

Electronic Supplementary Information

Discovery of a CHI3L1-Targeted Small Molecule Modulating Neuroinflammation in Alzheimer's Disease via DNA-Encoded Library (DEL) Screening

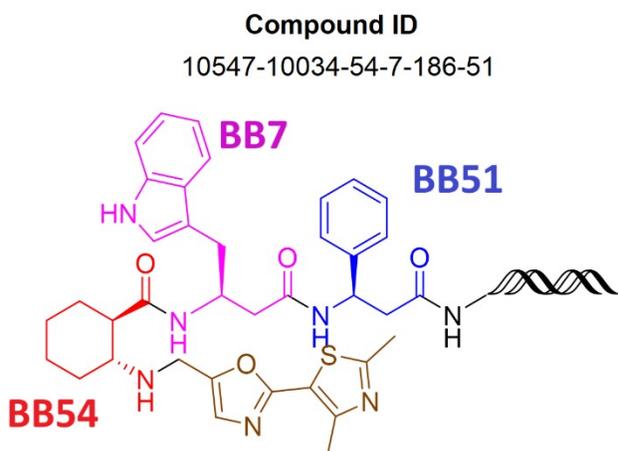
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Chemotype	Frequency
10034-X-7-X-51 BB7 at position 1,23	15 / 16 compounds
10034-54-7-X-51 BB51 at position 4	6 / 16 compounds

Figure S1. Building-block enrichment analysis of the **DEL-C1** family (Library 10034). The disclosed hit **DEL-C1** (10547-10034-54-7-186-51) is shown with enriched building blocks highlighted.

