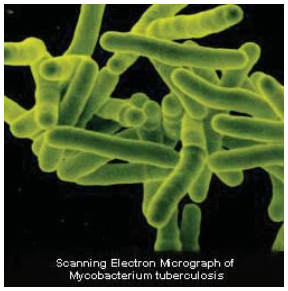
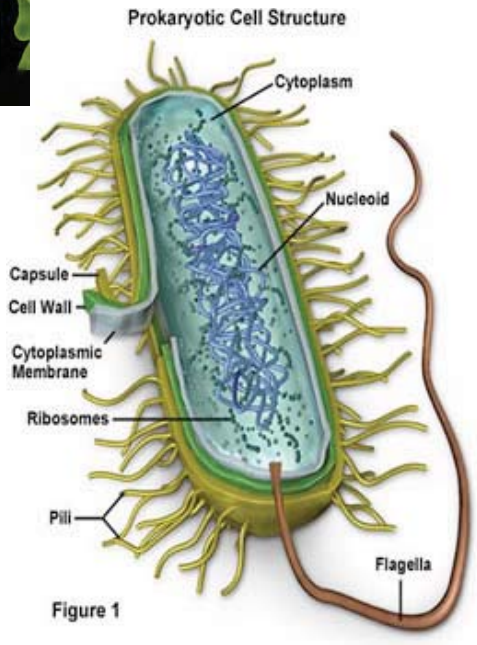
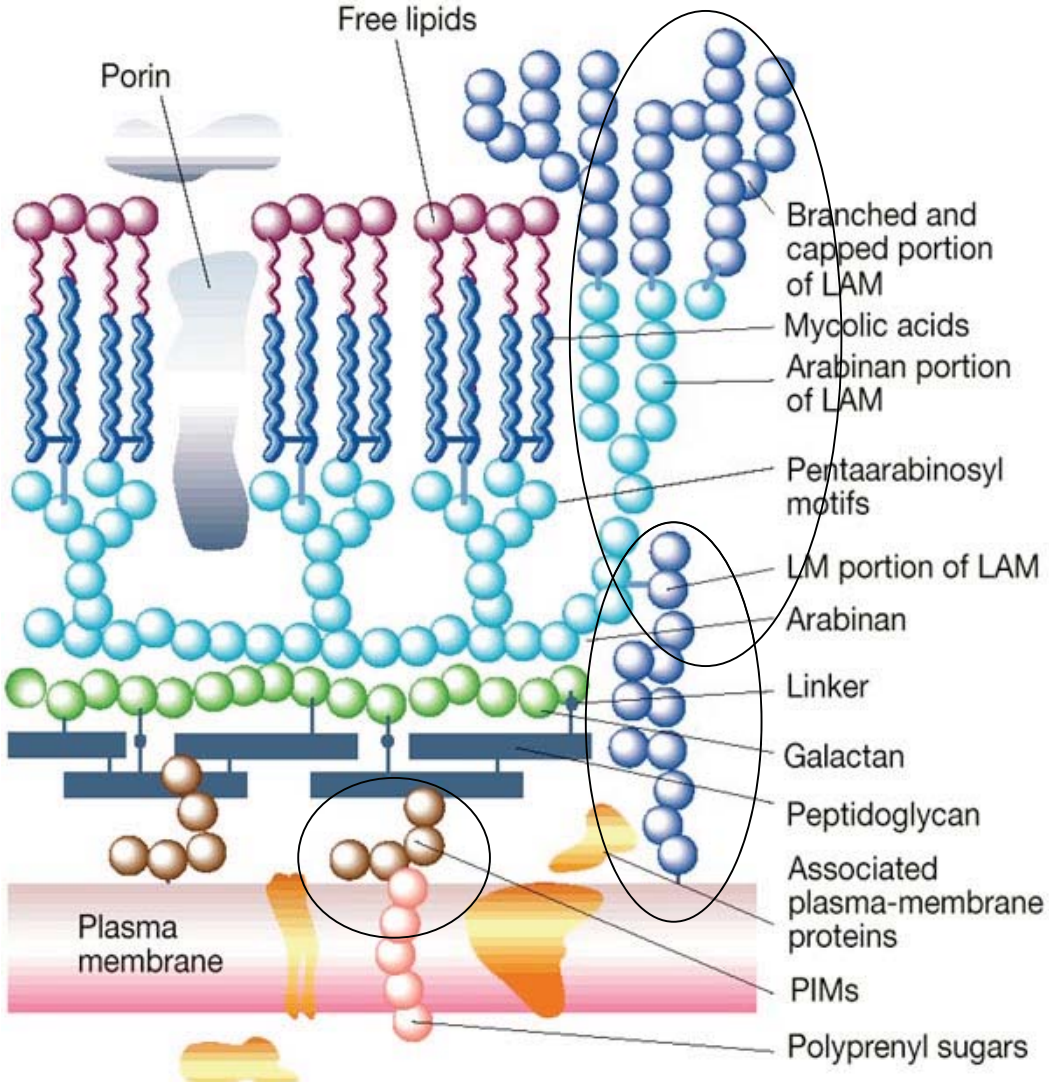
Tuberculosis and Mycobacteria Cell Wall

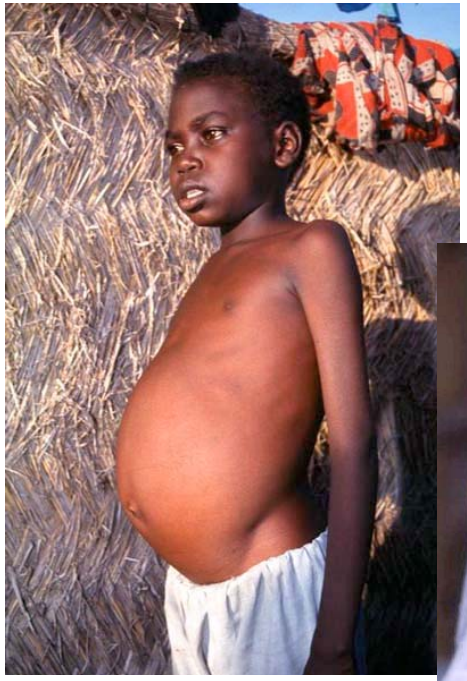






- TB infection is currently spreading at the rate of one person per second
- *"The single most lethal bacterial disease in the world"*

