ISGlobal Barcelona Institute for Global Health

IBEC Institute for Bioengineering of Catalonia

International conference on

Parasitology

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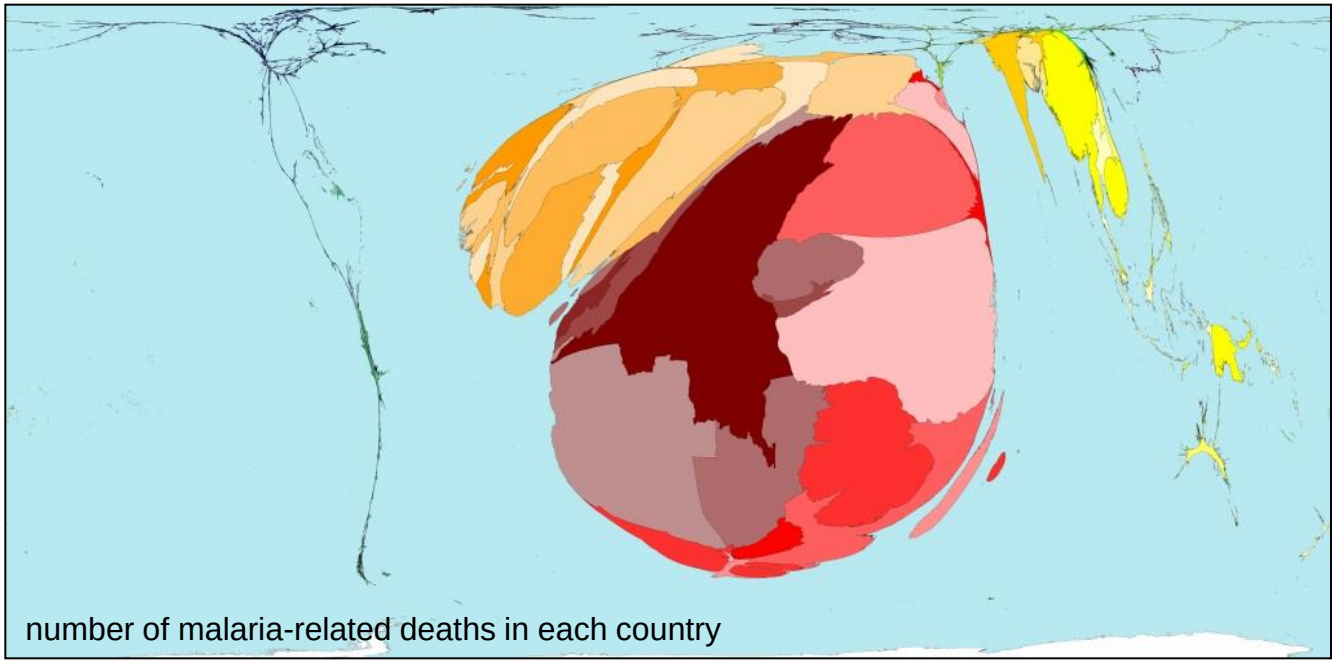
Nanomalaria Joint Unit
IBEC/ISGlobal

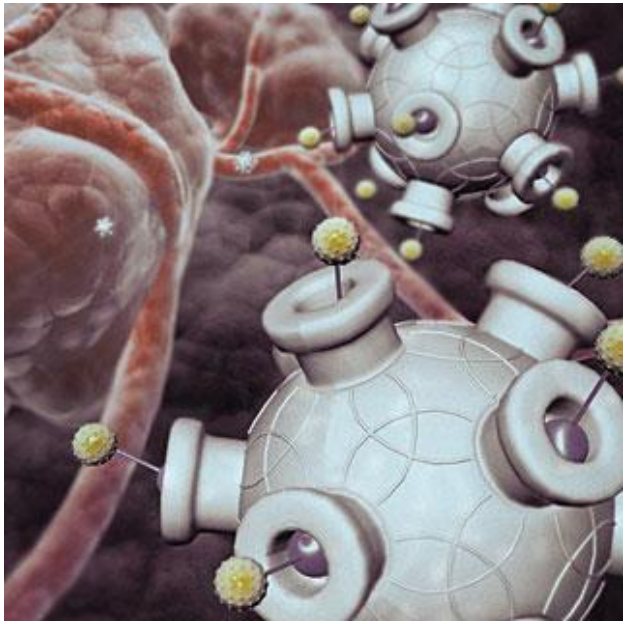
Polyamidoamine nanoparticles: From drug nanocarriers to vaccine adjuvants in malaria



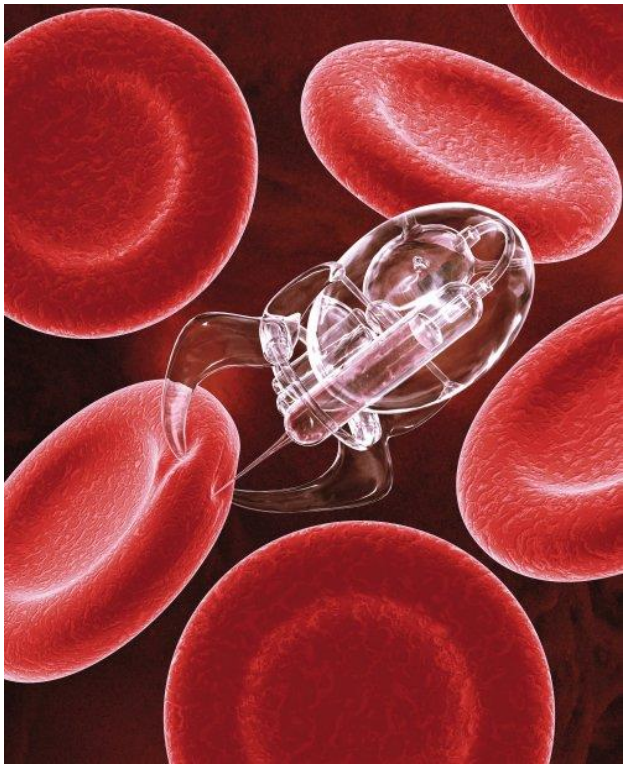
number of malaria-related deaths in each country

Nanomedicine against *Malaria*

Nanomedicine:
not for the developing world?

