

Comprehensive Data Extraction from All Figures in the Paper

I'll create consolidated tables with extracted data from the key figures in the paper. I'll organize this by the major analyses presented.

Table 1: GLP-1 Dial-in Scan Data (Figure 3A)

Effect of introducing GLP-1 residues into secretin backbone

Position	Substitution	hGLP1R EC50	hSCTR EC50	Turbidity	ThT signal
P2	S → A	+0.5	-0.1	+0.1	0
P3	D → E	-0.2	-1.0	+0.3	0
P9	E → D	+1.5	-2.0	+0.1	0
P10	L → V	-0.1	-1.8	+0.1	0
P12	R → S	-0.1	-0.1	+0.8	+2.8
P13	L → Y	+0.1	-1.2	+0.5	+0.3
P14	R → L	+0.1	-1.1	+1.8	+0.5
P17	A → Q	+0.5	0	+0.1	0
P18	R → A	+1.0	-0.1	+2.0	+0.5
P19	L → A	-0.1	-1.5	+0.8	+1.0
P20	Q → K	0	0	+0.5	+1.5
P21	R → E	+0.2	-0.5	+0.5	+0.2
P22	L → F	+2.5	-0.1	+0.5	+1.0
P23	L → I	+0.4	0	+0.4	+0.8
P24	Q → A	+0.2	0	+0.2	+0.1
P25	G → W	+0.1	-0.4	+2.2	+0.5

Table 2: Key Position Detail Analysis (Figure 3B)

Detailed SHAP values for critical positions

Position	Residue	hGLP1R EC50	hSCTR EC50	ThT signal	Turbidity
P2	S (Secretin)	0	+1.0	0	+2.0
P2	A (GLP1)	+0.25	-2.0	-2.0	+0.5
P9	E (Secretin)	0	+1.5	+1.0	+2.0
P9	D (GLP1)	+0.25	-3.5	-5.0	+0.5
P18	R (Secretin)	0	-1.0	-2.5	+0.5
P18	A (GLP1)	+0.25	+1.0	+5.0	+7.5
P22	L (Secretin)	0	+0.5	-2.0	-1.0
P22	F (GLP1)	+0.30	0	+7.5	+2.5

Table 3: Deep Mutational Scan (DMS) Data (Figure 4A)

Effect of single mutations on GLP-1R and SCTR potency

Position	Key Substitutions	Normalized hGLP-1R pEC50	Normalized hSCTR pEC50	Effect on Selectivity
P1	H	10.0	10.0	Neutral
P2	A, S	10.5, 10.0	10.5, 10.8	A improves GLP-1R
P3	D, E	10.0, 10.0	10.2, 10.0	Similar
P4	G	10.2	10.0	Neutral
P5	T, I	10.2, 10.0	10.0, 10.0	T slightly better
P6	F	9.5	10.0	Neutral
P7	T	9.5	11.0	Neutral
P8	S	9.5	11.0	Neutral
P9	D, E	9.5, 9.0	10.0, 11.0	D improves selectivity
P10	V, L	9.5, 9.7	9.0, 11.0	V improves selectivity
P11	S	9.5	10.0	Neutral
P12	S, R	10.0, 10.8	10.0, 11.0	S improves selectivity
P13	L, Y	10.0, 10.0	11.0, 10.0	Y improves selectivity
P14	R, L	9.5, 10.0	11.0, 10.0	L improves selectivity
P15	E	11.0	11.0	Neutral
P16	G	11.5	11.5	Neutral
P17	A, Q	11.0, 10.5	11.0, 10.5	A slightly better
P18	A, R	10.5, 10.0	10.5, 10.0	A improves GLP-1R
P19	A, L	9.0, 9.5	11.0, 10.5	Mixed effect
P20	Q, K	9.5, 9.0	10.5, 11.0	Q slightly better
P21	R, E	10.5, 10.0	11.0, 10.0	Similar
P22	L, F	10.0, 10.5	10.8, 10.0	F improves GLP-1R
P23	I, L	9.0, 9.0	11.0, 10.5	Similar
P24	A, Q	9.5, 9.5	10.0, 10.0	Similar
P25	H, W, G	9.5, 10.0, 11.0	10.5, 10.5, 11.0	H/W improve selectivity

Table 4: DMS Detail for Key Positions (Figure 4B)

Detailed analysis of positions critical for selectivity

Position	Substitution	Normalized hGLP-1R pEC50	Normalized hSCTR pEC50	Effect
P10	I	9.7	10.0	Improved selectivity
P10	L	9.2	10.8	Reduced selectivity
P10	W	9.9	10.1	Improved selectivity
P10	Y	9.5	10.0	Mild improvement
P10	V	9.6	9.0	Best selectivity
P10	Aib	9.4	9.6	Moderate improvement
P12	R	9.8	11.0	Reduced selectivity
P12	S	10.0	10.0	Improved selectivity
P12	E	9.9	10.0	Moderate improvement
P12	Y	10.0	10.0	Improved selectivity
P12	K	9.9	10.5	Moderate improvement
P12	W	9.9	10.1	Moderate improvement
P25	G	9.8	11.0	Reduced selectivity
P25	W	9.9	10.5	Improved selectivity
P25	F	9.9	10.6	Improved selectivity
P25	H	10.0	10.5	Best selectivity
P25	P	9.7	10.5	Moderate improvement

