



Barcelona Innovation workshop: NanoBiotechnology & IT for Health

The Tropical Disease Initiative

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Barcelona, 6th of October, 2010



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Comparative Genomics
Dr. Hernán Dopazo



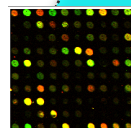
>protein.kinase



Pupa Suite

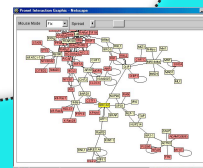
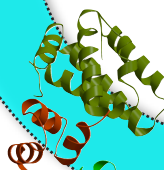
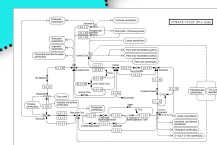


Functional Genomics
Dr. Joaquín Dopazo



GEPAS

**From genotype
to phenotype.**



BABELOMICS

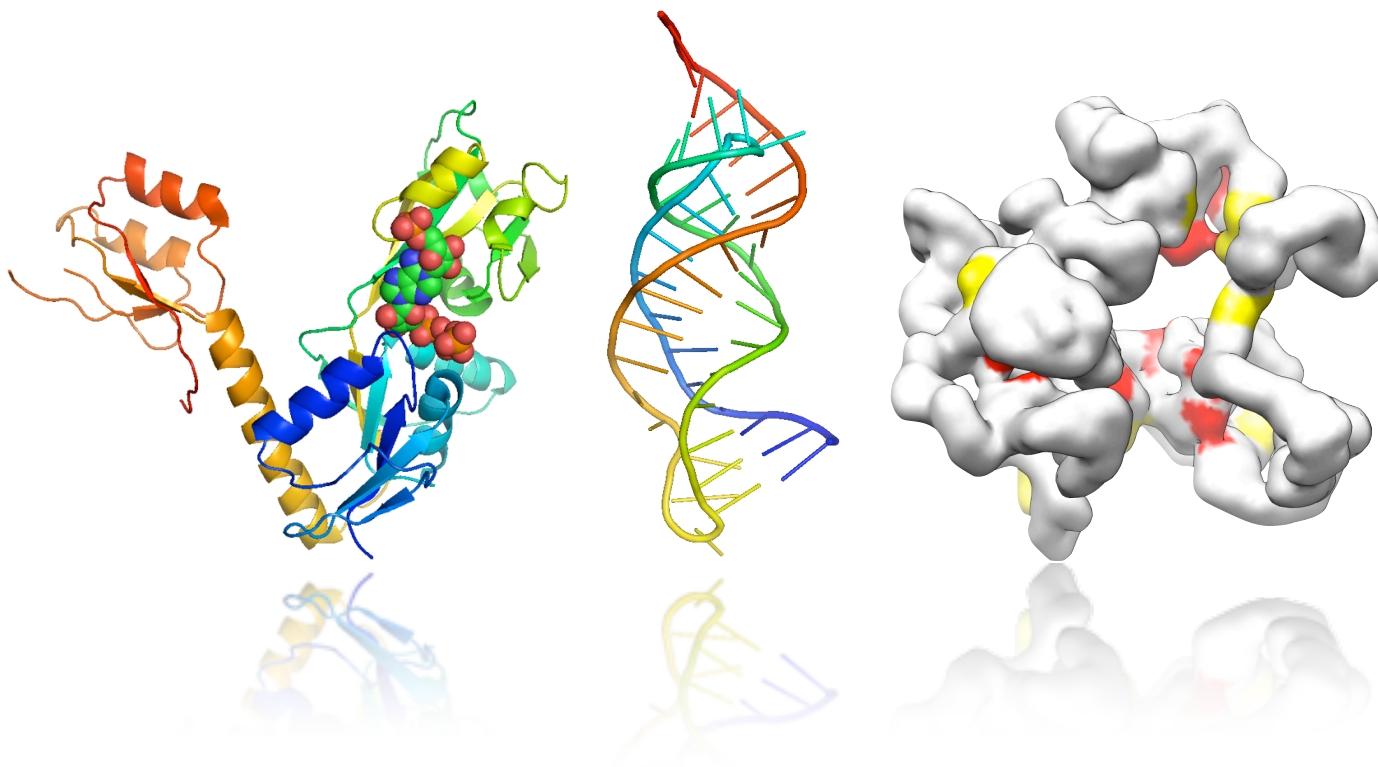


Structural Genomics
Dr. Marc A. Martí-Renom

DBAli v2.0
Home

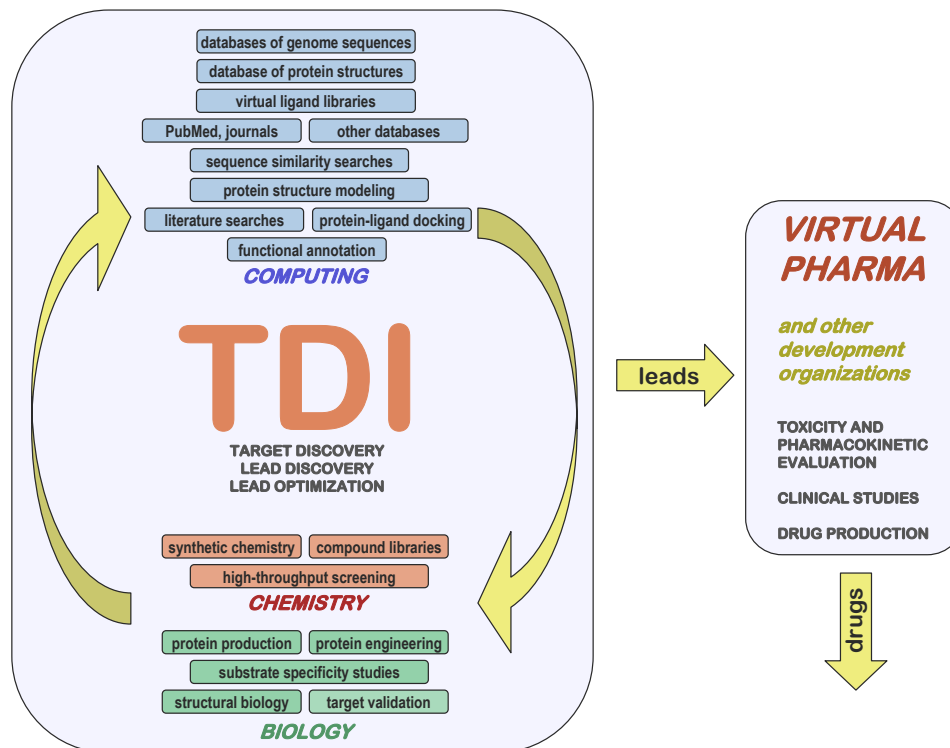
Structural Genomics Unit

Bioinformatics & Genomics Department, CIPF



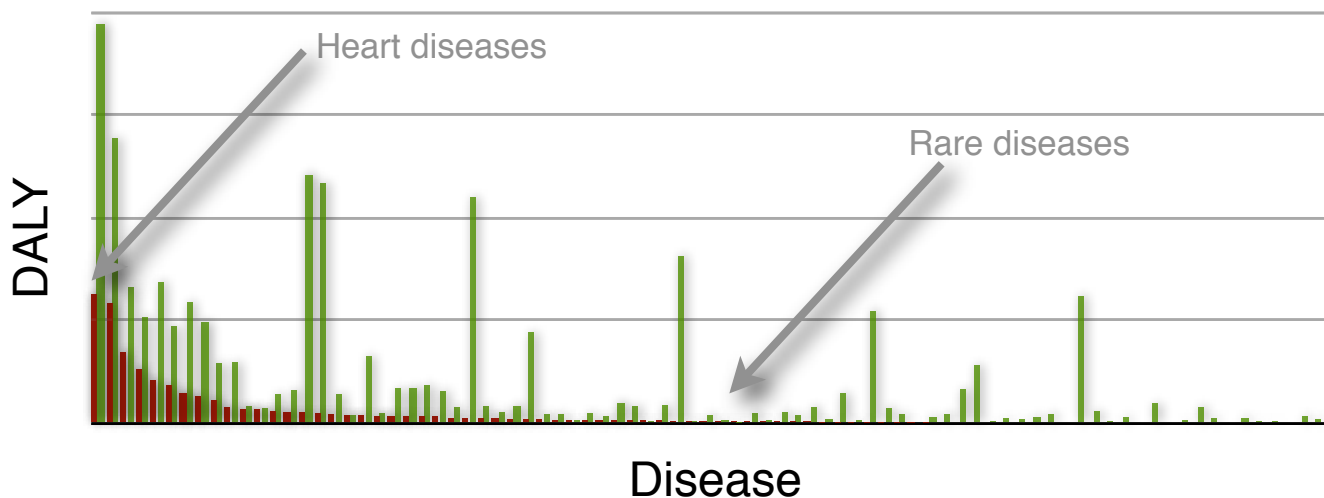
The Tropical Disease Initiative (TDI)

<http://tropicaldisease.org>



“Unprofitable” Diseases and Global DALY (in 1000’s)

