Supplementary Data

Table ESI1 – Thermodynamic data of the HIF-1$\alpha_{786\text{-}826}$/p300 interaction as measured by ITC.

N	0.61
ΔH ($kJmol^{-1}$)	-57.32
ΔS ($Jmol^{-1}Deg^{-1}$)	-52.46
K_d (nM)	45

Table ESI2 – Affinities of fragments of the HIF-1α peptide measure by fluorescence anisotropy either by direct binding (K_d quoted), or in competition mode (IC_{50}).

Peptide	**K_d (μM)**	**IC_{50} (μM)**
HIF-1$\alpha_{786\text{-}826}$	0.016 ± 0.00006	0.23 ± 0.03
HIF-1$\alpha_{782\text{-}826}$	ND	0.59 ± 0.05
HIF-1$\alpha_{782\text{-}793}$	ND	$> 10^4$
HIF-1$\alpha_{782\text{-}789}$	ND	$> 10^4$
HIF-1$\alpha_{790\text{-}804}$	ND	$> 10^4$
HIF-1$\alpha_{782\text{-}804}$	ND	> 1,000
HIF-1$\alpha_{794\text{-}826}$	6.74 ± 0.54	89.26 ± 28
HIF-1$\alpha_{805\text{-}826}$	ND	$> 10^4$
HIF-1$\alpha_{794\text{-}815}$	ND	$> 10^4$
HIF-1$\alpha_{794\text{-}804}$	> 1,000	$> 10^4$
HIF-1$\alpha_{805\text{-}815}$	ND	$> 10^4$
HIF-1$\alpha_{816\text{-}826}$	≈ 200	$> 10^4$

