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Società Italiana di Parassitologia

WORLD MALARIA DAY

Immunology taught by *Plasmodium falciparum*

Antonio Lanzavecchia

National Institute of Molecular Genetics, Milano
Vir Biotechnology, Bellinzona, Switzerland

Giovedì 29 aprile 2021 ore 15:00

Seminario web:
canale YouTube MediaEventi Università di Pisa

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Saluti introduttivi
Fabrizio Bruschi, Presidente Società Italiana di Parassitologia
Donatella Taramelli, Direttrice Italian Malaria Network

Discussione
Bruno Arcà, Università di Roma La Sapienza
Valentina Mangano, Università di Pisa
David Modiano, Università di Roma La Sapienza
Roberta Spaccapelo, Università di Perugia

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Il seminario si svolgerà in italiano

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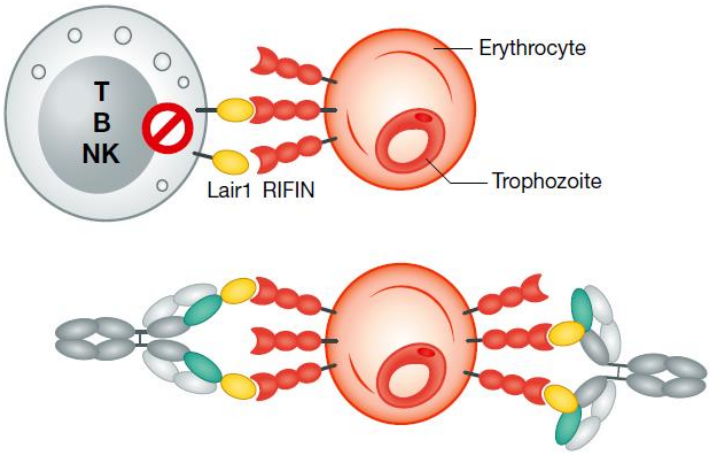
Abstract

Plasmodium falciparum uses multiple strategies to evade the human immune response. While infection is established by a small number of sporozoites that are largely ignored by the immune system, the abundant blood stage parasites use multiple and polymorphic variant surface antigens to avoid clearance and subvert the immune response. From volunteers immunized with irradiated sporozoites, we identified a family of potent neutralizing antibodies that bind to multiple sites of the CSP protein and represent a new tool for prophylaxis and for vaccine design. Using a systematic search for antibodies that bind broadly to infected erythrocytes, we discovered, in 10% of malaria-exposed individuals, a new class of antibodies generated by insertions of genomic DNA encoding human inhibitory receptors (LAIR1 or LILRB1) into antibody genes (at the V-DJ junction or in the switch region). LAIR1- and LILRB1-containing antibodies bind to different families of parasite RIFINs and opsonize infected erythrocytes. These findings demonstrate that the parasite uses multiple RIFINs to target inhibitory receptors as part of its evasion strategy. They also illustrate a new mechanism of diversification based on the insertion of host receptors into immunoglobulin genes, leading to the production of receptor-based antibodies, with implications for antibody and B cell engineering.

References: Tan et al., *Nature* 529:105 (2016); Pieper et al., *Nature* 549: 597 (2017); Tan et al., *Nat. Med* 24: 401 (2018); Chen et al. *Nature* (in press).



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Antonio Lanzavecchia

Antonio Lanzavecchia is known for his work on antigen presentation by B cells and dendritic cells, for his studies on T cell activation and on the cellular basis of immunological memory, and for the development of novel methods to isolate human monoclonal antibodies. Lanzavecchia was born in Italy and obtained a medical degree from the University of Pavia, where he specialized in pediatrics and in infectious diseases. From 1983 to 1999 he worked at the Basel Institute for Immunology and since 2000 as founding director of the Institute for Research in Biomedicine in Bellinzona, Switzerland. He has been Professor of Immunology at the University of Genova and at the Swiss Federal Institute of Technology, ETH Zürich. Lanzavecchia received the EMBO Gold Medal, the Cloetta Prize, the Robert Koch Prize, the Sanofi-Institut Pasteur prize and the Louis-Jeantet Prize and is a member of the EMBO and a foreign associate of the US National Academy of Sciences. Lanzavecchia is the scientific Founder of Humabs Biomed, now a subsidiary of Vir Biotechnology, where he is currently Senior Research Fellow. His academic research continues at the National Institute of Molecular Genetics in Milan.

Lanzavecchia's laboratory investigates the mechanisms of antibody-mediated resistance to infectious diseases. Using high-throughput cellular screens, the group interrogates human memory B cells and plasma cells and isolates potent and broadly neutralizing antibodies against a variety of targets, ranging from common pathogens to emerging viruses. These antibodies are developed for prophylaxis and treatment of infectious diseases and are used as tools to produce optimal vaccine components in a process of antibody-guided vaccine design. Besides these translational studies, the laboratory addresses fundamental aspects of the antibody response, such as the mechanisms that lead to the production of broadly neutralizing antibodies, and the relationship between infection and autoimmunity. The laboratory is also studying a new mechanism of antibody diversification through templated DNA insertions that they recently discovered in the context of the antibody response to malaria parasites.

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