Virosomes to Enhance the Immunogenicity of Synthetic Carbohydrates - A Leishmaniasis Vaccine Candidate



visceral leishmaniasis

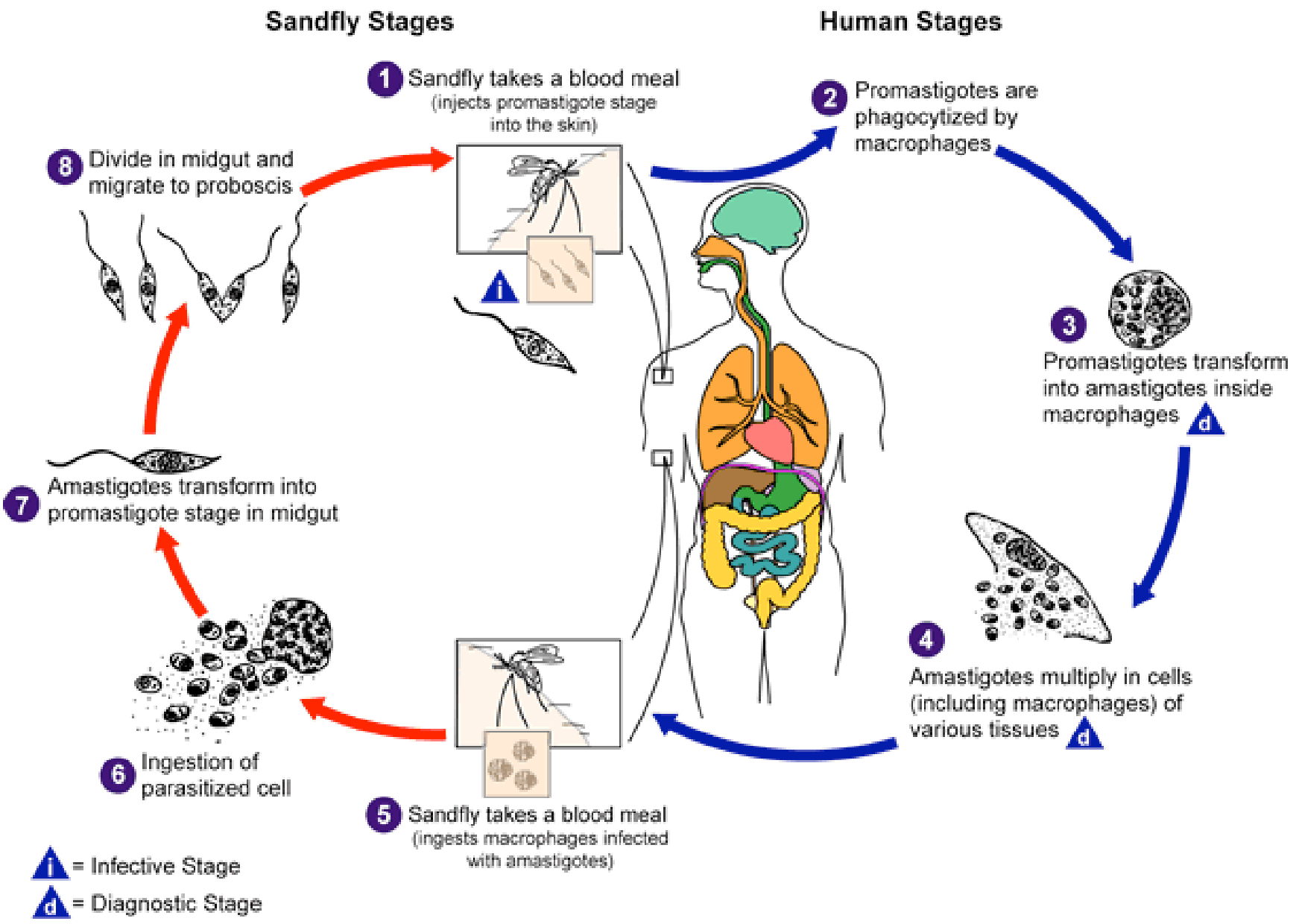
cutaneous leishmaniasis

diffuse cutaneous leishmaniasis

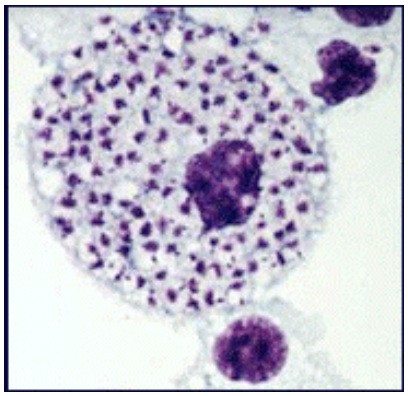
Mucocutaneous leishmaniasis

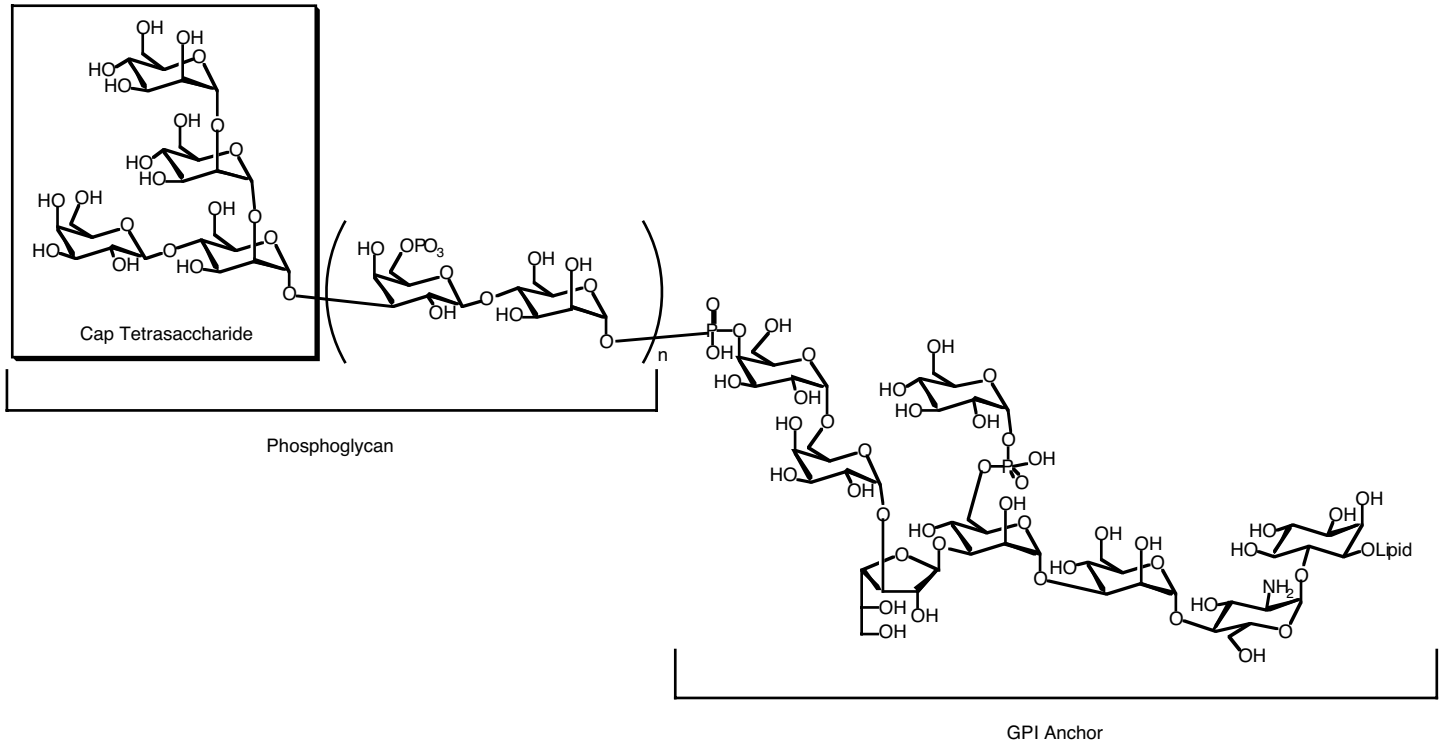
ACS Chem. Biol., 2006, *1*, 161-164.

