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Rifampicin-dependent antibody targets calcium-dependent epitopes on the glycoprotein IIb/IIIa complex

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Abstract

Drug-induced immune thrombocytopenia (DITP) is a major adverse drug effect mediated by drug-dependent antibodies (D-dAbs), which can be actuated by a wide range of medications including rifampicin. We characterized rifampicin-dependent antibody (Rif-dAb) from a tuberculosis patient who was treated with rifampicin and developed thrombocytopenia. Analysis included flow cytometry, monoclonal antibody immobilization of platelet antigens (MAIPA) assay, immunoprecipitation and an in vivo bioassay. Using five different monoclonal antibodies (mAbs) against various epitopes on the GPIb/IX (SZ1 and FMC25) and GPIIb/IIIa complex (AP2, SZ21 and SZ22) we found that the Rif-dAb binds glycoprotein (GP) IIb-IIIa but not GPIb-IX (another well known target for D-dAbs by MAIPA assay) . The binding of Rif-dAb to platelets was fully blocked by the anti-GPIIb/IIIa mAb (AP2), indicating that the Rif-dAb is not only specific for GPIIb/IIIa but also identical or close to the binding site of AP2 (calcium-dependent epitopes on the GPIIb/IIIa complex). Importantly, in our established nonobese, diabetic/severe immunodeficient mouse model of DITP, human platelets were rapidly cleared in vivo by co-injected Rif-dAb. The Rif-dAb-induced rapid platelet clearance was partially prevented by the treating mice with intravenous immunoglobulin (IVIG). Our results clearly show that: (1) thrombocytopenia is caused by the Rif-dAb and (2) IVIG treatment could partially inhibit in vivo platelet clearance by Rif-dAb, which may provide some guidance for the treatment of rifampicin-induced immune thrombocytopenia.

Biography

Simon X. Liang obtained his PhD in medicine at the University of Sydney in 2001. He did a post-doctoral research at Boston University School of Medicine from 2003 to 2005. Subsequently, he worked as a senior research scientist in St George Clinical School at the University of New South Wales. Since 2011, Dr. Liang has been appointed as a professor and head of the Department of Biochemistry and Molecular Biology at Liaoning Medical University, China. His researches focus on drug-induced immune thrombocytopenia. He has published 14 papers in reputed journals and served as a reviewer for four international journals.