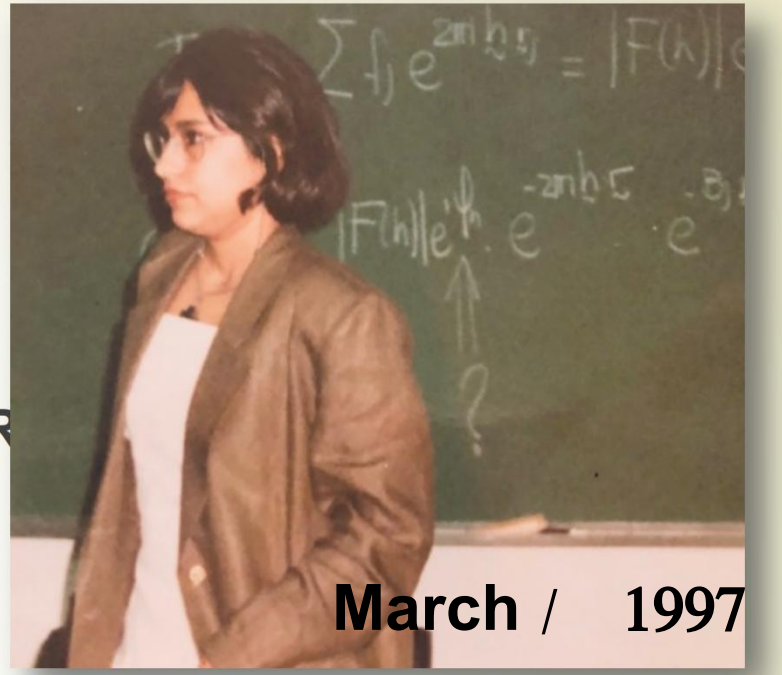
Glaucius Oliva – 60 anos

Cris/Cristininha/Cristy Nonato

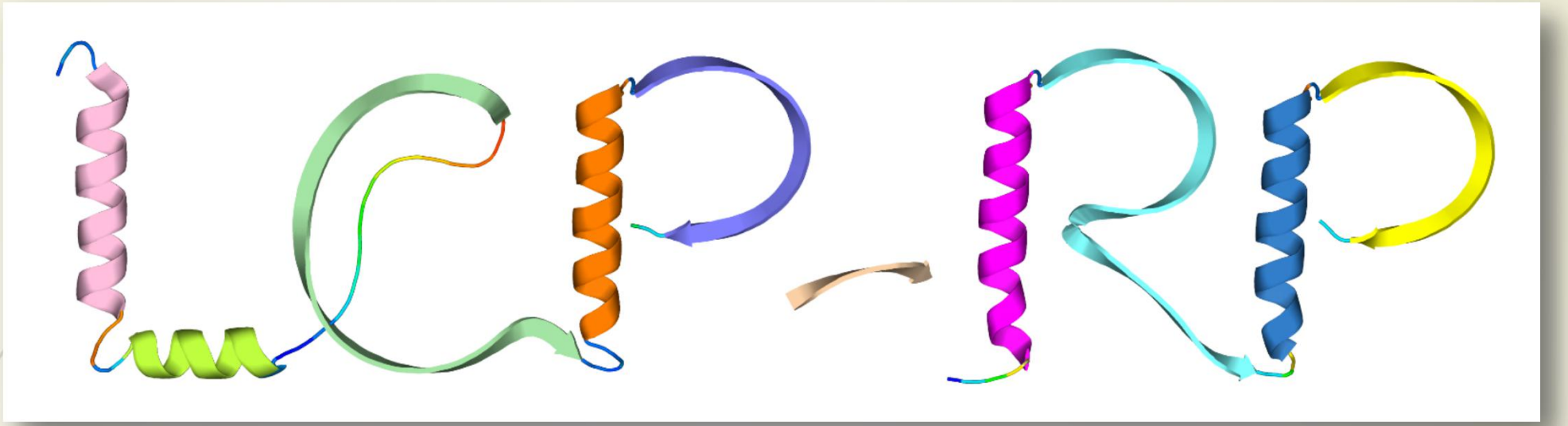
- “FAMILIES ARE LIKE BRANCHES ON A TREE. WE GROW IN DIFFERENT DIRECTIONS YET OUR ROOTS REMAIN AS ONE”

