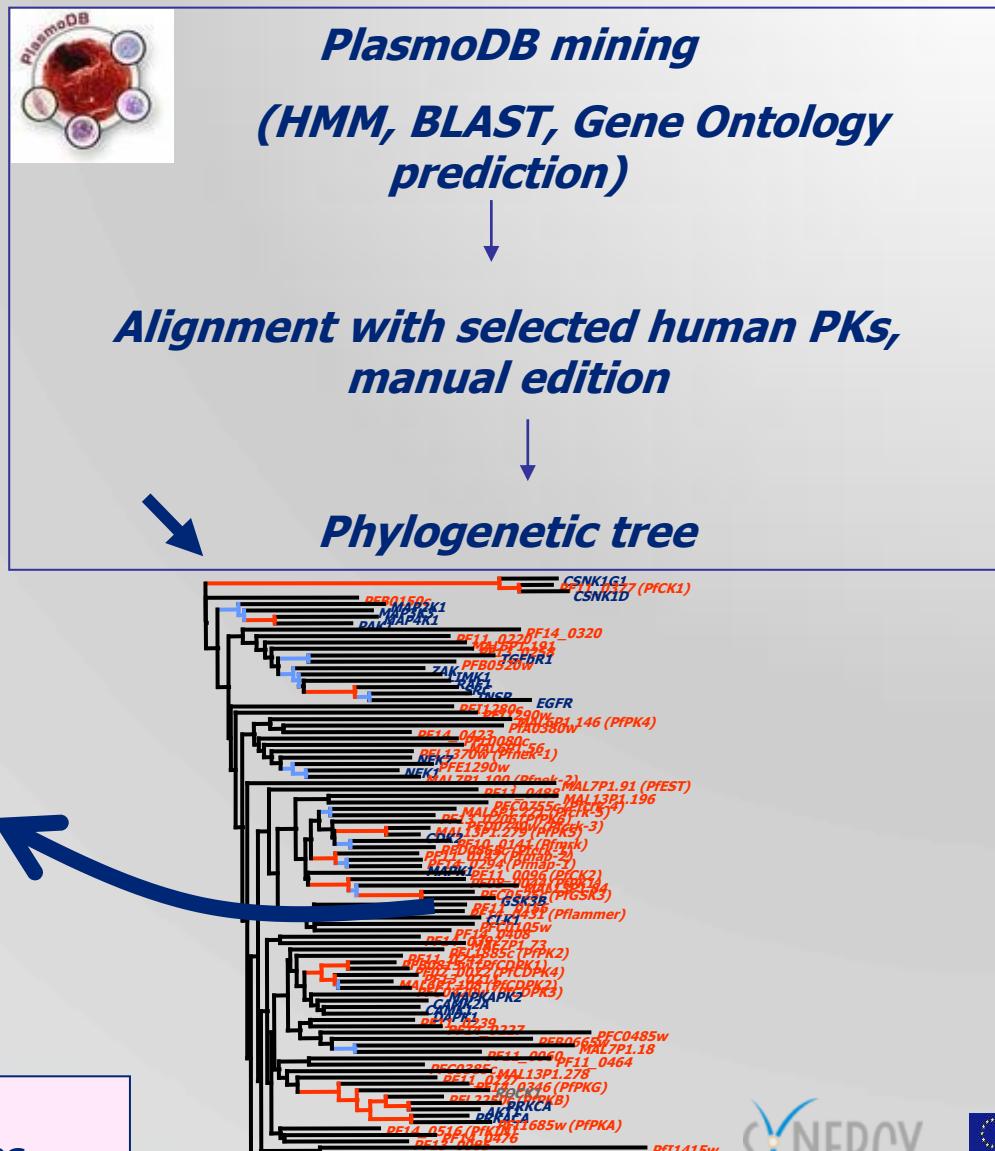
Baldauf, Science, 2003



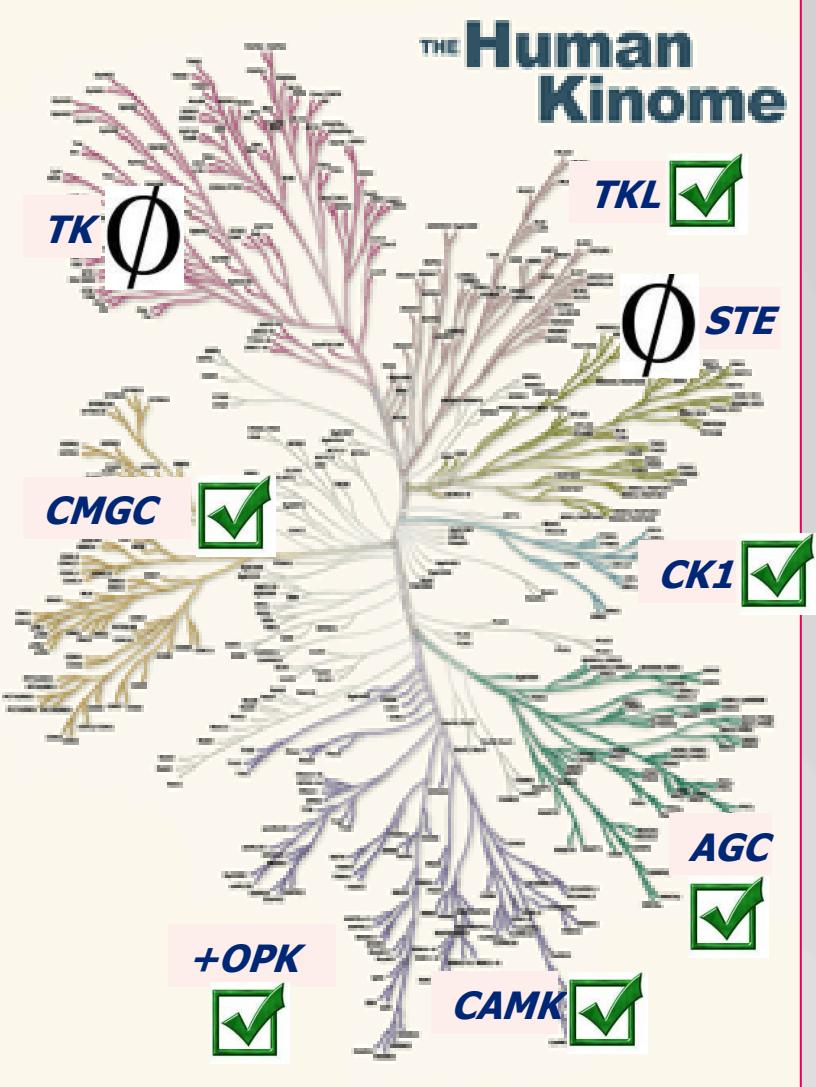
Plasmodium Life Cycle & Kinome



- **518 protein kinases (2% of genes)**
 - **Involved in essentially all cellular processes (30% of the proteome is phosphorylated)**

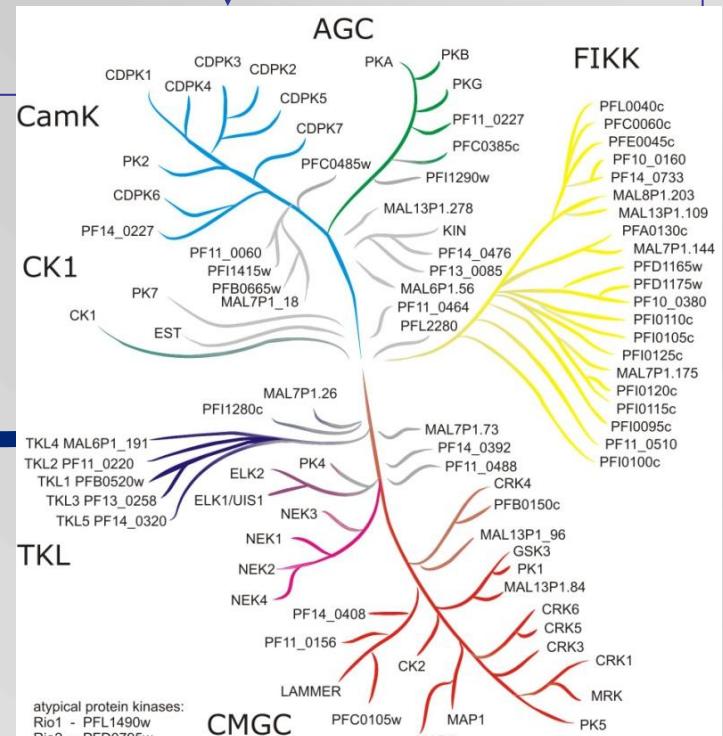


Plasmodium Life Cycle & Kinome



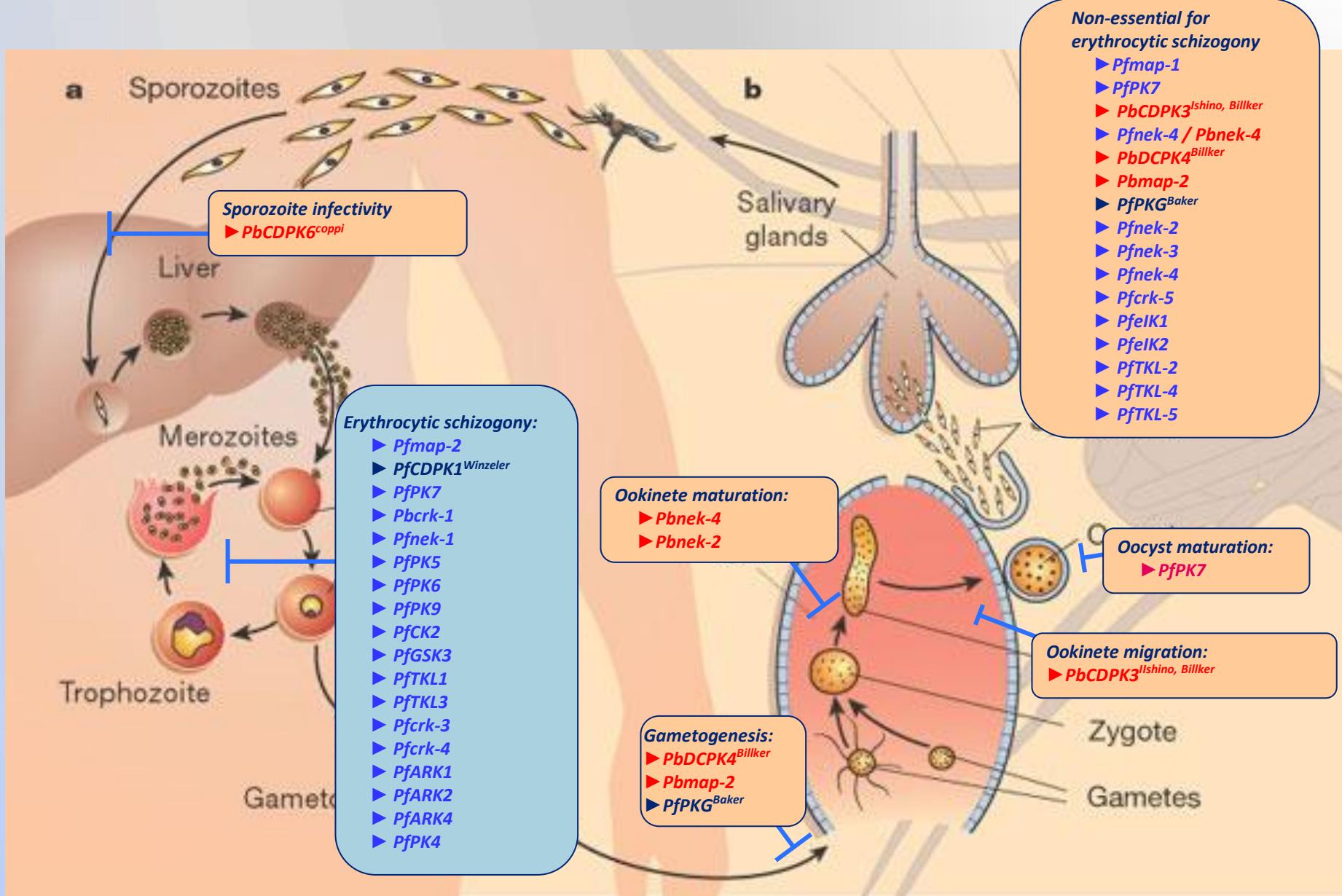
PlasmoDB mining
(HMM, BLAST, Gene Ontology prediction)