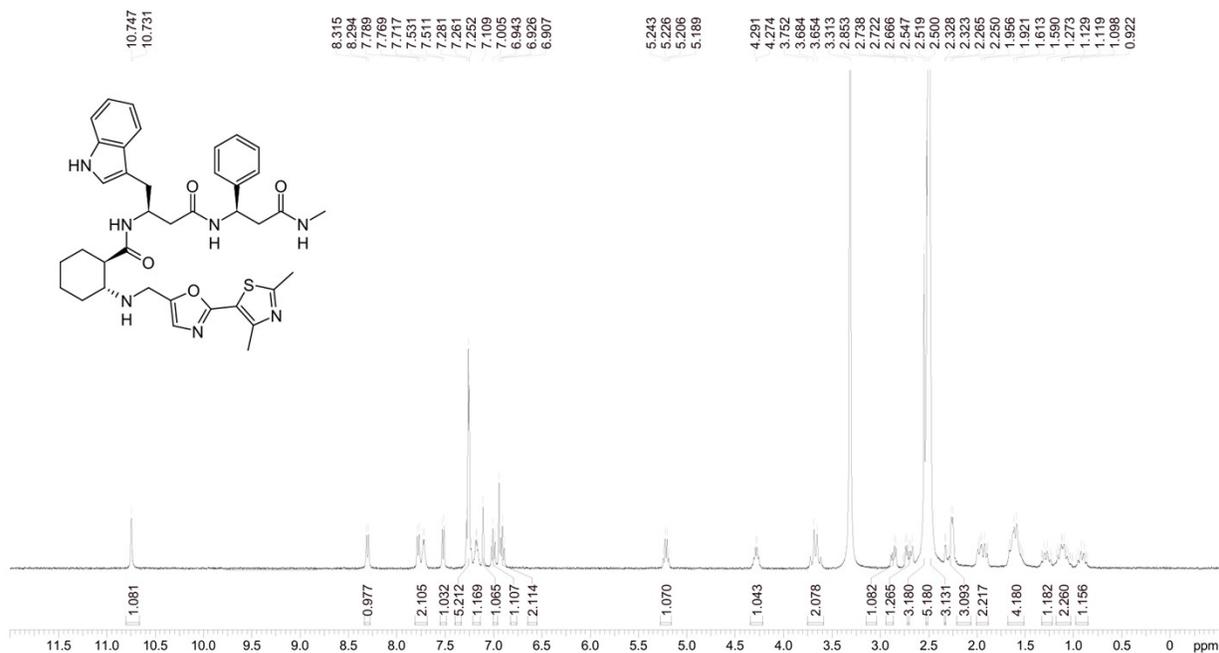
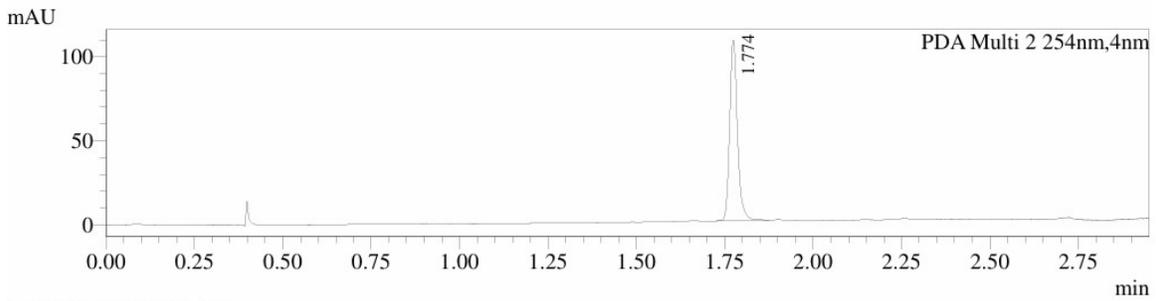
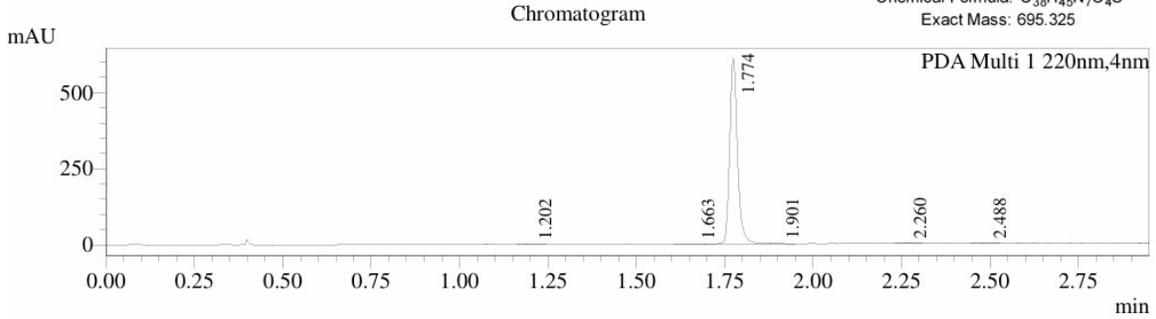
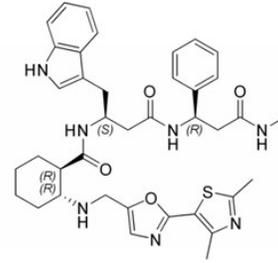


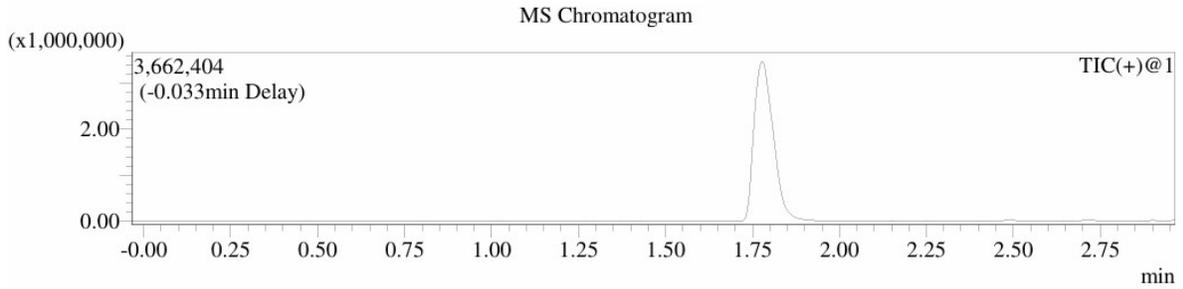
Figure S2. ¹H NMR spectrum of compound **DEL-C1** in DMSO-*d*₆.