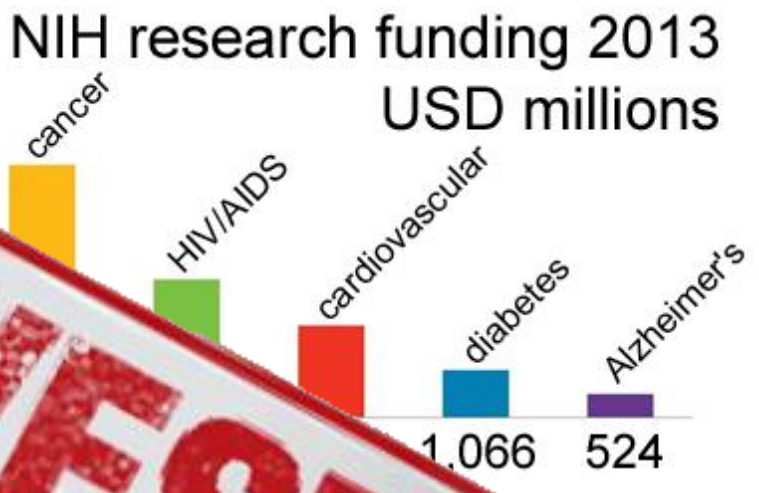


http://www.scientificamerican.com/



http://blog.zintro.com/

http://images.nationalgeographic.com/



Estimated annual g… nanomedicine+malaria … 200,000 USD

Web of Science search "nanomedicine+malaria" 30 hits (1/3 from our Unit)

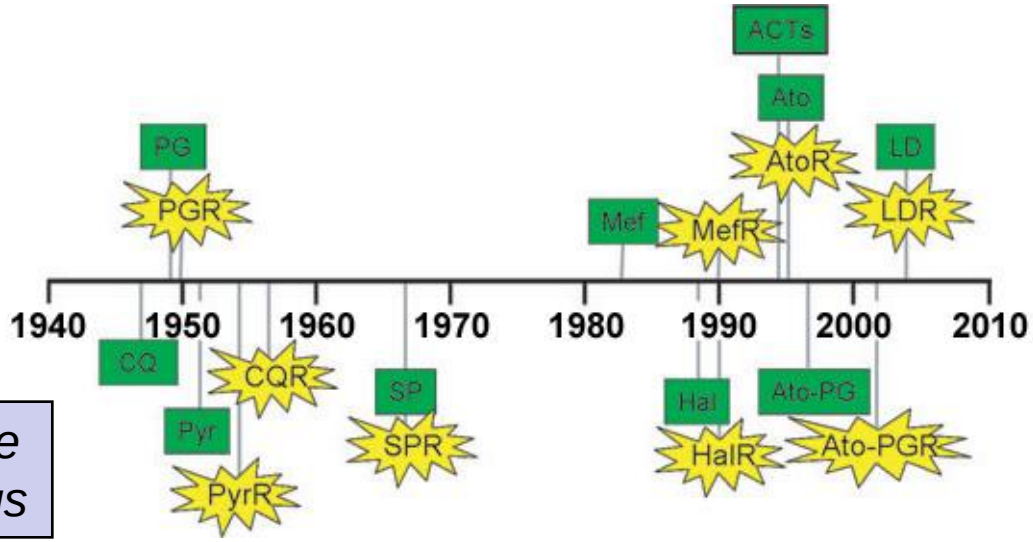
AMFm, Affordable Medicines Facility – malaria; AusAID, Australian Agency for International Development; CIDA, Canadian International Development Agency; DFID, Department for International Development; GF, Global Fund; PMI, President's Malaria Initiative; USAID, United States Agency for International Development; WB, World Bank

For the GF and PMI/USAID, funds from the last quarter of 2013 onwards are projected; for other agencies, funds from 2012 onwards are projected.

Source: See Box 3.1

Antimalarial strategies

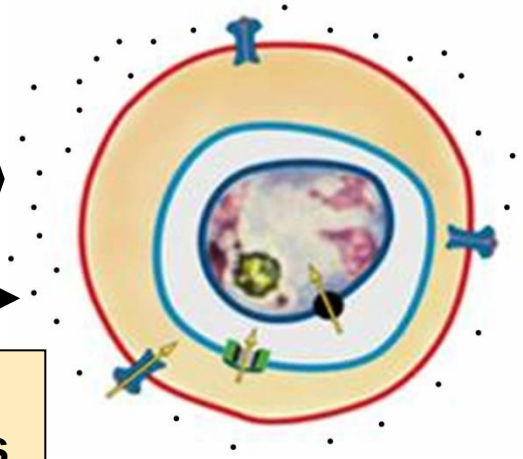
There is a pressing need for ***new*** therapeutic strategies against malaria, because the currently available treatments will not guarantee its eradication



*Development of **nanovectors** for the targeted delivery of antimalarial drugs*

Read and Huijben (2009) Evolutionary Applications 2:40

Currently available strategy for antimalarial drug delivery, where the drugs are free in the plasma.
pRBC-specific drug intake is usually poor in this situation.



Parasitized red blood cell (pRBC) ►

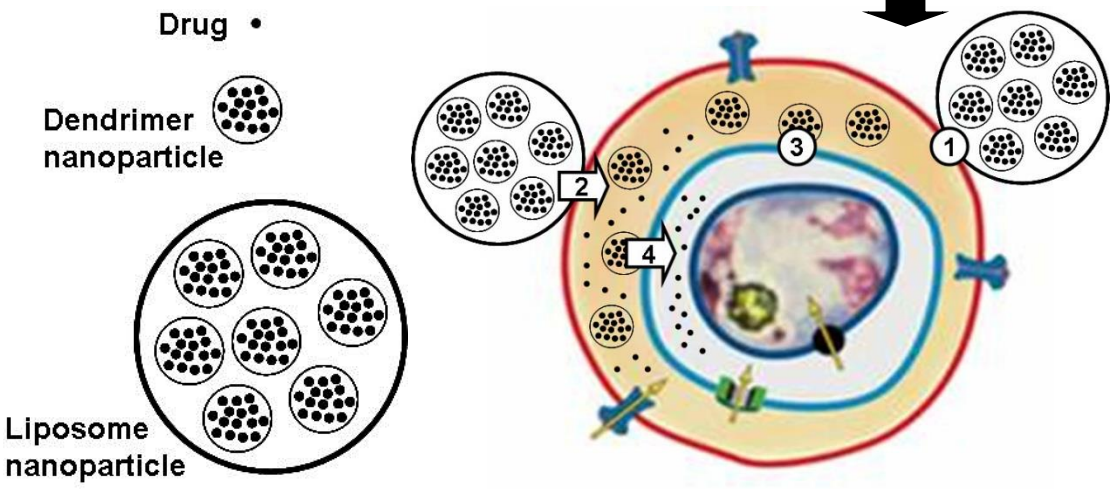
Our *proof-of-concept* strategy:

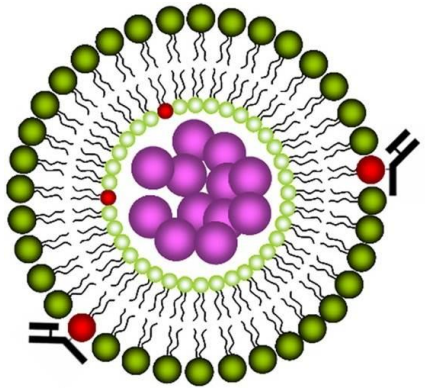
(1) Specific targeting of immunoliposomes towards pRBCs and docking to the pRBC plasma membrane.