TIMELINE

- (1997 – 1999) POS/ DOC @ IFSC/ USP – GLAUCIUS OLIVA
- (1999 – 2002) POS/ DOC @ CORNELL UNIVERSITY – JON CLAR
- (2002 – 2006) YOUNG RESEARCHER – FAPESP @ FCFRP – USP
- (2005) PEDRO WAS BORN
- (2006 – 2012) ASSISTANT PROFESSOR @ FCFRP – USP
- (2007) RAFAELA WAS BORN
- (2012 – NOWADAYS) ASSOCIATE PROFESSOR @ FCFRP – USP
- (2017 – 2018) SABATICAL AT THE BROAD INSTITUTE AT MIT AND HARVARD – STUART SCHREIBER
- (2018 – NOWADAYS) VICE/ COORDINATOR OF PPGCF/ FCFRP/ USP
- (2018 – NOWADAYS) VICE/ PRESIDENT OF THE BRAZILIAN CRYSTALLOGRAPHIC ASSOCIATION



March / 1997



LABORATÓRIO DE CRISTALOGRAFIA DE PROTEÍNAS FACULDADE DE CIÊNCIAS FARMACÊUTICAS DE RIBEIRÃO PRETO UNIVERSIDADE DE SÃO PAULO

- STRUCTURAL BIOLOGY APPLIED TO MEDICINAL CHEMISTRY

SUPERVISONS AND GRANTS

CONCLUDED

- 20 Undergrads
- 8 Master students
- 7 PhD students
- 6 pos/ docs

CURRENTLY

- 4 undergrads
- 2 master students
- 1 PhD student
- 1 pos/ doc

CONCLUDED

- 9 research projects
- 24 Scholarships
- 5 Scholarships abroad

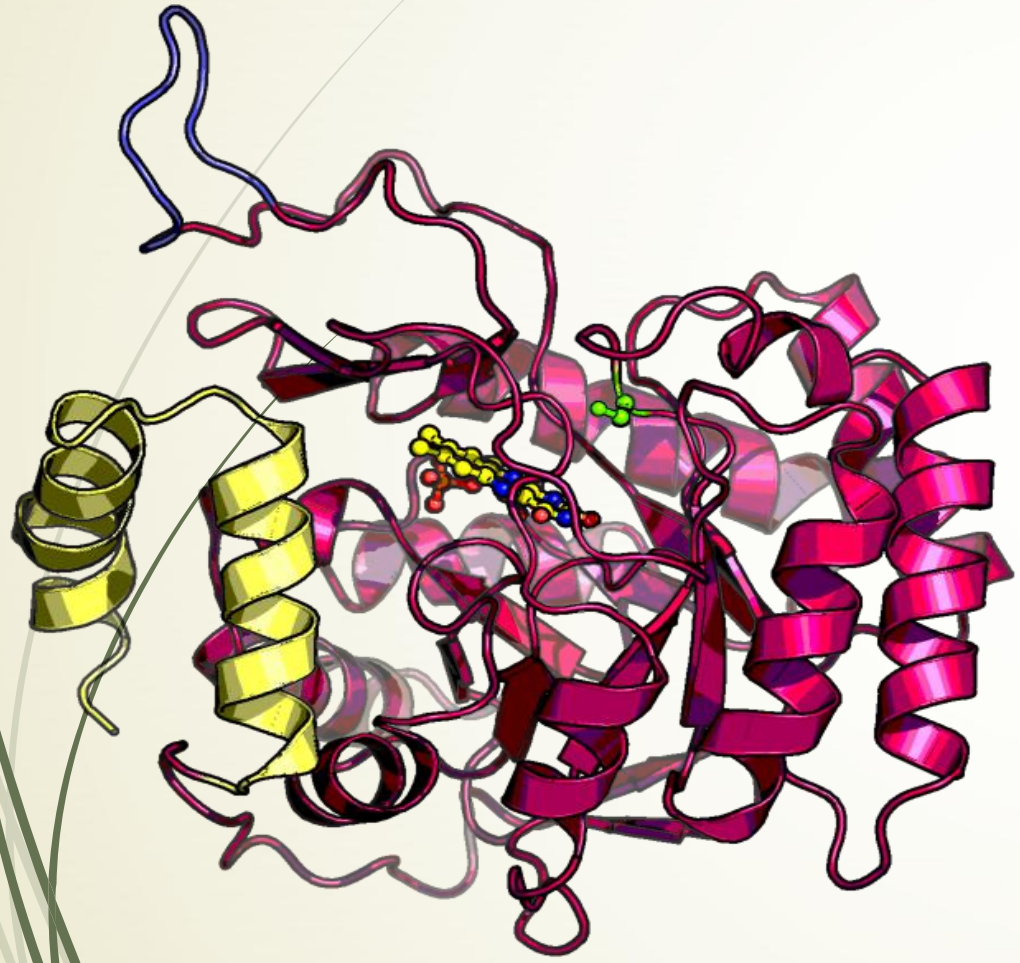
CURRENTLY

- 2 Research projects – Regular FAPESP/ Universal (CNPq)
- undergrads
- 5 Scholarships