LCMS REPORT

Compound ID : 10547-10034-54-7-186-51
Sample ID : EC23044-28-P1L1
Injection Date : 2025/1/10 12:03:35
Injection Vol : 4ul
Location : vial42
Acq Method : D:\method\5_95N_3min_220&254_POS.lcm
Org DataFile : D:\DATA\2025\2501\250110\EC23044-28-P1L1.lcd
Instrument : 05-LCMS-AK



- 1 PDA Multi 1 / 220nm,4nm
- 2 PDA Multi 2 / 254nm,4nm



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 Integration Result
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PDA Ch1 220nm							
Peak#	Ret. Time	Width	Height	Height%	Area	Area%	
1	1.202	0.051	1296	0.211	2732	0.287	
2	1.663	0.061	1061	0.173	2720	0.285	
3	1.774	0.039	608302	98.933	939603	98.623	
4	1.901	0.098	1616	0.263	3146	0.330	
5	2.260	0.040	1360	0.221	2372	0.249	
6	2.488	0.043	1226	0.199	2148	0.225	

PDA Ch2 254nm							
Peak#	Ret. Time	Width	Height	Height%	Area	Area%	
1	1.774	0.039	107542	100.000	164974	100.000	

Figure S3. LCMS report of compound DEL-C1.

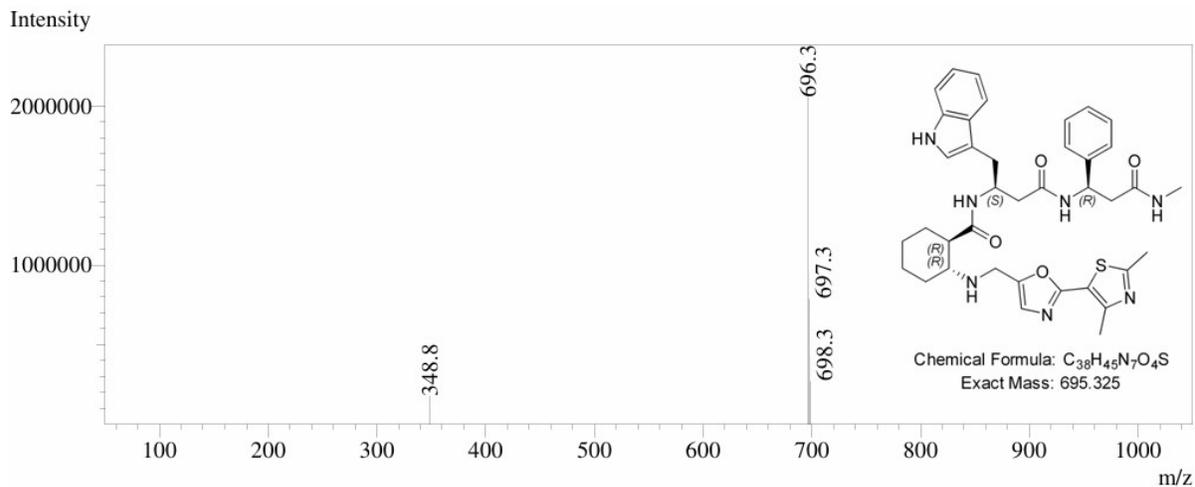
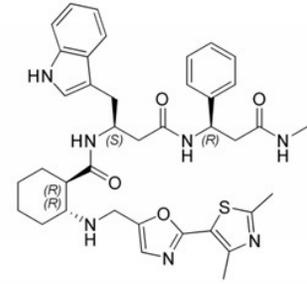