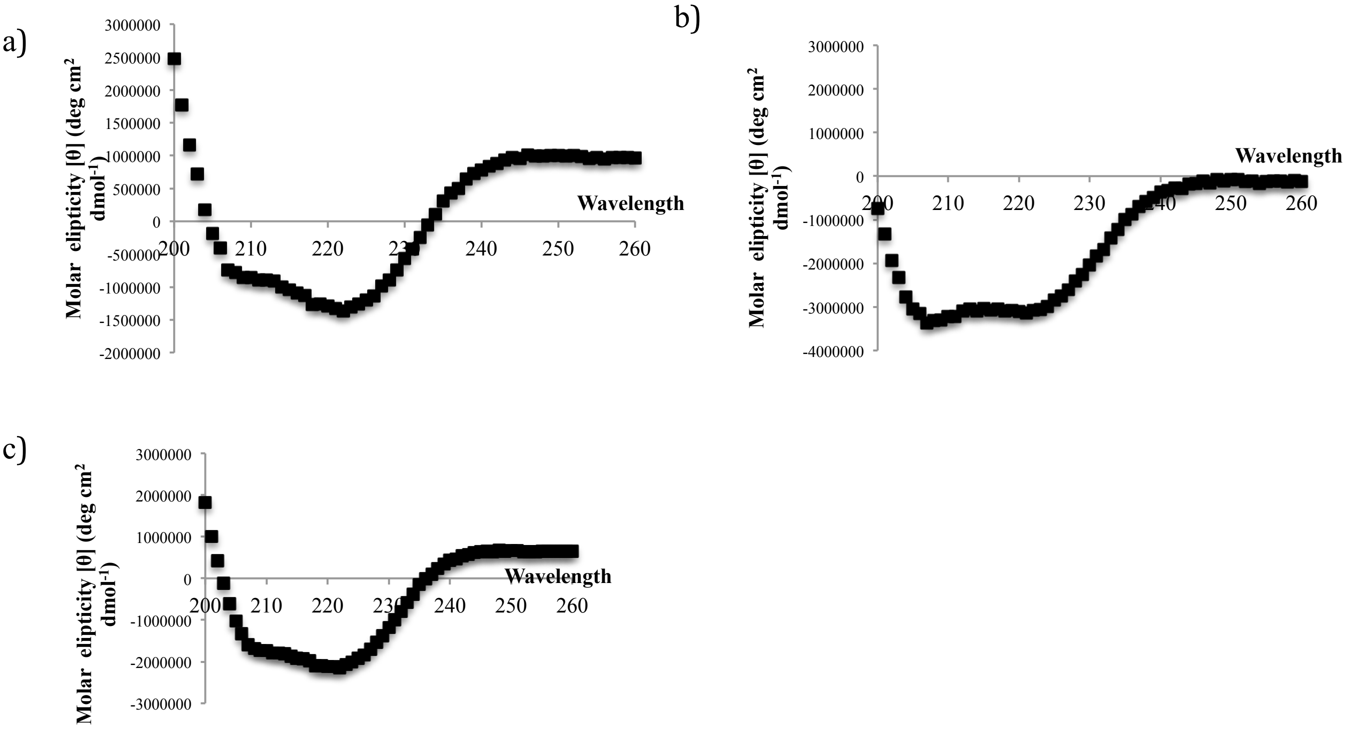
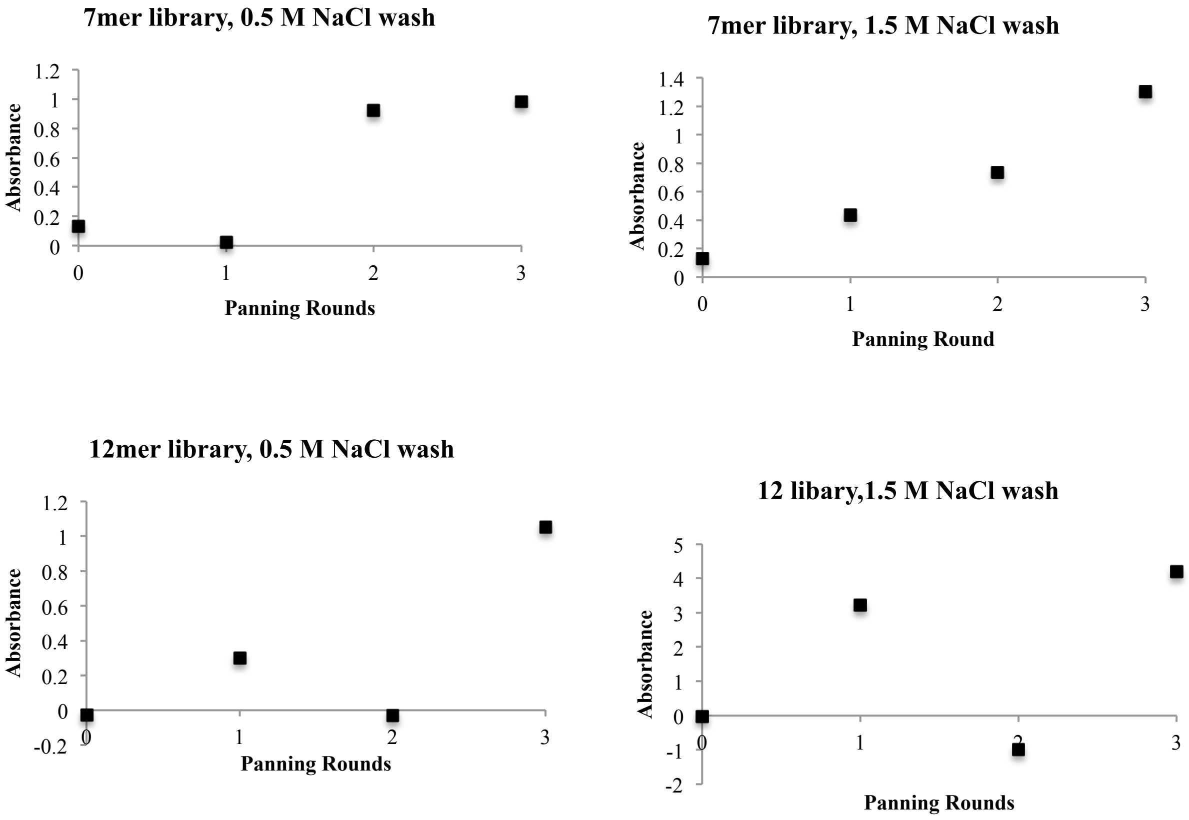