Alignment with selected human PKs,
manual edition

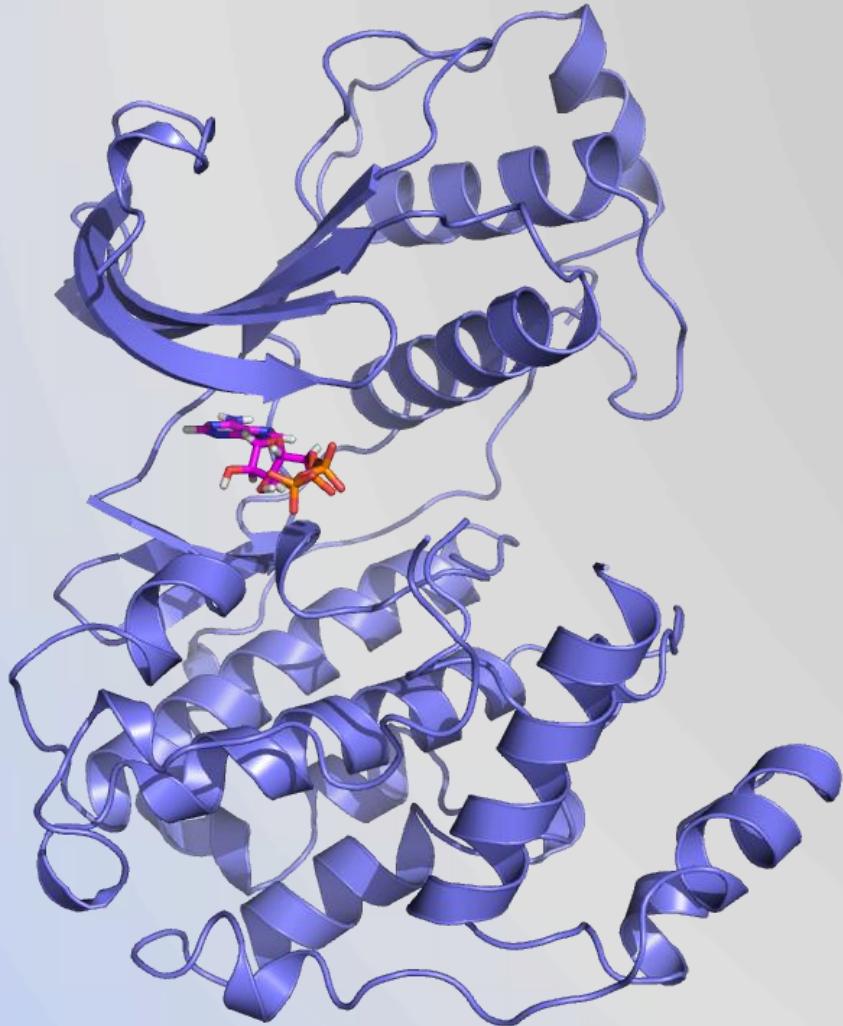


- 518 protein kinases (2% of genes)
- Involved in essentially all cellular processes (30% of the proteome is phosphorylated)

Plasmodium Life Cycle & Kinome



Target Model



- Starting point – no protein structure, no known ligand/inhibitor
- Initial model of PfMAP2 Kinase Protein built based on existing knowledge
- Library of Potential Inhibitors created (ca. 1.2 M structures)
- Virtual screening runs carried out at computing centres in Italy, Spain and USA
- Protein expressed in Monash, Australia and shipped to screening centre at Univ. Cincinnati where assays were developed and run

Homology Modelling

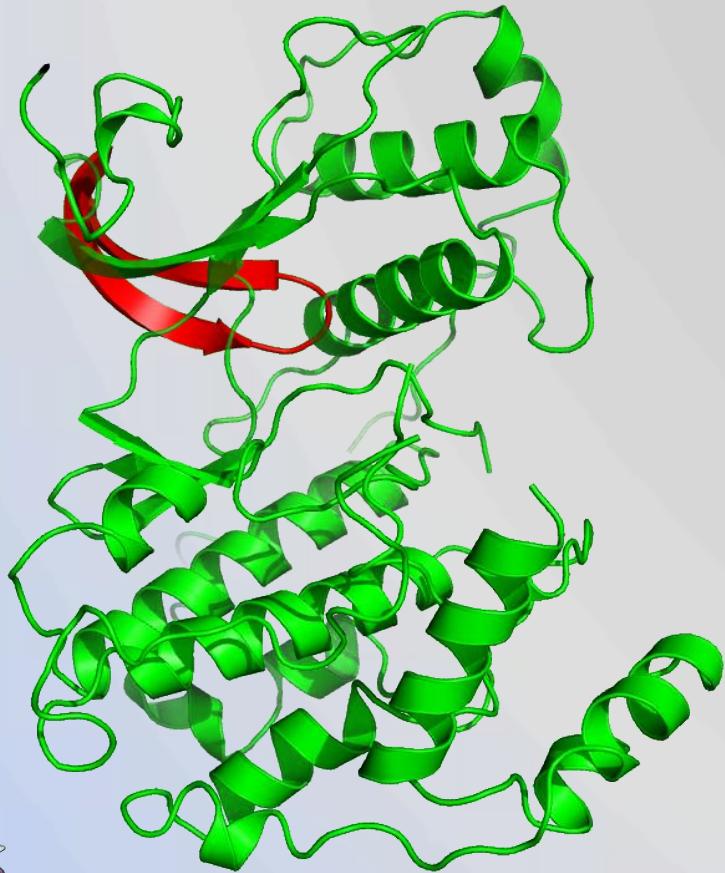
Alignment of Pfmap-2 with 1GOL and 1CM8

	70	80	90	100	110	120	130
_aln.p							
1go1A	-----	-----	-----	-----	-----	-----	-----
1cm8A	-----	-----	-----	-----	-----	-----	-----
pfmap2	DNIISKNCNIVEKKNNKSKEEKINIKEAI	IKNV	KVPDNYEIKHLIGRGSYGYVYL	AIDSKNANKNVAIKK			
_consrvd				*	*	*	***
1go1A	I-SPFEHQTYCQRTLREIKILLRFRHENIIGINDIIR-AP	TIEQM	KDVFYIVQDL	METDLYKLLKTQ-H			
1cm8A	LYRPFQSELF	AKRAYRELRL	LKHMRHEN	VIGLLDVFTPDET	LDFTDFYLVM	PMFMGTDLGKLMKHE-K	
pfmap2	VNRMFED	LIDCKRILREITIL	NRLKSDYI	IRLHDLI	IPEDLL-KFDELYIV	LEIADSDLKKLFKTP	IF
_consrvd	*	*	**	*	*	*	***
1go1A	LSNDHICYFLYQ	TLRGLKYIHSANVL	HRLDKPSN	LLNNTCDLKICDFGLARVADP			
1cm8A	LGEDRIQFLVYQ	MLKGLRYIHAAGI	IHRDLKPGNLAV	NEDCELKILD	DFGLARQADS		
pfmap2	LTEQHVKT	IYLNLLGEKF	IHESGIIHRDLKP	ANCLNQDCSVKICDFGLART	INSKDIDHIVNDLEE		
_consrvd	*	*	**	**	*****	*	**
1go1A	--DHDHTG-----	FLTEYVATRWYRAPEIMLNSKG	YTKSIDIWSVG	CILAEMLS			
1cm8A	--EM.	-----G.	VVTRWYRAPEVILNWMRYT	QTVDIWSVG	CIMAEMIT		
pfmap2	KEENE	EPGPHNKNLKKQLTSHVV	TRWYRAPELILLQEN	YNTNSIDIWSTGC	IFAELLNMMKSHINNPTN		
_consrvd			*****	*	**	****	***
1go1A	NRPIFP	GK	HYLDQLNHILGILGSPSQEDLN	CITINLKARNYLLSLPH	HNKVP		
1cm8A	TKL	FKG-----	DHLDQLKEIMKV	TGTPPAEFV	QRLQSDEAKNYMKGLPE	LEKKD	
pfmap2	RFP	LFPGSSCFPLSPDHNSK	VHEKSNRDQLN	IIFNVIGTP	PEEDLK	CITKQEVIKYIKLF	TRDGID
_consrvd	*	*		***	*	**	*
1go1A	WNRLFPNADSKAL	DL	DKMLTFNPHKR	IEVEQALAH	PYLEQYYDPS	DEPIAEAPFK	FDMEL-DDLPKE
1cm8A	FASILT	NASPLAVNL	LEKMLV	DAEQRV	TAGEALAH	PYFESLH	-----RTLD
pfmap2	LSKKY	SSISKEGI	DILLESMLRF	NAQKRITIDKAL	SHPYLK	DVRKENLEN	FSTEKIILPFDDWMVLSET
_consrvd	**	**		*	**	***	

PfMAP2 modelling

Three template pdbs selected:

