

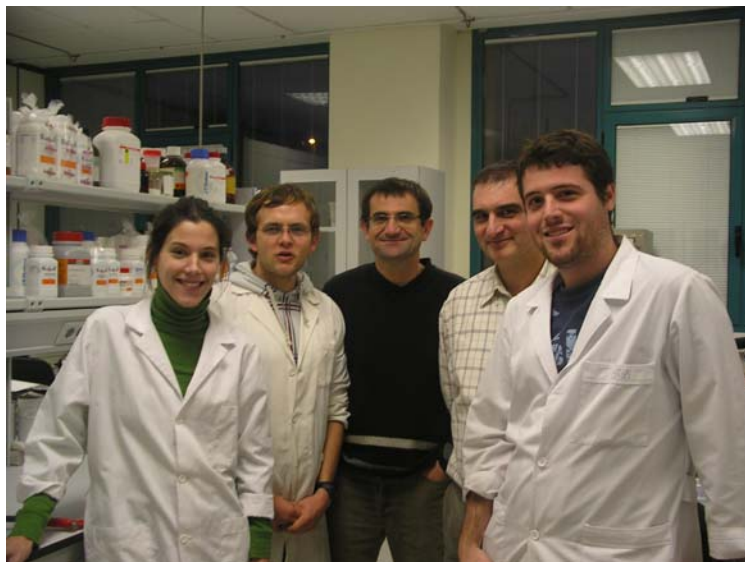


Cysteine-proteases inhibitors for Infectious Diseases

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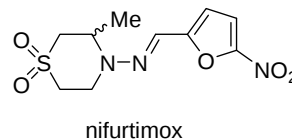
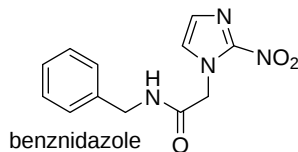


- Organic synthesis: synthetic methodology, synthesis of natural products
- Medicinal Chemistry: design and synthesis of cysteine proteases inhibitors



Chagas' disease

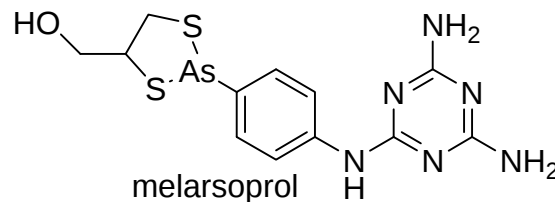
- 16 -18 millions in Latin-America, 50.000 deaths/yr., 90 millions under risk.
- Caused by protozoa *Trypanosoma cruzi*.
- The transmitter agent is *Triatoma* beetle.
- Cardiopathies, digestive lesions and neurological disorders, finally heart attack.
- The used drugs (benznidazole and nifurtimox) low efficient and secondary effects.





Sleeping sickness

- Half a million of people in Subsaharian Africa, 70 millions under risk.
- Caused by protozoa *Trypanosoma brucei*.
- The transmitter agent is tse-tse fly.
- Immunodeficiency, anemia and cardiac and endocrine disorders, and finally coma and death.
- The only drug (melarsoprol) is highly toxic.





Malaria

- Almost 40% of world population affected
- More than 3.000 millions under risk
- Caused by protozoa *Plasmodium falciparum*
- The transmitter agent is *Anopheles* mosquito
- The used drugs chloroquine and mefloquine show side effects and there is no total protection
- In Spain: 450 cases/yr. since 2000

TARGETS

Cysteine proteases from papain superfamily

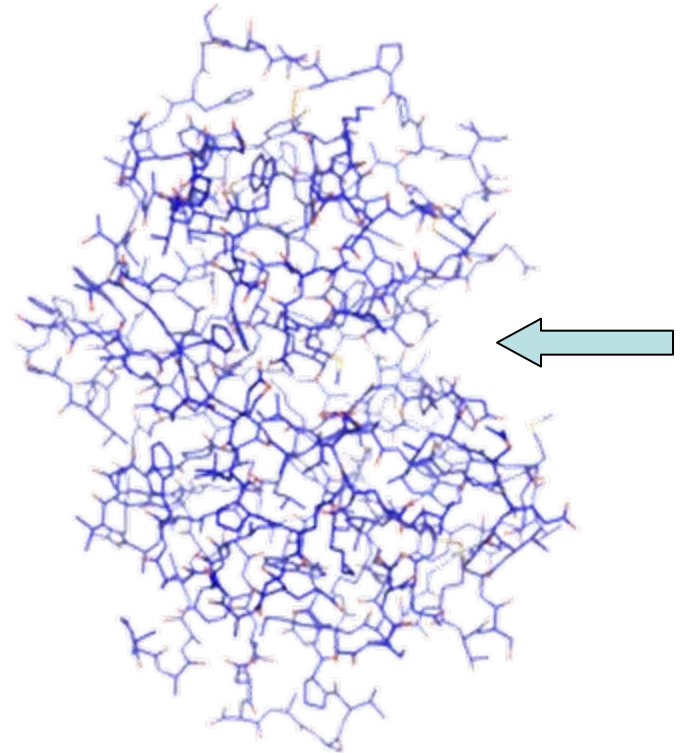
Cruzain (*Trypanosoma cruzi*)
(Chagas)