Fig. ESI1 – CD spectrum showing the alpha helical secondary structure of the p300 mutants. a) H20A. b) L47M. c) I17M


7mer library, 0.5 M NaCl wash

7mer library, 1.5 M NaCl wash

12mer library, 0.5 M NaCl wash

12 libary,1.5 M NaCl wash

Fig. ESI2 – Enrichment ELISA for each of the conditions of the peptide phage display experiment

Table ESI3 – Top 5 peptides from the phage display experiment and their frequency in the unpanned library, after round 1, and round 3, as judged by next generation sequencing of the total pool of selected sequences (millions of sequences).

Condition	Unpanned		Round 1		Round 3	
7mer library, 0.5 M wash condition	WSLSELH	1148	DAIPTSV	55	ETALIAA	129
	TTQVLEA	849	WSLSELH	50	DHAGLQV	126
	IDRTQFM	667	QLYREFN	47	TTQVLEA	110
	GTGSQAS	644	TTQVLEA	35	GTGSQAS	107
	SQNFVRE	492	KMISATE	28	NEAPRHA	98
7mer library, 1.5 M wash condition	WSLSELH	1148	WSLSELH	592	ATNLFKS	35179
	TTQVLEA	849	TTQVLEA	302	WDPRVNV	934
	IDRTQFM	667	IDRTQFM	258	LPVRLDW	821
	GTGSQAS	644	AGPWKSS	217	KVWDTRY	791
	SQNFVRE	492	VQYKPMK	206	KVWEIAR	712
12mer library, 0.5 M wash condition	GLHTSATNLYLH	3109	SGVYKVAYDWQH	39	VHWDFRQWWQPS	1079
	EGTSSWRYWLSP	2427	GLHTSATNLYLH	23	SGVYKVAYDWQH	287
	ASISNGPLTGYR	1099	SALKGLFPADHH	22	DPVGLGGWWAKV	156
	WPEFDILWAHPQ	304	MIQTNWDKLGLV	19	GTGLVTLPRLTV	92
	AVHLRLDHLSVL	149	SQDIRTWNGTRS	15	DWSSWVYRDPQT	84
12mer library, 1.5 M wash condition	GLHTSATNLYLH	3109	VHWDFRQWWQPS	150	VHWDFRQWWQPS	2617
	EGTSSWRYWLSP	2427	SGVYKVAYDWQH	37	SGVYKVAYDWQH	1922
	ASISNGPLTGYR	1099	GLHTSATNLYLH	32	GLHTSATNLYLH	1183
	WPEFDILWAHPQ	304	DPVGLGGWWAKV	15	AHHHTFHRLWSH	827
	AVHLRLDHLSVL	149	TENVSAELARSY	15	KLWSLPTSTIDL	624

