5th International Conference of translational medicine on pathogenesis and therapy of immunomediated diseases

Innate immunity, inflammation and experimental models of human diseases

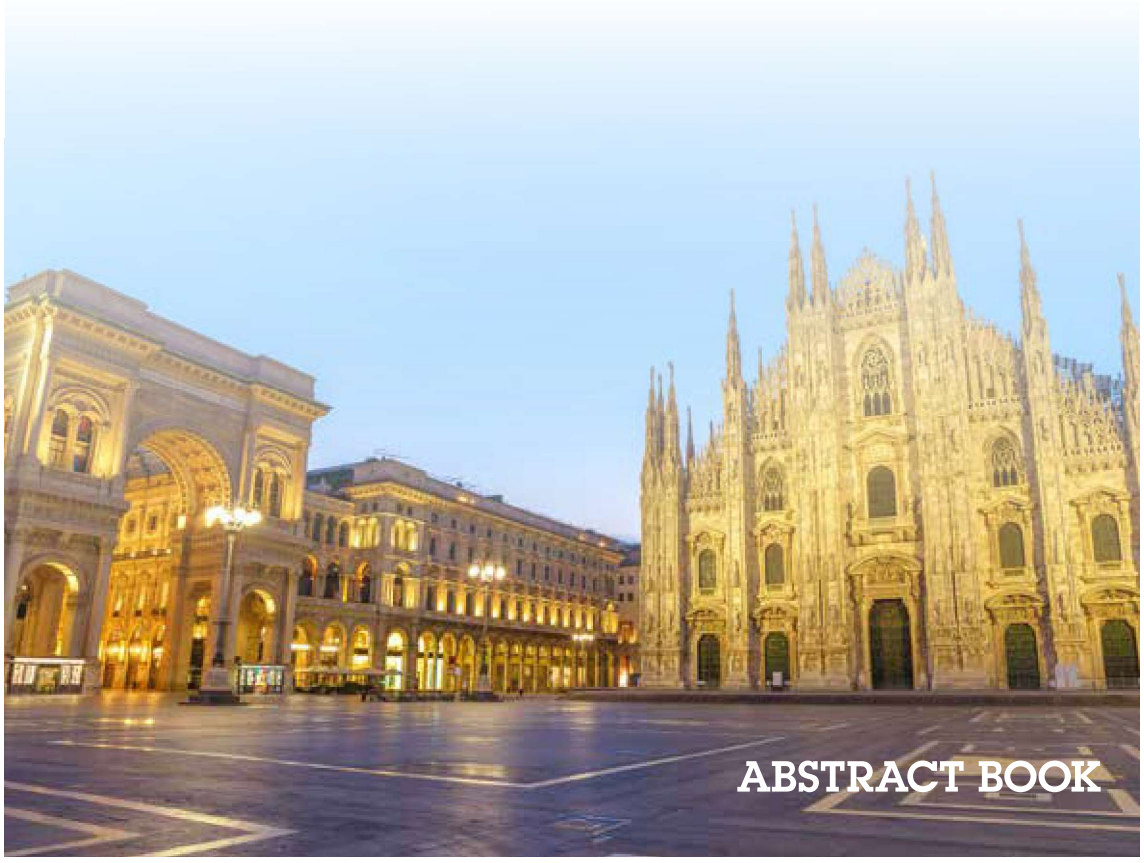
May 16th - 18th, 2019

Università degli Studi di Milano

Milan, Italy

SIICA
Società Italiana di Immunologia
Immunologia Clinica e Allergologia

www.translationalimmunology.it



P57

Innate immune response against Plasmodium falciparum gametocytes: phagocytosis and activation of bone marrow derived macrophages

Sarah D'Alessandro[1], Silvia Parapini[1], Valeria Messina[2], Francesco Silvestrini[2], Loredana Cavicchini[1], Paola Misiano[3], Donatella Taramelli[3], Nicoletta Basilico[1], Yolanda Corbett[4]

[1]Dipartimento di Scienze Biomediche, Chirurgiche ed Odontoiatriche, [3]Dipartimento di Scienze Farmacologiche e Biomolecolari, [4]Dipartimento di Bioscienze, Università degli Studi di Milano, Milan - Italy, [2]Dipartimento di Malattie Infettive, Istituto Superiore di Sanità, Rome - Italy

Gametocytes (GCT), the sexual stage of malaria parasites, develop in five stages (I-V). Stages I-IV are mainly sequestered in the extravascular compartment of the bone marrow, while stage V are released into circulation. Taken up by mosquitos during blood meals, they are responsible for malaria transmission. Few information are available about the role of innate immunity against GCT. The aim of this work was to study the phagocytosis of P. falciparum (Pf) GCT by bone marrow macrophages and their subsequent activation.
A method to evaluate phagocytosis was set up using the Pf transgenic strain 3D7elol-pfs16-CBG99 expressing the luciferase CBG99 under the control of the GCT-specific promoter pfs16 (D'Alessandro et al. 2016 JAC 71:1148). Immortalized bone marrow derived macrophages (BMDM) (Hornung V et al. Nat Immunol 2008;9:847) were incubated with immature (II-III) or mature (V) GCT for 2 or 24h. Non-internalized parasites were removed by a lysis step. The cell permeable substrate luciferin was added and phagocytosis was measured by reading the luminescence using a Synergy4 (Biotek) reader. Both immature and mature GCT were phagocytized by BMDM. Upon pre-incubation with Cytochalasin D, an inhibitor of cell phagocytosis, the luminescent signal disappeared, indicating that the method is suitable to study phagocytosis. The results were further confirmed by Giemsa staining and confocal microscopy, which showed the presence of parasites inside macrophages.
The activation of macrophages was evaluated by measuring the production of TNF-α (ELISA) and nitric oxide (Griess assay) in the supernatants of BMDM incubated with GCT. Mature GCT were more stimulatory than immature GCT.
An active interplay occurs between Pf GCT and BMDM suggesting an important, yet unexplored role of the innate immunity against the transmission stages of malaria. Moreover, the new luminescent method to quantify phagocytosis is reliable and can be adapted to different cell models.