To verify the binding of *Drosophila* Numb and Dab to the APP.ICD in GST-pulldown assays, similar assays were performed with the S\(^{35}\)-labeled *in vitro* translated human Dab2 and Numb proteins. Like their *Drosophila* counterparts, human Dab and Numb bound the NPTY-motif within the ICD of APP. Deletion of this motif or point mutations abolished or significantly reduced binding.

**Supplementary Figure 3** Interaction between APP.ICD and human Dab2 and Numb *in vitro*. 