MAIN PROJECTS

- DIHYDROOROTATE DEHYDROGENASE: **Human**, ***Plasmodium falcipurum***, ***Schistosoma mansoni***, ***Trypanosoma cruzi***, ***Leishmania major***, ***Leishmania braziliensis***, ***Pseudomonas aeroginosa***;
- FUMARATE HYDRATASE: **Human**, ***Schistosoma mansoni***, ***Trypanosoma cruzi***, ***Leishmania major***;
- NITROREDUCTASES: ***Trypanosoma cruzi***, ***Leishmania major***, ***Trypanosoma brucei***;
- HUMAN GALECTINS: ***Galectin 4***, ***galectin 12*** **and** ***galectin 1***;
- HUMAN PRION PROTEIN

SmDHODH – ATOVAQUONE REPORPUSING



Biochimie 158 (2019) 180–190

Contents lists available at ScienceDirect

Biochimie

journal homepage: www.elsevier.com/locate/biochi

Research paper

Structural basis for the design of selective inhibitors for *Schistosoma mansoni* dihydroorotate dehydrogenase

M. Cristina Nonato [a, *], Ricardo A.P. de Pádua [a], Juliana S. David [a], Renata A.G. Reis [a], Giovani P. Tomaleri [a], Humberto D'Muniz Pereira [b], Felipe A. Calil [a]

[a] Laboratório de Cristalografia de Proteínas, Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, 14040-903, Brazil
[b] Centro de Biotecnologia Molecular Estrutural, Instituto de Física de São Carlos, Universidade de São Paulo, São Carlos, SP, 13560-970, Brazil

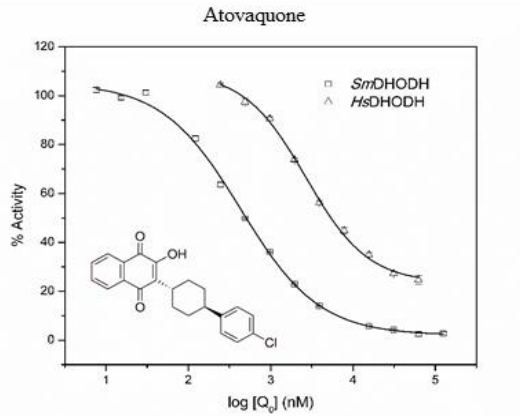


Table 1
Inhibitory potential (IC50) in nM for the compounds tested against *Hs*DHODH and *Sm*DHODH and their selectivity index. Error represents standard error of the fit. Single experiment in triplicate.

IC50 (nM)				
Enzyme	Atovaquone	Brequinar	DSM265	Teriflunomide
*Hs*DHODH	2600 ± 200	37 ± 2	7000 ± 1000	320 ± 40
*Sm*DHODH	430 ± 20	20000 ± 1000	21000 ± 1000	50000 ± 2000
Selectivity index	6 (*Sm*DHODH)	540 (*Hs*DHODH)	3 (*Hs*DHODH)	156 (*Hs*DHODH)

Table 11. *In vitro* effects of Compounds 2, 6i and 17 against 49-day-old adult *Schistosoma mansoni*.

Group	Incubation period (h)	Sex	Dead worms (%)[a]	Motor activity (%)[a]		Worms with tegumental alterations (%)[a]	
				Normal	Altered	Partial	Extensive
Control[b]	24	Male	0	100	0	0	0
		Female	0	100	0	0	0
	48	Male	0	100	0	0	0
		Female	0	100	0	0	0
	72	Male	0	100	0	0	0
		Female	0	100	0	0	0
	96	Male	0	100	0	0	0
		Female	0	100	0	0	0
PZQ[c]	24	Male	100	0	0	0	100
		Female	100	0	0	0	100
	48	Male	100	0	0	0	100
		Female	100	0	0	0	100
	72	Male	100	0	0	0	100
		Female	100	0	0	0	100
	96	Male	100	0	0	0	100
		Female	100	0	0	0	100
Compound 2							
50 µM	24	Male	17	17	66	17	50
		Female	0	17	83	17	0
	48	Male	17	17	66	50	50
		Female	17	0	83	33	66
	72	Male	17	0	83	0	100
		Female	66	0	33	0	100
	96	Male	66	0	33	0	100
		Female	66	0	33	0	100
Compound 6i							
5 µM	24	Male	0	100	0	0	0
		Female	0	83	17	0	0