Leishmania Life Cycle



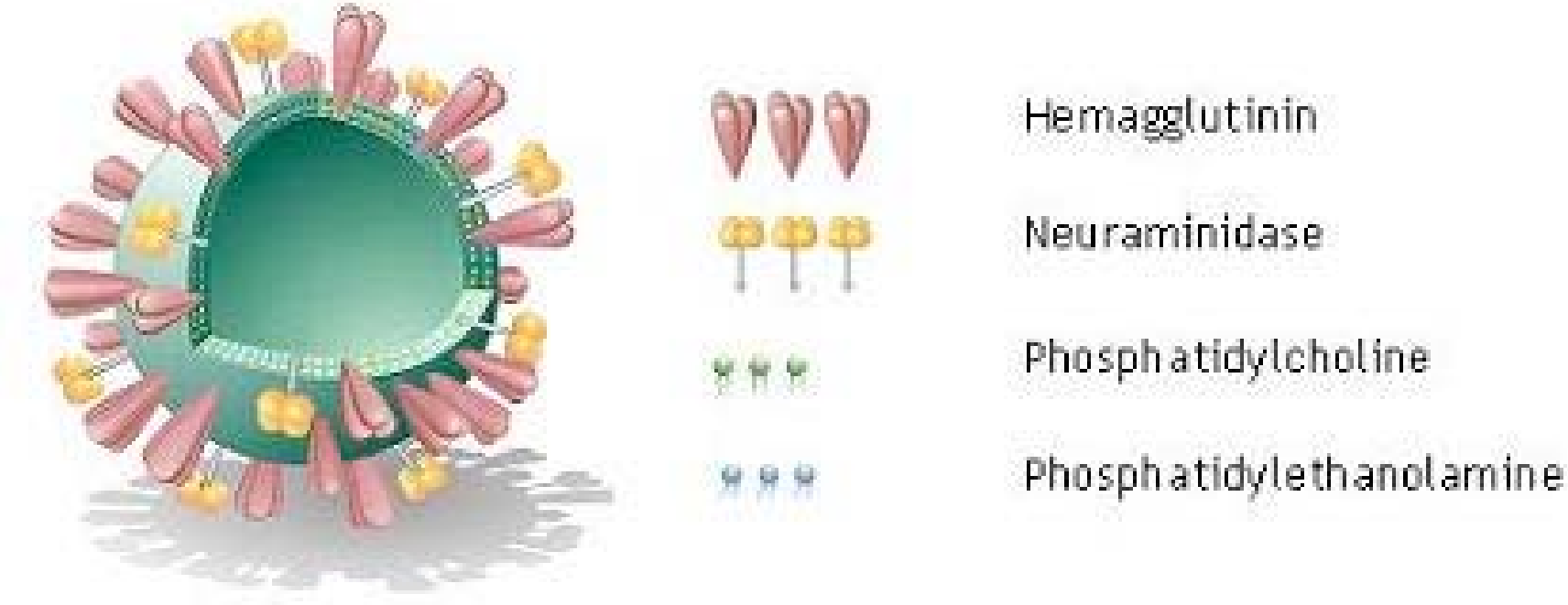
Preparation of a Potential *Leishmania* Vaccine





Virosomes as Vaccine Carrier Systems

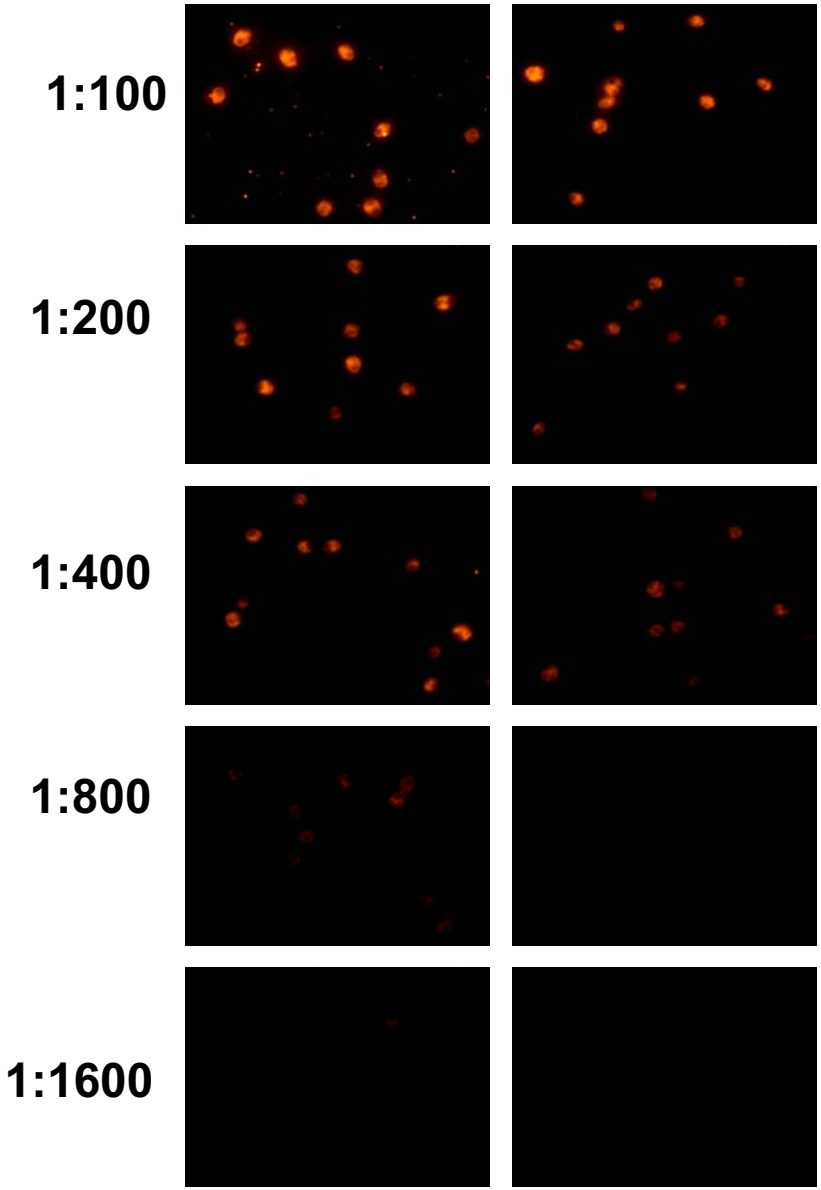
- Spherical, unilamellar vesicles
- Diameter 150 nm
- Reconstituted empty influenza virus envelopes
- Devoid of the nucleocapsid and viral genetic material
- Contrast to liposomes: contain functional viral envelope glycoproteins: influenza virus hemagglutinin (HA) and neuraminidase (NA)



