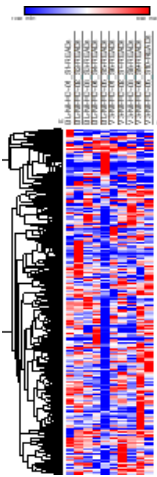


Immunity

Nilotinib: baseline
vs. 3 months



Significantly Altered miRNAs

hsa-miR-1-3p	hsa-miR-937-5p	hsa-miR-1233-5p
hsa-miR-144-5p	hsa-miR-6886-3p	hsa-miR-3188
hsa-miR-133a-3p	hsa-miR-4674	hsa-miR-766-5p
hsa-miR-1275	hsa-miR-326	hsa-miR-3677-5p
hsa-miR-5190	hsa-miR-1909-3p	hsa-miR-4634
hsa-miR-4655-5p	hsa-miR-3616-3p	hsa-miR-1307-5p
hsa-miR-5692c	hsa-miR-6794-5p	hsa-miR-203a-3p
hsa-miR-6893-3p	hsa-miR-1272	hsa-miR-4531
hsa-miR-4267	hsa-miR-200b-5p	hsa-miR-6813-5p
hsa-miR-4732-5p	hsa-miR-374b-5p	hsa-miR-496
hsa-miR-4262	hsa-miR-125b-2-3p	hsa-miR-487a-5p
hsa-miR-1301-3p	hsa-miR-6797-3p	hsa-miR-3605-3p
hsa-miR-4646-5p	hsa-miR-939-5p	
hsa-miR-5481	hsa-miR-3973	hsa-miR-4791
hsa-miR-4322	hsa-miR-548a-5p	hsa-miR-489-3p
hsa-miR-5089-3p	hsa-miR-19a-5p	hsa-miR-181b-3p
hsa-miR-153-5p	hsa-miR-302c-3p	hsa-miR-3064-3p
hsa-miR-95-5p	hsa-miR-378b	hsa-miR-644a
hsa-miR-3189-3p	hsa-miR-4653-3p	hsa-miR-892c-5p
hsa-miR-6829-3p	hsa-miR-6796-5p	hsa-miR-3118
hsa-miR-7153-3p	hsa-miR-920	hsa-miR-4252
hsa-miR-6773-5p	hsa-miR-4693-3p	hsa-miR-3134
hsa-miR-186-3p	hsa-miR-7976	hsa-miR-3934-3p
hsa-miR-3675-3p	hsa-miR-2115-3p	hsa-miR-3975
hsa-miR-454-5p	hsa-miR-656-3p	hsa-miR-4433b-3p
hsa-miR-5187-3p	hsa-miR-651-3p	hsa-miR-6818-3p
hsa-miR-519d-5p	hsa-miR-219b-5p	hsa-miR-8058
hsa-miR-892b	hsa-miR-4639-5p	hsa-miR-3925-3p
hsa-miR-34b-3p	hsa-miR-6840-3p	hsa-miR-4797-3p
hsa-miR-6715b-3p	hsa-miR-4638-5p	hsa-miR-3137
hsa-miR-1199-3p	hsa-miR-1243	
hsa-miR-6839-3p	hsa-miR-3674	