ATOVAQUONE

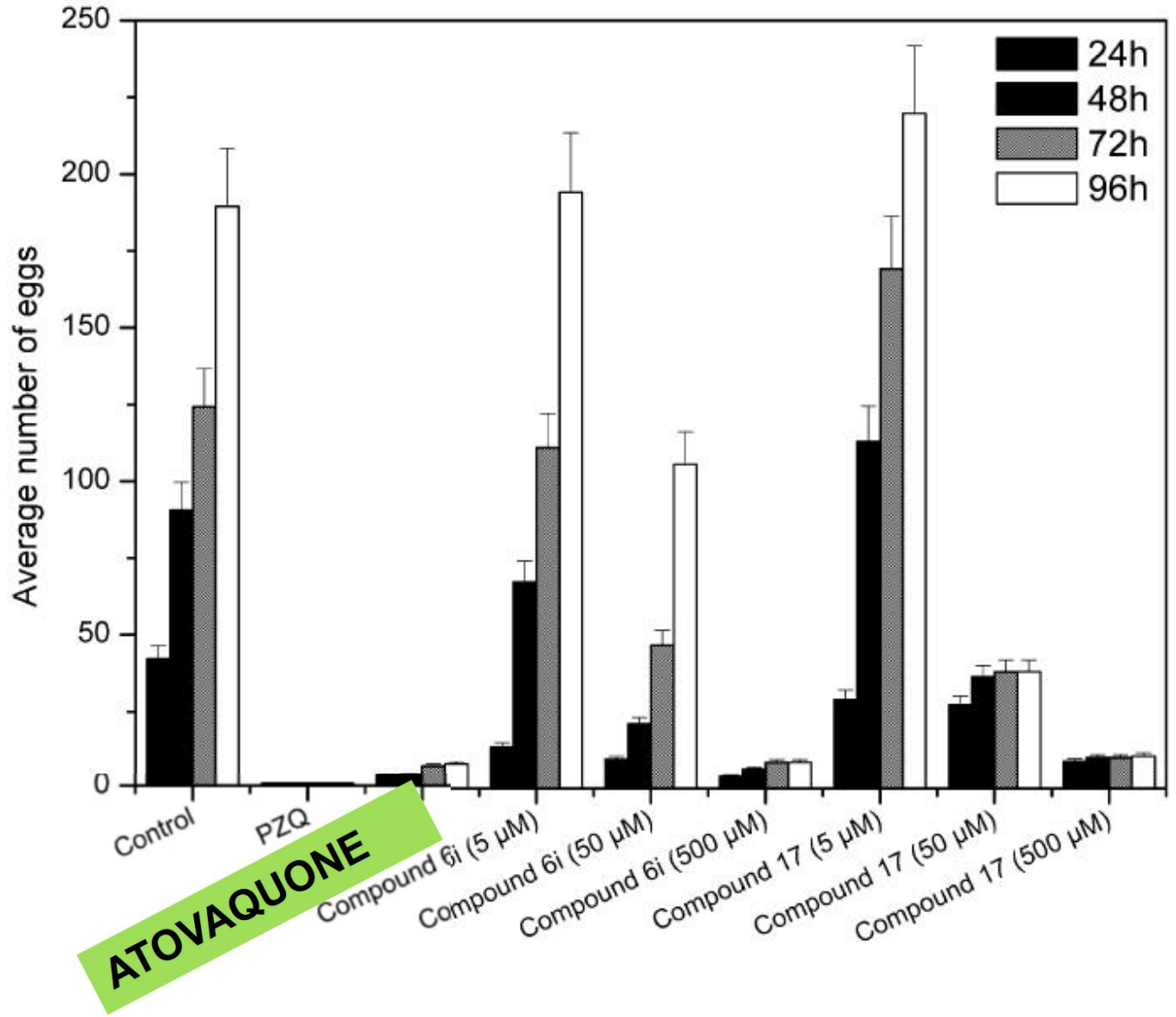


Figure 16. *In vitro* effect of Compounds 2, 6i and 17 on *Schistosoma mansoni* oviposition. Adult worm couples were incubated with Compounds 2, 6i and 17, and at the indicated time periods, the cumulative number of eggs per worm couple was assessed and scored using an inverted microscope. Values are means ± SD (bars) for six worm couples.