Rhodesain (*Trypanosoma brucei*)
(African trypanosomiasis)

Falcipain (*Plasmodium falciparum*)
(Malaria)

EhCP1 (*Entamoeba histolytica*)
(Amebiasis)

CP2 (*Giardia lamblia*)
(Giardiasis)



Highly potent irreversible cysteine proteases inhibitors

IC_{50} (nM)

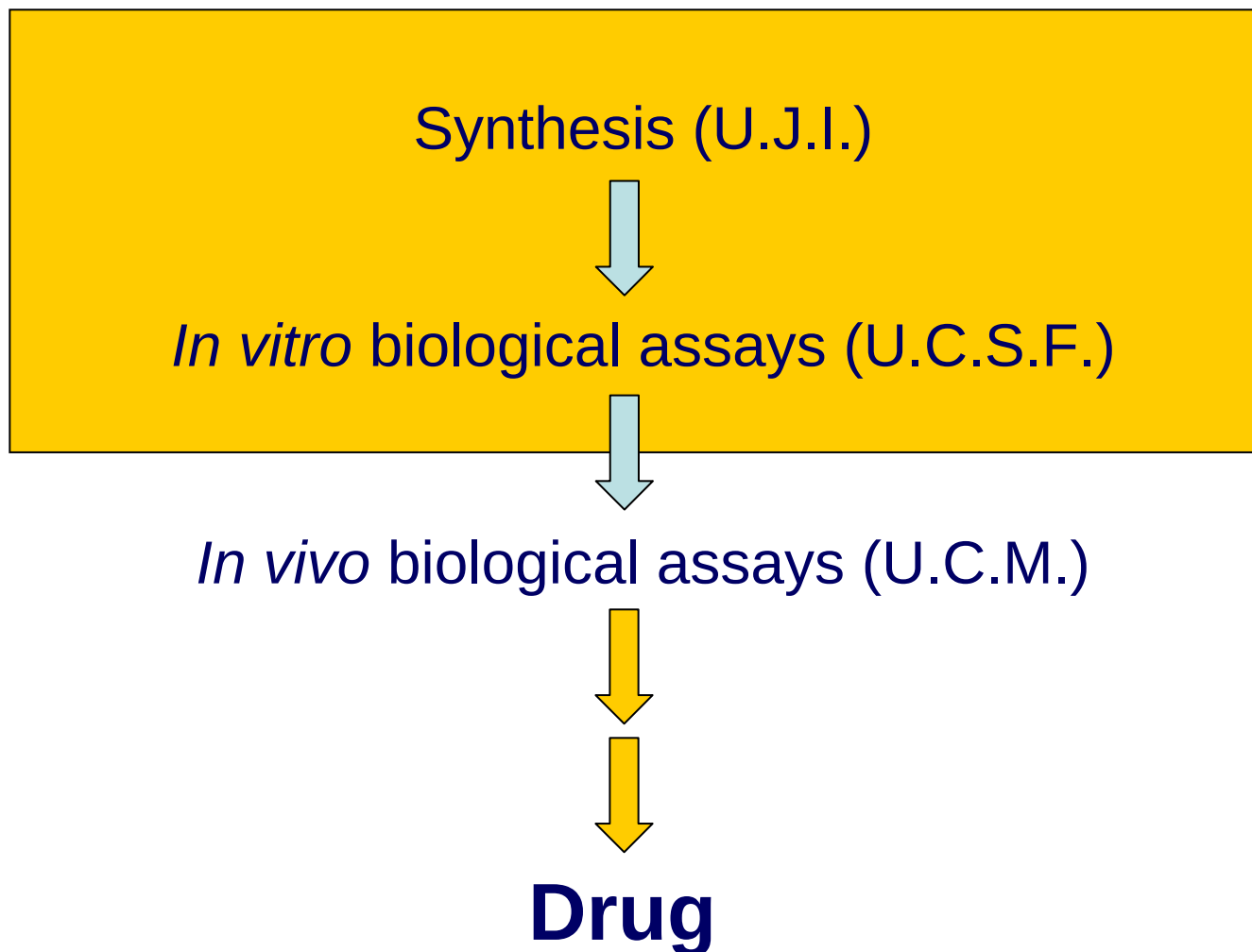
Comp	Cruzain	Rhodesain	<i>T.b.</i> CathepsinB
Q073	20	3.5	>>1000
Q074	50	30	400

Patente: P200701717.

PCT: PCT/ES2008/070116

Bioorg. Med. Chem. Lett. 2007, 17, 6697-6700.

Developing of inhibitors



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