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

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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 Ph.D. 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, He 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.

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