REPOSITIONING OF ANTIMALARIAL DRUGS FOR THE TREATMENT OF SCHISTOSOMIASIS BASED ON SELECTIVE INHIBITION OF *Sm*DHODH

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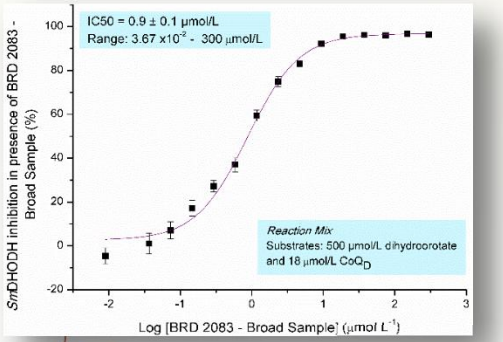
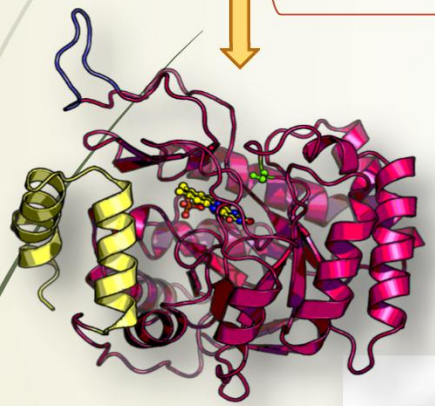
MMV Medicines for Malaria Venture





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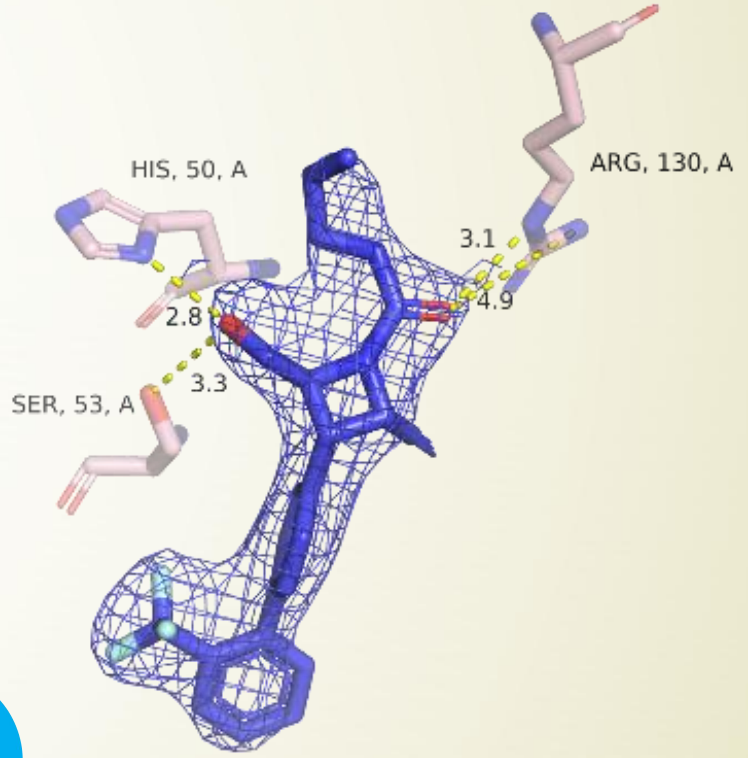

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Trypanosomatidae DHODHs

Biochimie 94 (2012) 1739–1748

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Research paper

Crystal structure of dihydroorotate dehydrogenase from *Leishmania major*

Artur T. Cordeiro [1], Patricia R. Feliciano, Matheus P. Pinheiro, M. Cristina Nonato*

Laboratório de Cristalografia de Proteínas, Departamento de Física e Química, Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Av. Café S/N, Monte Alegre, Ribeirão Preto 14040-903, S.P, Brazil

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Biochemical and Biophysical Research Communications 369 (2008) 812–817