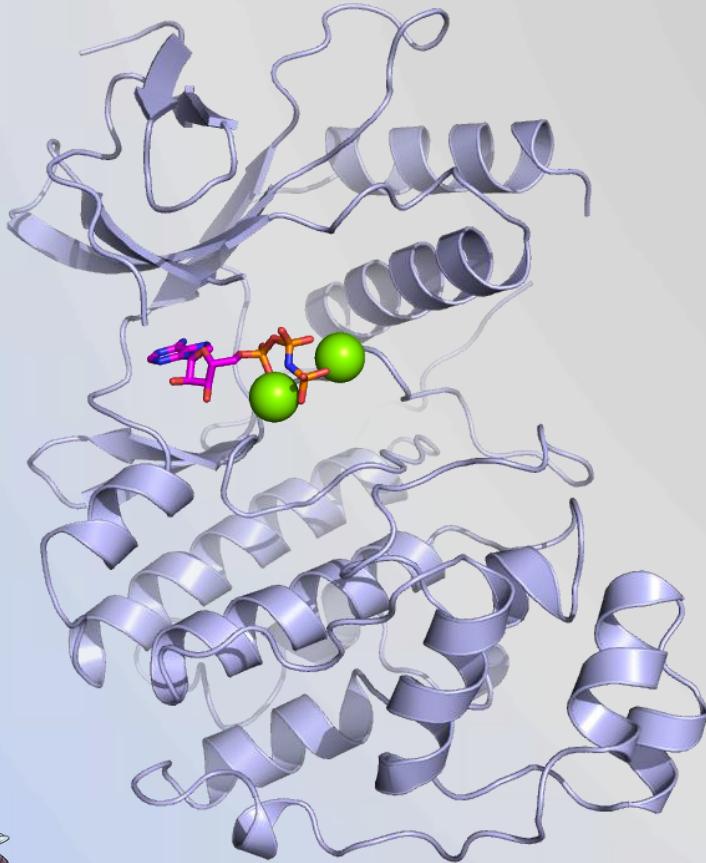
3N9X_PRE-RELEASE.pdb



PfMAP2 modelling

Three template pdbs selected:

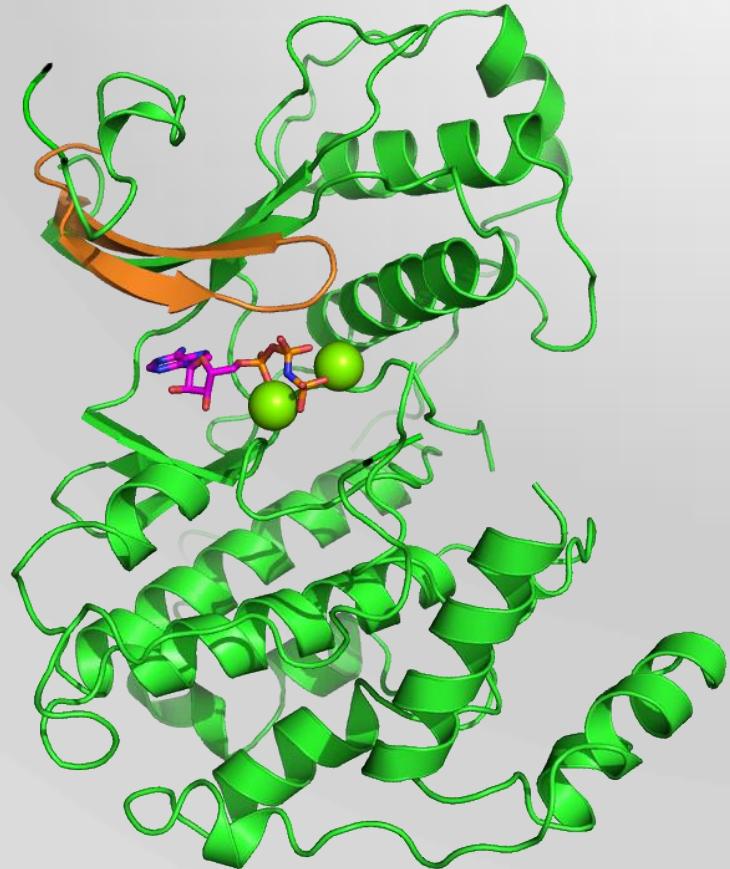
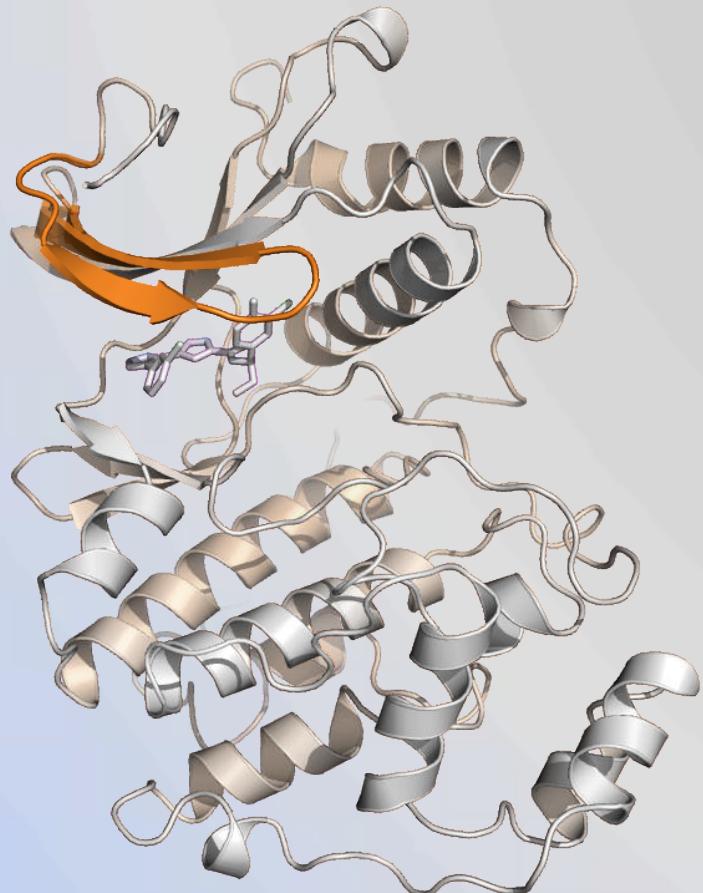
1CM8.pdb



PfMAP2 modelling

Three template pdbs selected:

2OJJ.pdb



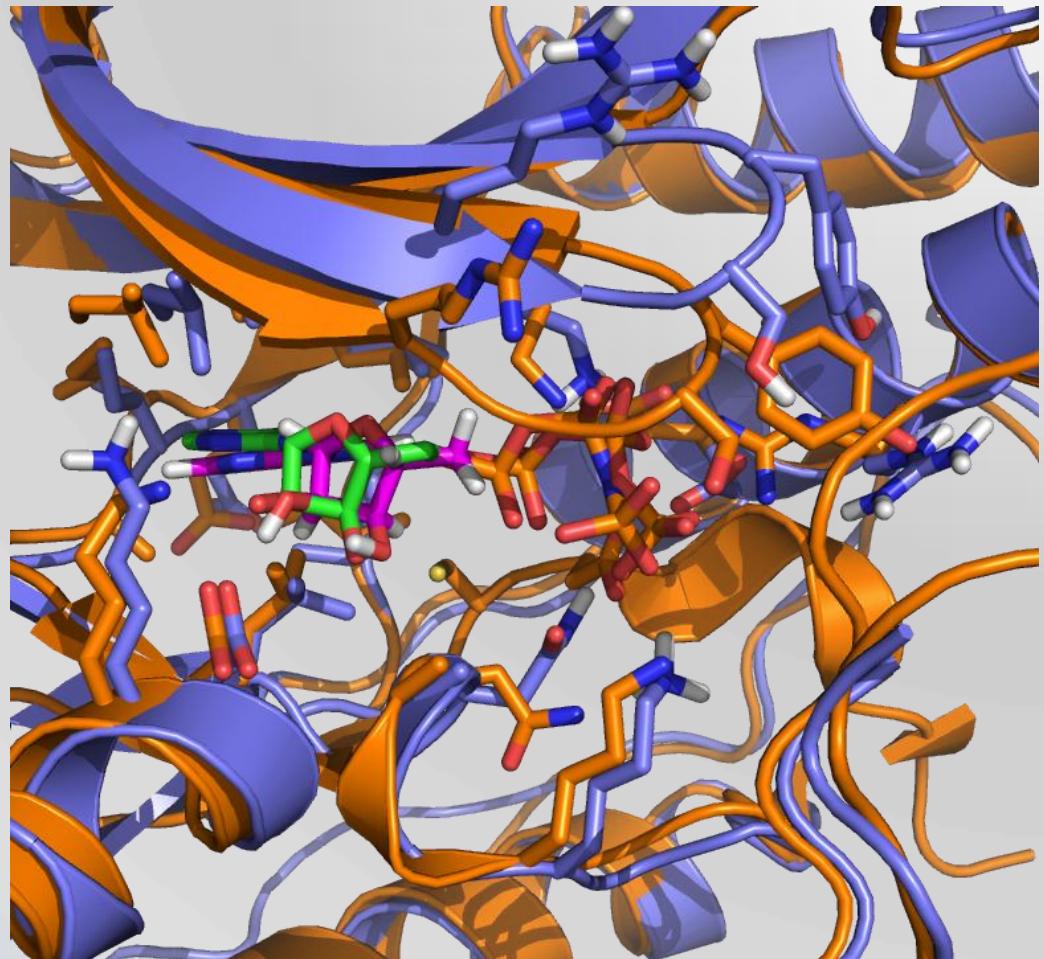
PfMAP2 Crystal Structure Model Comparison

