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A PEPTIDE MOIETY OF HUMAN A1-ACID GLYCOPROTEIN IS RECOGNIZED BY THE HEMOGLOBIN B-CHAIN ON MOUSE LIVER PARENCHYMAL CELLS

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ABSTRACT

Human α1-acid glycoprotein (AGP), a serum glycoprotein, is known to have anti-inflammatory activity. We recently reported that AGP was mainly incorporated into the liver in mice via a receptor-mediated pathway, although the mechanism for this was largely unknown. The objective of this study was to identify the specific cellular surface protein that recognizes the peptide moiety of AGP. Pharmacokinetic studies of ^{111}In-AGP and recombinant glycan-deficient ^{111}In-AGP (rAGP) in mice demonstrated that both AGPs are mainly distributed to the liver and kidney, but hepatic and renal uptake clearance of rAGP was higher than that for AGP. Hepatic uptake of rAGP was inhibited in the presence of a 100-fold excess of unlabeled AGP, indicating that the hepatic uptake of rAGP shared a common route with that of AGP and that it recognized the peptide moiety of AGPs. In ligand blotting analyses using crude cellular membrane fraction of mice liver, a band corresponding to a 16 kDa protein was observed to bind to both AGPs. Interestingly, MALDI/TOFMS and Western blotting analyses indicated that this 16 kDa protein is the hemoglobin β-chain (HBB). It therefore appears that HBB is associated with the hepatic uptake of AGP via a direct interaction with its peptide moiety.