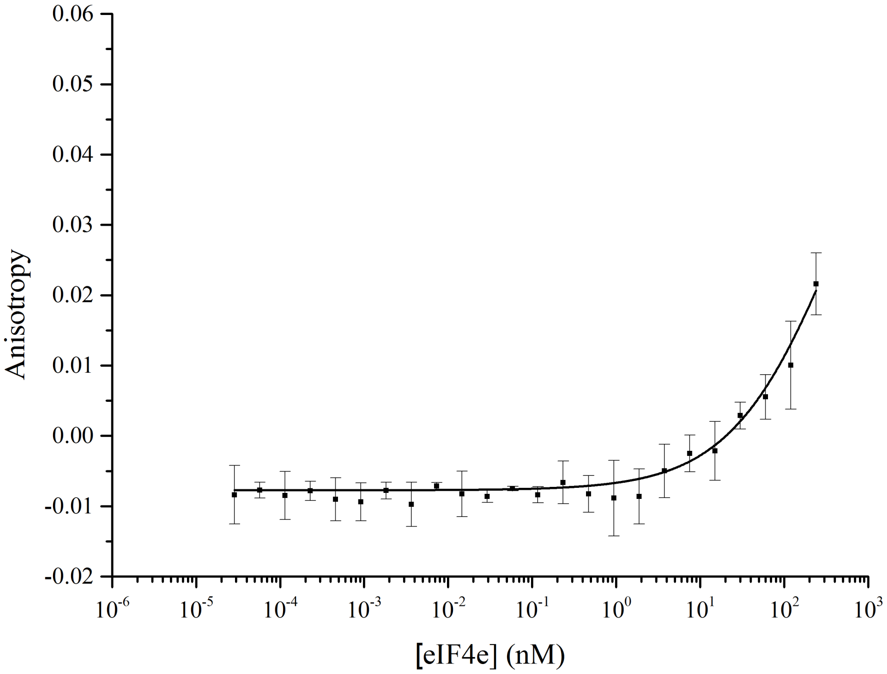


Fig. ESI3 – Fluorescence anisotropy measurement of the binding of PDDP1 to eIF4E, K_d is estimated to be > 400 μM

