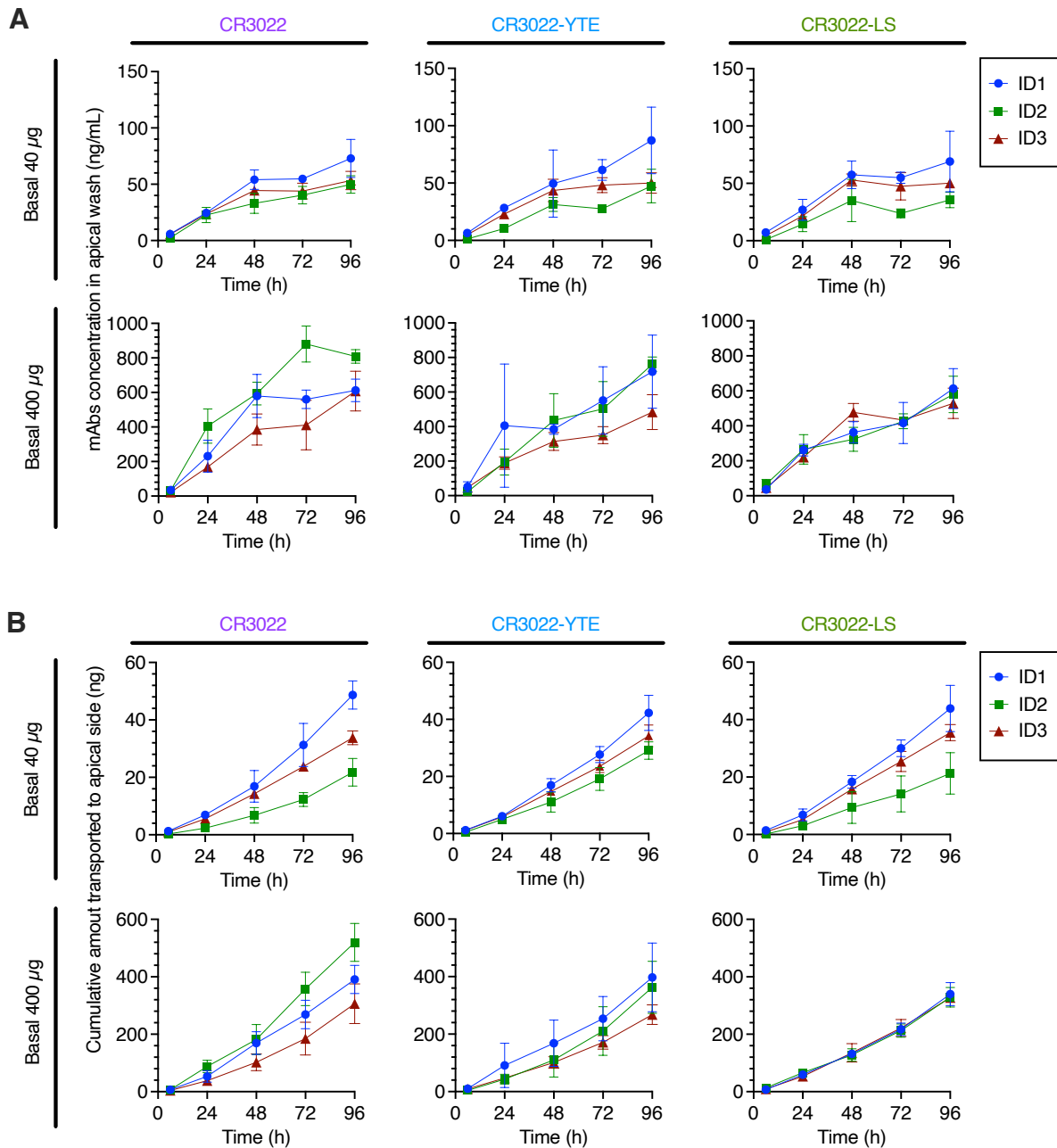
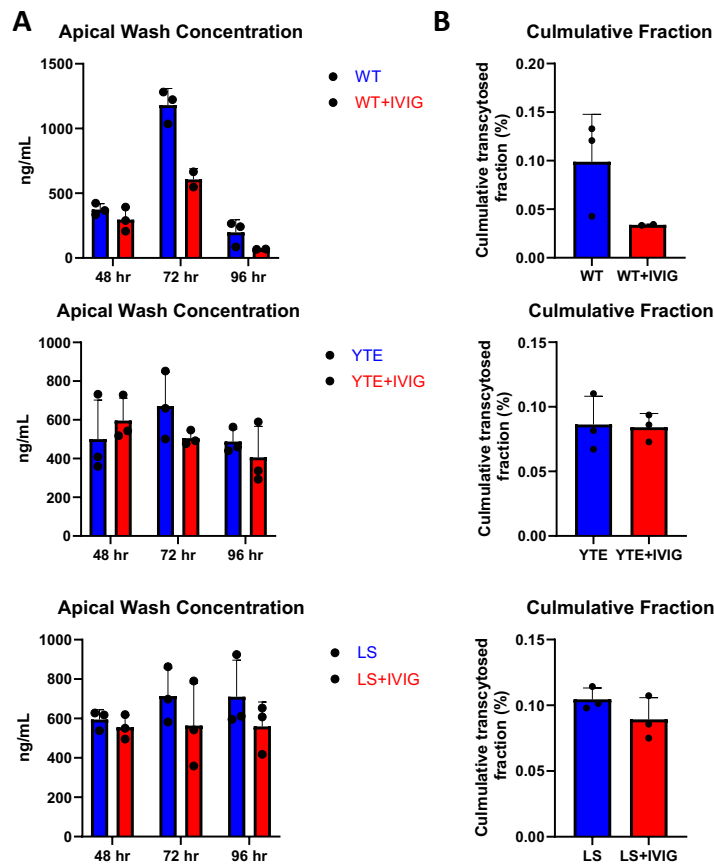