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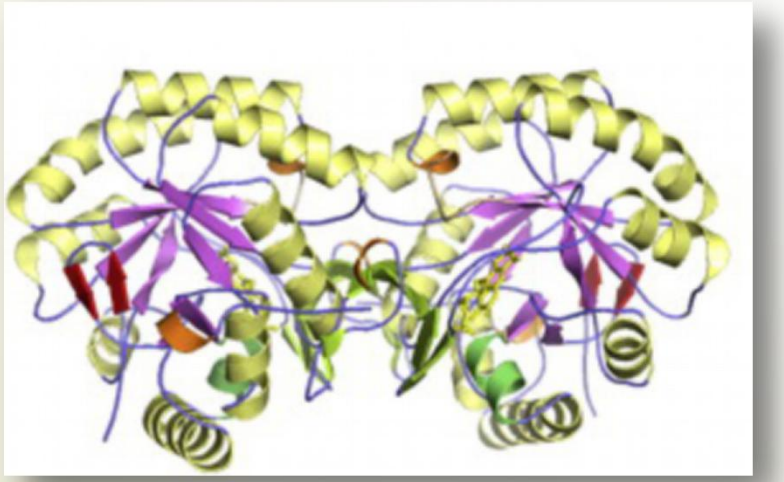
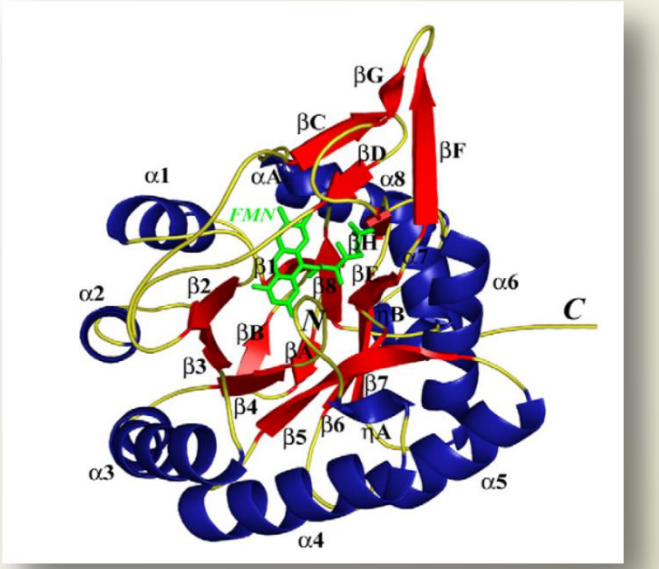
Crystal structure of *Trypanosoma cruzi* dihydroorotate dehydrogenase from Y strain

Matheus P. Pinheiro [a], Jorge Iulek [b], M. Cristina Nonato [a,*]

[a] *Laboratório de Cristalografia de Proteínas, Departamento de Física e Química, Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto S.P. 14040-903, Brazil*

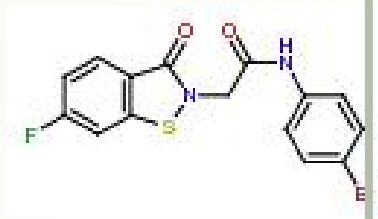
[b] *Setor de Ciências Exatas e Naturais, Departamento de Química, Universidade Estadual de Ponta Grossa, Ponta Grossa P.R. 84030-000, Brazil*