3NIE.pdb protein structure by SGC was released August 11, 2010

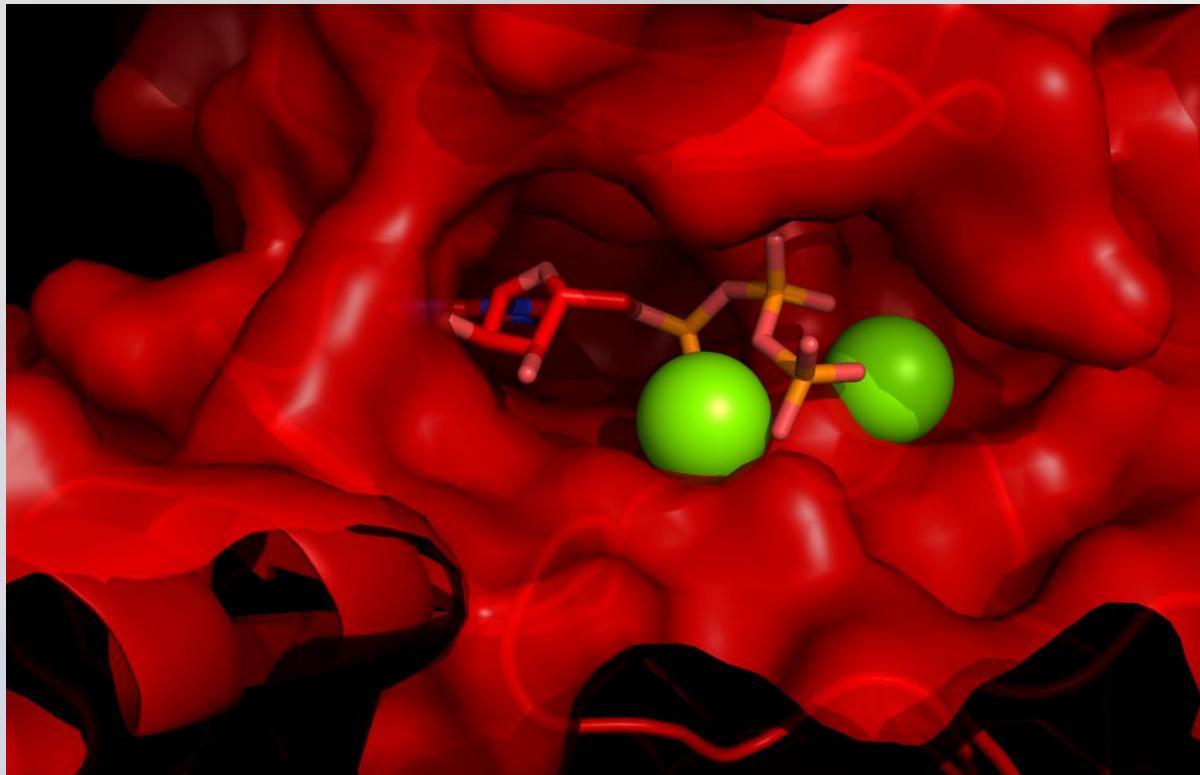
Overall, our model was quite accurate

Conformation of ATP was modelled well

Binding pocket residues were mostly ok

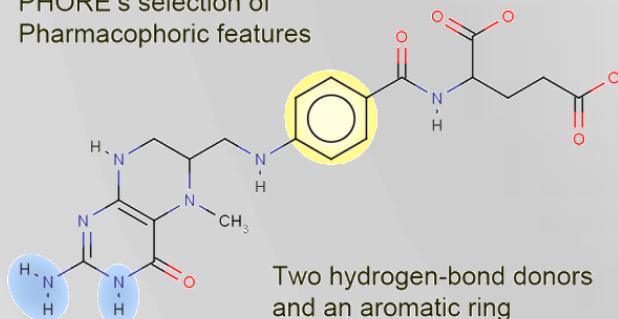


Binding Pocket

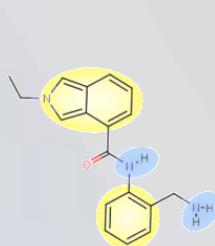


Pharmacophore-based Screening

PHORE's selection of Pharmacophoric features



PHORE's library of compounds



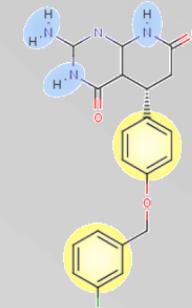
Compound-ID 001
aromatic ring
2 donors



Compound-ID 002
Only one donor



Compound-ID 003
No aromatic ring

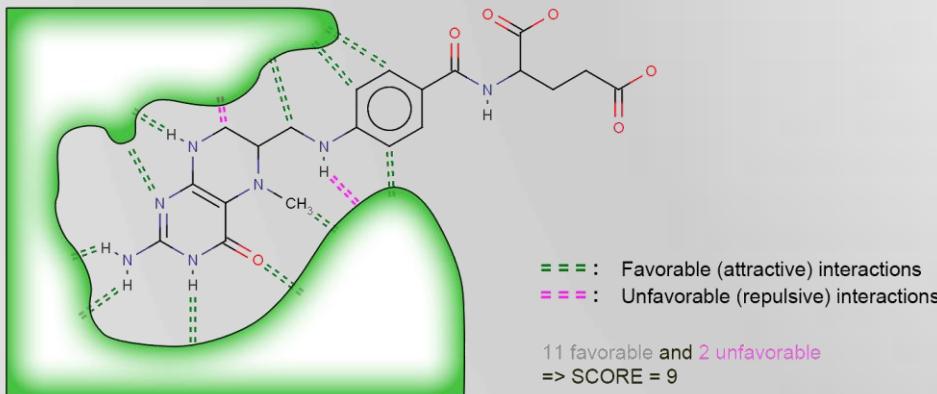


Compound-ID 004
aromatic ring
2 donors

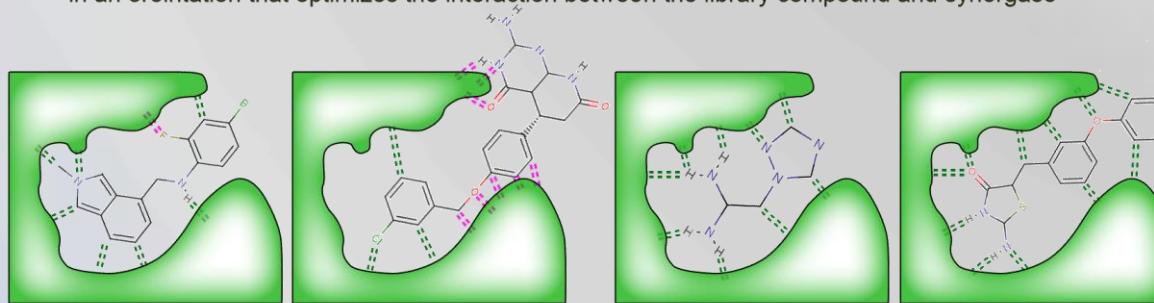
PHORE's activity hits prediction: compound-IDs 001 and 004

Dock Screening Prediction

γ -synergie bound to synergase (schematic depiction)

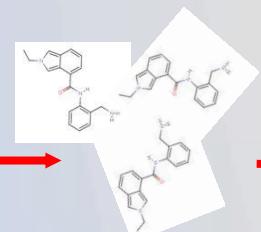


Each member of DOCK's library of compounds is placed in the binding pocket of synergase in an orientation that optimizes the interaction between the library compound and synergase

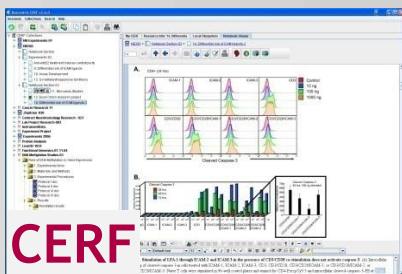


DOCK's activity hits prediction: compound-IDs 005 and 006

SAM Workflow



Data



Refine Predictions

SYNERGY



Refine Predictions

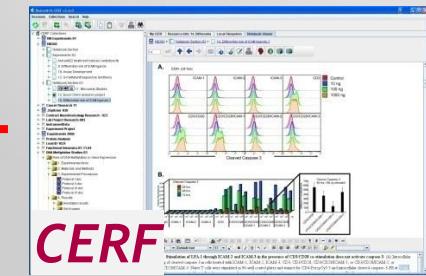
SYNERGY



Data



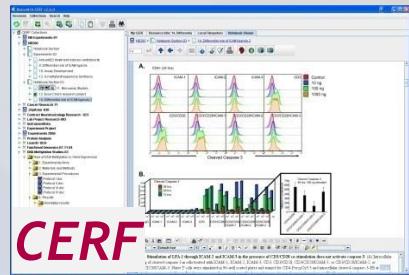
OpenTox



Toxicity Predictions



Data



Decision Dashboard

Compound ID	Phore	VS	Dock	Dock 2	Binding Prediction Stoplight	Saturation Binding Assay	Binding Assay Stoplight
AA0002	1	1	0	0	Green	Green	Green
AA0003	1	1	1	1	Green	Red	Red
AA0004	0	0	0	0	Red	Red	Red
AA0005	1	1	1	1	Green	Green	Green
AA0006	0	1	0	0	Red	Red	Red

SYNERGY

(Safer) Drug Leads

Data Entry & Analysis

Rescentris CERF v2.6.0

Sessions Collections Search Help

CERF Collections

- NB-Experiments-01
- NB260
 - Notebook Section
 - Experiments-02
 - Anti-erbB2 treatment induces cardiotoxicity
 - 9. Differential role of ICAM ligands
 - 10. Assay Development
 - 13. β -methylanthraquinone Synthesis
 - Notebook Section-03
 - 11. Microarray Studies
 - 12. Excel Chem research project
 - 14. Differential role of ICAM ligands-2
 - Cancer Research 11
 - JSpitzner-038
 - Contract Neurotoxicology Research - 003
 - Lab Project Research-003
 - InstrumentData
 - Experiment Project
 - Experiments 2006
 - Protein Analysis
 - Lead ID-1034
 - Functional Genomics-07-11-04
 - DNA Methylation Studies-03
 - Role of DNA Methylation in Gene Expression
 - 1. Experimental Aims
 - 2. Materials and Methods
 - 3. Experimental Procedures
 - Protocol I.doc
 - Protocol II.doc
 - Protocol III.doc
 - Protocol IV.doc
 - 4. Results
 - Annotated results
 - Gel Images
 - Sequencing Gel 1.jpg
 - Sequencing Gel 2.jpg
 - Gel 3.jpg
 - Spreadsheets
 - Raw Data_1.xls
 - RUIL12.XLS
 - 5. Conclusions
 - jspitzner

Controlled Vocabularies

My CERF Resource Info: 14. Differential role of ICAM ligands-2 Local Filesystem Notebook Viewer

NB260 > Notebook Section-03 > 14. Differential role of ICAM ligands-2

A. CD4+ (24 hrs)

CD3

Control
10 ng
100 ng
1000 ng

Cleaved Caspase 3

B.