Pevion Inc. Berne Switzerland

Immunofluorescence Staining of Parasites

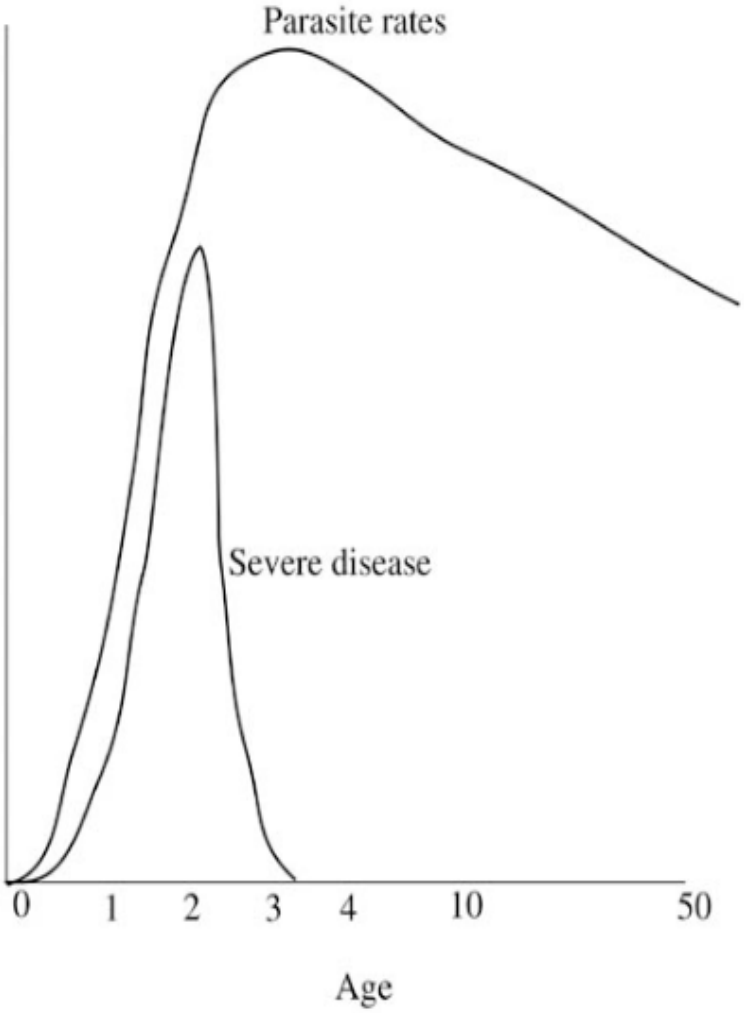
anti-HA-glycan immuneserum



anti-PE-glycan immuneserum

An Anti-Toxin Malaria Vaccine

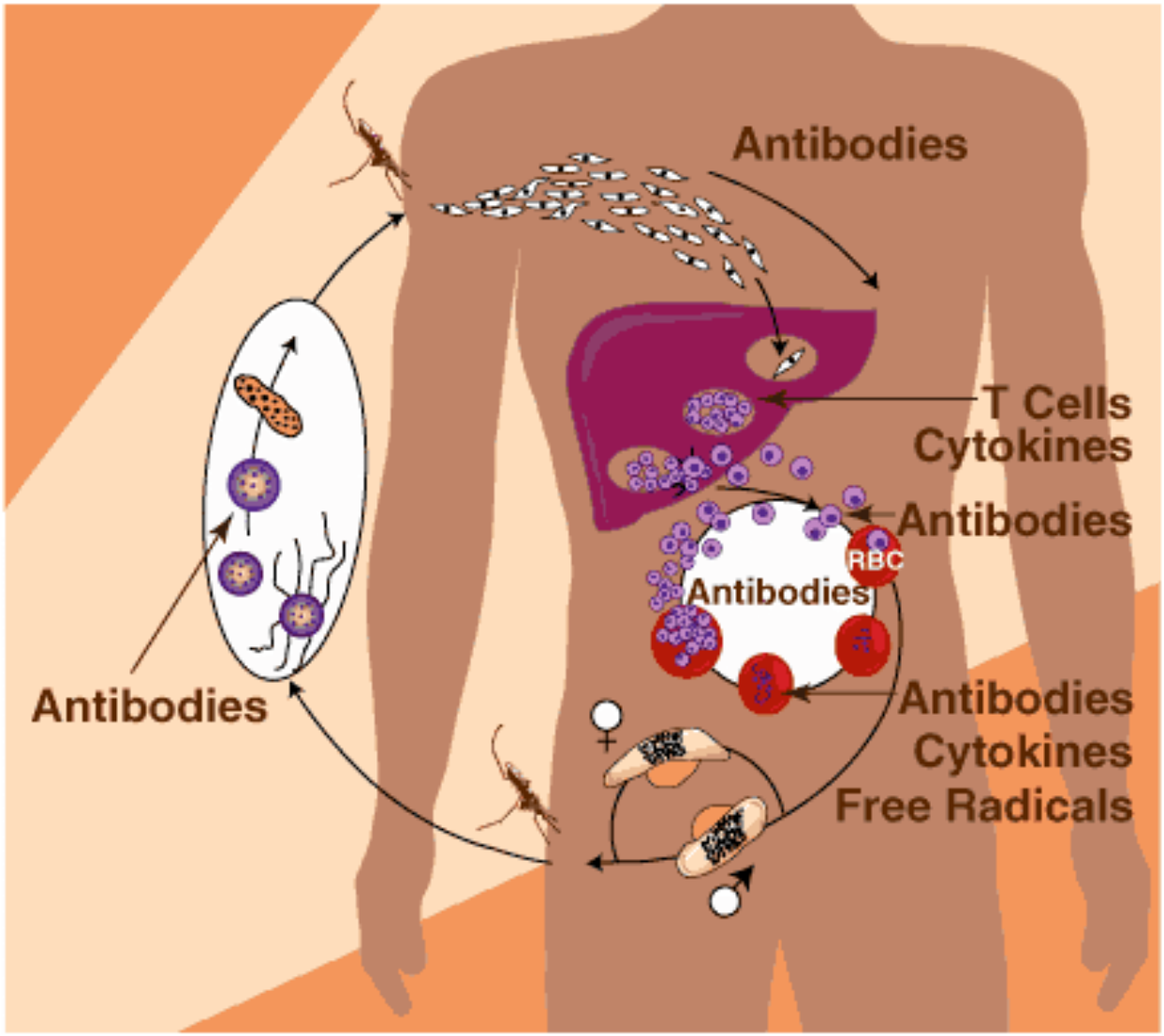
Clinical and Anti-parasite Immunity to Malaria