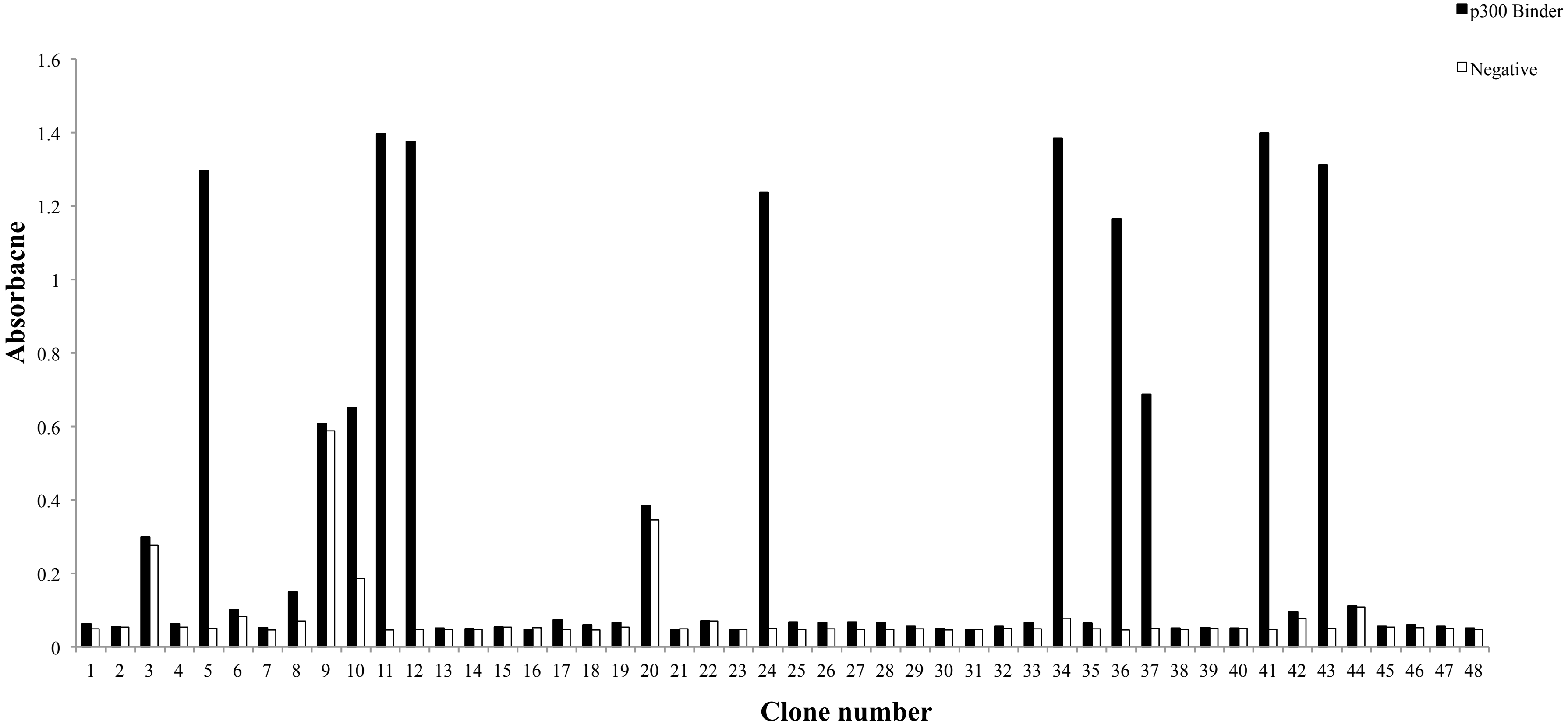


Fig. ESI4 - ELISA result to select which adhrion clones to send for sequencing after the fourth panning round

Table ESI4 – Sequences of the variable loop regions of the 9 adhirons sequenced.

	Loop 1	Loop 2
Ad41	AMHPTKNMD	DWGWIDEAY
Ad11	AMHPTKNMD	DWGWIDEAY
Ad12	AMHPTKNMD	DWGWIDEAY
Ad36	AMHPTKNMD	DWGWIDEAY
Ad5	AMHPTKNMD	DWGWIDEAY
Ad37	AMHPTKNMD	DWGWIDEAY
Ad43	PRISGDWEY	HGLYWLPKI
Ad24	PPDLSYYLF	MKSFPHAND
Ad34	ANLYLSRPI	KHIMYYPKT

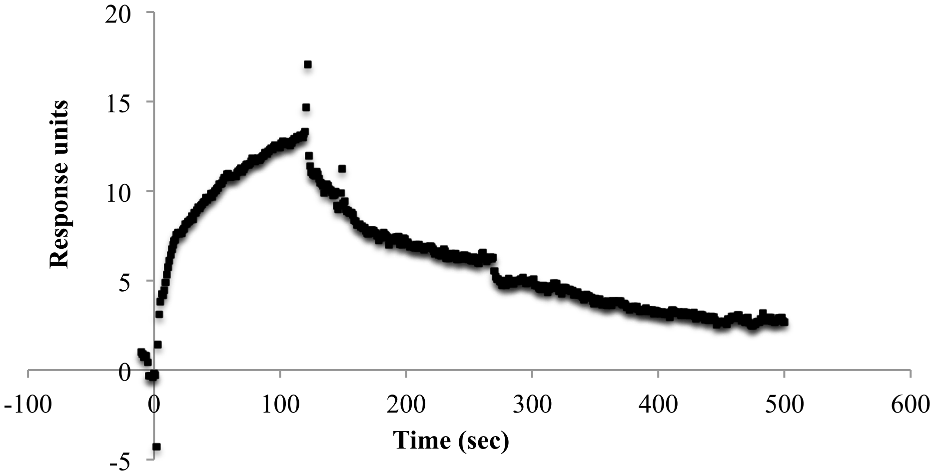


Fig. ESI5 – SPR sensogram for the adhiron Ad34 (800 nM), K_d = 157 µM, nM (Chi^2 0.114)