inhibited

disinhibited

ABL1	CACNG3	COL1A2	FZD10	IFNA4	KHDC1	MEF2D	PLEKHA2	RPS6KA3
ACTB	CACNG7	COL5A3	FZD2	IFNA6	KLK10	MMP1	PLEKHA3	RPS6KB1
ACTR3	CALM1	CREB1	FZD9	IFNAR1	KLK12	MMP1	PLEKHA4	RPS6KB1
ADAMTS4	CALM5	CREB3	FZD9	IFNLR1	KLK15	MMP1	PLEKHA4	RPS6KB1
AHR	CANX2G	CREB3L1	GNAI2	IKBKG	KLK2	NCK1	PPP1R14B	RSK2
AKT2	CANX4	CREB3L4	GNAI2	IL10	KLK4	NECTIN2	PPP2C8	SIRPB1
ALOX12	CASP10	CRK	GNAQ	IL10RA	KLK5	NFYAT2	PPP2R3A	SFRP1
AP1G1	COL2	CSF1	GNAI1	IL17F	KLK9	NFYAT2	PPP2R3B	SFRP5
AP1G2	CCR1	CSF3	GNG13	IL18	KLRL1	NGF	PPP2R3B	SH2B3
AP1G2	CCR4	CSNK1D	GNG2	IL1R1	KLRC2	NLK	PPP2R3D	SIRPB1
AP2M1	CCR5	CSNK1G1	GNG3	IL1RL1	KLRC4-KLRK1	NOS2	PRKCA	SMAAD3
AP2C	CCR8	CXCL12	HAVCR2	IL1RL2	KLRD1	NOTCH2	PRKCD	SMO
APOC1	CD18	DOX5B	HLAA	IL2	KRAS	NOTCH3	PRKCE	SOC22
APOC2	CD209	DEFB132	HLAC	IL22	LCN2	NOTCH4	PSEN1	SOC33
APOC4	CD3E	DEFB	HLA-DQB	IL24	LIMK1	OSM	PSENEN	SOSL
APOD	CD4	DKK3	HLA-DQB1	IL25	LIMK2	PAK1	PTFA	SPR1
APOL1	CD81	DOX1	HLA-DQB5	IL27RA	LTBR	PAK2	PVN	SRC
APPC3	CD86	ELK1	HLAF	IL2RA	LYVE1	PAK3	RAB11B	STAT1
ATF3	CD8B	F2RL1	HRAS	IL2RB	MMPR	PAK4	MAC2	STAT2
ATF7	Cdc42	FADD	HSP90B1	IL32	MAP2K7	PDGF1B	RAP2B	STAT3A
BHL2	CEBPB	FOS	ICOS	IL4	MAP3K13	PIK3R6	RASD2	TCTF12
CSAR1	CFL1	FOXO3	IFIT2	IL5	MAP3K8	PLA2G2D	RHOA	TGFB3
CANAL5	CLTC	FOXQ3	IFNA1	IL9R	MAP3K9	PLA2G6	RHOE	TGFB3
CANAL203	CLU	FSCN1	IFNA17	IRS4	MAPK3	PLCD3	RHOE	TLN1
CANR2	COL11A2	FN1	IFNA2	ITGAL	MAPKAPK2	PLCH2	RHOE	TLN1
CANR3	COL1A1	FZD1	IFNA21	JMD16	MAVS	PLD1	RHOE	TLN1
ACTG1	CASP8	DAPP1	GNAI3	IL13	KIR2DL4	PONA	PPP3R1	SOC54
ACTR3	CASP9	DEFB118	GNAI2	IL17A	KIR3DL1	PCYOX1	PPP3R2	SOST
ACTR3	CCL5	DEFB123	GNAI5	IL18	KIR3DL3	PCYOX1	PPP3R2	SOST
ADRB1B	CND1	DEFB44/DEFB48	GNAI5	IL18R1	KLK7	PDPR1	PRKCG	TBX21
AIFM1	CCR7	DGKB	GNG10	IL1A	KLK8	PIK3CD	PRKCG	TCF4
AP1S1	CD138	DHX58	GNG11	IL1RAP	LAR1	PIK3CG	PRKCG	TGFB2
APOM	CD226	DRAG3	GNG12	IL20	LEP	PIK3R5	PRKCG	TGFB2
APR6	CD244	DKK1	GNG5	IL23R	LGAL5	PLA2G12B	PSEN2	TNFRSF138
ARG1	CD247	DKK2	GZMB	IL26	MAF	PLA2G2A	PTEN	TNFRSF13C
APPC1A	CD36	DLL4	HIST1	IL27	MAP2K3	PLA2G2E	PTGDR2	TNFRSF10
APPC4	CD40LG	DEFB2K2	HLA-B	IL2RA	MAP3K2	PLA2G2F	PTPRN2	TNFRSF11
B2M	CD69	FAS	HLA-DMB	IL3	MAP3K6	PLA2G4D	RAB7A	TNFRSF9
BCL1D	CD74	FASLG	HLA-DQB1	IL31	MAPK1	PLA2G4F	RAP1B	TGFB3
BCL2L1	CFL2	FCER1G	HLA-C	IL33	MAPK13	PLCE1	RAP2A	TGFB3
BLNK	CHP1	FCGR1A	HNF1A	IL4R	MICA	PLD3	RASD2	TNFRSF5
CANB1	CHTA	FCGR2A	HSP41A	IL6ST	MIRAS	PON1	RASD5	TNFRSF5
CANAL1A	CLTA	FCGR3A/FCGR3B	HSP90	IL7R	MIR	POU2F1	RELA	ULBP1
CANAL1E	COL3A1	FBNP1	IFH1	IRAK3	NCF2	PPP1CA	RHOE	VCAM1
CANAL1	CSNK1E	FZD2	IFNA2	IRAK4	NCK2	PPP1CB	RHOE	VCAM1
CANAL2D1	CTL4	FZD3	IFNGR1	IRF7	NF1L3	PPP1R34C	RASD2	WIF1
CANR4	CXCL1	GAB2	IFN	IRF9	NFYAT2	PPP1R3D	SIRPB1	WNT10B
CANR2	CXCL10	GFI1	IFNLR1	ITGB1	NOTUM	PPP1R7	SFRP2	WNT11
CANR8	CXCL8	GNAI3	IFNW1	ITGB2	NRAS	PPP2R1B	SH2B3	WNT2B
CASP6	CXCR6	GNAI4	IKBK	ITPR1	OSMR	PPP2R2A	SH2D1A	WNT7B
CASP7	CYC5	GNAI5	IL10RB	KIR2DL1	PAMP4	PPP2R3A	SIGLEC7	