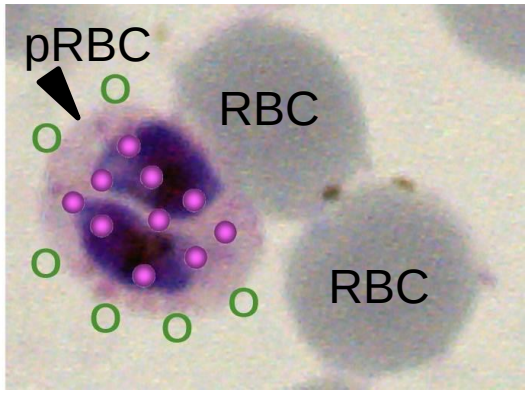
(2) Delivery of immunoliposome cargo to the pRBC cytosol through membrane fusion, to overcome the lack of endocytic processes in erythrocytes.

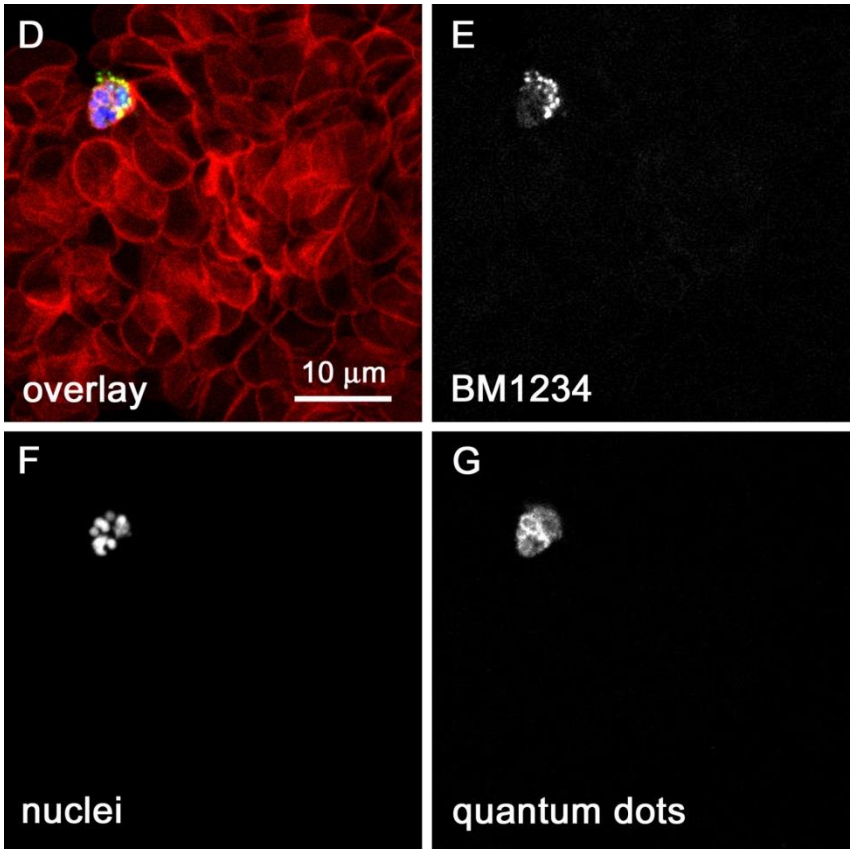
(3) Specific PVM recognition and docking of nanoparticles.

(4) Release of the drug from biodegradable nanoparticles in the RBC cytosol and inside the PV.









100% efficacy *in vitro*, in both ways: *all* pRBCs, *not a single* RBC (90 min)

A *magic bullet* against malaria?

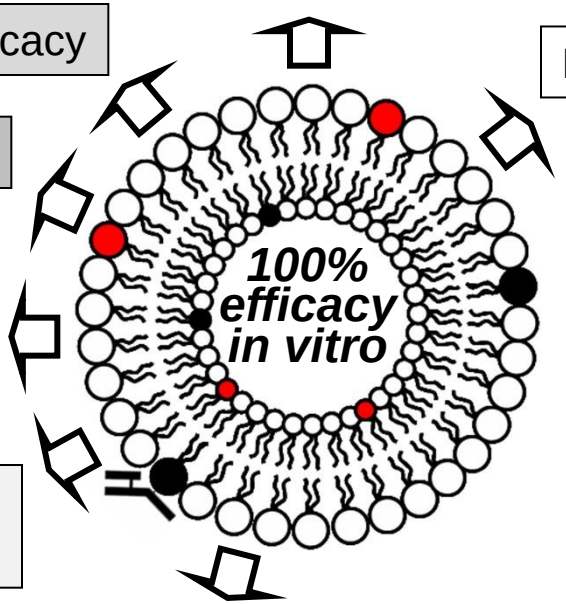
How far are we from a magic bullet against malaria?

Better targeting

Better encapsulation efficacy

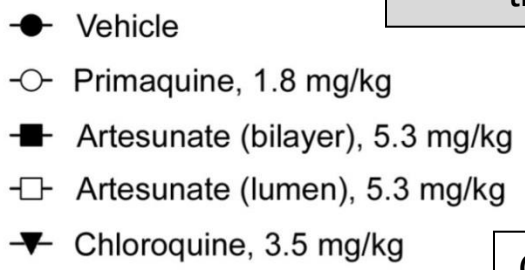
Better drugs

Better efficacy *in vivo*

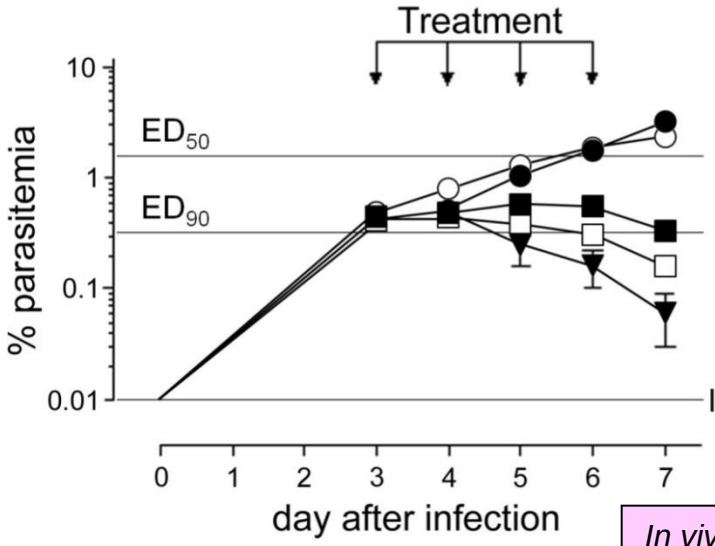


New targets (transmission stages in the mosquito?)