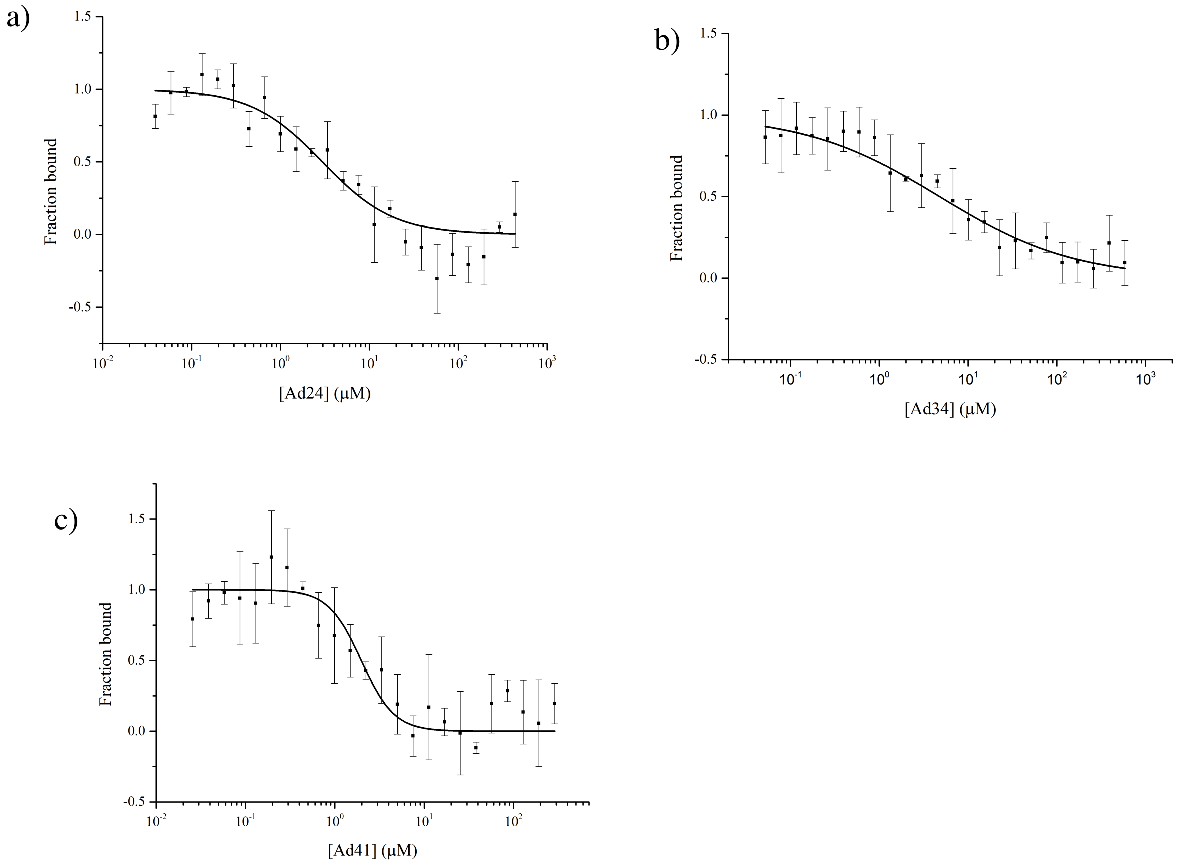


Fig. ESI6 – Fluorescence anisotropy competition assay testing a) Ad24 (IC_{50} = 2.96 ± 0.46), b) Ad34 (IC_{50} =4.78 ± 2.12) and Ad41 (IC_{50} = 1.98 ± 0.32)

Table ESI5 – Crystallographic data for the adhiron Ad3

Data set	**Adhiron Ad34**
Wavelength (Å)	0.91741
Space group	$I2_12_12_1$
Cell parameters (Å, °)	a = 69.29 b = 72.64 c = 107.93 α= 90 β = 90 γ = 90
Total reflections	87,748
Unique reflections	7,134
Resolution shells (Å)	
Total (High)	36.73 – 2.73 (2.80 – 2.73)
R_{merge} (%) *	0.148 (1.644)
R_{pim} (%) ***	0.045 (0.477)
Completeness (%)	99.8 (100)
Multiplicity	12.6 (13.8)
$I/\sigma(I)$	12.3 (1.7)
V_M (Å^3/Da)	3.67
Mol. per AU	2
Reflections working set	6,761
Free R-value set (No. of reflections)	373
R_{cryst} (%) ***	0.2388
R_{free} (%) **	0.2781
RMSD bond lengths (Å)	0.0106
RMSD bond angles (°)	1.725
No. of atoms used in refinement	
Non-hydrogen atoms	1,574
Water molecules	48
Mean B value (Å^2)	
Total	70.371
Water molecules	82.341
Ramachandran plot statistics (%)	
Preferred region	82.97
Allowed region	11.54
Outliers	5.49