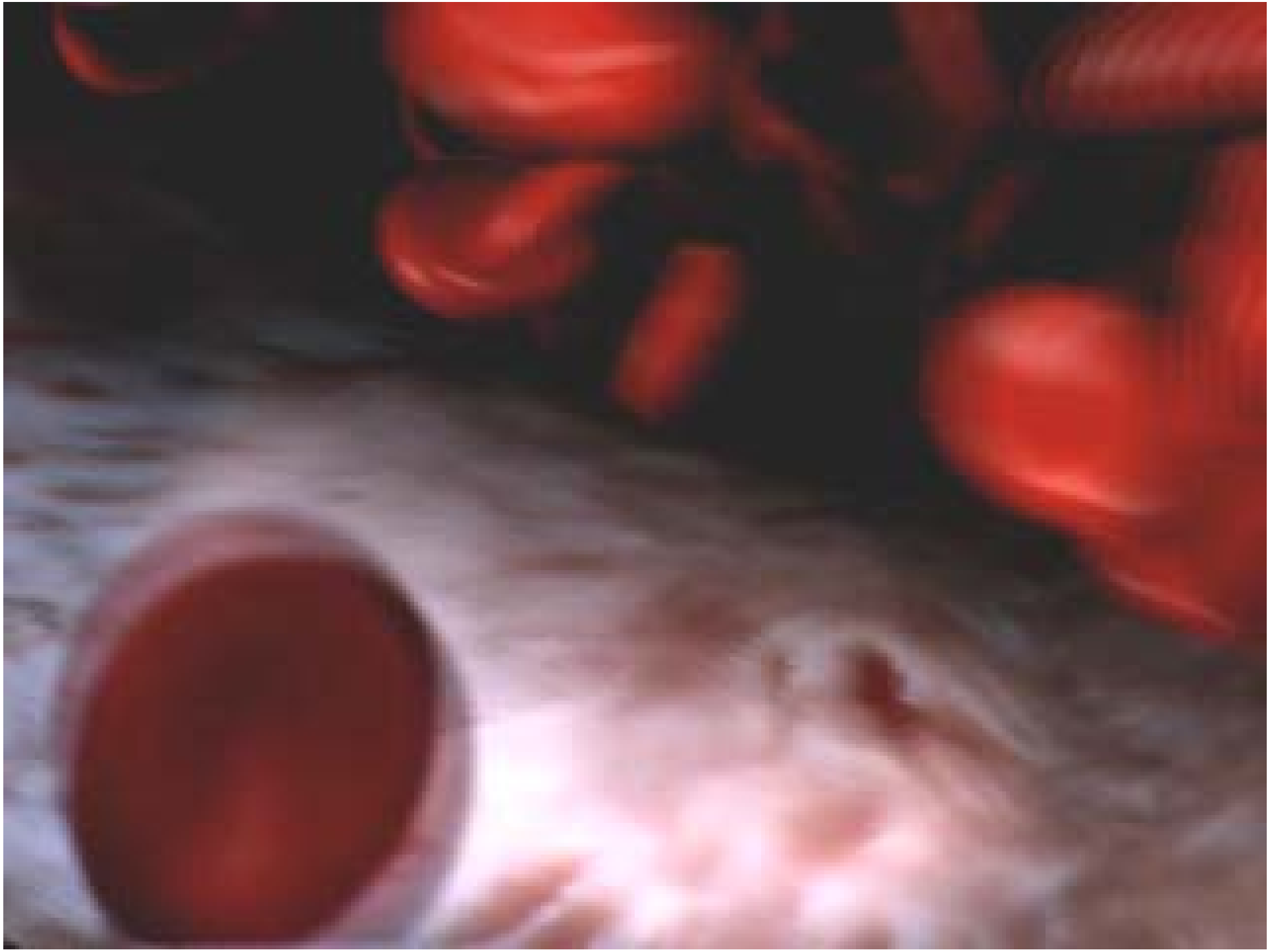


- many protein-based vaccines explored
- carbohydrate-based vaccines
  very successful against other diseases

Malaria Statistics (1994 WHO Estimate)
- 40% of world population at risk
- 5% infected (300 million people)
- 100 million clinical cases
- 2-3 million deaths (1% of cases fatal
  (predominantly children < 5 years)

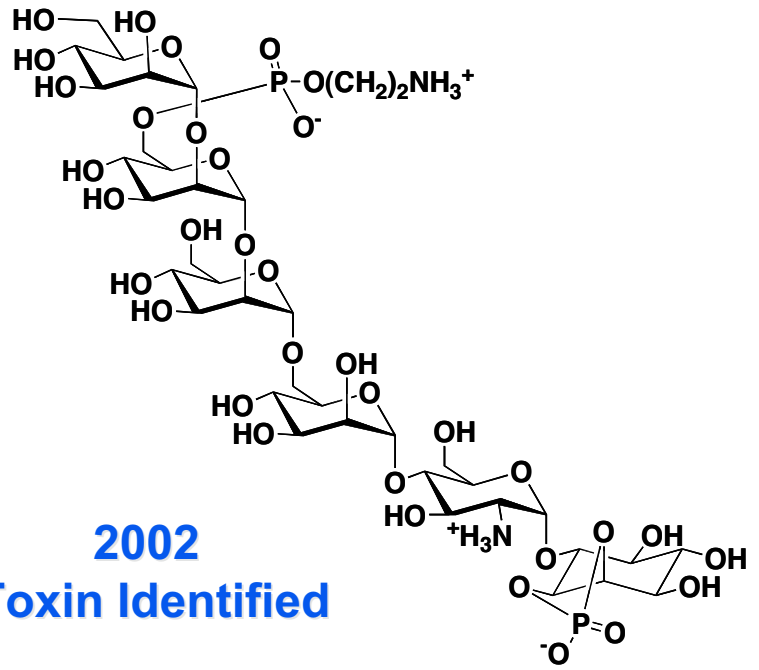
The *Plasmodium falciparum* Life Cycle





An Anti-Toxin Malaria Vaccine

1896
Golgi Postulates Malaria Toxin



2002
Toxin Identified

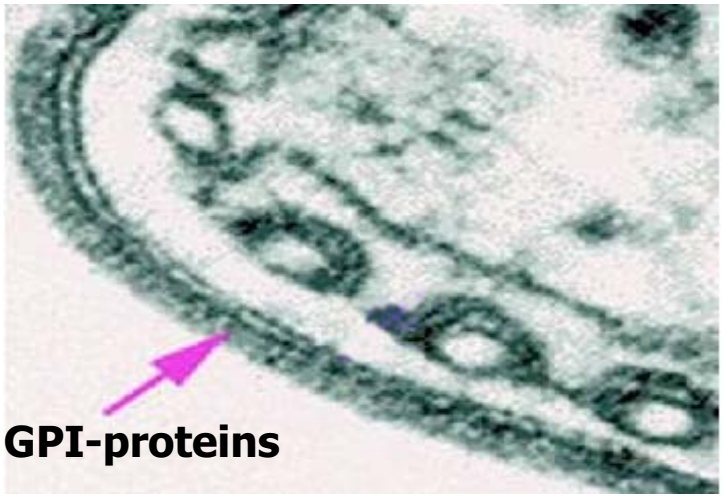
1) Substance isolated from *P. falciparum* - structure postulated