New applications (vaccines)



Oral administration (smaller size, new structures)



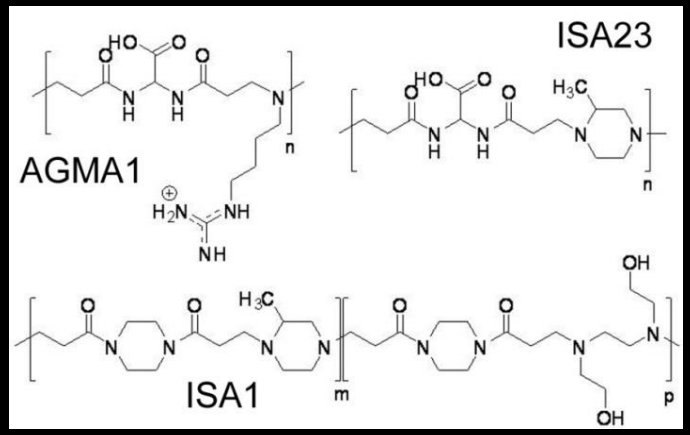
In collaboration with GlaxoSmithKline

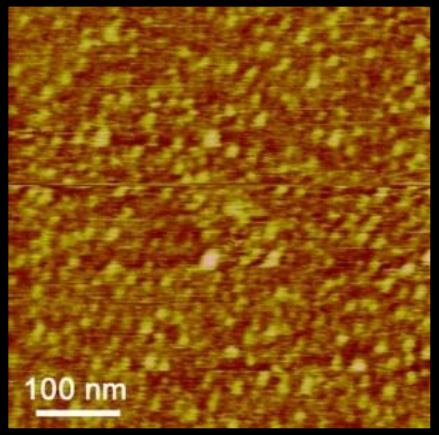
GlaxoSmithKline

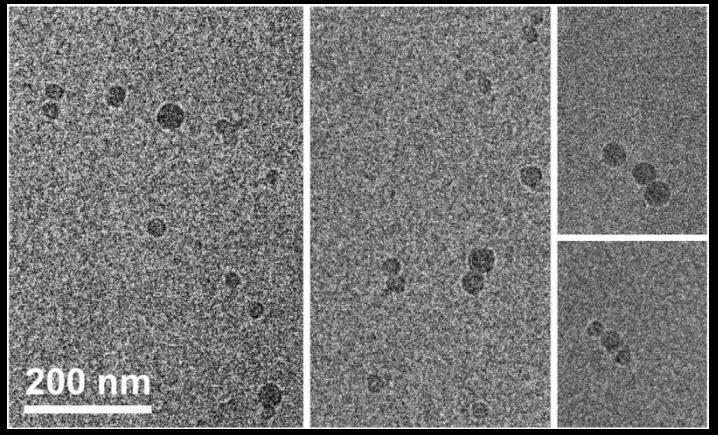
In vivo activity of immunoliposomal antimalarials: so, so…

Better capsules <u>and</u> better targeting

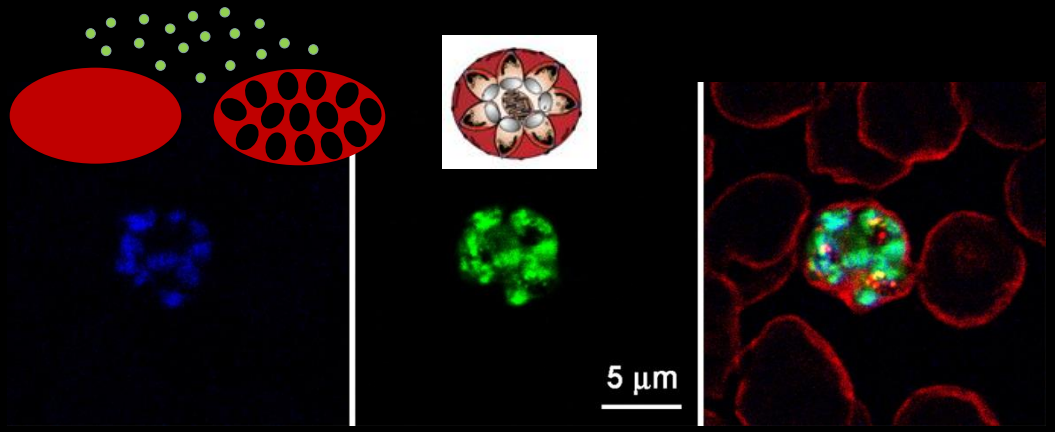
Polyamidoamine (PAA)-based nanoparticles





