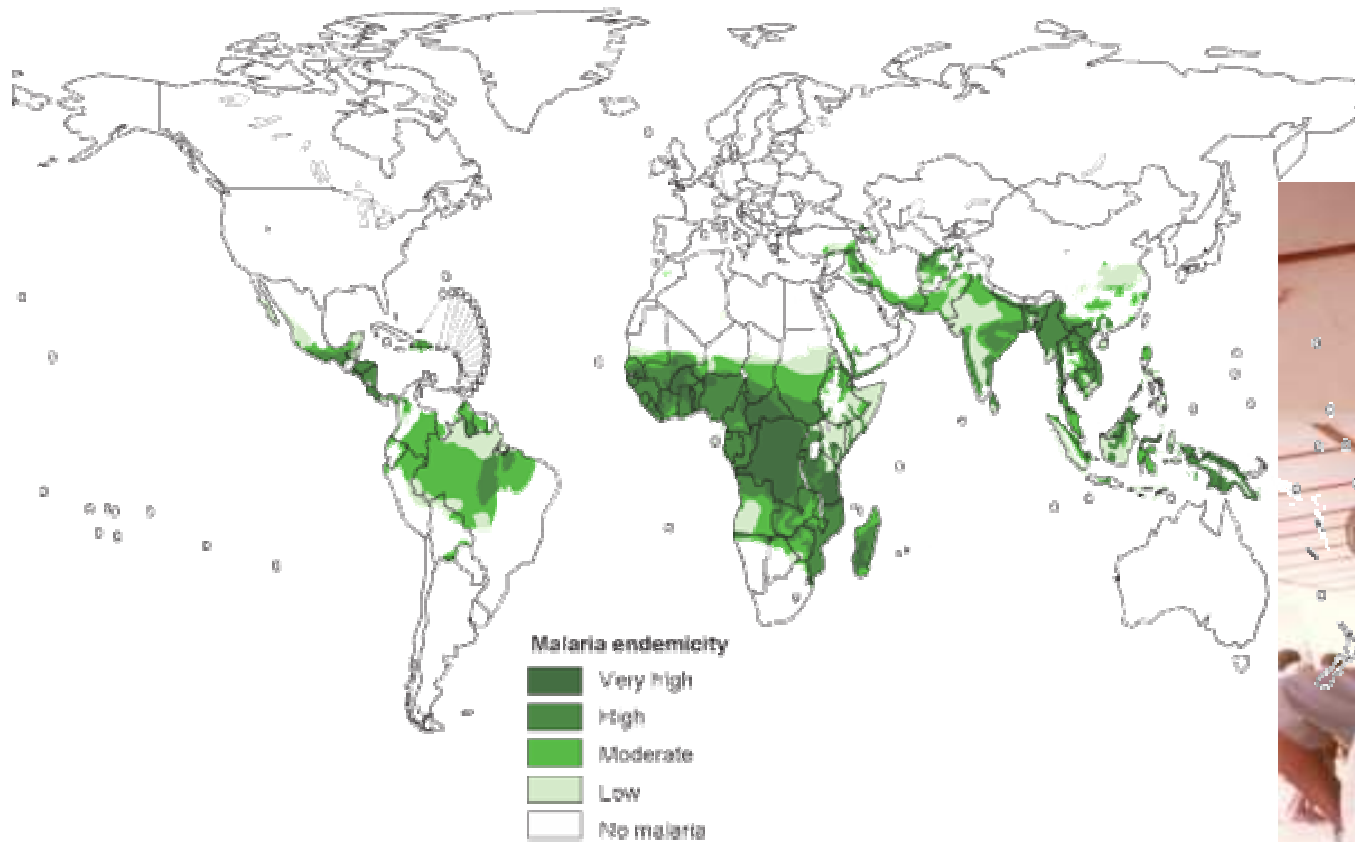


Developing Vaccines for Malaria

Dr. Kavita Singh
Malaria Vaccine Development Program
ICGEB, New Delhi

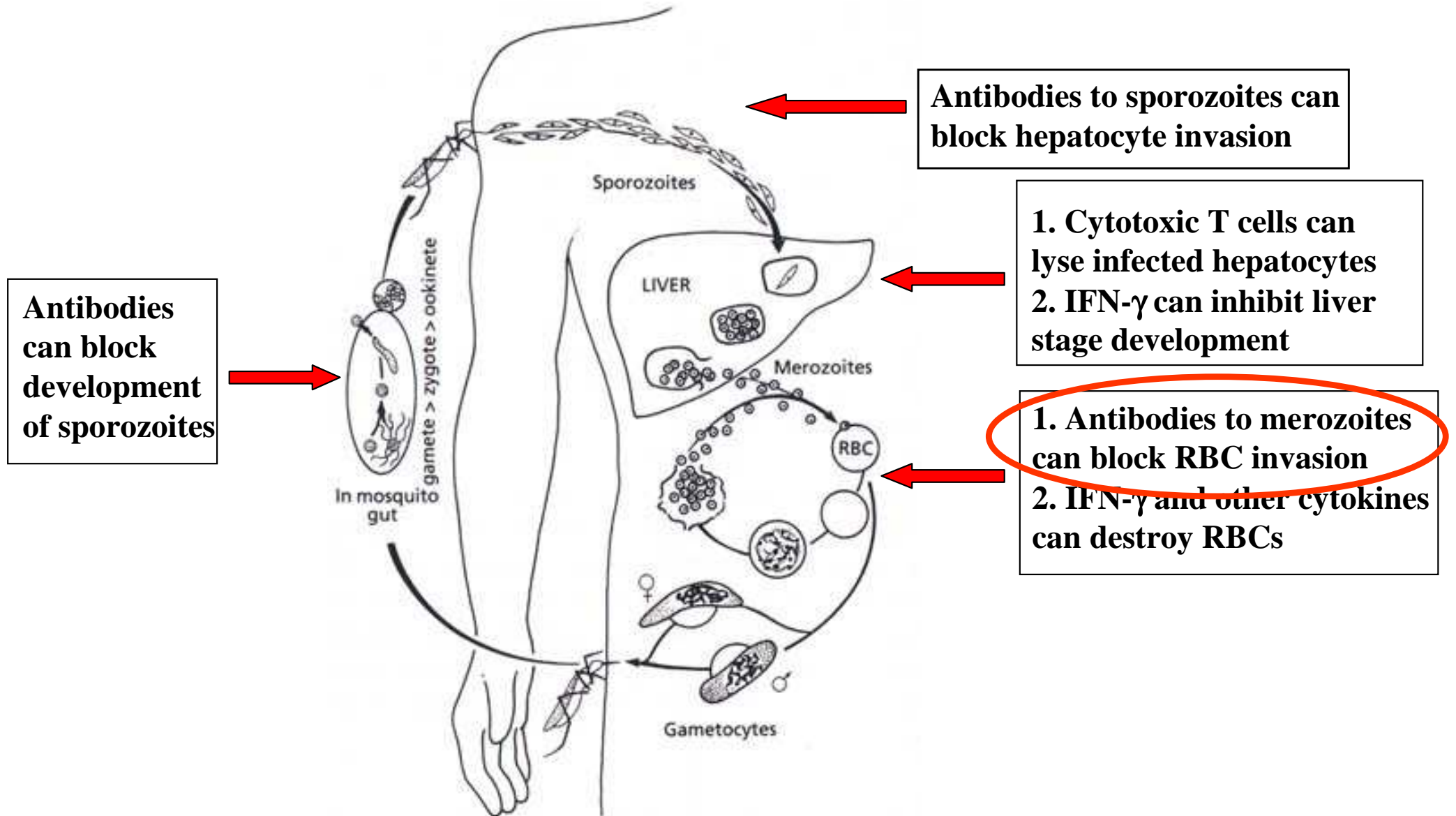
Developing Vaccines for Malaria



- 500 million cases of *P. falciparum* malaria per year
- 1-2 million deaths from malaria per year
- 75-90 million cases of *P. vivax* malaria per year
- Severe vivax malaria



