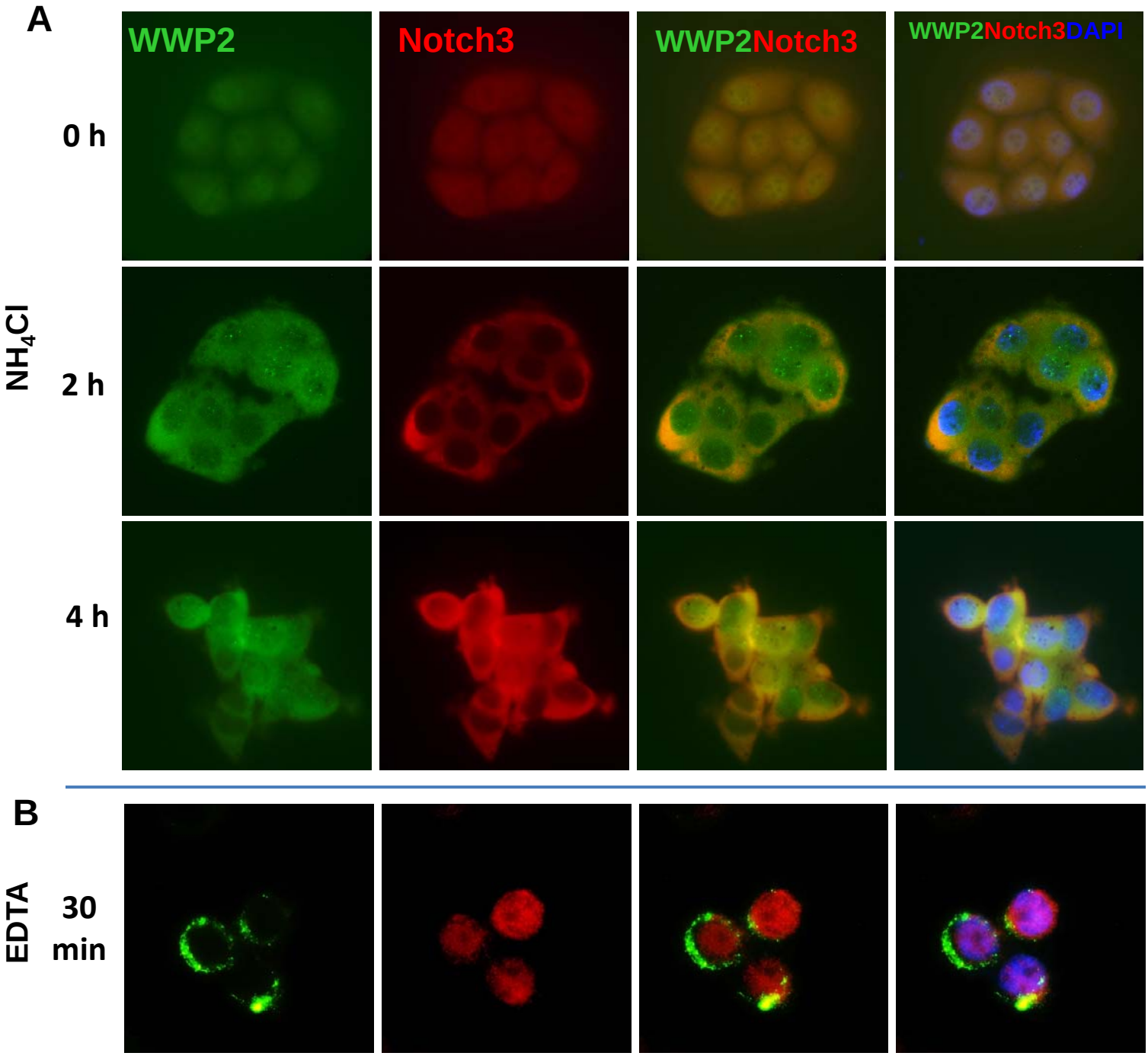

Fig. S2. Localization of WWP2 and Notch3 in cancer cells treated with NH_4Cl. MCF7 cells were treated with either NH_4Cl (A) or EDTA (B) for the indicated time and cells were subjected to immunofluorescence staining. In NH_4Cl treated cells, WWP2 and Notch3 protein fragments are co-localized. However, in EDTA treated cells, WWP2 and N3-ICD are located in different cellular compartments. As shown in Fig. 4, NH_4Cl treatment resulted in release and cytoplasmic accumulation of N3-NEXT while EDTA treatment induces release and nuclear accumulation of N3-ICD.