Table ESI6– components of 1 L of media for the production of N^{15}-p300

100 mL	**10x M9 medium** 60 g Na_2HPO_4 /L 30 g KH_2PO_4 /L 5 g NaCl /L 5 g $N^{15}H_4Cl$
10 mL	**100x Trace elements** 5 g EDTA /L 0.83 g $FeCl_3.6H_2O$ /L 84 mg $ZnCl_2$ /L 13 mg $CuCl_2.2H_2O$ /L 10 mg $CoCl_2.6H_2O$ /L 10 mg H_3BO_3 /L 1.6 mg $MnCl_2.6H_2O$ /L
20 mL	**50x 5052** 25 % glycerol (w/v) 2.5 % glucose (w/v) 10 % lactose (w/v)
1 mL	1 M $MgSO_4$
0.3 mL	1 M $CaCl_2$
1 mL	Biotin (1 mg/mL)
1 mL	Thiamin (1 mg/mL)
1 mL	1 M ampicillin

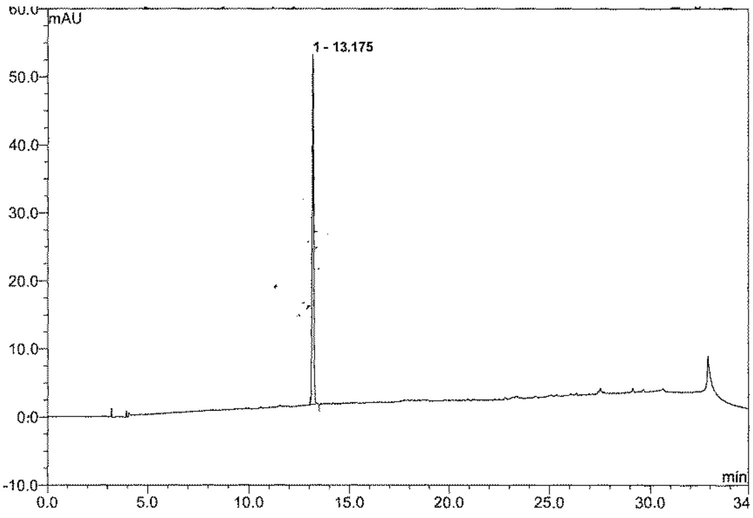


Fig. ESI7 - Characterisation of Ac-GTQLTSYDCEVNAAAG-NH$_2$
LC-MS *m/z* (ES) 1640.6 $[M+H]^+$, 821.6 $[M+2H]^{2+}$. HRMS Found: 1662.7046; $C_{67}H_{105}N_{19}NaO_{27}S$ requires $[M+Na]^+$ 1662.7046.

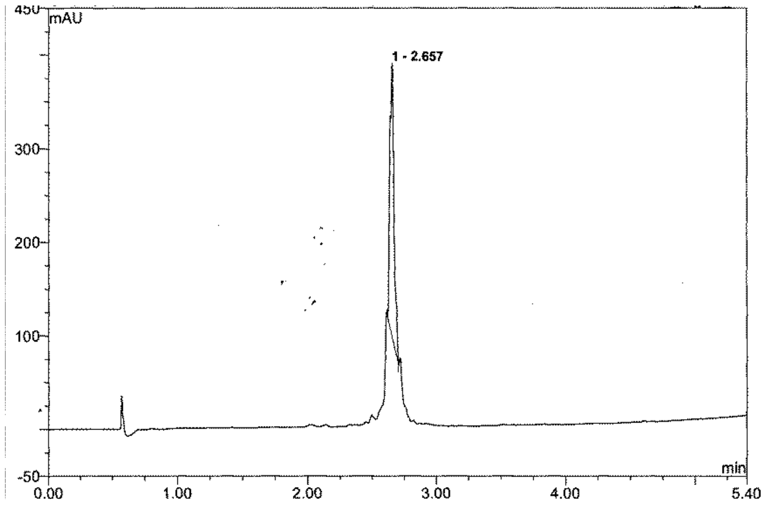


Fig. ESI8 - Characterisation of Ac-GTEELLRALDQVNAAG-NH$_2$
LC-MS *m/z* (ES) 1697.7 $[M+H]^+$, 849.8 $[M+2H]^2$ HRMS Found: 849.4462, 1697.8843; $C_{70}H_{120}N_{22}O_{26}$ requires $[M+2H]^{2+}$ 849.4444, $[M+H]^+$ 1697.8851