Malaria Vaccine Design - Points of Intervention



Difficulties and challenges

- ❑ Complex parasite life cycle
- ❑ Immune evasion mechanisms
- ❑ Lack of surrogate measures of protection
- ❑ No predictive animal models
- ❑ Proof of concept requires field trials

Malaria Vaccine Development at ICGEB

Blood stage vaccines

- Parasite proteins involved in invasion of RBCs
- Lead vaccine candidates
 - *P. falciparum*: JAIVAC-1 (EBA175 + PfMSP1)
 - *P. vivax*: PvRIL (Duffy binding protein)
- Process development for production of rec. vaccines
- Pre-clinical studies
- Basic research to develop vaccine pipeline
 - PfMSP1₁₉ – MSP3
 - EBA175 + PfRh/TRAMP

Current Status – JAIVAC-1 (PfF2 + PfMSP1₁₉)

➤ Basic Research

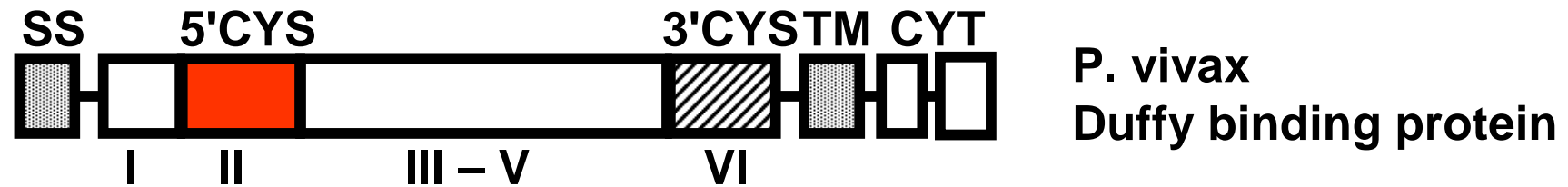
➤ Process Dev and cGMP Production of PfF2 and PfMSP1₁₉

- ✓ Process development (10L) – ICGEB
- ✓ Immunogenicity in small animals – ICGEB
- ✓ Formulation with Montanide ISA720 selected for clinical dev.
- ✓ Tech transfer and cGMP production – Bharat Biotech, Hyderabad

➤ Pre-clinical/Clinical Development

- ✓ Pre-clinical tox – Intox, Pune (Mar 2009)
- ✓ Submission of IND to DCGI for conduct of Phase I trial
- ✓ Phase I – Safety and immunogenicity in healthy adults

Vaccine for *P. vivax* : PvRII



- *P. vivax* dependent on binding Duffy antigen for RBC invasion
- PvDBP mediates interaction with Duffy antigen
- Receptor binding domain of PvDBP maps to region II (PvRII)¹
- PvBP-DARC mediates junction formation during invasion²
- Antibodies to Duffy binding domain block invasion in vitro³ available