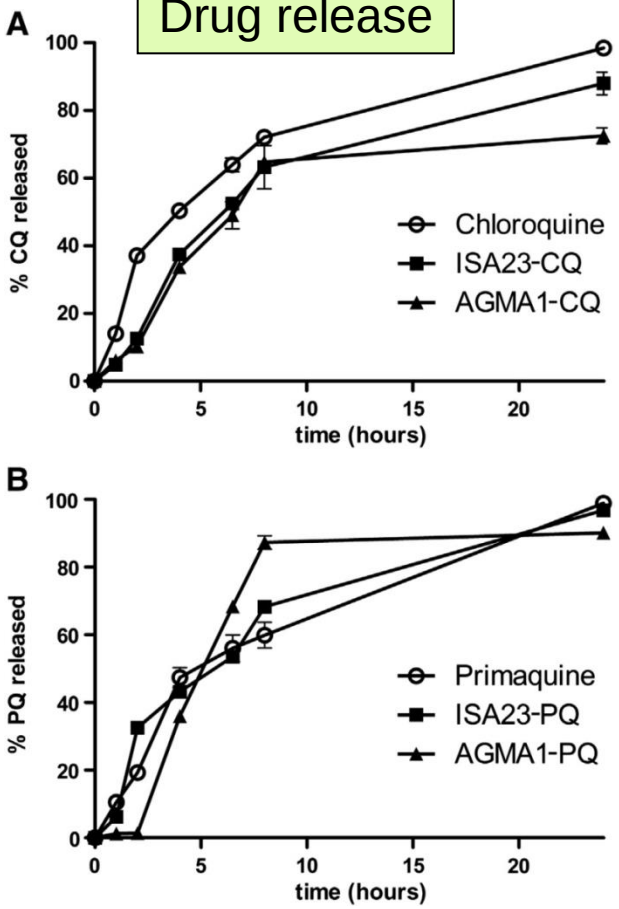


In collaboration with Dr. Elisabetta Ranucci, University of Milano, Italy



Polyamidoamine (PAA)-based nanoparticles

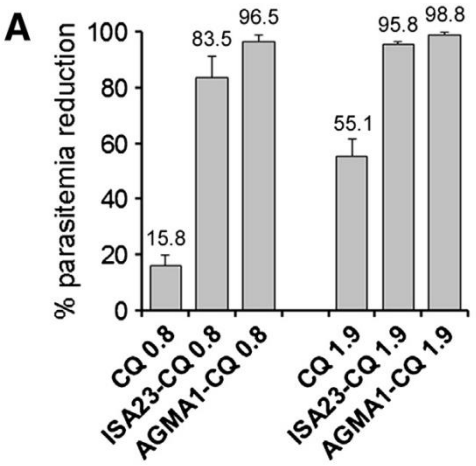
Drug release

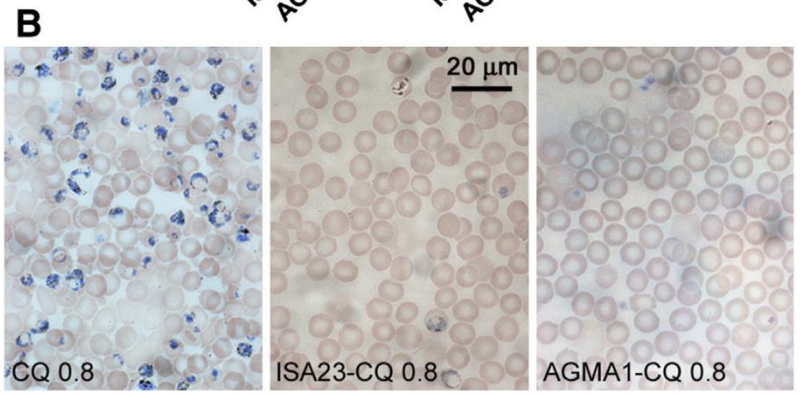


Estimated extra cost for increasing 10-fold the *in vitro* efficacy of CQ/liter:

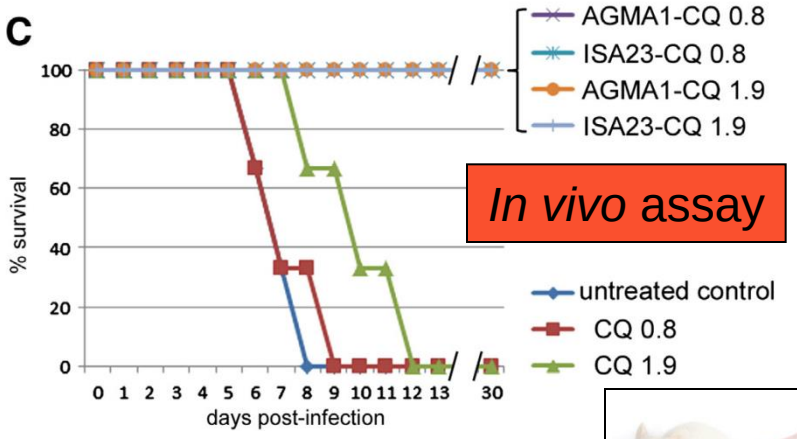
51 € (immunoliposome/CQ)
1 € (heparin-liposome/CQ)
40 ¢ (PAA-derived polymer/CQ)
0.5 ¢ (dendrimers C,D/CQ)