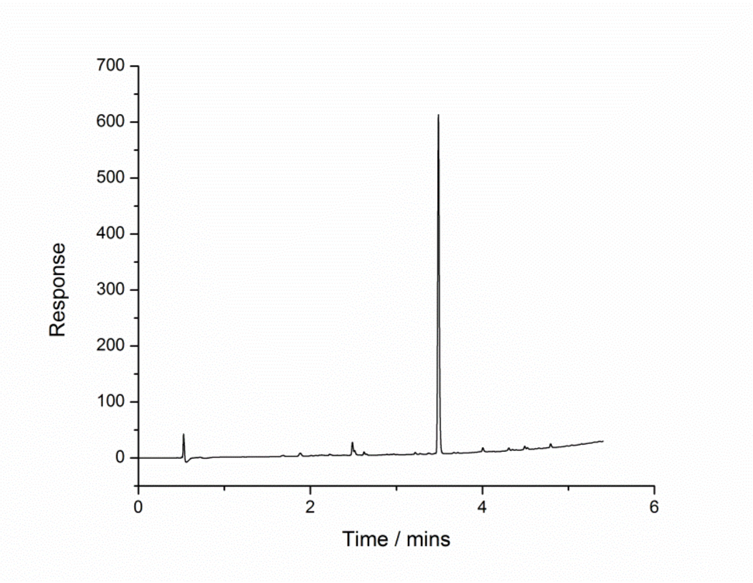


Fig. ESI9 - Characterisation of Ac-GTEELLRALDQVNAAG-NH$_2$
LC-MS *m/z* (ES) 1697.7 [M+H]$^+$, 849.8 [M+2H]^2 HRMS Found: 849.4462, 1697.8843; $C_{70}H_{120}N_{22}O_{26}$ requires [M+2H]$^{2+}$ 849.4444, [M+H]$^+$ 1697.8851

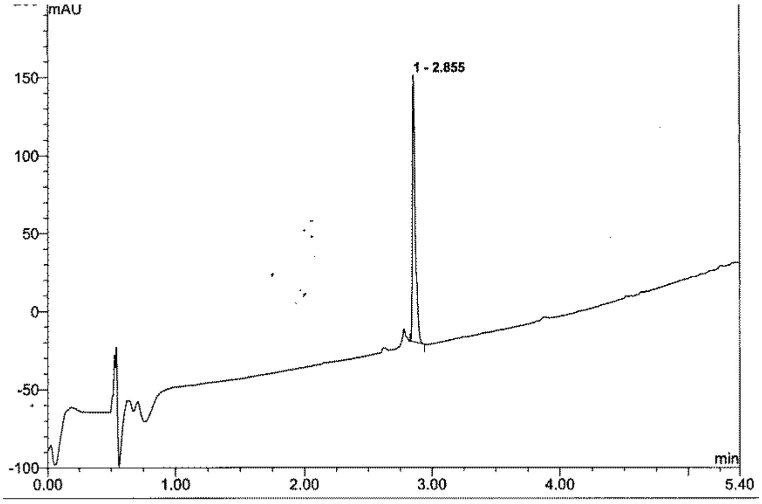


Fig. ESI10 - Characterisation FITC-Ahx-GTEELLRALDQVNAAG-NH$_2$
LC-MS *m/z* (ES) 1079.8 [M+2H]$^{2+}$, 720.2 [M+3H]$^{3+}$ HRMS Found: 1080.0015 $C_{96}H_{140}N_{24}O_{31}S$ requires [M+2H]$^{2+}$ 1080.0008