2) Synthesis of structure to confirm assignment

3) Use synthetic molecule as anti-toxin vaccine candidate

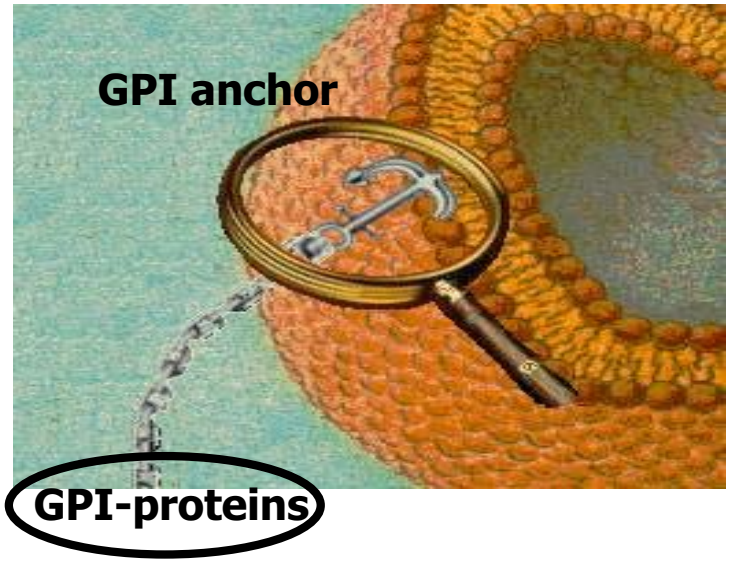
Nature, 2002, *418*, 785

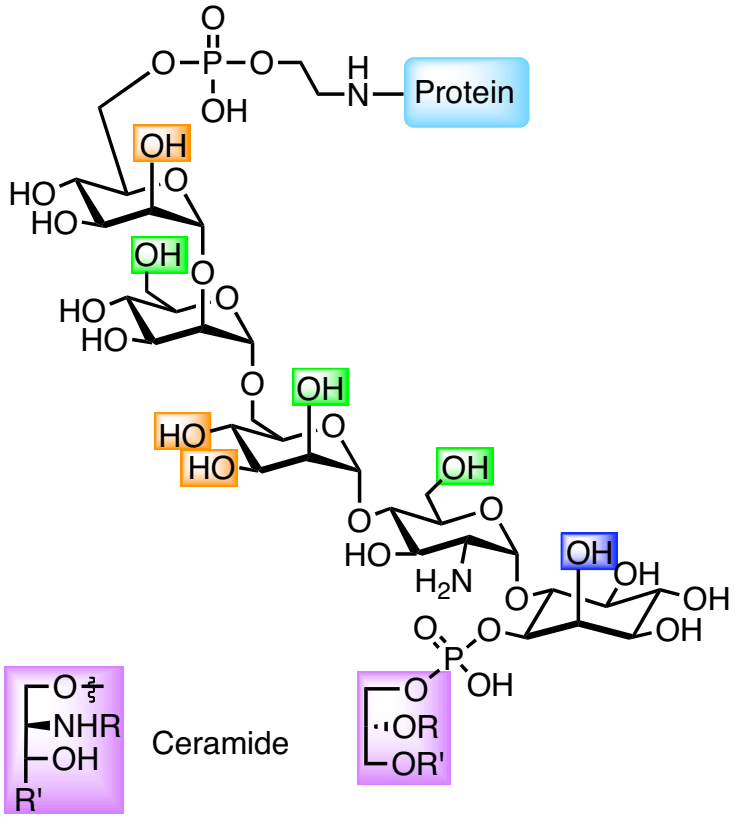
Glycosyl Phosphatidyl Inositol (GPI): Structure



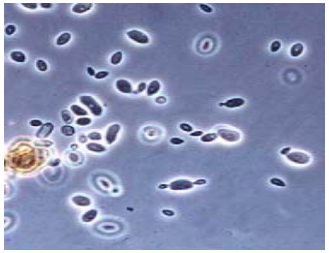
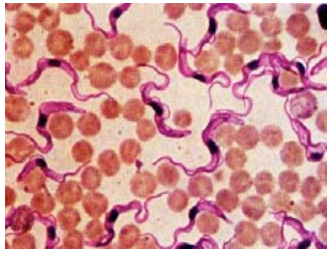
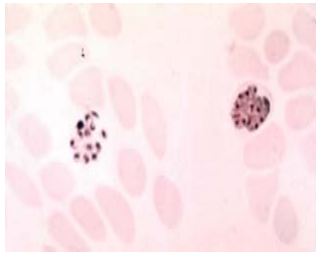
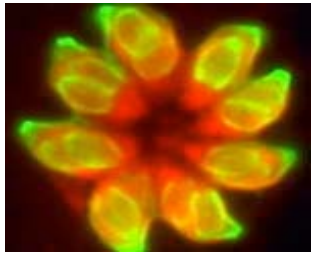
>GPI-proteins

