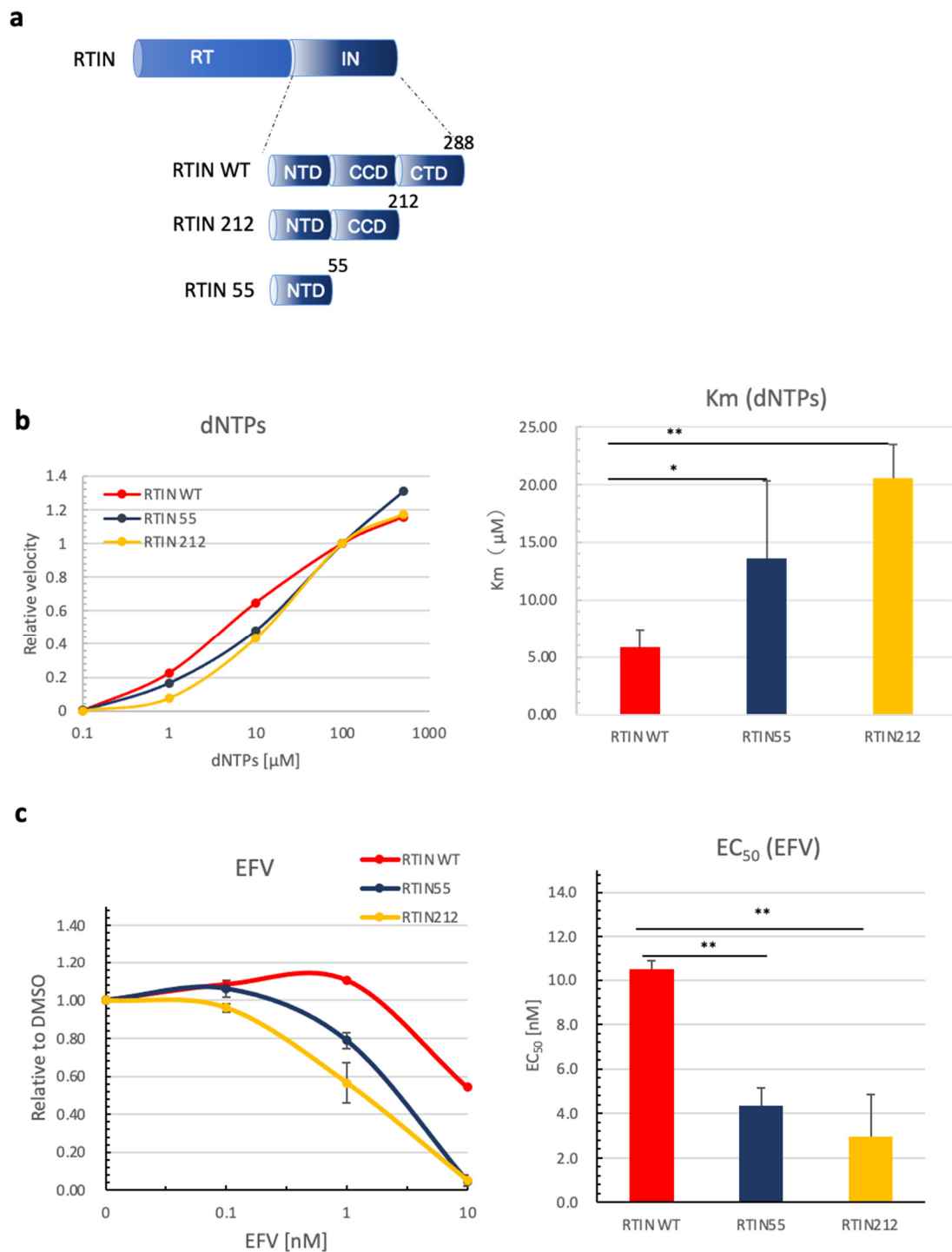


Supplementary Figure S1. SEC profiles of rRTIN. **a.** Purified rRTIN was subjected to a size-exclusion column of Superdex 75 increase 100/300 GL (Cytiva). Retention volume (ml) for each main peak is indicated. To estimate protein size, a molecular weight marker (MWM, Sigma-Aldrich) was also subjected to the same column independently. Locations of MWM proteins are shown on the top with size (kDa) and retention volume (ml). **b.** Fractions of major peaks were subjected to SDS-PAGE followed by staining with Coomassie brilliant blue. Lanes: M (size marker), F1 (fractions of #2-4), F2 (fractions of #5-11), F3 (fractions of #12-14), F4 (fractions of #15-17). Band corresponding to RTIN (molecular weight: 96,466) is indicated. **c.** Major peak fractions (F1-F3) were pooled and subjected to a size-exclusion column of Superdex 200 increase 100/300 GL (Cytiva) as described in **a.**



Supplementary Figure S2. Contribution of IN domains on RTIN functions. **a.** rRT carrying IN NTD (residues 1-55, RTIN 55), NTD and CCD (residues 1-212, RTIN 212) or NTD, CCD and CTD (residues 1-288 RTIN WT) are schematically illustrated. **b.** *In vitro* reverse transcription assay was performed in the presence of different concentrations of dNTP. Levels of R/u5 products were measured and are shown as velocity values relative to the level at 100 μM of dNTPs as 1.0 (left). K_m to dNTPs for each form of RTIN was calculated as

described in Figure 4 (right). Data are shown with means \pm SD (n=3). **c.** *In vitro* reverse transcription assay was performed in the presence of different concentrations of efavirenz (EFV). Levels of R/u5 products were measured and are shown as values relative to the level with solvent (DMSO) only as 1.0 (left). EC₅₀ of EFV for each rRTIN was determined by calculating drug concentration to inhibit 50% of RDDP activity in solvent only (right). Data are shown with means \pm SD (n=3). Student's *t* analysis showed significant differences between RTIN WT and either RTIN 55 or RTIN 212 (*p<0.05, **p<0.01).