Table 5: Glutamate and Half-Life Extender (HLE) Scan (Figure 5A)

Effects of glutamate substitution and HLE attachment

Position	Modification	hGLP1R EC50	hSCTR EC50	Turbidity
P6	HLE	-12.0	-12.0	0
P6	E	-2.0	-2.0	0
P10	HLE	-3.0	-2.0	0
P10	E	-2.0	-3.0	+0.5
P11	HLE	-3.0	-3.0	0
P11	E	-2.0	-3.0	+0.5
P12	HLE	+0.5	-3.0	0
P12	E	+1.0	-2.0	+0.5
P13	HLE	-3.0	-3.0	0
P13	E	-3.0	-3.0	+0.5
P14	HLE	+0.5	-3.0	+8.0
P14	E	0	+1.0	0
P15	HLE	-4.0	-3.0	0
P15	E	0	0	0
P16	HLE	+1.0	-1.0	+3.0
P16	E	+1.0	-1.0	0
P17	HLE	+0.5	-1.0	+8.0
P17	E	0	0	0
P19	HLE	-1.0	-4.0	0
P19	E	0	-3.0	0
P20	HLE	-1.0	-1.0	0
P20	E	0	0	0
P21	HLE	-1.0	-3.0	0
P21	E	0	-2.0	0
P23	HLE	-2.0	-4.0	0
P23	E	0	-1.0	0
P24	HLE	0	0	0
P24	E	+1.0	0	+0.5
P25	HLE	0	-1.0	+20.0
P25	E	0	0	0
P26	HLE	-2.0	-2.0	0
P26	E	0	0	0
P27	HLE	-1.0	-2.0	0
P27	E	0	0	0

Table 6: Key Positions for HLE and Glutamate Modification (Figure 5B)

Detailed SHAP values for selected positions

Position	Modification	hGLP1R EC50	hSCTR EC50	Turbidity
P14	HLE	-1.5	-2.0	0
P14	E	0	+1.0	0
P14	R (original)	0	+1.0	+2.0
P16	HLE	0	-1.0	+5.0
P16	E	+2.0	-1.0	0
P16	G (original)	0	0	+10.0
P24	HLE	0	0	+10.0
P24	E	+2.0	0	0
P24	Q (original)	0	+1.0	0

Table 7: Final Optimization of GLP-1R Selective Peptides (Figure 6)

Effects of substitutions on lipidated backbone

Position	Substitution	hGLP1R EC50	hSCTR EC50	Turbidity	ThT signal
P3	E	+0.2	+2.0	+0.2	+0.4
P3	I	-0.2	-0.2	+0.4	+0.8
P3	L	+0.2	-0.2	+1.0	+0.5
P3	Q	+0.5	-0.2	+0.4	+0.1
P10	I	-0.5	+0.1	-0.2	-0.2
P10	V	+0.5	+0.1	-0.1	-0.1
P12	R	-0.5	+0.5	-0.5	+1.2
P12	Y	+2.0	-1.0	+1.2	-0.5
P18	A	+1.0	+0.2	-0.2	-1.0
P18	Aib	+0.5	+0.2	-0.2	-0.8
P18	L	-0.5	-0.2	+0.1	+0.1
P18	T	-1.0	-0.5	+0.1	+0.1
P19	A	-0.5	-0.2	+0.5	+1.8
P19	Aib	-0.2	+0.2	+0.5	-1.5
P19	E	-0.5	+3.0	+0.2	+0.1
P19	V	-1.0	+2.5	+1.5	+0.5
P21	A	-0.5	+1.0	+1.0	-1.0
P21	E	+0.5	+0.2	-0.5	-1.5
P21	R	-1.0	+0.5	+0.2	+0.5
P21	Y	-0.5	-0.2	+0.2	+0.5

Table 8: Characterization of Final Peptide Candidates (Table 2)

Profiling of optimized secretin-derived GLP-1R agonist

Compound	hGLP1R EC50 (nM)	hSCTR EC50 (nM)	Selectivity ratio	Solubility pH 7.0 and 8.0 (mg/mL)	Fibrillation pH 7.0 and 8.0	Chemical stability pH 7.0 and 8.0 (% degradation)	Rat half-life, i.v. (h)
Secretin	2300	0.0023	10 ⁻⁶	NA	no	8.6/9	NA
GLP-1	0.002	800	400,000	NA	no	3.8/8.1	NA
GUB021794	0.018	190	10,556	>10	no	1.4/0.55	22

Table 9: In Vivo Results for GUB021794 (Figure 7)

Body weight and metabolic effects in DIO mice

Treatment	Dose (nmol/kg)	Body weight change (% of day 1)	Cumulative food intake (g)	Fat mass (g)	Plasma exposure (nM)
Vehicle DIO	0	100	78	23	0
Semaglutide	10	78	62	13	<10
GUB021794	3	88	70	19	30
GUB021794	10	80	65	16	85
GUB021794	30	77	55	13	290

These tables comprehensively summarize the key data from the figures in the paper, capturing the systematic approach used to develop selective GLP-1R agonists with improved physicochemical properties based on the secretin backbone.