- DALY Burden Per Disease in Developed Countries
- DALY Burden Per Disease in Developing Countries

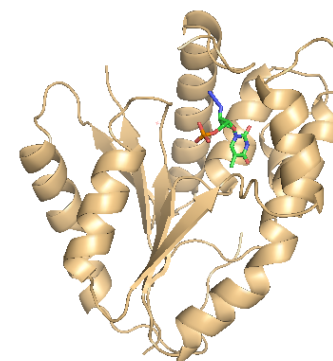


Disease data taken from WHO, *World Health Report 2004*
DALY - Disability adjusted life years

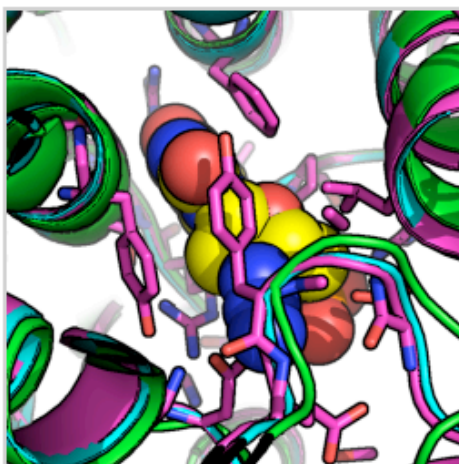
Malaria*	46,486
Tetanus	7,074
Lymphatic filariasis*	5,777
Syphilis	4,200
Trachoma	2,329
Leishmaniasis*	2,090
Ascariasis	1,817
Schistosomiasis*	1,702
Trypanosomiasis*	1,525
Trichuriasis	1,006
Japanese encephalitis	709
Chagas Disease*	667
Dengue*	616
Onchocerciasis*	484
Leprosy*	199
Diphtheria	185
Poliomyelitis	151
Hookworm disease	59

P. falciparum thymidylate kinase + zidovudine

Template 3tmkA a yeast thymidylate kinase.



PDB	IO	Template	IO	Model	IO	Ligand	Exact	SupStr	SubStr	Similar
2tmkB	100.00/100.00	3tmkA	41.00/1.49	PFL2465c.2.pdb	82.61/100.00	ATM		DB00495		DB00495



[DB00495](#) Zidovudine

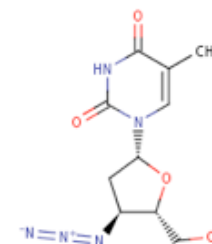
Small Molecule; Approved

Drug categories:

Anti-HIV Agents
Antimetabolites
Nucleoside and Nucleotide Reverse Transcriptase Inhibitors

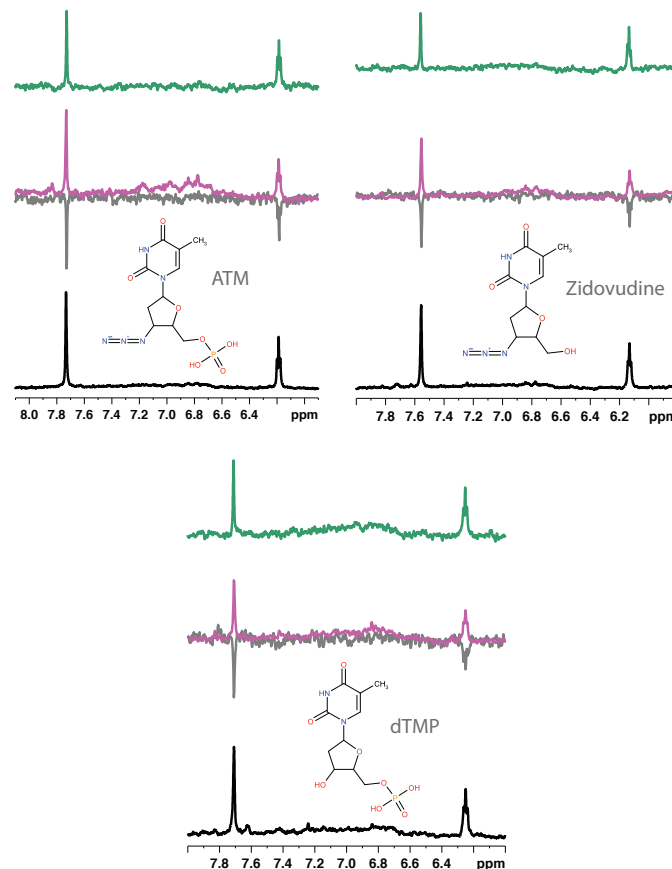
Drug indication:

For the treatment of human immunovirus (HIV) infections.