In vitro assay

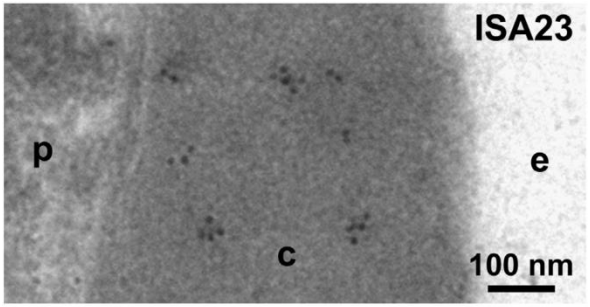


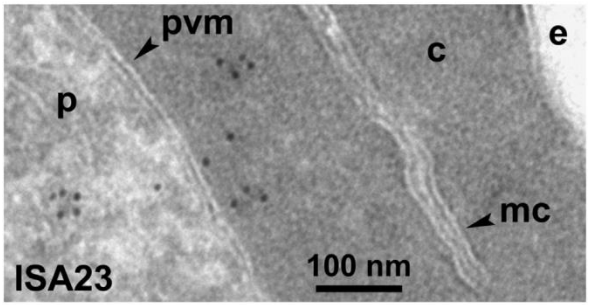


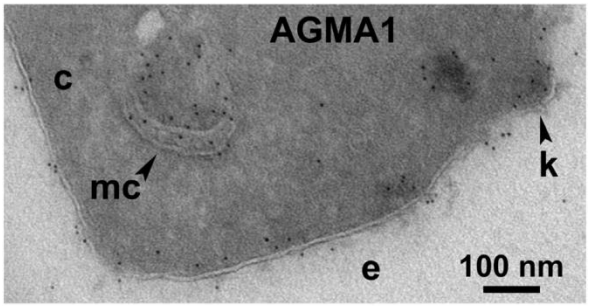
In vivo assay

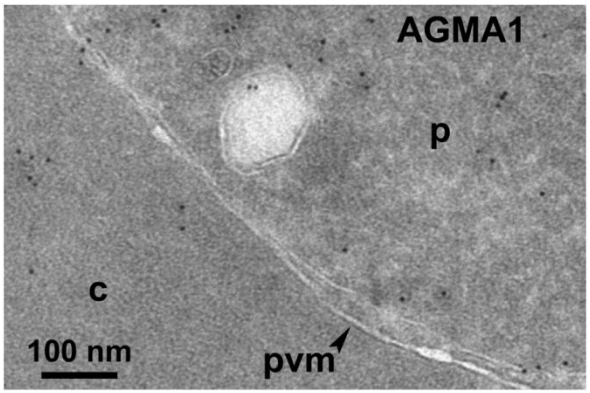


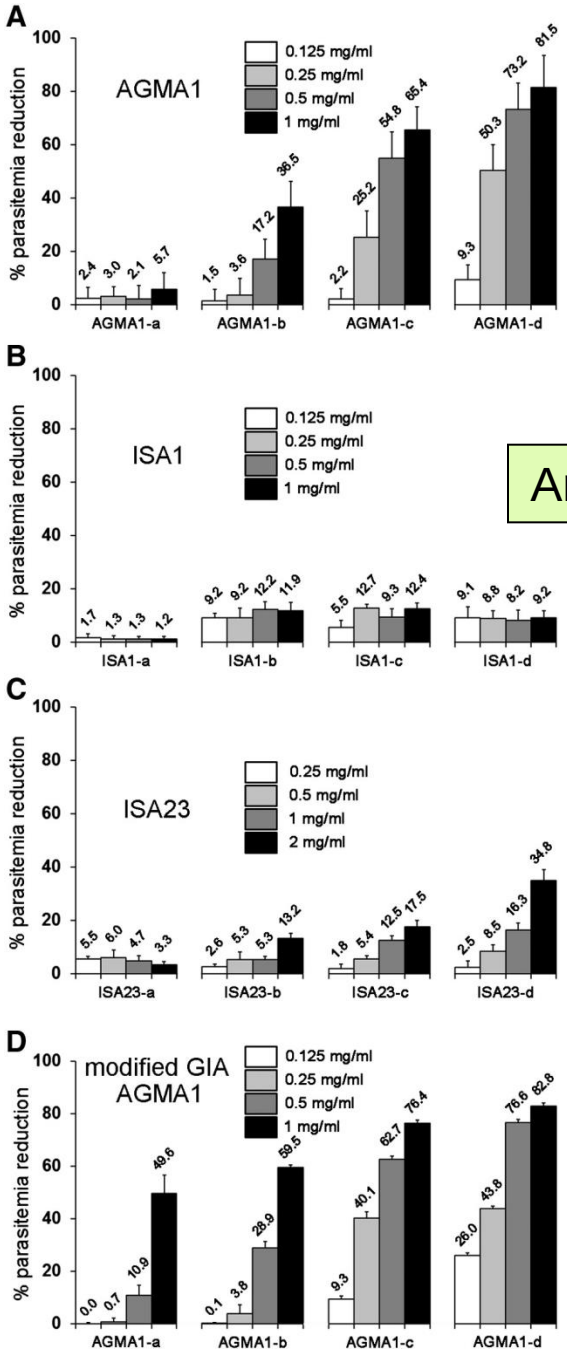
GlaxoSmithKline





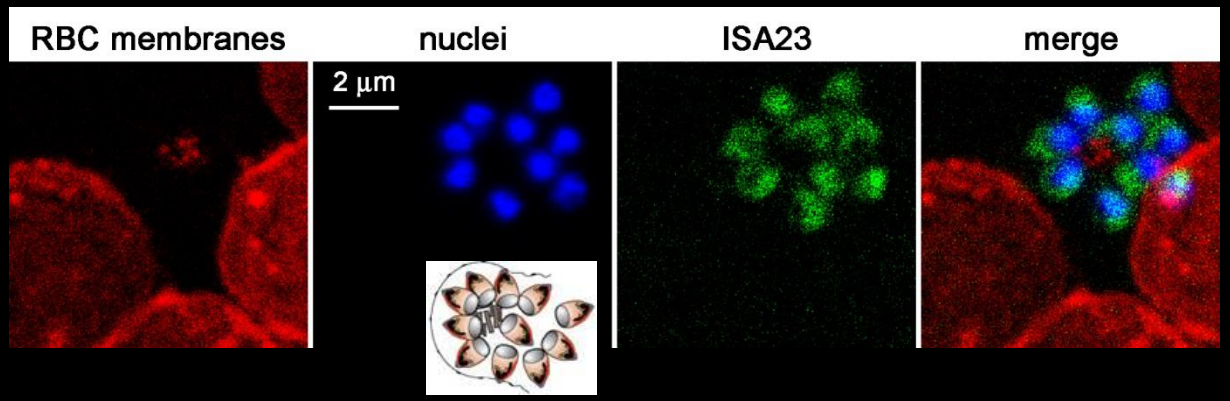


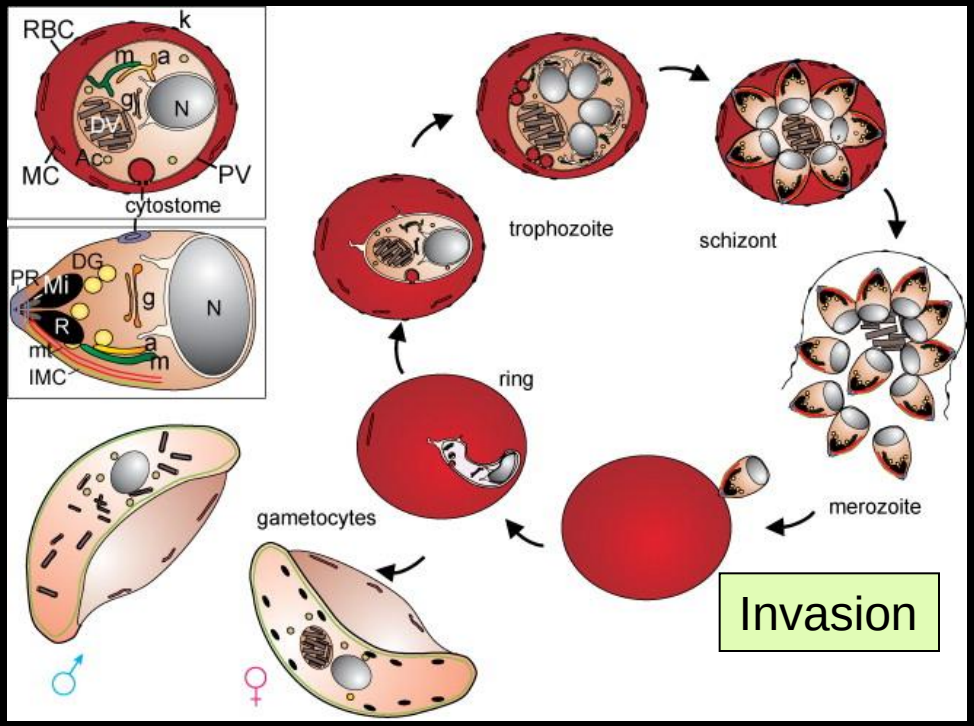


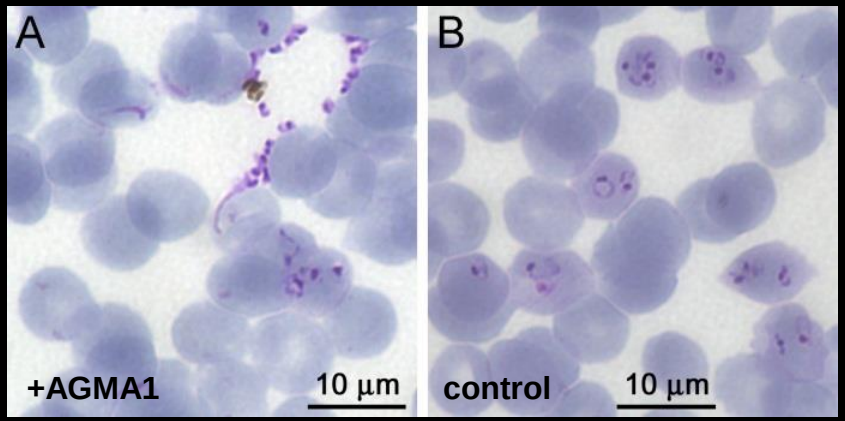


Antimalarial activity of PAAs

New antimalarial strategies (II)