Pathways

- T lymphocyte-mediated apoptosis
- Cytokine Production and Signaling
- PI3K Signaling in B lymphocytes
- T & B Cell Receptor Signaling
- CD28 Signaling in T helper cells
- Crosstalk between Dendritic Cells and Natural Killer Cells
- MIF regulation of Innate Immunity
- NFkB Signaling
- Th1 and Th2 Activation

Figure S1. miRNAs targeting genes associated with innate and adaptive immunity are altered following nilotinib treatment. Gene ontology analysis revealed 38 upregulated and 55 downregulated miRNAs that target 476 genes experimentally observed to be associated with immunological processes, including B and T cell receptor signaling, inflammatory cytokine production, and innate immune cell crosstalk.

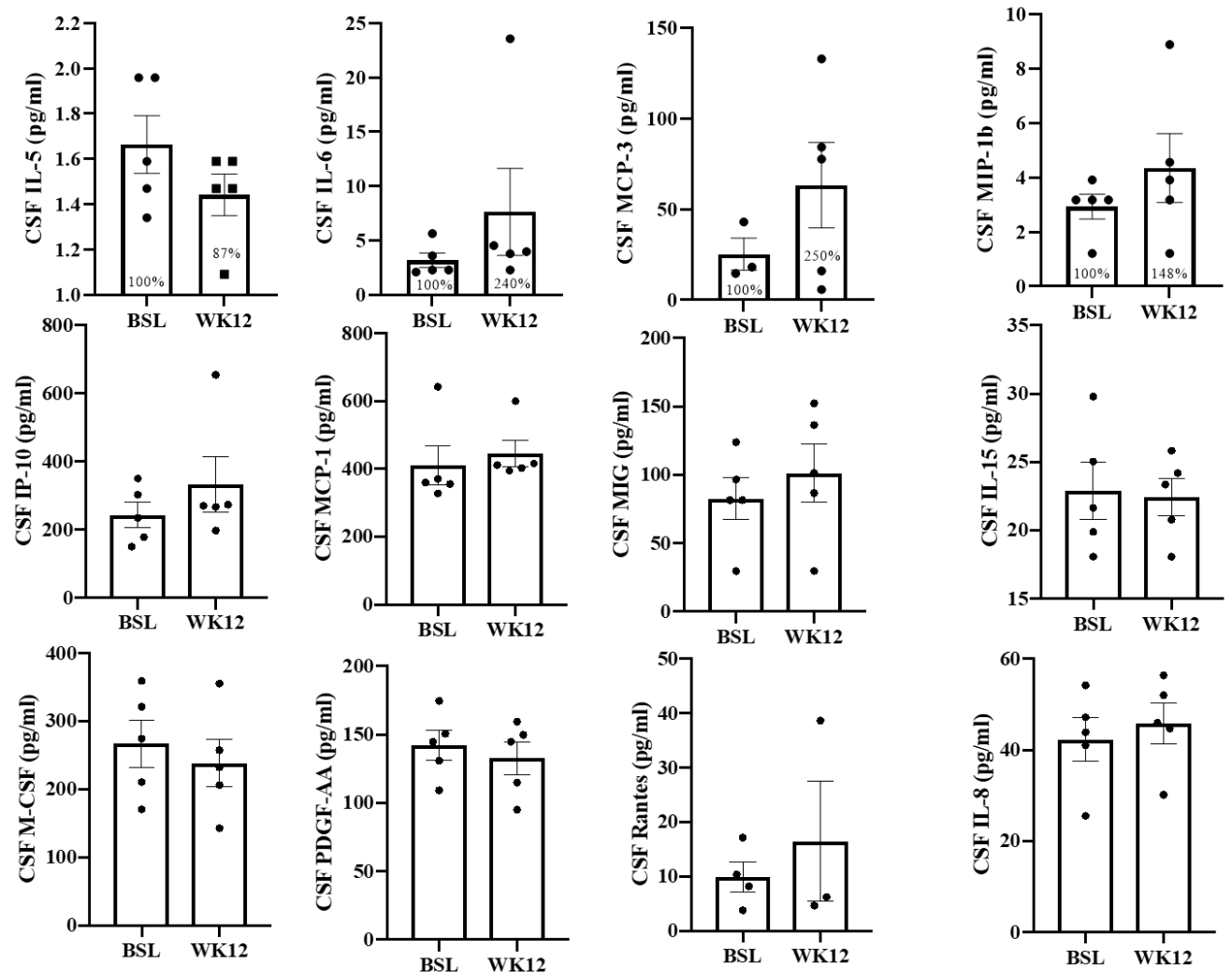


Figure S2. ELISA concentrations inflammatory markers in the CSF following nilotinib treatment.

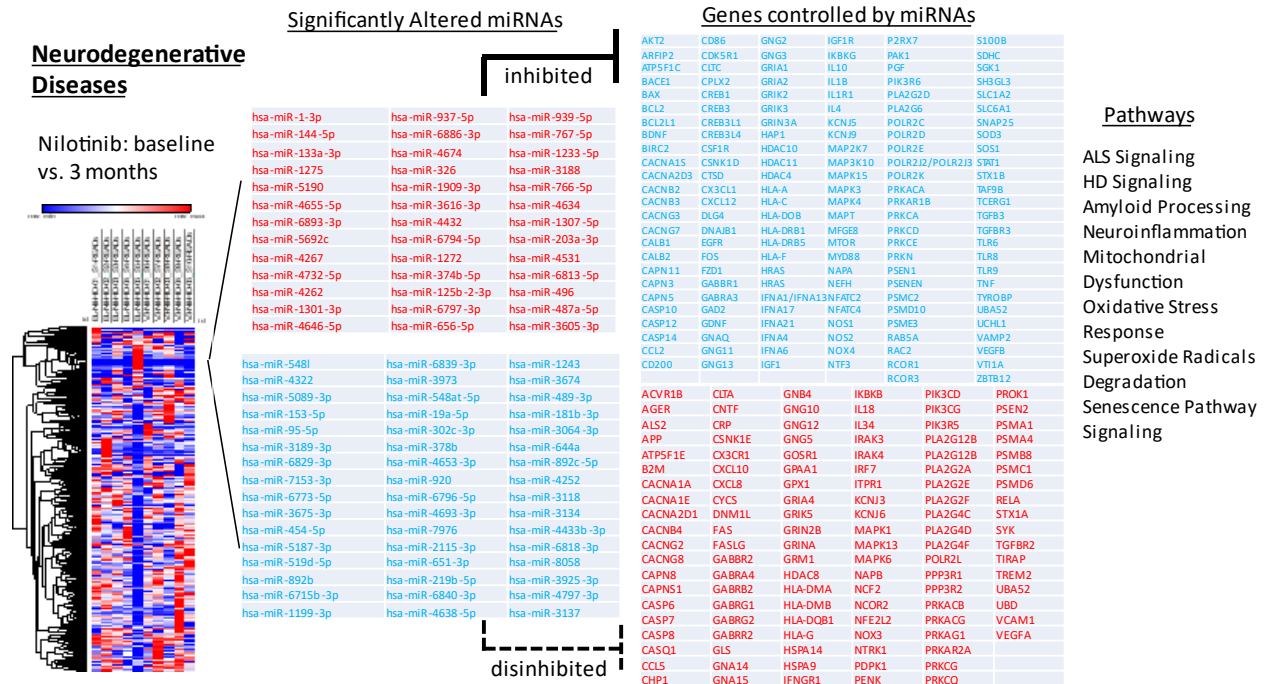


Figure S3. miRNAs targeting genes associated with various neurodegenerative disorders are altered following nilotinib treatment. Gene ontology analysis revealed 39 upregulated and 48 downregulated miRNAs that target 268 genes experimentally observed to be associated with neurodegenerative diseases including AD, PD, ALS, and HD.