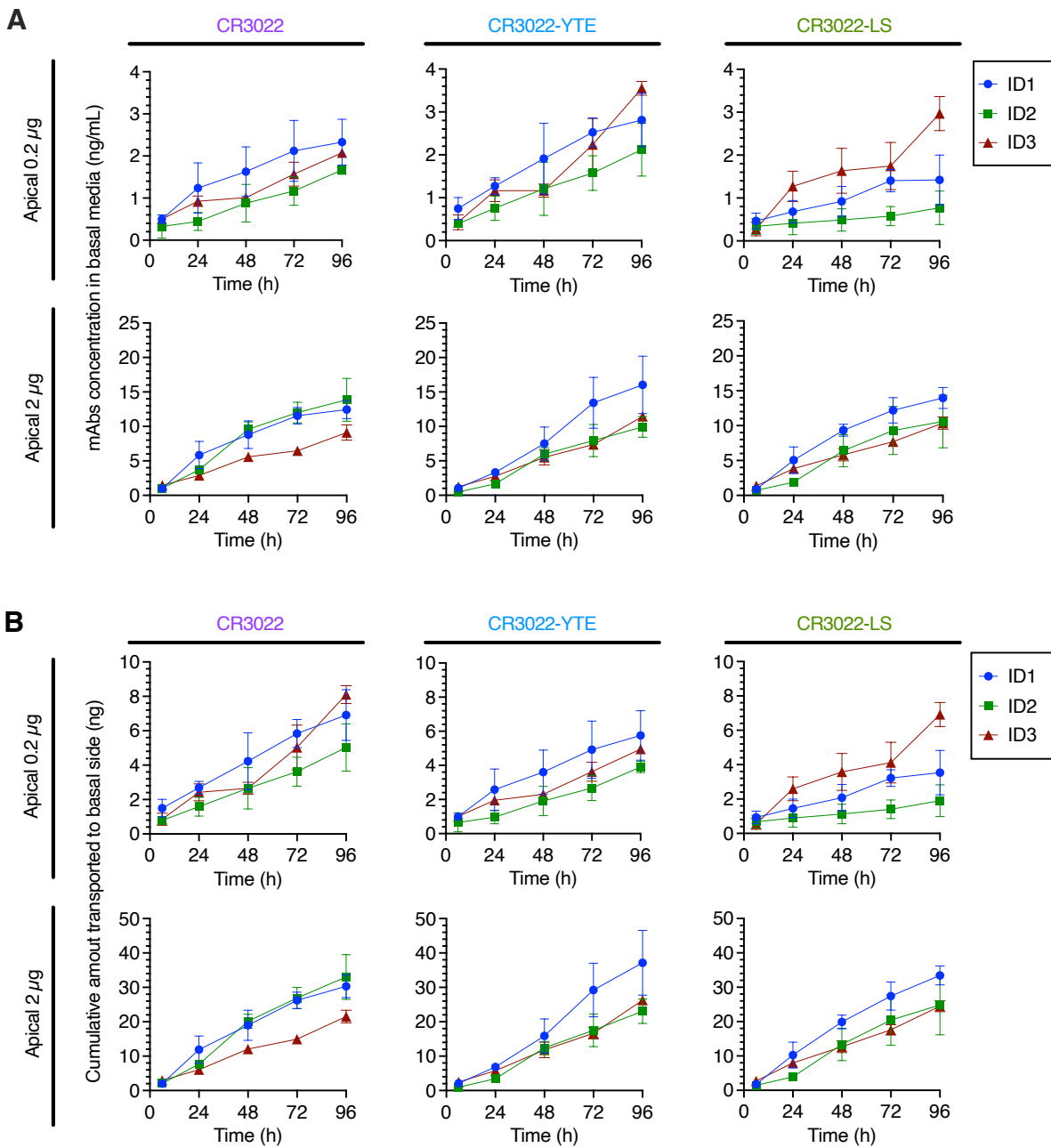
## Supplementary Materials

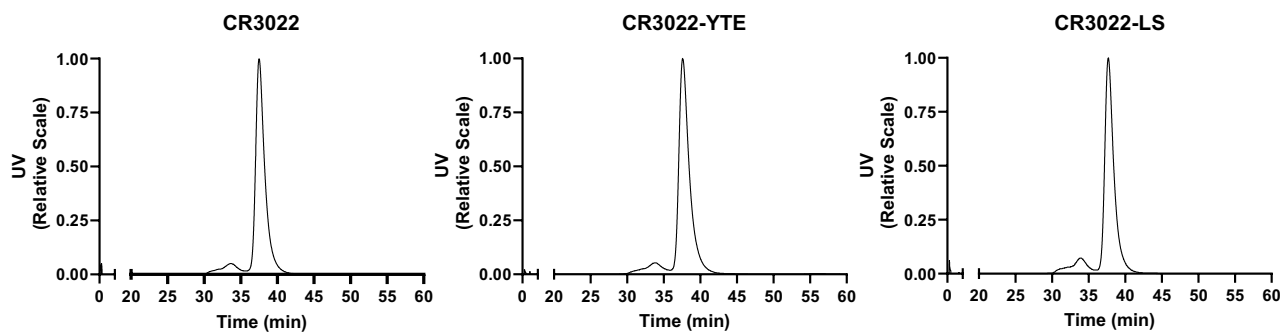


**Figure S1.** Patient ID-based comparison of basal-to-apical transport of CR3022 and its variants across WD-HAE cell culture **(A)** The mAb concentration in the apical wash over time at basal doses of 40 and 400 µg. **(B)** The cumulative amount of mAbs transported to the apical side over time at basal doses of 40 and 400 µg.



**Figure S2.** Effect of IVIG on the basal-to-apical transport of CR3022, CR3022-YTE and CR3022-LS across WD-HAE cell culture. **(A)** The concentration of various CR3022 variants in the apical wash on Day 2, Day 3 and Day 4 following basal dosing of 400  $\mu\text{g}$ , with or without co-application of IVIG (4 mg). **(B)** The cumulative amount of CR3022 variants transported to the apical side over 4 days, with or without IVIG (4 mg).





**Figure S4:** Size-exclusion chromatography multi-angle light scattering (SEC/MALS) assessment of purity of CR3022 variants. The % of the UV corresponding to the monomer peak is 91.3, 88.4, and 91.0% for CR3022, CR3022-LS, and CR3022-YTE respectively.

mAb	Dose ( $\mu$ g)	Time (h)	<i>P</i> values for mAb concentration in apical wash		<i>P</i> values for cumulative amount transported	
			vs CR3022-YTE	vs CR3022-LS	vs CR3022-YTE	vs CR3022-LS
CR3022	20	6	0.949	0.944	0.951	0.944
		24	0.635	0.719	0.704	0.765
		48	0.938	0.794	0.759	0.992
		72	0.994	0.790	0.957	0.998
		96	0.955	0.748	0.996	0.940
CR3022-YTE	20	6		1.000		1.000
		24		0.990		0.994
