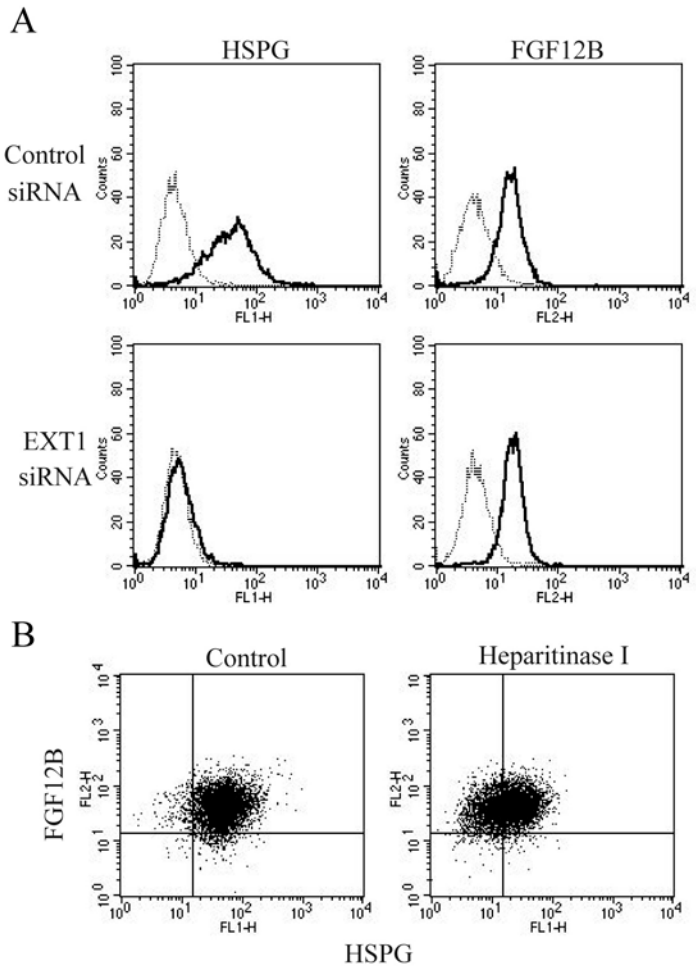

FIGURE S2. **Inhibition of FGF12 internalization by heparin.** *A,* In order to identify the mechanism of FGF12 internalization, the expression of HSPG was down-regulated in IEC6 cells by siRNA-mediated repression of EXT1, which was required for polymerization of the heparan sulfate (HS) chain (35). IEC6 cells were transfected with Stealth RNAi targeting the *EXT1* gene (EXT1 siRNA) using Lipofectamine RNAiMAX in accordance with the manufacturer's instructions (Invitrogen) and incubated for 48 h to inhibit heparan sulfate (HS) chain synthesis. Mock transfection was performed with control Stealth RNAi (Control siRNA). These transfectant cells were incubated with 1 μg/ml Alexa Fluor 568-labeled FGF12B for 24 h. Then, they were stained with an anti-HS antibody (10E4) (Seikagaku Kogyo, Tokyo, Japan) and subjected to flow cytometry to assess the level of FGF12 internalization and cell surface expression of HSPG. Surprisingly, FGF12B could be internalized into IEC6 cells without any cell surface expression of HSPG. *B,* IEC6 cells were incubated with 10 mU/ml of heparitinase I (Seikagaku Kogyo) for 60 min to digest the HS chains and then incubated with 1 μg/ml Alexa Fluor 568-labeled FGF12B for 24 h. The treated cells were subjected two-color flow cytometric analysis to assess the level of FGF12B internalization and cell surface expression of HSPG. Two-color flow cytometric analysis showed that heparitinase I treatment increased the population of cells with a low expression of anti-HS antibody epitope compared with an untreated control; however, the rates of Alexa Fluor 568-positive fluorescent cells was not reduced in this cell population.