Table S1. Demographics and Adverse Events.

Patient ID	Nil-HD-001	Nil-HD-002	Nil-HD-003	Nil-HD-004	Nil-HD-005	Nil-HD-006	Mean +/- SD	
Age	62	47	61	63	58	50	56.83 ± 6.74	
Gender	M	F	M	F	M	M		
Weight (kg)	84.1	58.7	65.3	82.9	82.13	97.1	78.37 ± 13.97	
Height (cm)	177.3	171.8	178	158.9	178.2	176	172.58 ± 8.07	
BMI	26.8	19.89	20.61	32.83	25.86	31.35	26.11 ± 5.95	
Race	White	White	White	White	White	White		
Ethnicity	Not Hispanic or Latino	Hispanic or Latino	Not Hispanic or Latino	Not Hispanic or Latino	Not Hispanic or Latino	Not Hispanic or Latino		
Selective serotonin reuptake inhibitor	Zoloft (Sertraline)	-	-	-	-	Prozac (Fluoxetine)		
	No. AEs (%)	No. AEs (%)	No. AEs (%)	No. AEs (%)	No. AEs (%)	No. AEs (%)	Total No. of Adverse Events (%)	
Psychiatric Disorders	Irritability 1 (5.2%)					Obsessive compulsive disorder 1 (5.2%)	2 (10.5%)	
Nervous System Disorders	Headache 1 (5.2%)	Headache 1 (5.2%)		Headache 1 (5.2%)			3 (15.8%)	
Skin Disorders	Folliculitis 2 (10.5%)						2 (10.5%)	
Digestive System Disorders		Stomach pain 1 (5.2%)					1 (2.5%)	
Respiratory Tract Disorders		Sinus 1 (5.2%) Runny nose (5.2%)	Flu 1 (5.2%)	Flu 1 (5.2%)			4 (21%)	
General Disorders			Fatigue 1 (5.2%)	Cold sore 1 (5.2%) Dry skin 2 (10.5%) Fatigue 1 (5.2%) Allergies 1 (5.2%)		Motion sickness 1 (5.2%)	7 (36.84%)	
No. of AEs per patient (%)	4 (21%)	4 (21%)	2 (10.5%)	7 (36.84%)	0 (0%)	2 (10.5%)	19 (100%)	
EKG QTc interval (ms)								
Patient ID	Screening	Baseline	0.5 Month	1 Month	1.5 Month	2 Month	3 Month	4 Month
Nil-HD-001	440	426	438	417	435	427	424	415
Nil-HD-002	459	433	426	432	447	438	442	Remote visit
Nil-HD-003	389	400	400	410	Remote visit	Remote visit	416	403
Nil-HD-004	414	425	413	Remote visit	Remote visit	Remote visit	431	428
Nil-HD-005	422	423	425	417	426	416	418	422
Nil-HD-006	403	402	407	384	408	410	408	388

Table S2. Exploratory Clinical Outcomes.

	Baseline (Mean ± SD)	3 Mths (Mean ± SD)	4 Mths (Mean ± SD)	BSL Vs 3 Mths (p value)	3 Mths Vs 4 Mths (p value)
MOCA	26.50 ± 2.74	25.83 ± 3.0	28.4 ± 1.14	0.25	0.1563
Timed up and go	10.05 ± 2.0	12.02 ± 2.38	10.25 ± 1.64	0.1563	0.0781
TMT-B	120.2 ± 79.15	120 ± 74.69	116.2 ± 72.44	0.5	0.5
UHDRS-m (motor score)	28 ± 13.89	27.33 ± 13.63	28.33 ± 10.88	0.375	0.125
Apathy (Partner)	21.5 ± 4.37	23 ± 5.1	21.83 ± 4.79	0.125	0.4531
Apathy (Participant)	23 ± 3.69	26.17 ± 2.32	24.17 ± 2.4	0.1875	0.125
Irritability (Partner)	14.17 ± 4.79	15.83 ± 4.22	17.17 ± 4.12	0.3125	0.3281
Irritability (Participant)	15.17 ± 8.04	17 ± 9.14	19 ± 6.03	0.375	0.4063