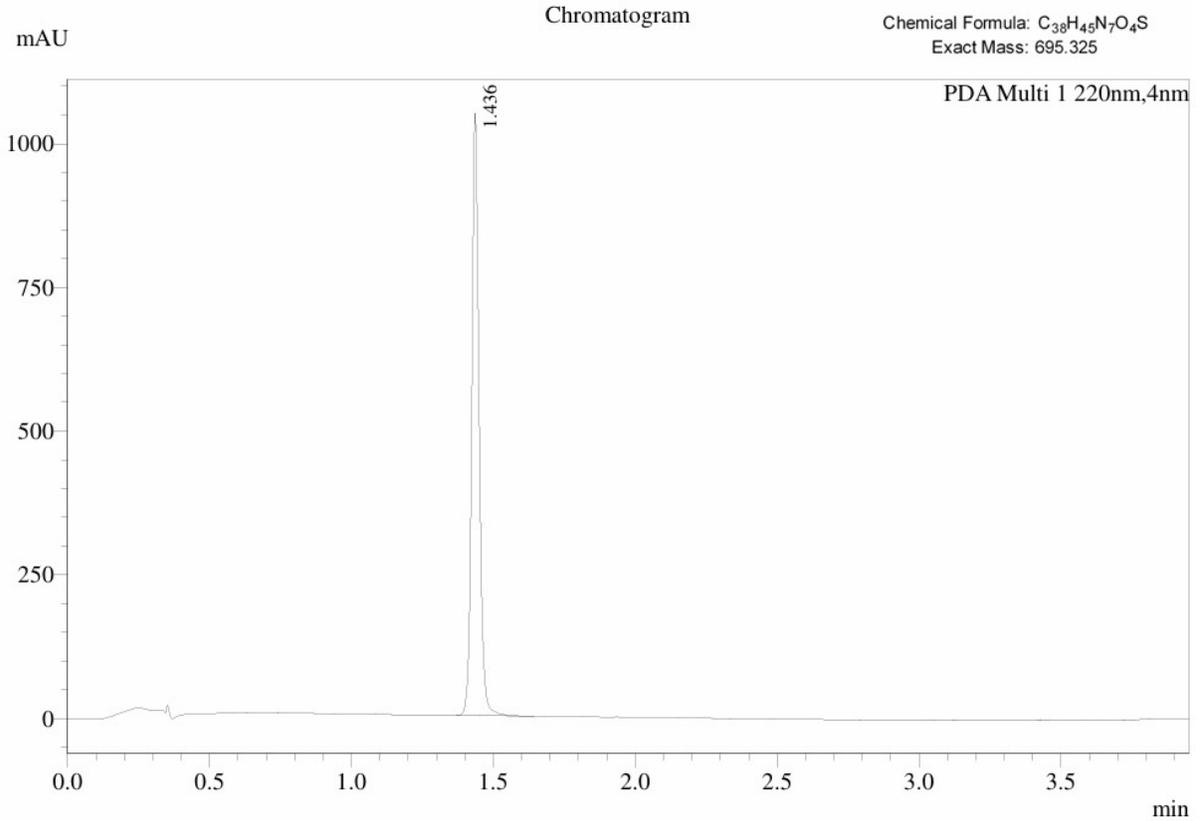
Figure S4. Mass spectrum of compound DEL-C1.

HPLC REPORT

Compound ID : 10547-10034-54-7-186-51
Sample ID : EC23044-28-P1H1
Injection Date : 2025/1/10 11:33:59
Injection Vol : 4ul
Location : vial41
Acq Method : D:\Method\10_80AB_4min_220&254.lcm
Org DataFile : D:\DATA\2025\2501\250110\EC23044-28-P1H1.lcd
Instrument : 05-HPLC-C



