Supplemental information
Figure S1. Deuterium uptake plots of heavy chain briakinumab and the briakinumab variant peptides. Deuterium incorporation of unbound briakinumab (red), FcRn-bound briakinumab (blue), unbound briakinumab variant (green), FcRn-bound briakinumab variant (purple) was determined in triplicate experiments at 15 s, 1 min, 1 h, 2.5 h and 5h and plotted with 1x standard deviation (in most cases the SD was lower than the size of the data point marker). The 90 % D$_2$O control is shown in orange at the last time point.
Figure S2. Deuterium uptake plots of light chain briakinumab and the briakinumab variant peptides. Deuterium incorporation of unbound briakinumab (red), FcRn-bound briakinumab (blue), unbound briakinumab variant (green), FcRn-bound briakinumab variant (purple) was determined in triplicate experiments at 15 s, 1 min, 1 h, 2.5 h and 5h and plotted with 1x standard deviation (in most cases the SD was lower than the size of the data point marker). The 90 % D₂O control is shown in orange at the last time point.
Figure S3. Sequence coverage map of briakinumab and the briakinumab variant A) heavy chain and B) light chain.
**Figure S4.** Deuterium uptake plots of heavy chain ustekinumab peptides. Deuterium incorporation of unbound ustekinumab (red), FcRn-bound ustekinumab (blue) was determined in triplicate experiments at 15 s and 1 h and plotted with 1x standard deviation (in most cases the SD was lower than the size of the data point marker). The 90 % D₂O control is shown in green at the last time point.
Figure S5. Deuterium uptake plots of light chain ustekinumab peptides. Deuterium incorporation of unbound ustekinumab (red), FcRn-bound ustekinumab (blue) was determined in triplicate experiments at 15 s and 1 h. and
plotted with 1x standard deviation (in most cases the SD was lower than the size of the data point marker). The 90 % D2O control is shown in green at the last time point.

**Figure S6.** Sequence coverage map of ustekinumab A) heavy chain and B) light chain.
Figure S7. Comparison of theoretical deuterium uptake of unstructured peptides of briakinumab and the briakinumab variant. Theoretical deuterium uptake of peptides containing the R to A substitution: A) 13-39, B) 50-74 and C) 92-101 of briakinumab (blue) and the briakinumab variant (orange) at time points 0.1 s, 1 s, 15 s, 1 h, 2.5 h and 5 h. The theoretical uptake for random coil peptides was calculated using intrinsic exchange rates of Bai et al. (18)
Figure S8. Sequence alignment of ustekinumab and briakinumab LC. Sequence alignment performed with Clustal Omega. (*) indicates a fully conserved residue, (:) indicates conservation between residues with strongly similar properties, and (.) indicates conservation between residues with weakly similar properties. (20)