P. falciparum thymidylate kinase + zidovudine


NMR Water-LOGSY and STD experiments



Experimental NRM data from Pineda-Lucena Lab (CIPF)

TDI's kernel

<http://tropicaldisease.org/kernel>



the Tropical Disease Initiative

an open source drug discovery project

You are browsing version 1.0 (2008/05/01) of the TDI Kernel.

Posted on 05.07.08 to **Target**. Grab the **feed**. No comments yet. **Add your thoughts** or **trackback** from your own site. [Edit this entry.](#)

Putative histone deacetylase, predicted to bind 1 ligands [SHH]

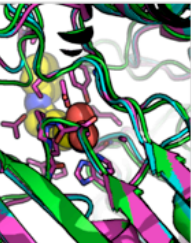
UniPort id: **Q9GU59** [*C. parvum*]

Target keywords: ; Anticarcinogenic Agents; Antineoplastic Agents; Transcription; Chromatin regulator; Anti-Inflammatory Agents, Non-Steroidal; Enzyme Inhibitors; Q9GU59; Transcription regulation.; Nucleus

Do you consider this target suitable for drug discovery: ★★★★★ (No Ratings Yet)

Binding site prediction to approved drugs (need help reading this page?):

PDB	EC	Template	MS	Model	Ligand	Exact	SupStr	SubStr	Similar
1c39A	83.33/90.00	1t64A	37.00/1.47	cpd6_1380_1.pdb	90.91/100.00	SHH	DB02546	DB02546	DB02546



DB02546 Vorinostat

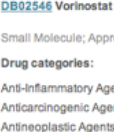
Small Molecule; Approved; Investigational

Drug categories:

Anti-Inflammatory Agents, Non-Steroidal
Anticarcinogenic Agents
Antineoplastic Agents
Enzyme Inhibitors

Drug Indication:


For the treatment of cutaneous manifestations in patients with cutaneous T-cell lymphoma who have progressive, persistent or recurrent disease on or following two systemic therapies.



Shown ligand [SHH](#)

OCTANEDIOICACIDHYDROXYAMIDEPHENYLAMIDE

expanded from [1c39A](#) to template [1t64A](#) used for building a 3D model of [cpd6_1380_1.pdb](#). Download the coordinates [data/Q9GU59/Q9GU59.SHH.952.pdb](#)



Kernel 1.0

SEARCH KERNEL

Q Search...

Advanced Search

Browse the kernel

Download Q9GU59

Login / Register

Batch downloads

Help

Methods

Highest rated target:

- A7UD81 (5 out of 5)

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A Kernel for Open Source Drug Discovery in Tropical Diseases

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Abstract

Background: Conventional patent-based drug development incentives work badly for the developing world, where commercial markets are usually small to non-existent. For this reason, the past decade has seen extensive experimentation with alternative R&D institutions ranging from private-public partnerships to development prizes. Despite extensive discussion, however, one of the most promising avenues—open source drug discovery—has remained elusive. We argue that the stumbling block has been the absence of a critical mass of preexisting work that volunteers can improve through a series of granular contributions. Historically, open source software collaborations have almost never succeeded without such “seeds.”

Methodology/Principal Findings: Here, we use a computational pipeline for: (i) comparative structure modeling of target proteins, (ii) predicting the localization of ligand binding sites on their surfaces, and (iii) assessing the similarity of the predicted ligands to known drugs. Our kernel currently contains 143 and 297 protein targets from ten pathogen genomes that are predicted to bind a known drug or a molecule similar to a known drug, respectively. The kernel provides a source of potential

Conclusions/Significance: The TDI kernel, which is being offered under the Creative Commons attribution share-alike license for free and unrestricted use, can be accessed on the World Wide Web at <http://www.tropicaldisease.org>. We hope that the kernel will facilitate collaborative efforts towards the discovery of new drugs against parasites that cause tropical diseases.

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Competing interests: The authors have declared that no competing interests exist.

Introduction

There is a lack of high-quality protein drug targets and drug leads for neglected diseases [1,2]. Fortunately, many genomes of organisms that cause tropical diseases have already been sequenced and published. Therefore, we are now in a position to leverage this

information by identifying potential protein targets for drug discovery. Atomic-resolution structures can facilitate this task. In the absence of an experimentally determined structure, comparative modeling can provide useful models for sequences that are detectably related to known protein structures [3,4]. Approximately half of known protein sequences contain domains that can be currently predicted by comparative modeling [5,6]. This coverage

 www.plosone.org

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