Biology and control of malaria parasite transmission

Activities at Istituto Superiore di Sanità
and opportunities for Italy - South Africa collaborations

Pietro Alano

Bilateral Workshop on Transmissible Diseases: HIV/AIDS, Tuberculosis and Malaria
Italy-South Africa Collaborative Workshop on the occasion of the Italian Research Day in the world, Pretoria, 5 April 2019

Chronic asymptomatic infections significantly contribute to transmission

Data meta analysis from 48,840 participants in 121 clinical trials (70% Africa; 28% Asia; 2% America) indicates that low asexual parasite density, no fever and anaemia are predictors of gametocytaemia.

WWARN Gametocyte Study Group (2016) BMC Medicine 14:79

The majority of gametocyte carriers have submicroscopic gametocytaemias

Data meta analysis from general population and clinical patients from studies in 8 countries (6 in Africa and 2 in SE Asia) indicates that majority of gametocyte carriers have submicroscopic gametocytaemia.

rev in Bousema & Drakeley (2011) Clin. Microbiol. Rev. 24:377

Submicroscopic gametocyte carriers significantly contribute to transmission

A longitudinal study by membrane feeding assay with *A. gambiae* on 130 randomly selected individuals in two malaria endemic villages in Burkina Faso showed that 29% of infectious individuals were microscopy negative, contributing to 17% of mosquito infections.

Ouédraogo et al (2015) Journal Infect Dis. 213: 90

A. gambiae feeding assays with 171 *P. falciparum* infected blood samples from Burkina Faso and Kenya children and *A. dirus* feeding assays with 94 *P. vivax* blood samples from western Thailand farmers demonstrated infectiousness of submicroscopic (even RT-PCR negative!) gametocytaemias.

Churcher et al. (2013) eLife 2:e00626; Kiattibutr et al (2017) Int J Parasitol 47: 163

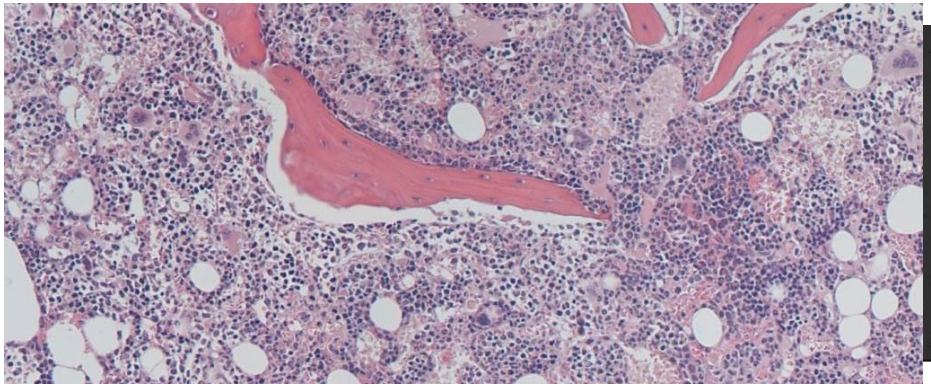
Understanding and contrasting human-to-mosquito malaria parasite transmission

The challenges:

- Characterizing host parasite interplay in the maturation of the parasite transmission stages
  Fundamental biology

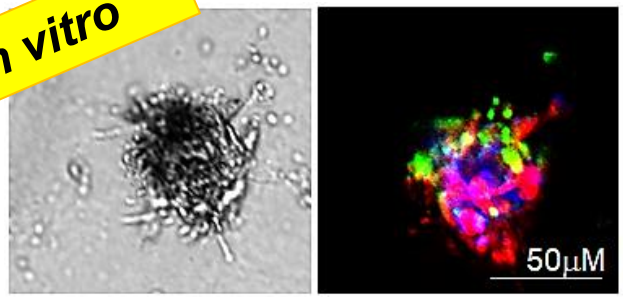
- Developing/using tools to map the malaria parasite transmission reservoir
  New, functionally predictive diagnostics

- Developing drugs active against the non proliferative transmission stages in infected indivduals
  Transmission blocking drug discovery



3D co-culture of human bone marrow mesenchymal stem cells (**hBM-MSC**) *& P. falciparum* **gametocytes**

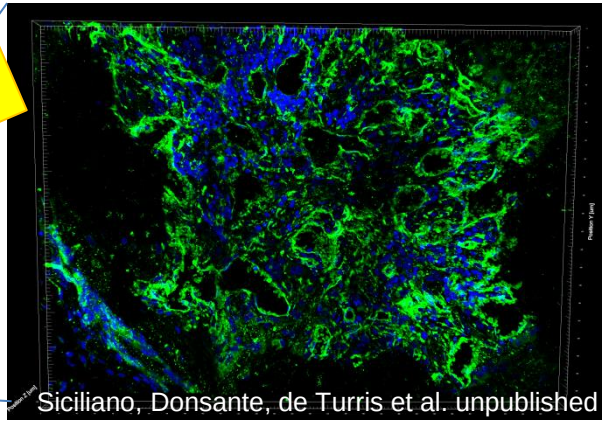
in vitro



Messina et al 2018 Front Cell Infect Microbiol. 8:50

A humanised mouse model of ectopic bone marrow "ossicle"

in vivo



Siciliano, Donsante, de Turris et al. unpublished

Sacchetti *et al.,* 2007 Cell; Serafini *et al.,* 2014 Stem Cell Res.

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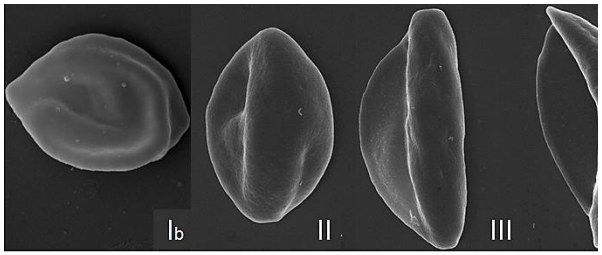

Development of transmission blocking drugs

Development of HTS cell-based assays for chemical library screening

- Luciferase assays with bioluminescent gametocytes (Cevenini, Camarda et al. 2014 Anal. Chem.)
- High content imaging phenotypic assays (Lucantoni, Silvestrini et al 2015 Scientific Reports)

Development of ♂ ♀ gcyte-specific assays and identification of gcyte-selective drugs – ISARP (ISS, Univ. Pretoria, CSIR Pretoria, Univ. Milan)

P. falciparum gametocyte HTS of a 125k chemical diversity library for gcyte-selective and dual (gcyte-asex) active compounds.
Hit identification and validation by orthogonal and selectivity assays on asexual parasites and host cells

Support for building future collaborations!

Research grants
Bilateral schemes of call for proposals

Education and early career
Co-supervised fellowships for young researchers

Mobility
Support for short term visits, skill/technology transfer, seminars, grant writing.

ngiyabonga kakhulu

ke a leboha

grazie

thank you

ngiyabonga

ke a leboga

ndo livhuwa

ndza nkhensa

sibonga

dankie

ke a leboga kudu