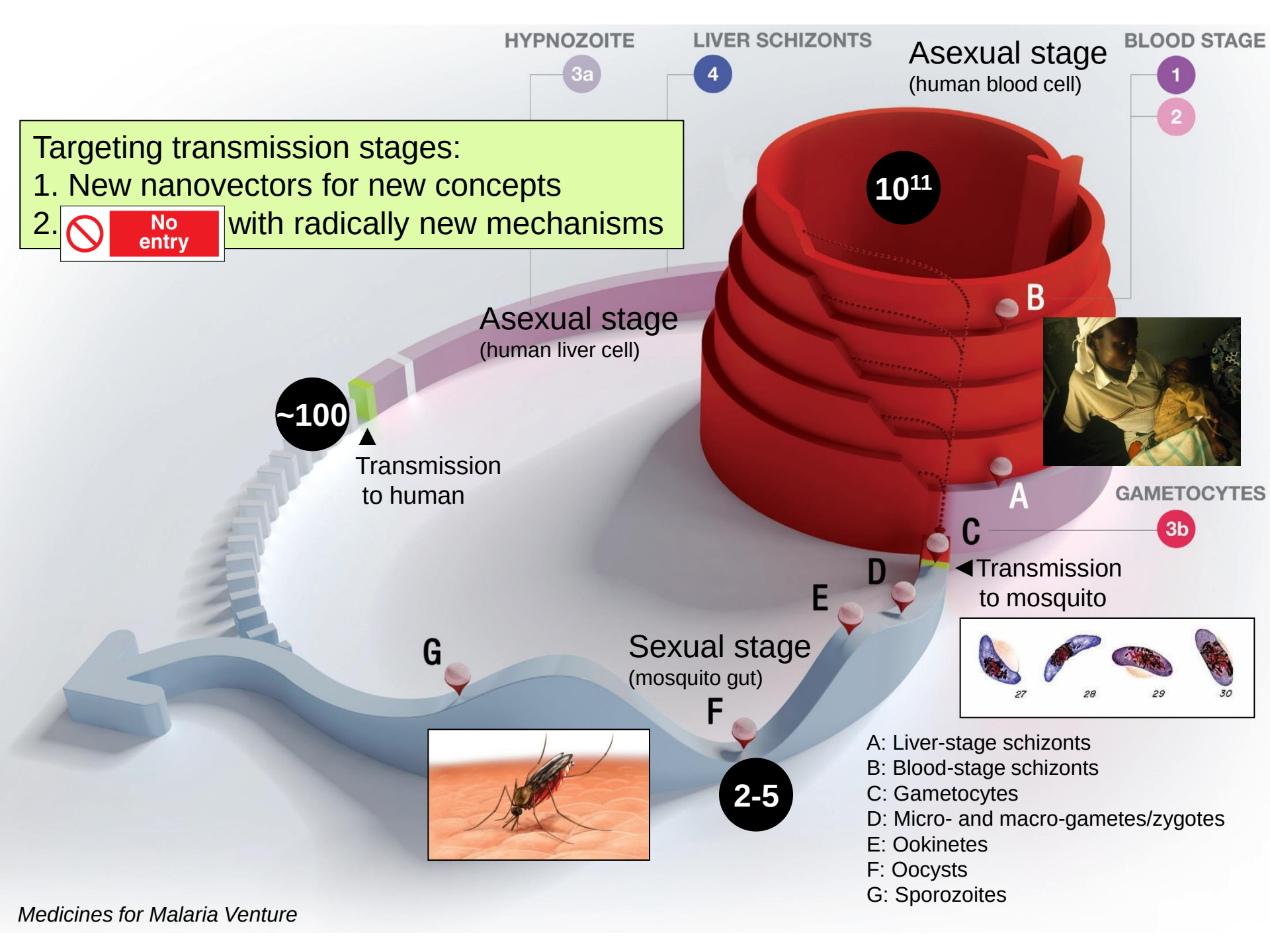






PAAs as invasion-blocking agents?
(vaccination approach)

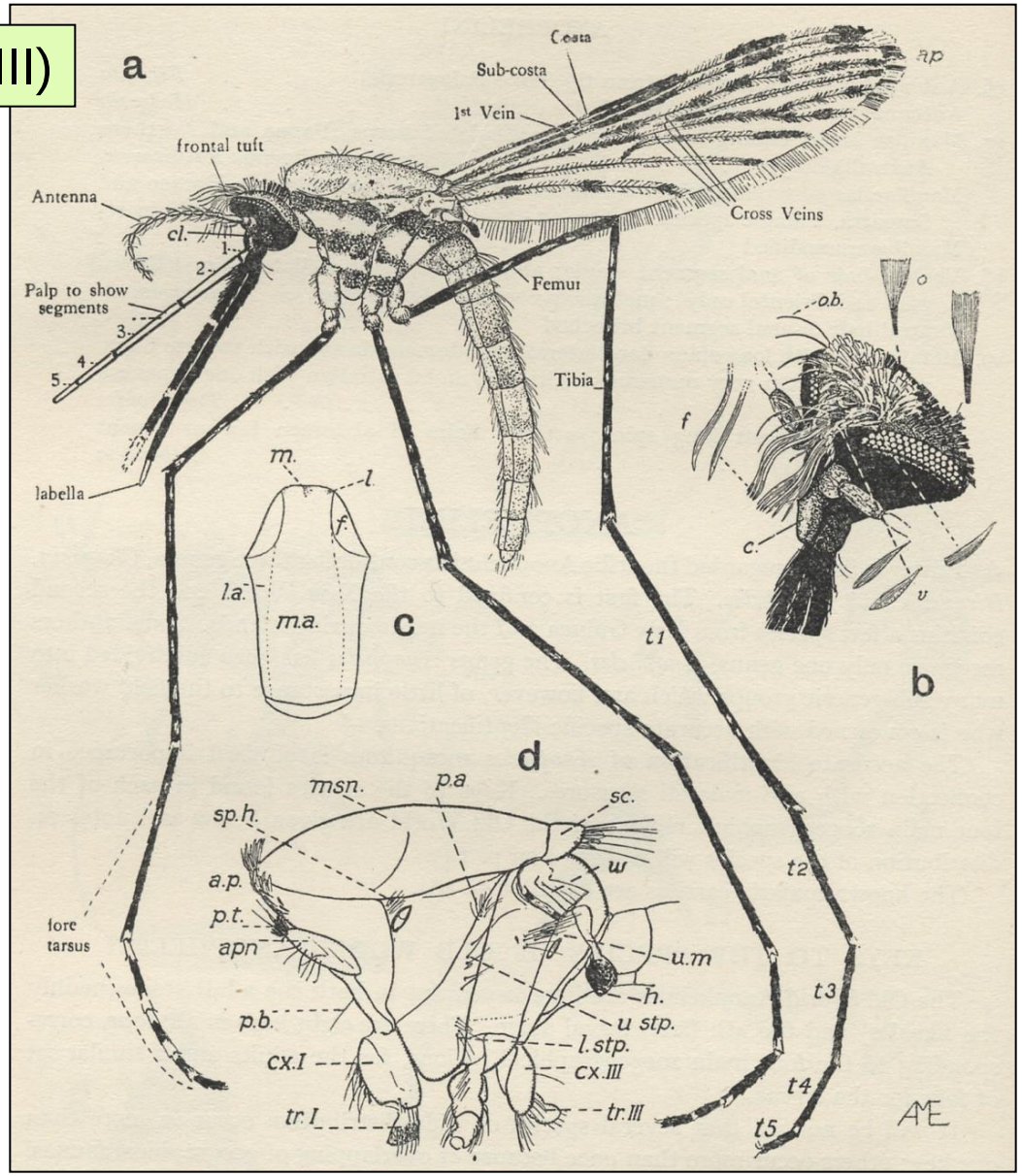
The *Plasmodium falciparum*-infected red blood cell
Tilley L, Dixon MW, Kirk K
Int J Biochem Cell Biol 2011 Jun;43(6):839-42