		48		0.589		0.688
		72		0.844		0.974
		96		0.572		0.967
CR3022	200	6	0.484	0.078	0.484	0.078
		24	0.997	0.957	0.998	1.000
		48	0.026*	0.039*	0.518	0.660
		72	0.151	0.051	0.165	0.224
		96	0.936	0.260	0.275	0.179
CR3022-YTE	200	6		0.514		0.513
		24		0.977		0.998
		48		0.981		0.971
		72		0.845		0.982
		96		0.427		0.963

**Table S1.** Summary statistics of basal-to-apical transport experiments of CR3022 and its variants across WD-HAE cell culture. One-way ANOVA analysis was performed using the data in Figure 2. \* $p < 0.05$ : indicates a statistical significance difference.

mAb	Dose ( $\mu$ g)	Time (h)	<i>P</i> values for mAb concentration in basal media		<i>P</i> values for cumulative amount transported	
			vs CR3022-YTE	vs CR3022-LS	vs CR3022-YTE	vs CR3022-LS
CR3022	20	6	0.912	0.507	0.656	0.659
		24	0.802	0.999	0.581	0.895
		48	0.813	0.993	0.596	0.823
		72	0.580	0.928	0.224	0.417
		96	0.503	0.999	0.105	0.659
CR3022-YTE	20	6		0.292		0.204
		24		0.825		0.330
		48		0.871		0.274
		72		0.369		0.017*
		96		0.531		0.016*
CR3022	200	6	0.416	0.610	0.416	0.610
		24	0.078	0.709	0.073	0.694
		48	0.200	0.675	0.163	0.650
		72	0.953	0.980	0.874	0.959
		96	0.889	0.992	0.986	0.975
CR3022-YTE	200	6		0.942		0.942
		24		0.316		0.313
		48		0.632		0.586
		72		0.994		0.974
		96		0.830		0.926

**Table S2.** Summary statistics of apical-to-basal transport experiments of CR3022 and its variants across WD-HAE cell culture. One-way ANOVA analysis was performed using the data in Figure 4. \* $p < 0.05$ : indicates a statistical significance difference.