Chemical Formula: C₃₈H₄₅N₇O₄S
Exact Mass: 695.325



Integration Result

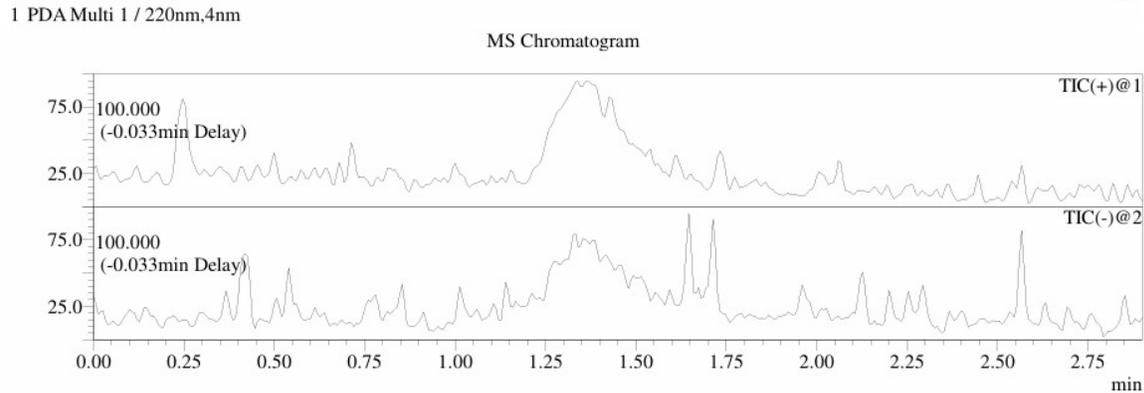
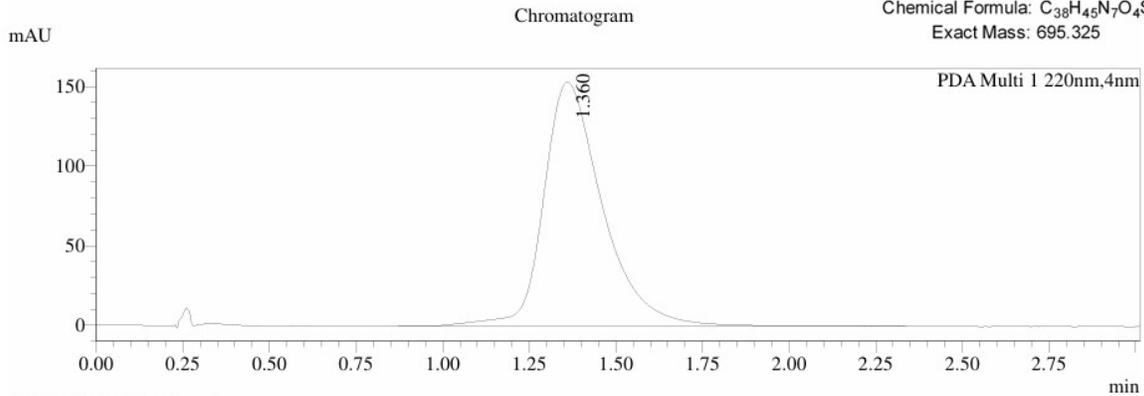
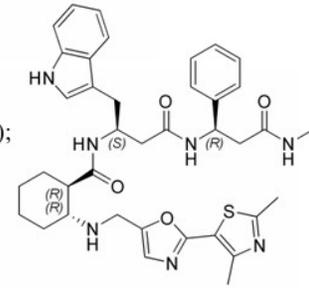
PDA Ch1 220nm						
Peak#	Ret. Time	USP Width	Height	Height%	Area	Area%
1	1.436	0.045	1048546	100.000	1878382	100.000
Total			1048546	100.000	1878382	100.000

Figure S5. HPLC purity of compound DEL-C1.

Chiral SFC Report

Compound ID : 10547-10034-54-7-186-51
 Sample ID : EC23044-28-P1_E6
 Injection Vol : 2ul
 Location : Tray3 vial17
 Acq Method : D:\method\IG-3-MeOH(DEA)-40-3mL-35T.lcm
 Org DateFile : E:\DATA\2025\202501\20250114\EC23044-28-P1_E6.lcd
 Injection Date : 2025/1/14 12:13:40
 Instrument : CAS-05-ANA-SFC-E(SHIMADZU LC-30ADsf)

Method details: "Column:Chiralpak IG-3 50x4.6mm I.D., 3um
 Mobile phase: Phase A for CO2, and Phase B for MeOH(0.05%DEA);
 Isocratic elution: B in A for 40%
 Flow rate: 3mL/min;
 Detector: PDA;
 Column Temp: 35C;Back Pressure: 100Bar"



Integration Result

Peak Table

Peak#	Ret. Time	Height	Height%	USP Width	Area	Area%	Resolution(USP)
1	1.360	153241	100.000	0.294	1830564	100.000	--

Figure S6. Chiral SFC report of compound DEL-C1.