Median Fluorescence

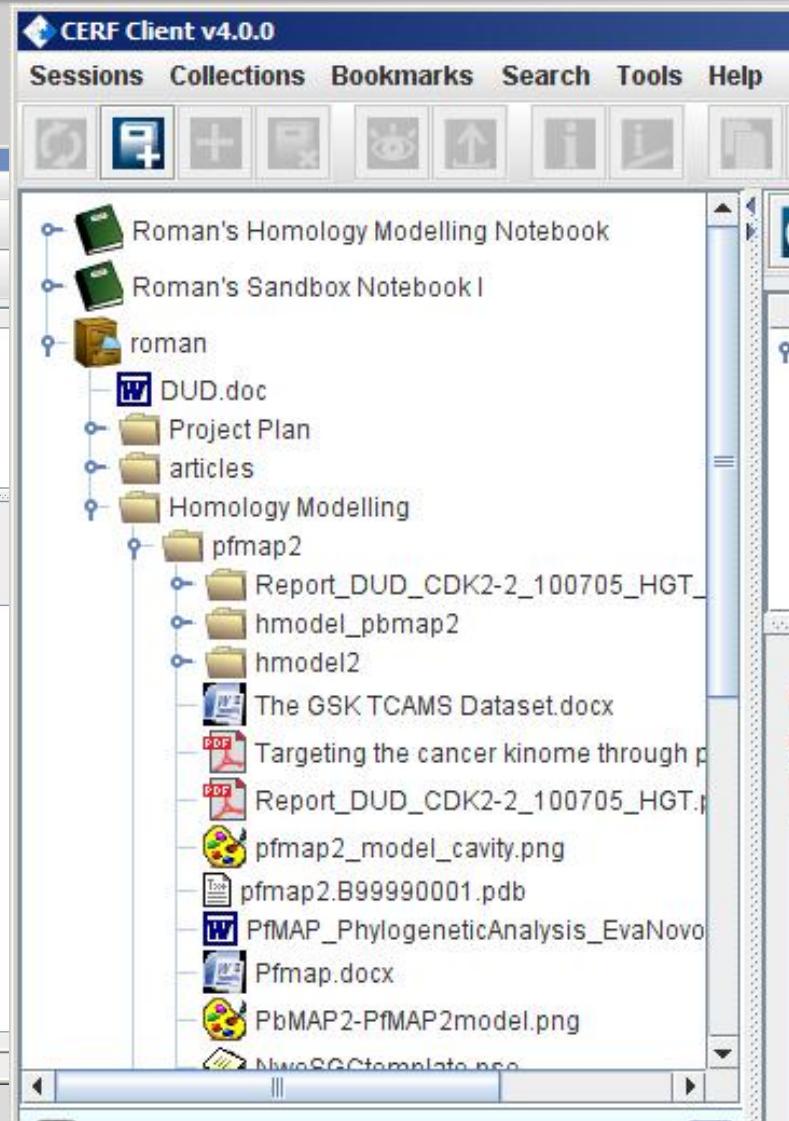
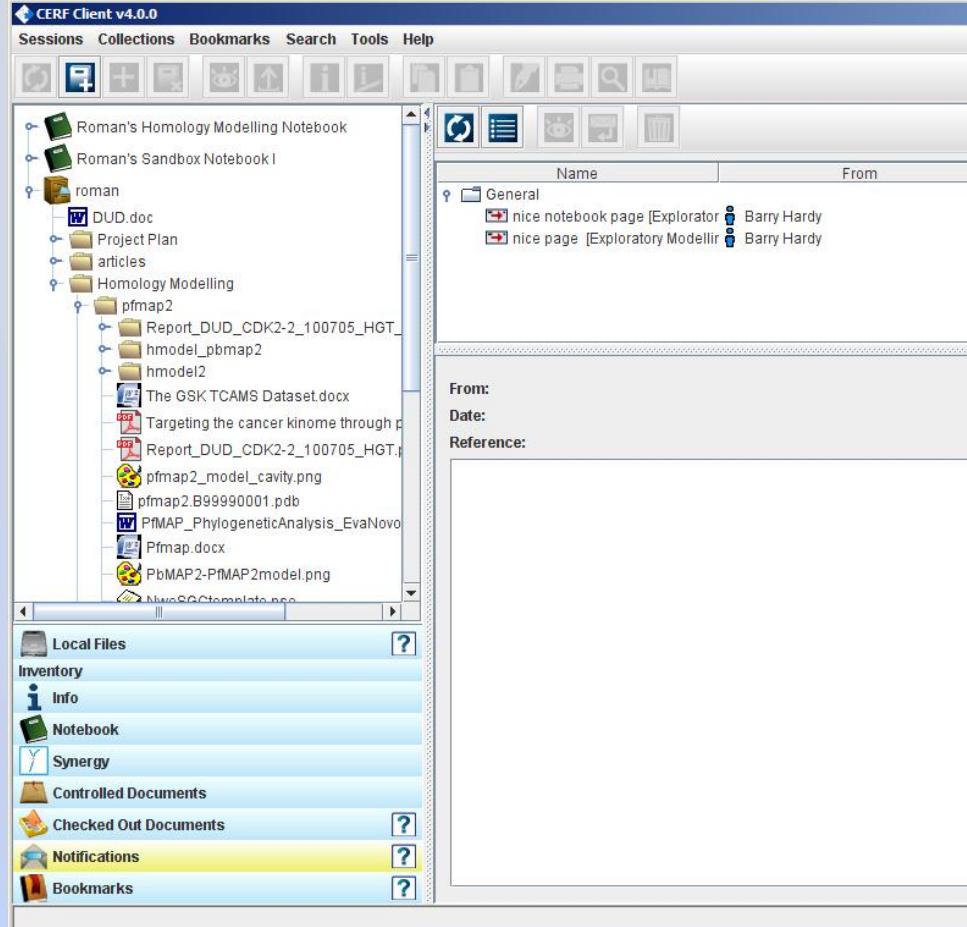
Cleaved Caspase-3 48 hrs, 100 ng stimulant

Fig. 1. Stimulation of LFA-1 through ICAM-2 and ICAM-3 in the presence of CD3/CD28 co-stimulation does not activate caspase-3. (A) Intracellular staining of cleaved-caspase 3 in cells treated with ICAM-1, ICAM-2, ICAM-3, CD3, CD3/CD28, CD3/CD28/ICAM-1, or CD3/CD28/ICAM-2, or CD3/CD28/ICAM-3. Naive T cells were stimulated in 96-well coated plates and stained for CD4-PercpCy5.5 and intracellular cleaved-caspase-3-PE at 24 hrs.

Visualisation

Collaborative Electronic Research Framework (CERF)

File cabinets to store data etc



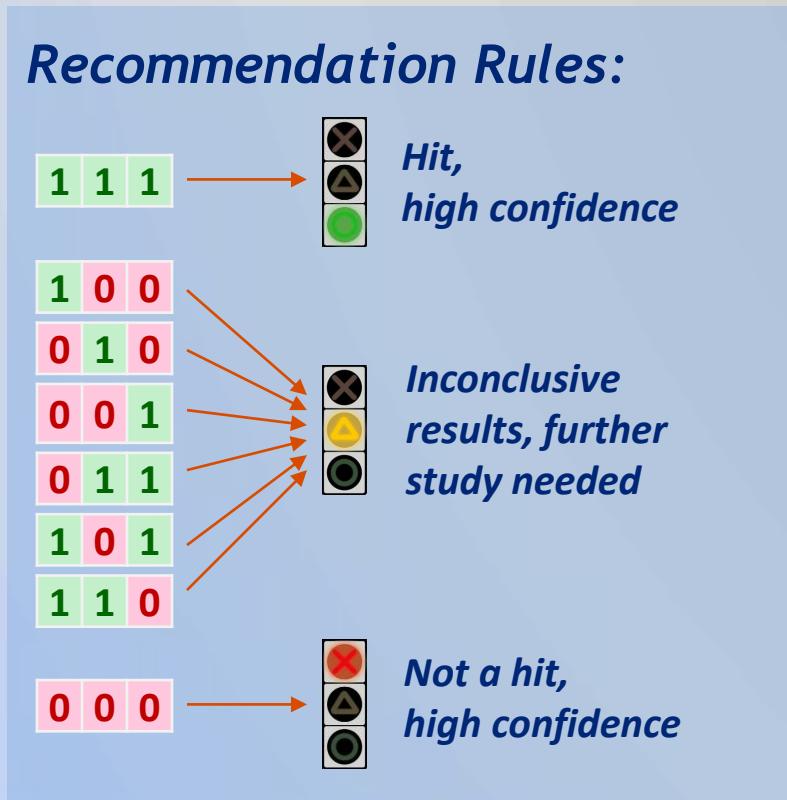
Template Spreadsheets to Document Computations

Computational Analysis Form (Roman Affentranger, Tuesday, September 7, 2010 10:55:19 AM)					
	fx:				
1	A	B	C	D	E
2	Operator Name (if different from Notebook user):	Roman	Operator Organization:	Douglas Connect	
3	Computer Operating System & Version	Fedora 10	Computer architecture	x86_64	
4	Name of computational software	MODELLER	Version of software	9v8	
5	Analysis Performed	Template Selection for PfMAP2 step 1: get list of template candidates			
6	Method (Steps - use as many as you need):				
7	1. Preparation of PfMAP2 sequence in MODELLER format		pfmap2.ali		
8	2. Building a sequence profile		build_profile.py		
9	3. Remove template candidates with low ID or small overlap		manual		
10	4. Download selected pdb files		get_pdb.sh		
11	5. Structural alignment of template candidates		salign.py		
12					
13	Parameters used	Default parameters were used for all MODELLER scripts			
14	Sample input file	pfmap2.ali			
15		Script	Input	Output	
16	Reference Files (inputs and outputs) - attach as links	build_profile.py	pfmap2.ali	build_profile.prf	
17				build_profile.log	
18				build_profile.ali	
19		get_pdb.sh	pdb-list.dat	get_pdbs	
20		salign.py	get_pdbs	salign.log.gz	
21				pfmap2-salign-templates.tree	
22				pfmap2-salign-templates.pap	
23				pfmap2-salign-templates.ali	
24					

SAM ICT Architecture



Resolving Inconclusives



ELN

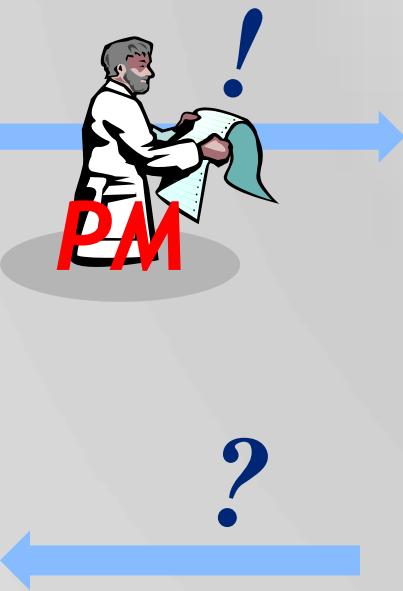
Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
1	0	1	XX	△	○