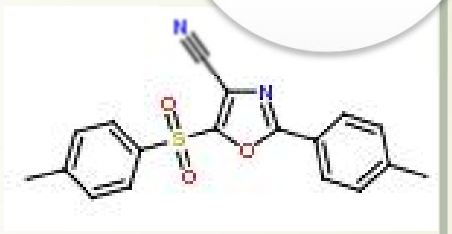


INHIBITOR SEARCH FOR TRYPDHODHS BY HTS-HIGHTHROUPUT SCREENING

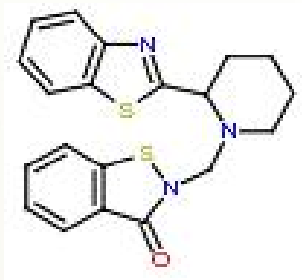
Small diversity (EasySet) Potency assay



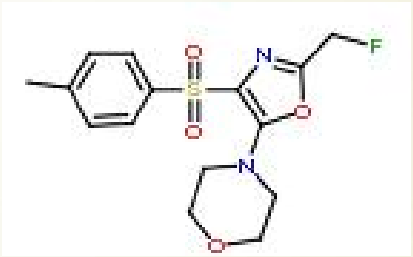
$IC_{50} = 0.257\ \mu M$



$IC_{50} = 1.3\ \mu M$

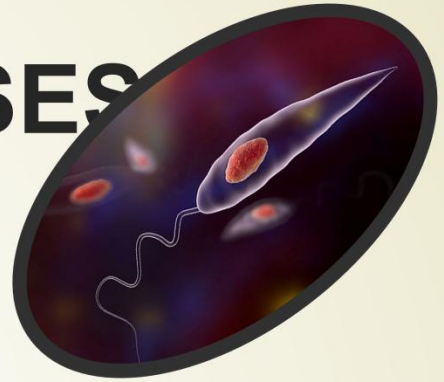


$IC_{50} = 1.1\ \mu M$



$IC_{50} = 2.2\ \mu M$

TRYPANOSOMATIDADE FUMARASES

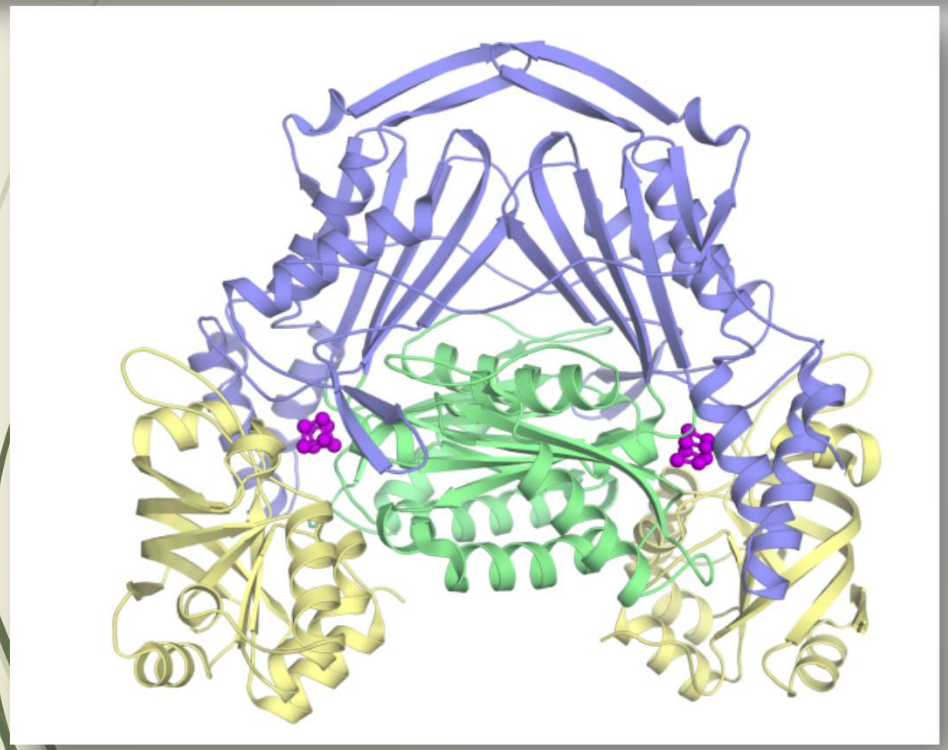


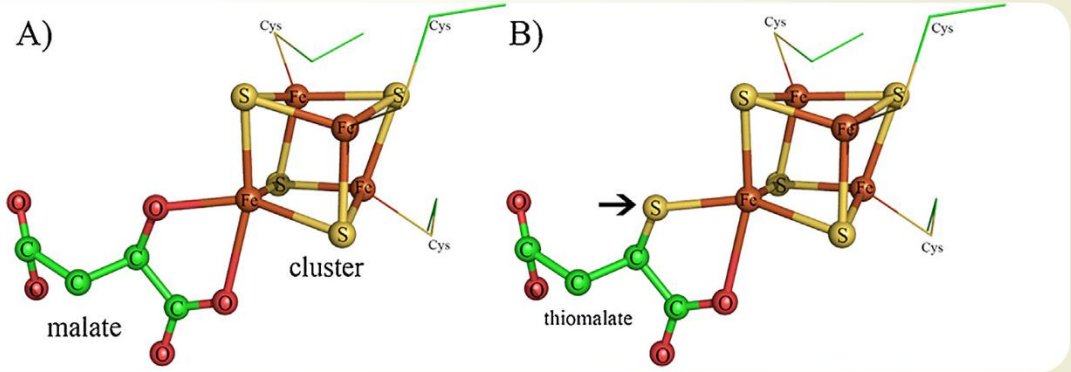
PNAS

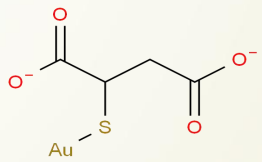
Crystal structure of an Fe-S cluster-containing fumarate hydratase enzyme from *Leishmania major* reveals a unique protein fold

Patricia R. Feliciano[a,b,c], Catherine L. Drennan[b,c,d,1], and M. Cristina Nonato[a,1]

[a]Laboratório de Cristalografia de Proteínas, Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, São Paulo 14040-903, Brazil; [b]Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA 02139; [c]Department of Biology, Massachusetts Institute of Technology, Cambridge, MA 02139; and [d]Howard Hughes Medical Institute, Massachusetts Institute of Technology, Cambridge, MA 02139