>Free GPIs





Glycosyl Phosphatidyl Inositol (GPI): Occurrence


Yeast *T. brucei* *P. falciparum* *T . gondii* Human

High copy (10-20 Million per cell) Low copy

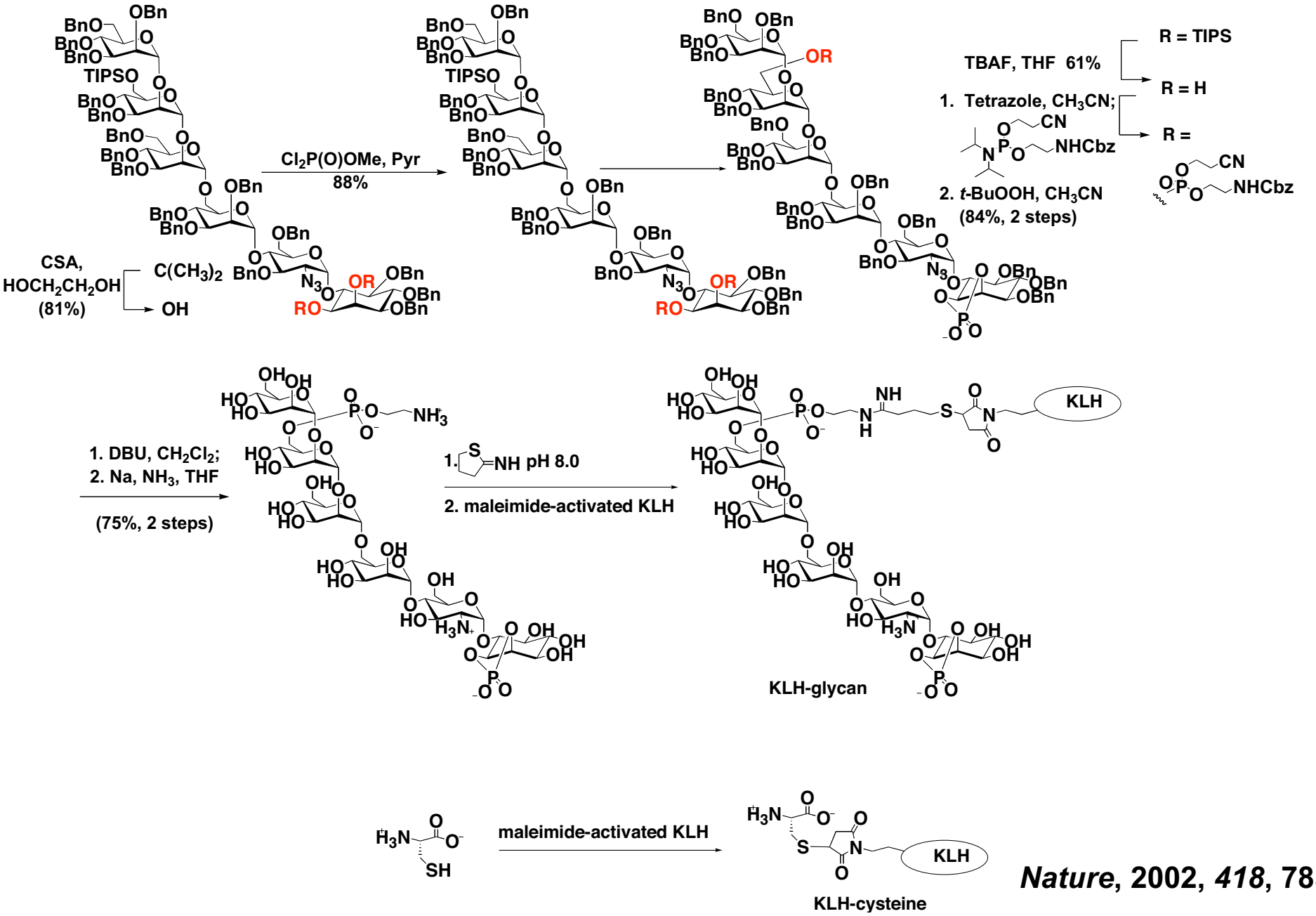
Exoenzymes e.g. alkaline phosphatase,

Adhesion molecules e.g Neural cell adhesion molecules

Complement regulatory proteins e.g. DAF, CD59

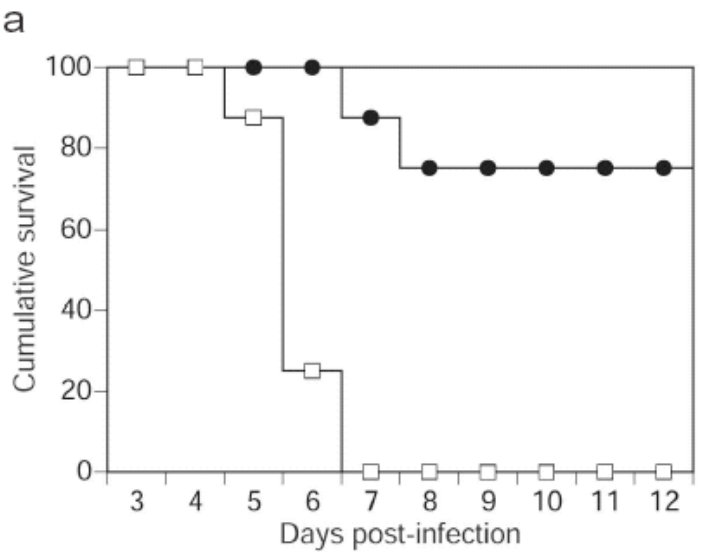
Protozoa surface antigens e.g. SAG1, MSP1

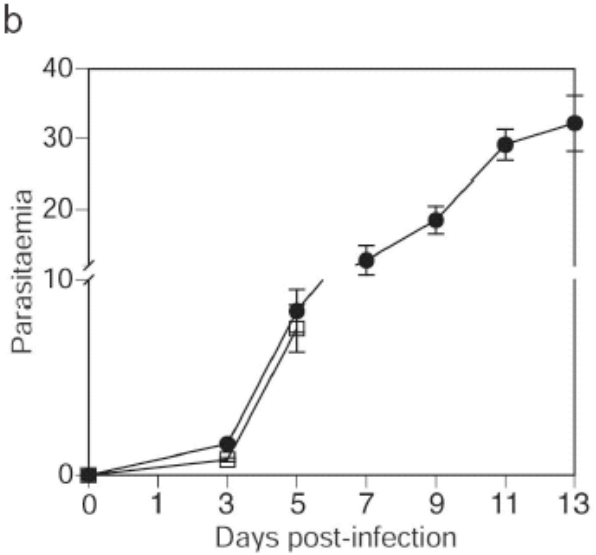
Synthesis of a Malaria Vaccine Candidate