Synergy

Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
1	0	1	XX	△	○

OpenTox

Resolving Inconclusives



ELN

	Model 1	Model 2	Model 3	
	1	0	1	

- Assay 1 - Assay 2 - Assay 3

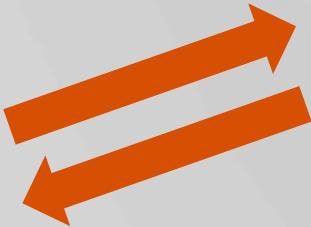
Synergy

	Model 1	Model 2	Model 3	
	1	0	1	

- Assay 1 - Assay 2 - Assay 3

OpenTox

Resolving Inconclusives



ELN

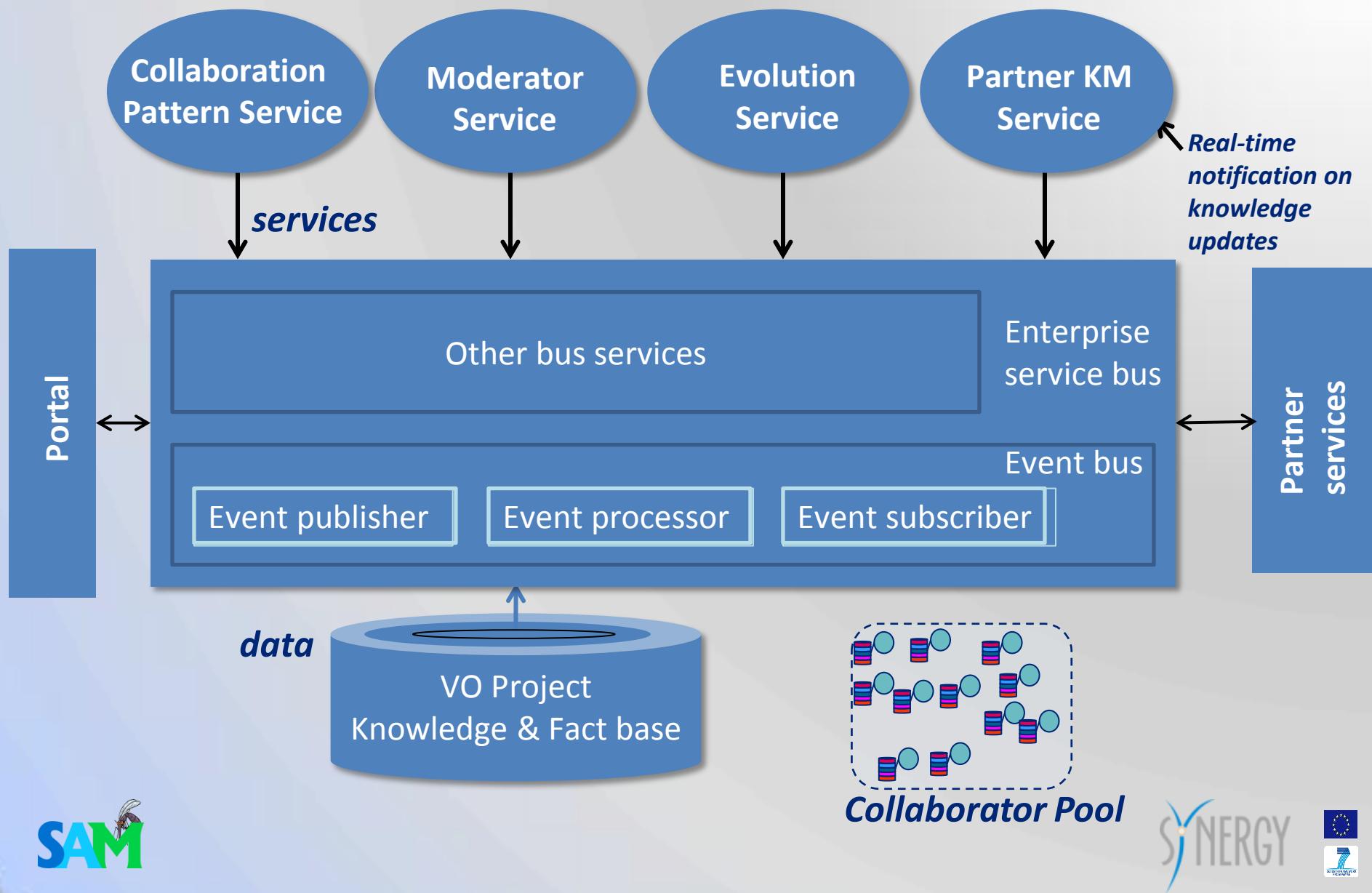
	Model 1	Model 2	Model 3	
	1	0	1	
- Assay 1				
- Assay 2				
- Assay 3				

Synergy

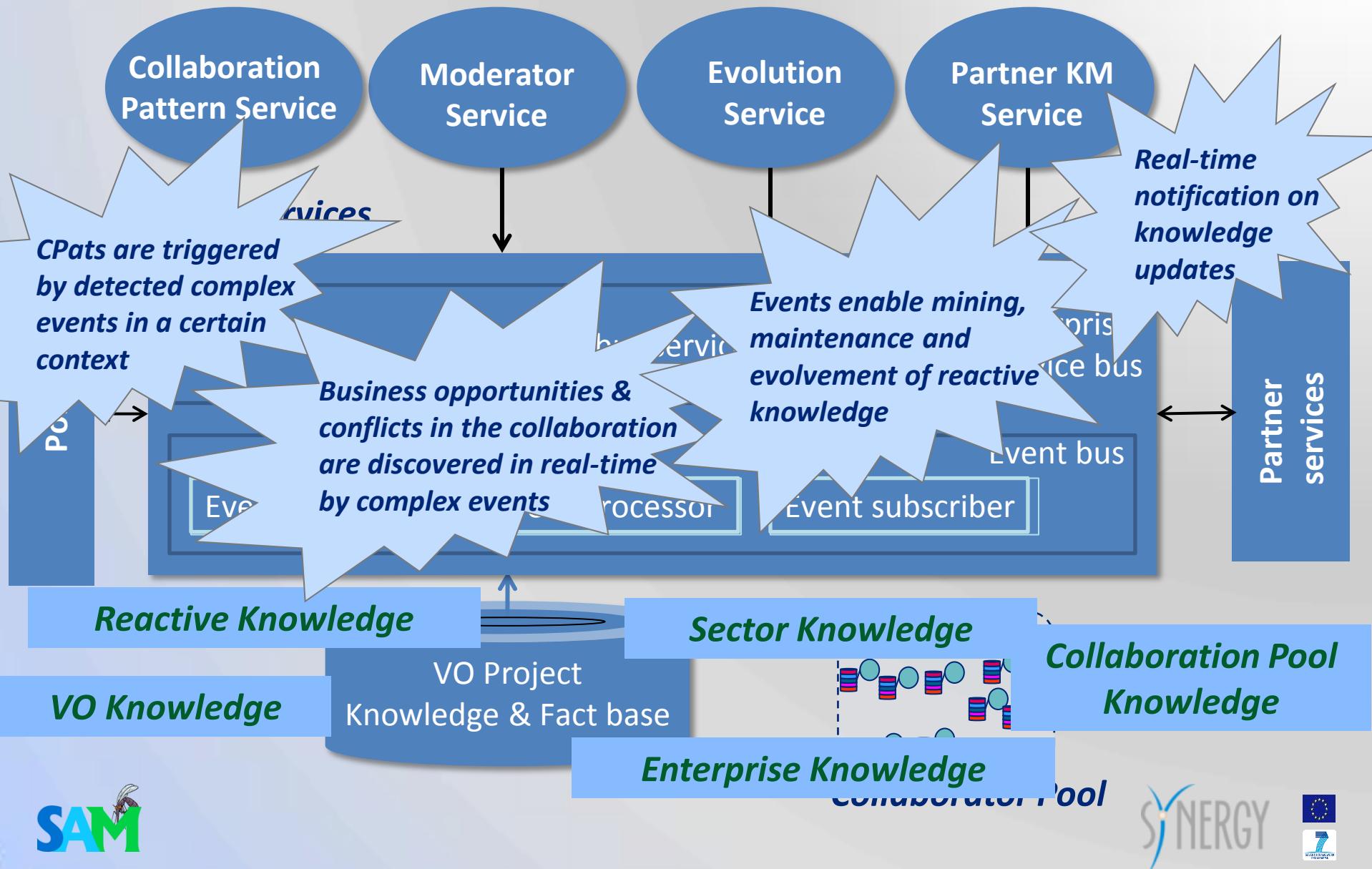
	Model 1	Model 2	Model 3	
	1	0	1	
- Assay 1				
- Assay 2				
- Assay 3				

