

### Supplementary Table S1: Development of various pro-Abs with different blocking fold

We identified good candidate pro-Abs that achieved  $\geq 100$ -fold blocking with targeted Ags including pro-infliximab,  $\alpha$ -hu-CD19, PD-1, IL-1 $\beta$ , CTLA-4, mouse PD-1 and mouse CD3 Ab. In contrast, the bad pro-Abs did not reach 100-fold such as  $\alpha$ -mouse CTLA-4, human EGFR and CD52 Ab. (-: not shown in the Table 1)

Targeted Ag	Blocking fold	Linker
Good blocking ability ( $\geq 100$ fold)		
human TNF $\alpha$ (pro-Infliximab <sup>[19]</sup> )	395	L3
human CD19	269	L1
human PD-1	250	L2
human IL-1 $\beta$	186	L4
human CTLA-4	150	L2
mouse PD-1	135	L3
mouse CD3	114	-
Bad blocking ability (<100 fold)		
mouse CTLA-4	82	L3
human EGFR	49	L4
human CD52	20	-