Medicines for Malaria Venture

New antimalarial strategies (III)

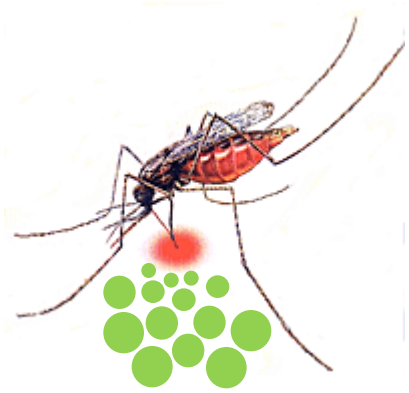
Anopheles



A Handbook for the Identification of Insects of Medical Importance
John Smart
British Museum, London, 1948

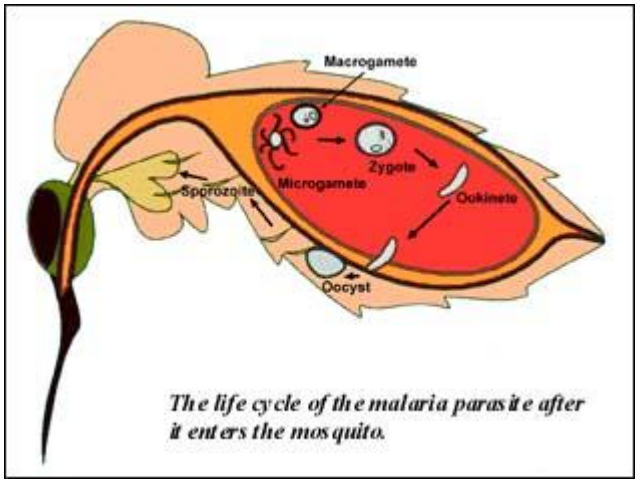
Antimalarial targeted drug delivery to the mosquito?

Antimalarial targeted drug delivery to *Plasmodium* stages in the mosquito vector

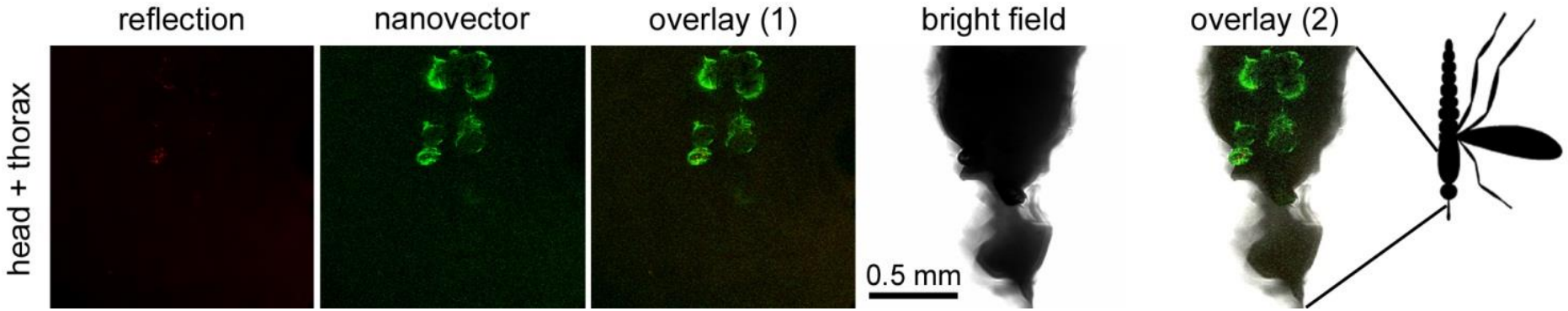


Nanovectors
in sugar meal

Anopheles atroparvus



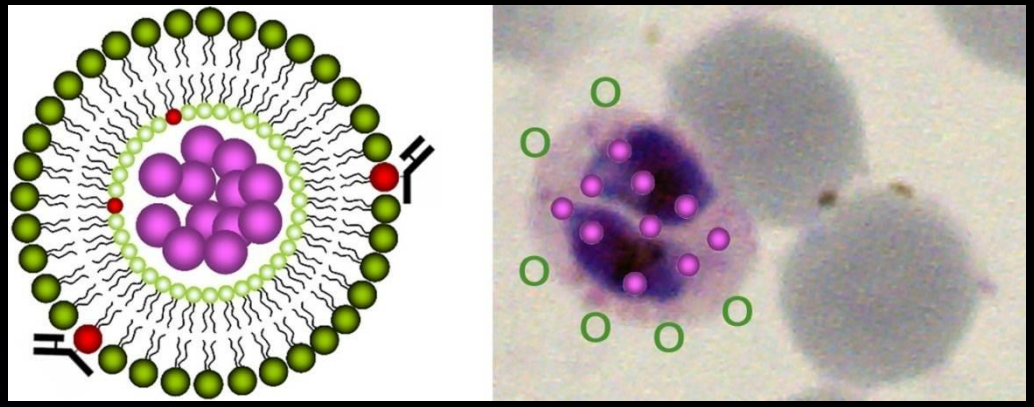
Polyamidoamine (PAA)-based nanoparticles



In collaboration with Dr. Krijn Paaijmans
ISGlobal

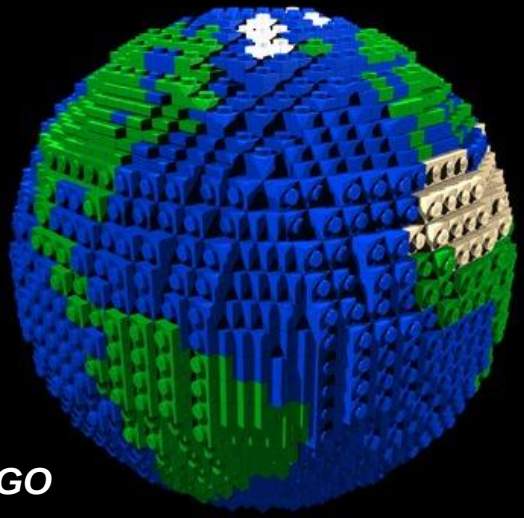
The toy kit against malaria

Russian dolls



Magic bullets

Nanomedicine *can* be an option for diseases of poverty



LEGO

Trojan horse

Acknowledgments:

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Generalitat de Catalunya (Consolidated Research Group 2009-SGR-760)
Fondazione Cariplo, Italy (project 2013-0584)