OpenTox

SYNERGY Service Support



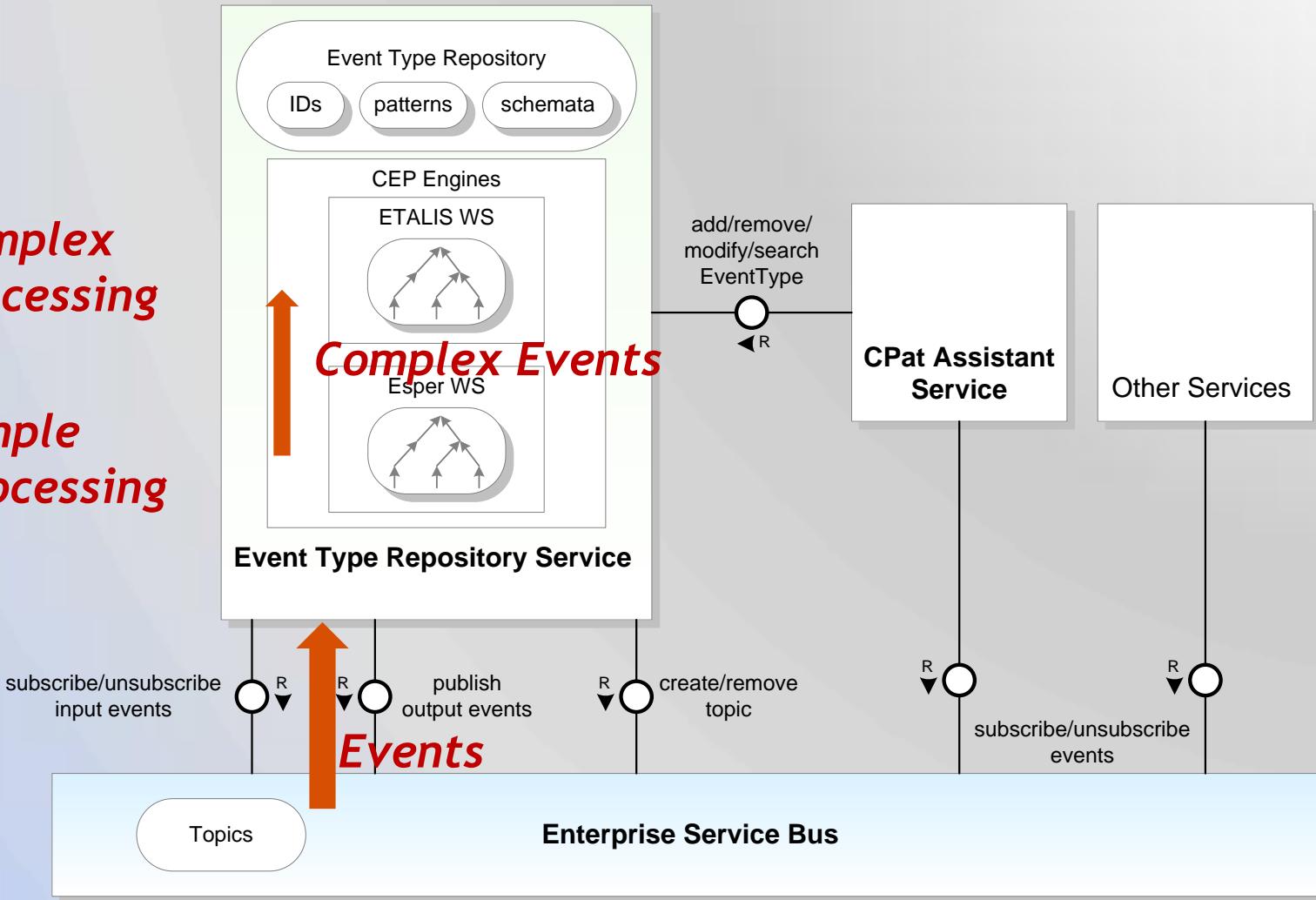
SYNERGY Service Support



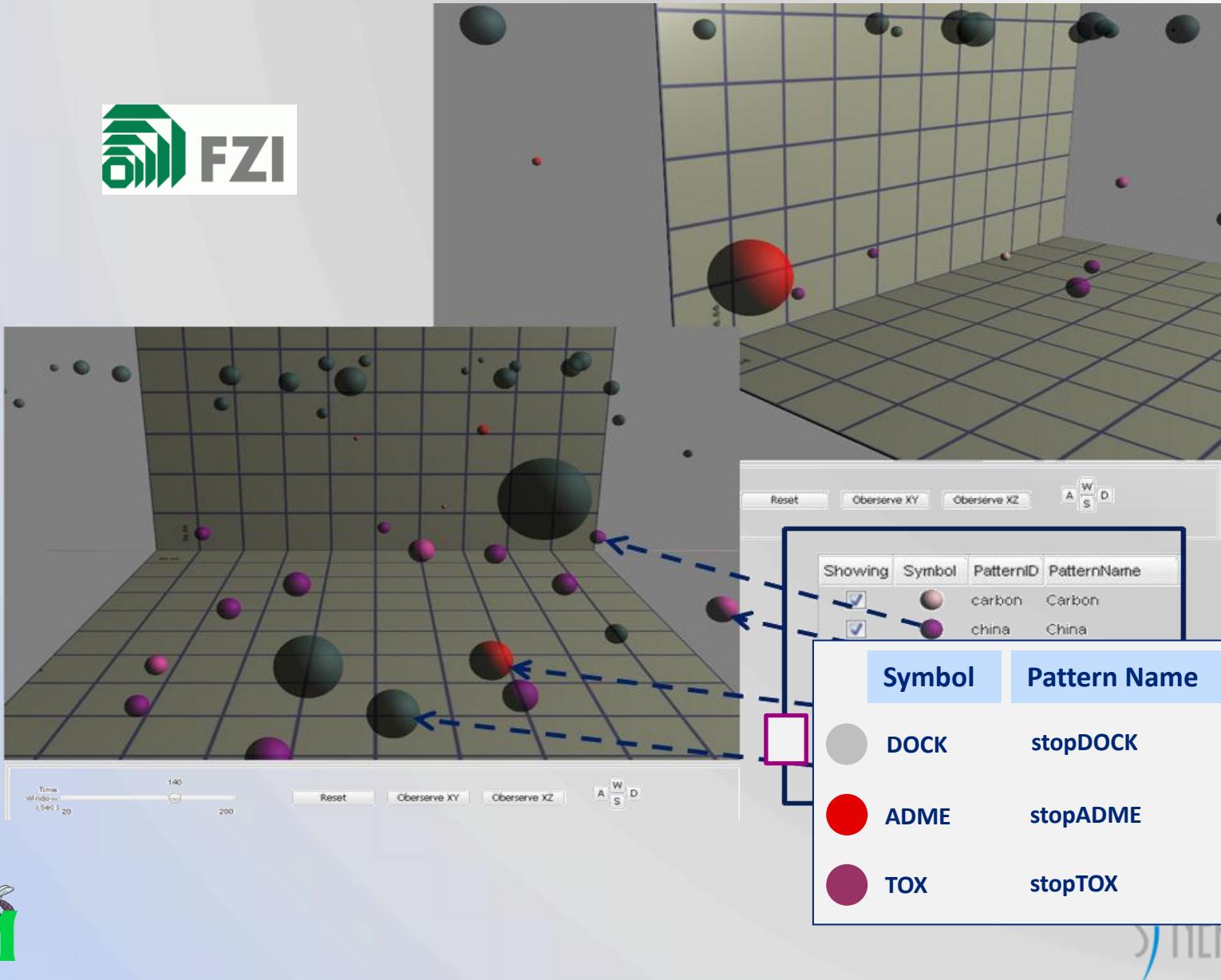
SYNERGY Complex Event Processing

Complex processing

Simple processing

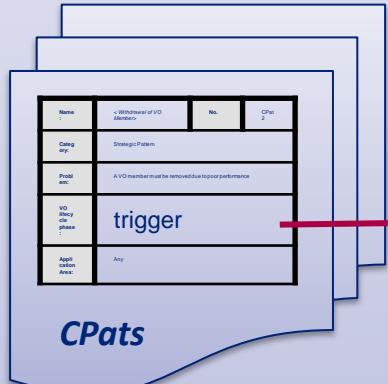


Complex Events Stream



Collaboration Patterns

How are the building blocks of communication (ie. events) identified?



Where are they represented?

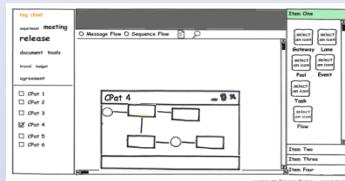
events from trigger definitions

Event Type Repository

1. Identifier
2. Pattern
3. Schema

other communication primitives in SYNERGY

Where are they put to use?



CPat Editor

pub/sub



PETALS ESB



Esper CEP

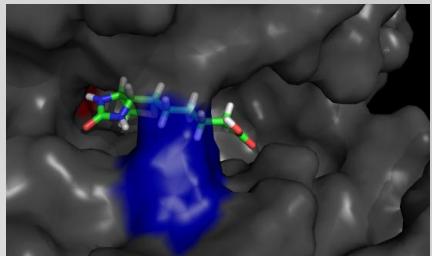
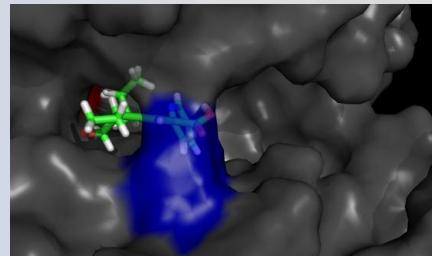


ETALIS iCEP

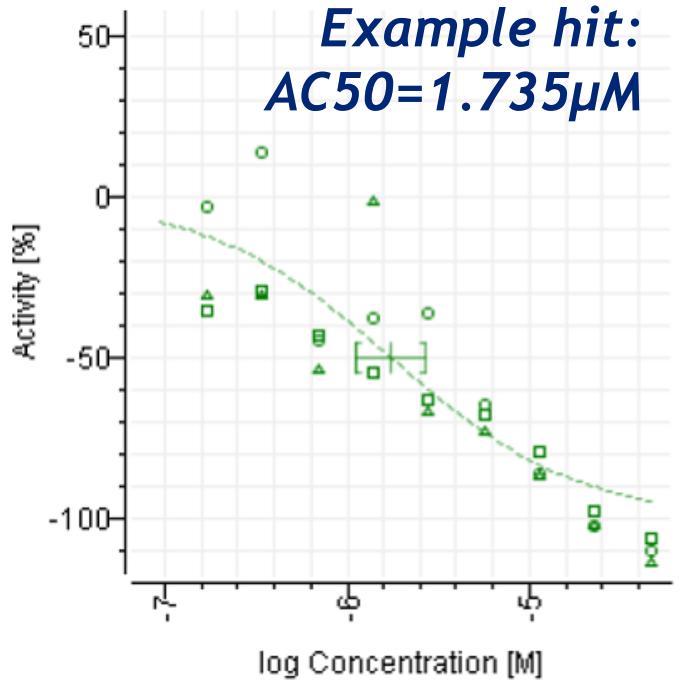
Who are the end consumers?

SYNERGY Services

Preliminary Results



Example hit:
 $AC50=1.735\mu M$



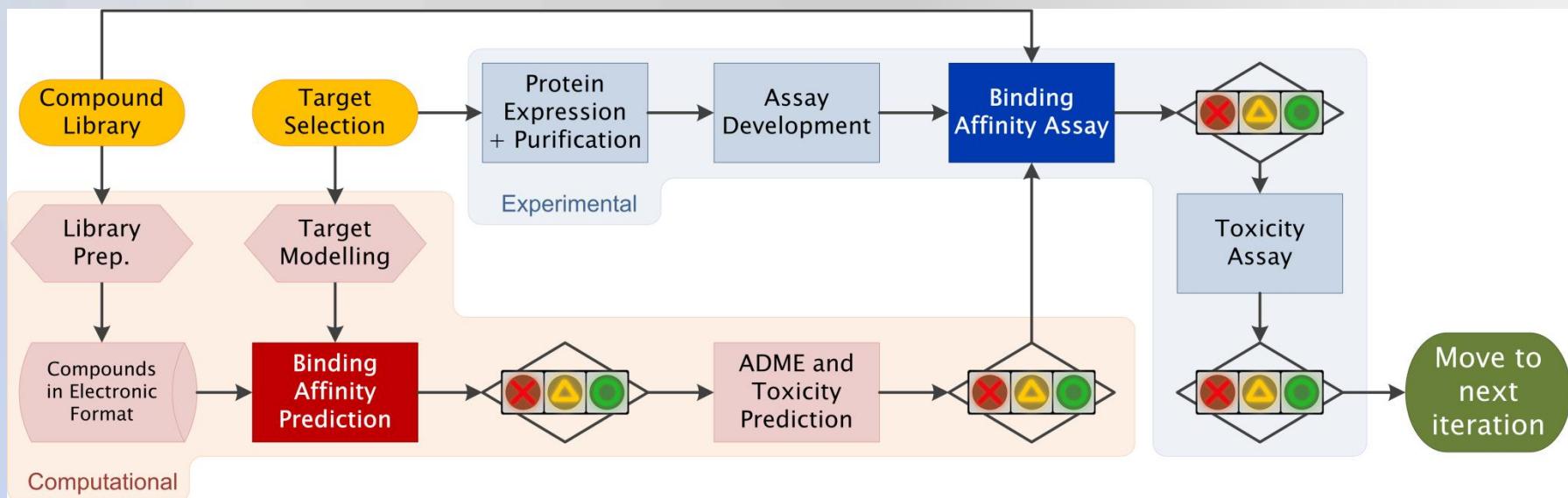
Pharmacophore Search

- Found 696 fits in library of >300,000 compounds
- Evaluated energies by free energy simulations
- Binding assays run for 588 compounds

Docking predictions

- 996 compounds predicted as consensus between three docking screens (AutoDock, Vina, Glide)
- Binding assays are currently in progress

Incorporation of Holistic Predictive ADME & Toxicity



Predictive toxicology model building

The screenshot shows a Mozilla Firefox browser window with the URL <http://apps.ideaconsult.net:8180/ToxPredict/user/4996263b-0d7c-4fec-8b68-15e38c29e7cd/4/step3>. The page title is "Models - Mozilla Firefox". The main content area displays the "ToxPredict" application with a progress bar at the top showing "Step 1: Search Select structure(s)", "Step 2: Verify structure Verify structure", "Step 3: Models Select prediction models", "Step 4: Estimate Estimate", and "Step 5: Results Display results". A "NEXT" button is visible. Below the progress bar is a table listing various endpoints and their associated models, descriptors, training datasets, and algorithms.