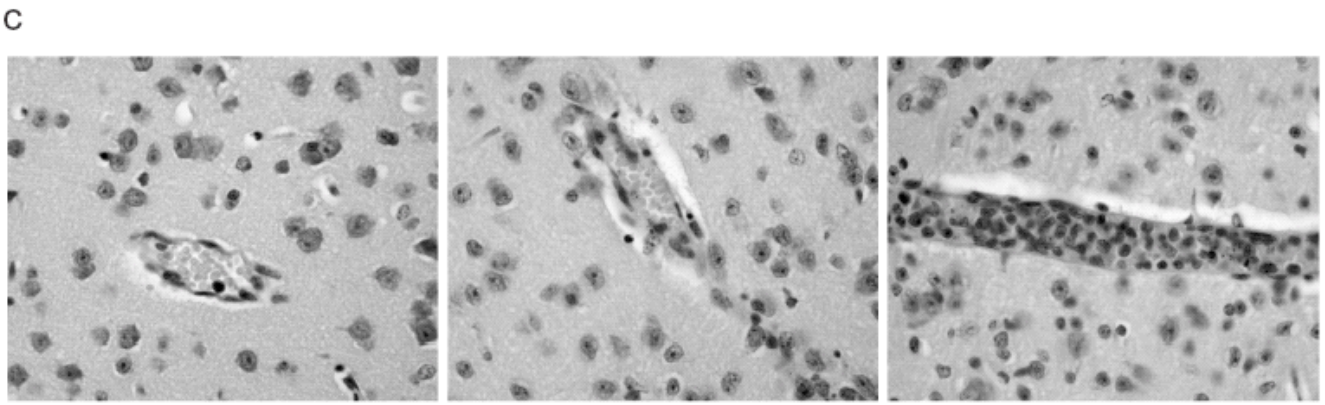
Nature, 2002, *418*, 785

Vaccines vs Controls

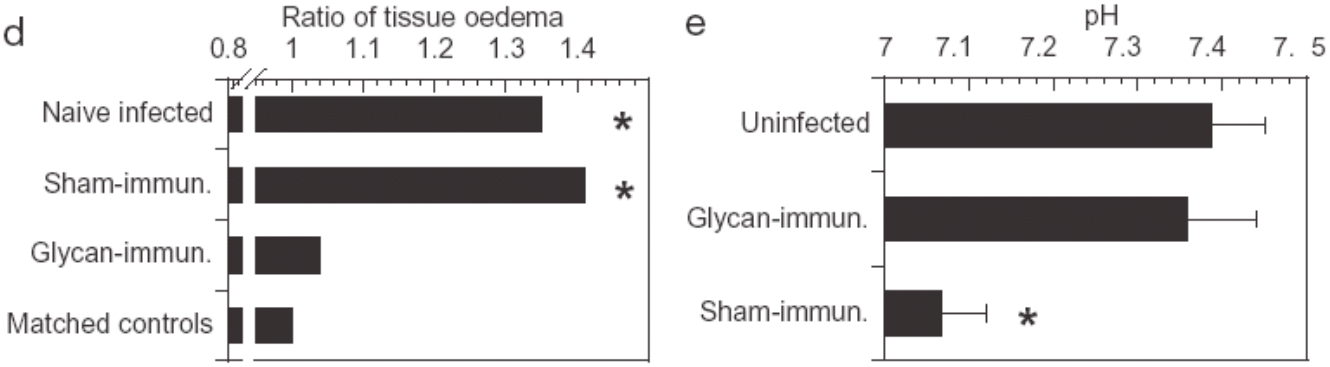




Survival and parasitaemia

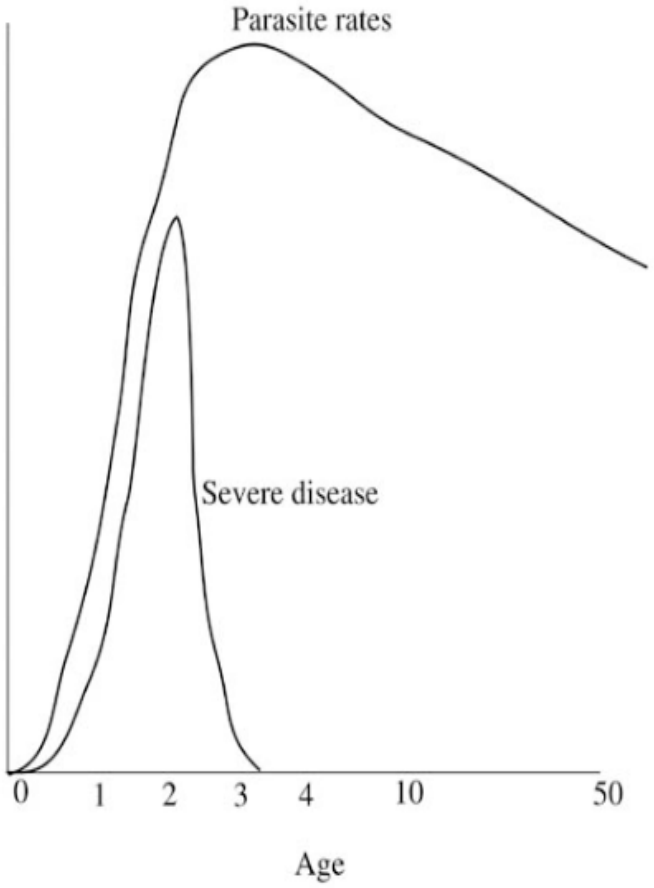


Cerebral Histology

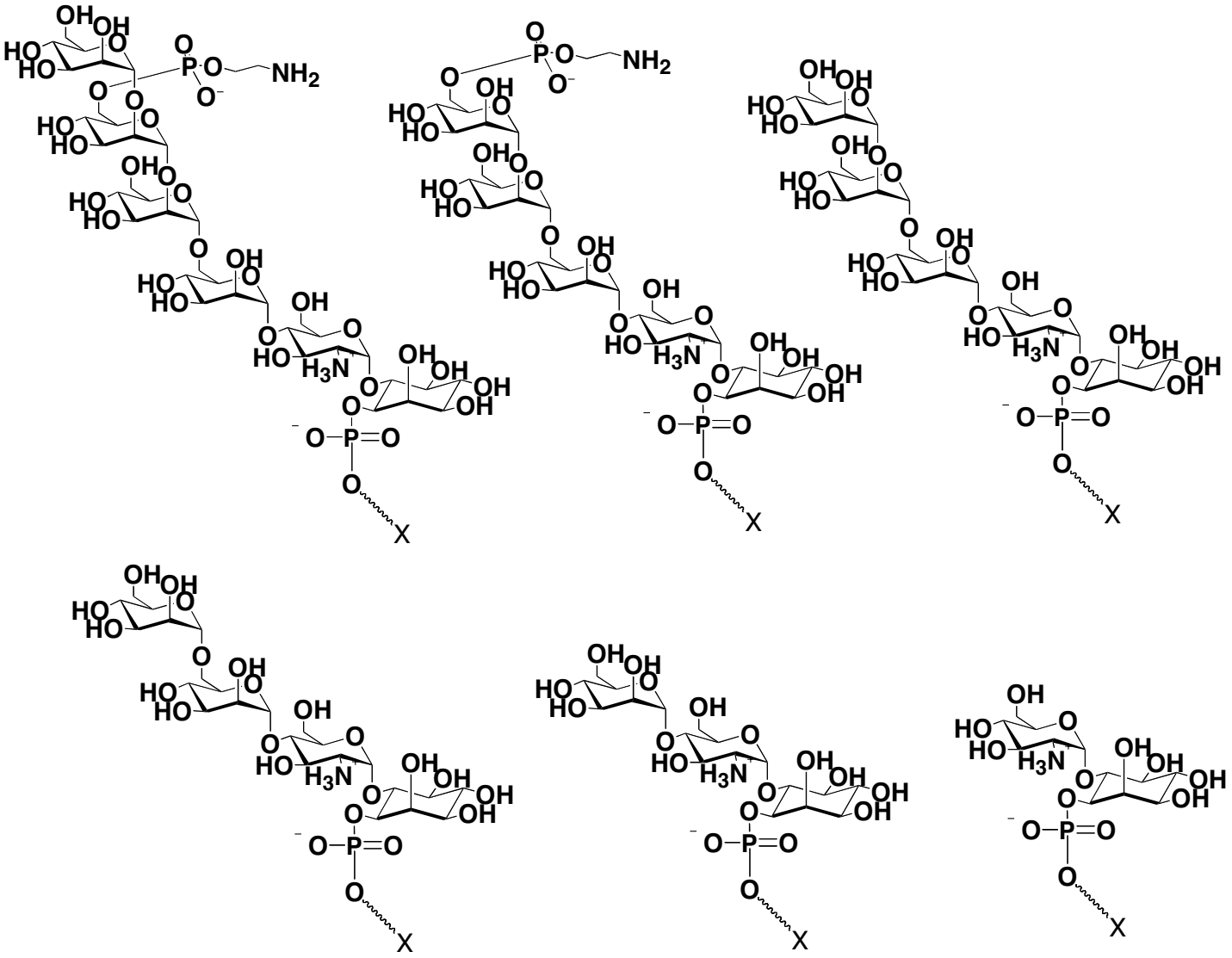


Systemic Pathology

Does an Anti-GPI Response Protect from Malaria Mortality?



Tools for Epitope Mapping & Biosynthesis Investigations



Chem. Eur. J. 2005, *11*, 2493.

GPI Microarray Results - Summary

- Fine specificities and titers differ between exposed and naive populations
- Children of mothers with specific antibodies have no antibodies
- Disease specific antibodies decline in migrants to about 40% in three years

Specific GPI Antibodies Protect Adults in Endemic Areas from Severe Disease

Induction of GPI-specific Antibodies Should Protect Naive Individuals and Small Children from Severe Disease

ETH Zurich Group

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