1. Chitnis and Miller J Exp Med 1995

2. Singh et al., Mol Microbiol 2004

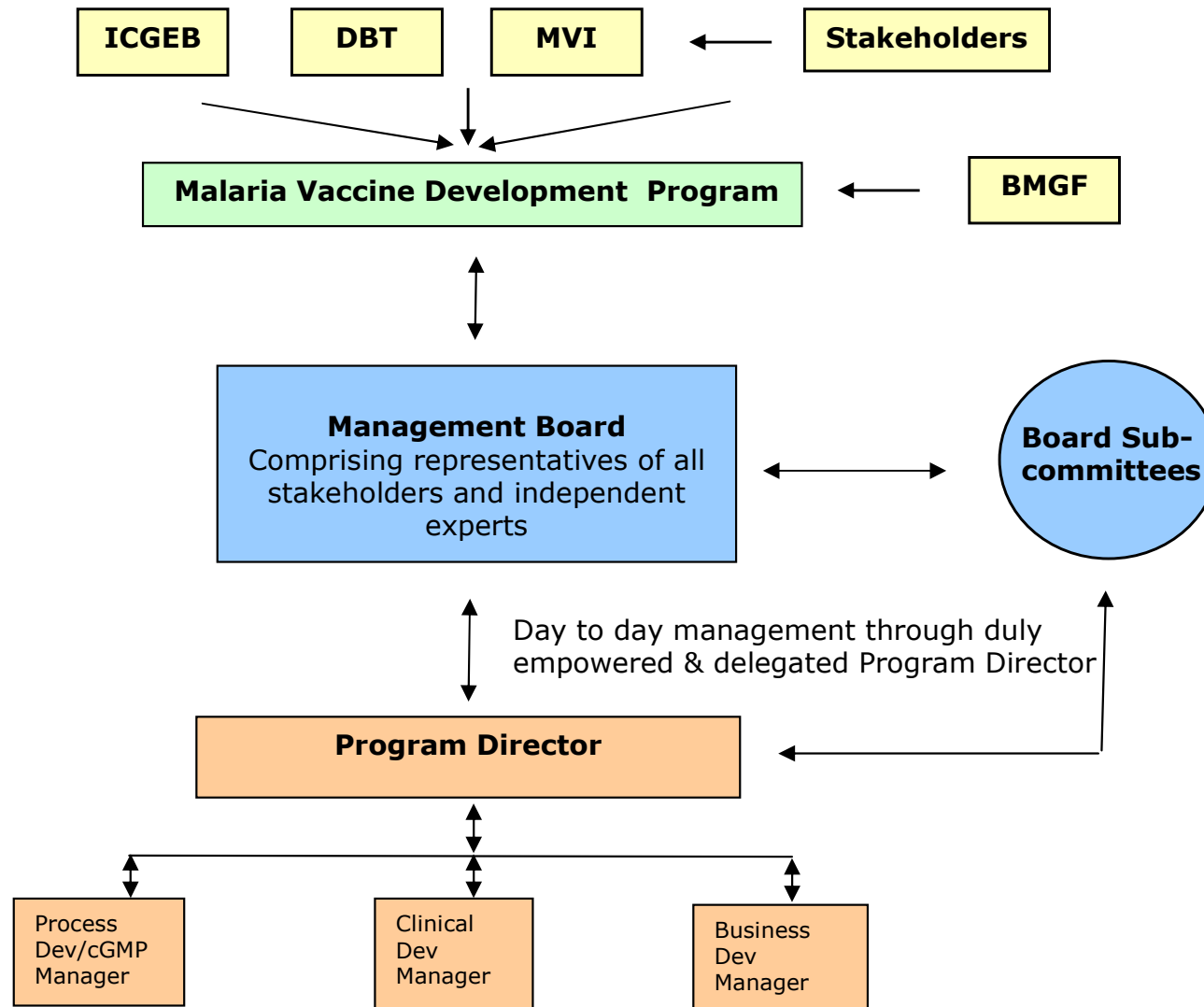
3. Singh et al Mol Biochem Parasitol 2002

4. Hans et al. Mol Microbiol 2005

5. Singh et al. Nature 2006

6. King et al. PNAS 2008

Malaria Vaccine Development Program - Structure



MVDP Workplan

- ❑ Technology transfer and GMP production of PvRII
- ❑ Planning the clinical development of PvRII
- ❑ Clinical development of JAIVAC-1 (PfF2 + PfMSP1₁₉)
- ❑ Selection of other vaccine candidates and adjuvants for clinical development
- ❑ Development of field trials sites in India

Collaboration with MVDP

- ❑ Access to malaria vaccine candidates and antigens from ICGEB
- ❑ Access to India's strengths in Process development and manufacture
- ❑ Access to Indian CROs for Clinical development
- ❑ Availability of funds from Indian government for malaria vaccine development
- ❑ In due course field sites for testing vaccines in India
- ❑ Build synergy with other efforts to accelerate malaria vaccine development