Endpoint	Model	Descriptors	Training dataset	Algorithm
	OpenTox model created with TUM's kNNregression model learning web service.	YES		http://opentox.informatik.tu-muenchen.de:8080/Opentox-dev/algorithm/kNRegression
Carcinogenicity	ToxTree: Benigni/Bossa rules for carcinogenicity and mutagenicity	-		ToxTree: Benigni/Bossa rules for carcinogenicity and mutagenicity
Dissociation constant (pKa)	ToxTree: pKa	-		pKa
Endpoints	ToxTree: Structure Alerts for the in vivo micronucleus assay in rodents	-		ToxTree: Structure Alerts for the in vivo micronucleus assay in rodents
Endpoints	ToxTree: Michael acceptors	-		ToxTree: Michael acceptors
Eye irritation/corrosion	ToxTree: Eye irritation	-		ToxTree: Eye irritation
Human health effects rules	ToxTree: Extended Cramer rules	-		ToxTree: Extended Cramer rules
Human health effects	ToxTree: ILSI/Kroes decision tree for TTC	-		ToxTree: ILSI/Kroes decision tree for TTC
Skin irritation/corrosion	ToxTree: Skin irritation	-		ToxTree: Skin irritation

Simple building of predictive toxicology applications based on well-established methods and databases



Applications and Models based on OpenTox Web Services will be applied holistically to drug design libraries to help guide decisions on chemistry directions and classes...

Predictive toxicology model building

A screenshot of a Mozilla Firefox browser window titled "Models - Mozilla Firefox". The address bar shows the URL "http://apps.ideaconsult.net:8180/ToxPredict/user/4006/f23b7d7c-ffec-5b68-15e8-20a77ef11a/clean3". The main content area displays the "ToxPredict" demo application. On the left, there's a sidebar with two steps: "Step 1: Search Select structure(s)" and "Step 2: Verify structure Verify structure". Below this is a table with columns "Endpoint" and "Model". The table lists various endpoints and their corresponding models, such as "Carcinogenicity" using "OpenTox model created by TUM's KNNregression machine learning web service." and "Dissociation constant (pKa)" using "ToxTree: pKa". A large map of Europe is shown in the center, with several green circular markers placed on it, representing data points. At the bottom left of the application window, there's a "Done" button.

Endpoint	Model
Carcinogenicity	OpenTox model created by TUM's KNNregression machine learning web service.
Dissociation constant (pKa)	ToxTree: pKa
Endpoints	ToxTree: Structure A the in vivo micronucleus rodents
Endpoints	ToxTree: Michaelis constants
Eye irritation/corrosion	ToxTree: Eye irritation
Human health effects	ToxTree: Extended Cramer rule of five
Human health effects	ToxTree: ILSI/Kroes tree for TTC
Skin irritation /corrosion	ToxTree: Skin irritation

Simple building blocks,
application modules,
methods and services

*Distributed applications,
integrating wide range of data,
models, prediction methods*

Predictive toxicology model building

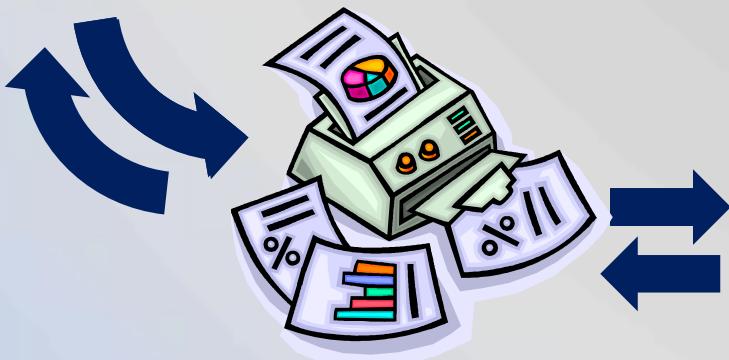
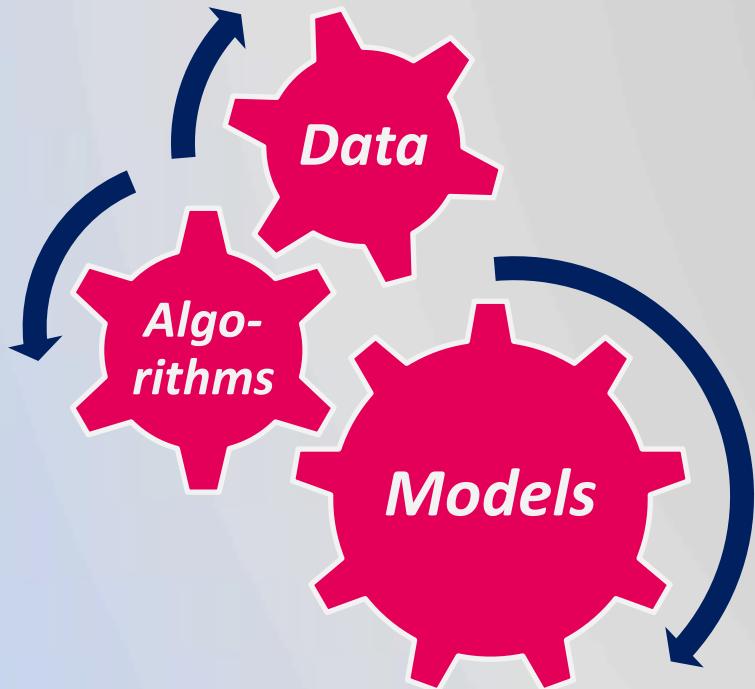
A screenshot showing two windows side-by-side. On the left is the "ToxPredict" demo application, which has a sidebar with steps "Step 1: Search" and "Step 2: Verify structure". Below this is a table of endpoints and models, including "Carcinogenicity" (TUM's KNN regression model), "Dissociation constant (pKa)" (ToxTree), and "Human health effects" (ToxTree). On the right is the "Taverna Workbench 2.1.0" interface, displaying a complex workflow diagram with various nodes like "ask_username", "choose_trainset", "upload_trainset", "wait_for_trainset", "calculate_descriptors", "get_features_of_trainset", "wait_for_testset", "choose_prediction_feature", "learn_model", "wait_for_learned_model", "apply_model_to_testset", and "wait_for_prediction".

Simple building blocks for distributed applications across a wide range of methods and models

Distributed applications across a wide range of methods and models

Integration into workflow systems for computational biology

Predictive toxicology model building



ELN

	Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
<chem>CN1C=CC=C1</chem>	-	-	-	○△	○△	○△

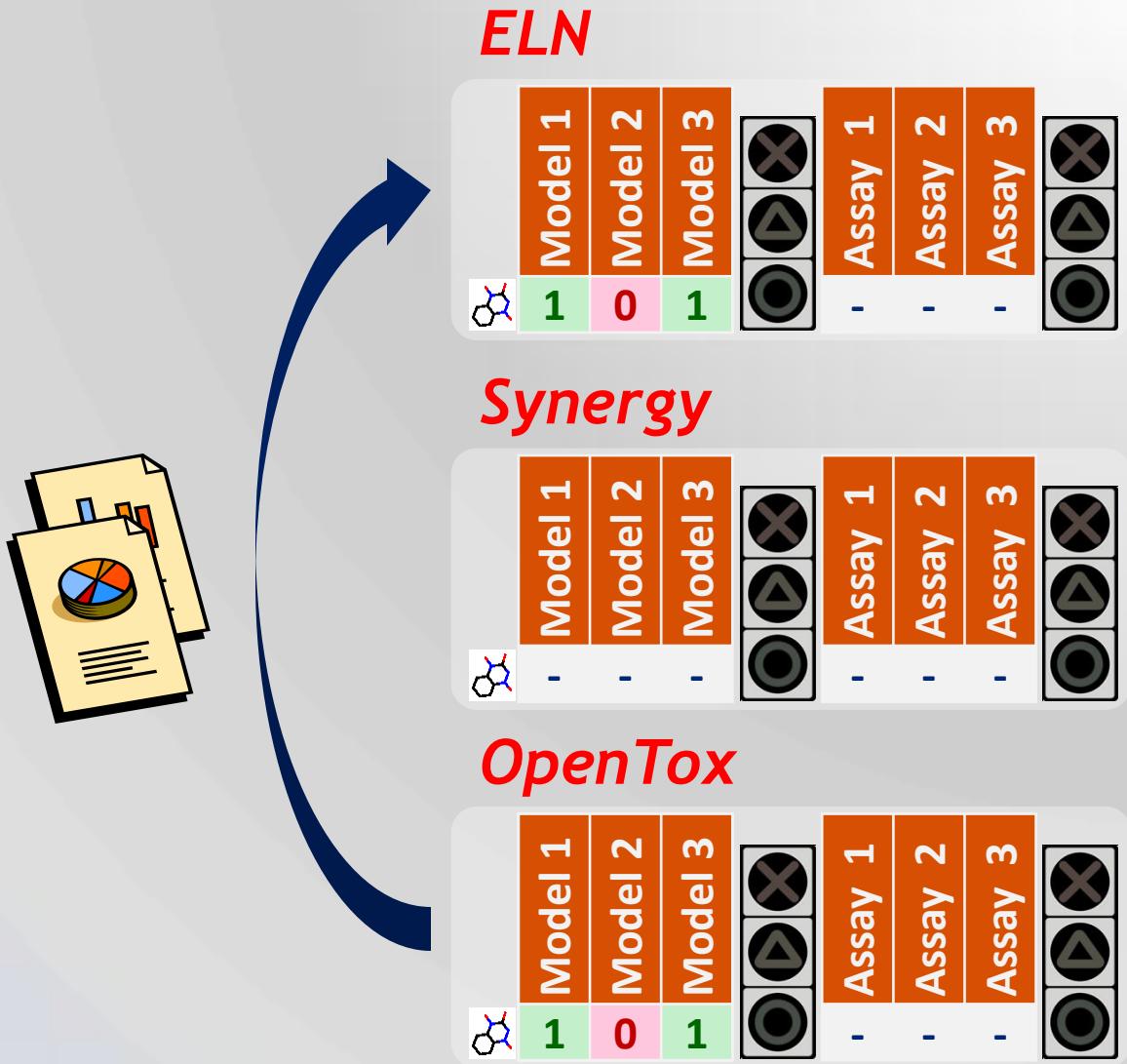
Synergy

	Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
<chem>CN1C=CC=C1</chem>	-	-	-	○△	○△	○△

OpenTox

	Model 1	Model 2	Model 3	Assay 1	Assay 2	Assay 3
<chem>CN1C=CC=C1</chem>	1	0	1	○△	○△	○△

Predictive toxicology model building





Current Realities (we can impact on):

- 1) Nearly half of the parents of these children in Namibia will die of AIDS
- 2) These children will be infected with malaria
- 3) They will not receive medical care or drugs for either of these diseases

If you would like to get involved in our Scientists Against Malaria work,
please contact us!

barry.hardy -(at)- douglasconnect.com

www.scientistsagainstmalaria.net