- **Treatment of arthritis**
- **Low toxicity in human**

CUTANEOUS LEISHMANIASIS
CELL CULTURE AND IN VIVO ASSAYS

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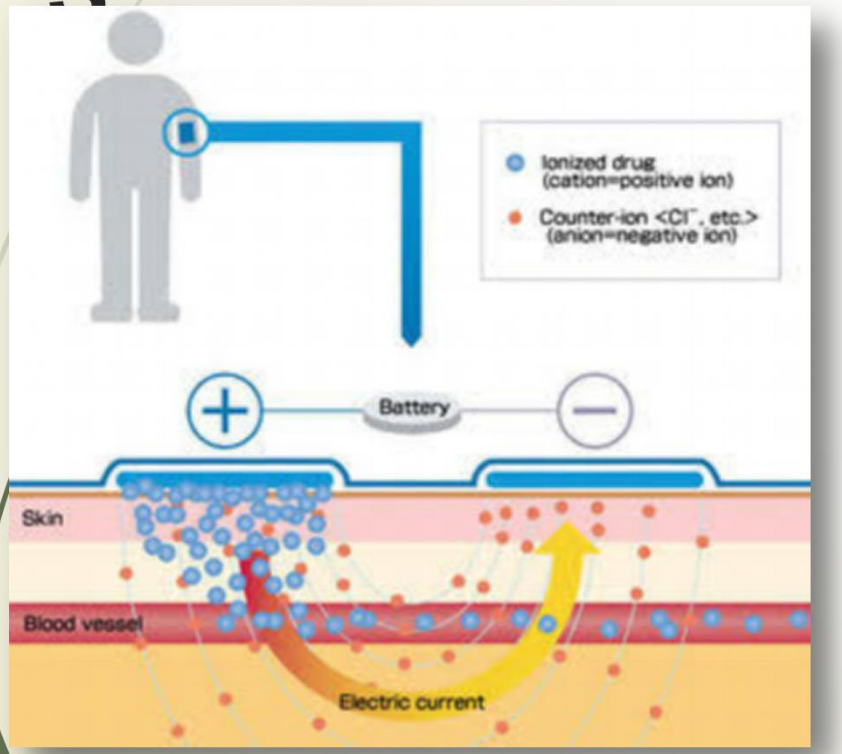

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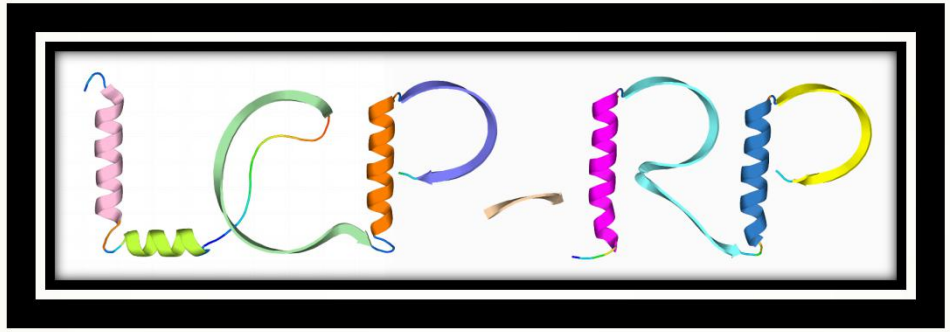

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30 YEARS OR SO OF PROTEIN CRYSTALLOGRAPHY IN BRAZIL: The green olive BR800 co


ENTREVISTA Glaucius Oliva
Estruturas complexas
Autodeclarado domador de moléculas, físico aliá pesquisa científica à gestão administrativa
Maria Guimarães / RETRATO Léo Ramos Chaves
A paixão de Glaucius Oliva por domar proteínas para o desenvolvimento de fármacos nasceu na graduação, de um desafio de engenharia: descobrir como unir dezenas de pecinhas de plástico na forma de uma molécula de mioglobina. Foram meses de trabalho para calcular a posição e a orientação exatas de cada átomo e posicioná-los, todos, furando as partes encaixando-as em arames cortados no comprimento preciso. A partir daí, o estudante de engenharia elétrica sabia o que queria fazer.
Só não sabia que esse interesse científico exigiria também que se dedicasse desde o início da carreira a congregar especialistas em áreas diferentes para trabalhar em conjunto e a convencer agências de fomento e instituições de pesquisa a financiá-los. Glaucius Oliva tornou-se então um destacado gestor, tanto em grandes projetos interdisciplinares como à frente do Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), que presidiu entre 2011 e 2015. Professor no Instituto de Física de São Carlos da Universidade de São Paulo (USP), atualmente dirige o Centro de Pesquisa e Inovação em Biodiversidade e Fármacos (CIBFar), um dos Centros de Pesquisa, Inovação e Difusão (Cepid) financiados pela FAPESP.
Oliva concedeu esta entrevista em sua sala decorada pelo modelo molecular montado há cerca de 40 anos (com ele na foto ao lado) em um instituto praticamente vazio às vésperas do Natal. Seu laboratório estava ativo.
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