

Supplementary Information. Average fluorescent intensity and background of 1 fM, 100 aM, and 10 aM **F508C** target concentrations hybridized to the multiplexed array. Bracketed signals are less than 3X the signal standard deviation and are below the signal to-noise range. Each probe correctly identified its complementary target except for the 10 aM concentrations, where no signal was acceptable.

1fM concentration (~6000 target molecules)

Target	Probe	Hybridization \pm s.d	Mean background \pm s.d.	Signal \pm s.d
F508C	F508C	543.02 \pm 0.71	472.23 \pm 5.0	70.79 \pm 5.1
	IL2	485.39 \pm 2.3	476.96 \pm 8.0	{8.43} \pm 8.3
	IL6	390.63 \pm 0.87	375.91 \pm 5.2	{14.72} \pm 5.3
F508C	F508C	777.90 \pm 4.7	674.48 \pm 3.2	103.42 \pm 5.7
	IL2	765.69 \pm 19	748.92 \pm 3.4	{16.77} \pm 19
	IL6	708.57 \pm 5.7	682.36 \pm 9.5	{26.21} \pm 11
F508C	F508C	703.75 \pm 5.1	634.20 \pm 5.4	63.55 \pm 7.4
	IL2	777.46 \pm 9.3	750.04 \pm 0.1	{27.42} \pm 9.3
	IL6	717.21 \pm 1.8	708.36 \pm 8.5	{8.85} \pm 8.7

100 aM concentration (~600 target molecules)

Target	Probe	Hybridization \pm s.d	Mean background \pm s.d.	Signal \pm s.d
F508C	F508C	562.58 \pm 7.7	534.29 \pm 1.1	28.29 \pm 7.8
	IL2	462.58 \pm 4.9	459.53 \pm 5.3	{3.05} \pm 7.2
	IL6	418.61 \pm 4.9	411.43 \pm 2.5	{7.18} \pm 5.5
F508C	F508C	625.22 \pm 4.7	578.69 \pm 9.3	46.53 \pm 10
	IL2	605.45 \pm 7.2	576.92 \pm 7.5	{28.53} \pm 10
	IL6	592.46 \pm 5.8	569.00 \pm 8.2	{23.46} \pm 10
F508C	F508C	560.79 \pm 8.5	522.17 \pm 2.2	38.62 \pm 8.5
	IL2	481.01 \pm 12	454.20 \pm 4.0	{26.81} \pm 13
	IL6	403.38 \pm 6.3	382.27 \pm 3.4	{21.11} \pm 7.2

10 aM concentration (~60 target molecules)

Target	Probe	Hybridization \pm s.d	Mean background \pm s.d.	Signal \pm s.d
F508C	F508C	540.21 \pm 3.8	528.14 \pm 2.6	{12.07} \pm 4.6
	IL2	462.29 \pm 2.9	454.85 \pm 0.72	{7.44} \pm 3.0
	IL6	394.15 \pm 2.9	390.44 \pm 2.2	{3.71} \pm 3.6
F508C	F508C	542.71 \pm 6.3	522.22 \pm 4.2	{20.49} \pm 7.6
	IL2	468.10 \pm 3.3	453.78 \pm 7.0	{14.32} \pm 7.7
	IL6	403.58 \pm 5.7	389.80 \pm 5.4	{13.78} \pm 7.9
F508C	F508C	255.92 \pm 5.7	244.78 \pm 5.1	{11.14} \pm 7.6
	IL2	238.97 \pm 4.0	228.31 \pm 2.5	{10.66} \pm 4.0
	IL6	330.52 \pm 9.0	322.35 \pm 7.3	{8.17} \pm 12

Average fluorescent intensity and background of 1 fM, 100 aM, and 10 aM **IL2** target concentrations hybridized to the multiplexed array. Bracketed signals are less than 3X the signal standard deviation and are below the signal-to-noise range. Each probe correctly identified its complementary target except for the 10 aM concentrations, where no signal was acceptable.

1fM concentration (~6000 target molecules)

Target	Probe	Hybridization \pm s.d	Mean background \pm s.d.	Signal \pm s.d
IL2	F508C	550.17 \pm 7.5	530.43 \pm 1.8	{19.74} \pm 7.7
	IL2	677.08 \pm 8.1	563.99 \pm 7.7	113.09 \pm 11
	IL6	449.16 \pm 1.4	445.99 \pm 3.9	{3.17} \pm 4.1
IL2	F508C	465.82 \pm 1.4	454.84 \pm 3.6	{10.98} \pm 3.8
	IL2	517.38 \pm 2.6	429.42 \pm 0.92	87.96 \pm 2.8
	IL6	467.82 \pm 5.3	459.81 \pm 3.0	{8.01} \pm 6.1
IL2	F508C	443.34 \pm 5.6	439.64 \pm 3.5	{3.70} \pm 6.6
	IL2	503.31 \pm 6.6	432.52 \pm 5.6	70.79 \pm 8.7
	IL6	432.13 \pm 2.8	431.11 \pm 2.1	{1.02} \pm 3.5

100 aM concentration (~600 target molecules)

Target	Probe	Hybridization \pm s.d	Mean background \pm s.d.	Signal \pm s.d
IL2	F508C	348.98 \pm 8.3	304.31 \pm 2.9	{13.58} \pm 8.8
	IL2	381.23 \pm 4.8	312.38 \pm 3.0	39.30 \pm 5.7
	IL6	484.34 \pm 11	384.96 \pm 5.7	{20.42} \pm 12
IL2	F508C	341.42 \pm 2.1	327.47 \pm 4.5	{13.95} \pm 5.0
	IL2	378.20 \pm 7.8	343.14 \pm 6.6	35.06 \pm 10
	IL6	471.38 \pm 13	466.21 \pm 11	{5.17} \pm 17
IL2	F508C	413.63 \pm 1.2	410.73 \pm 2.6	{2.90} \pm 2.9
	IL2	455.26 \pm 6.5	410.69 \pm 2.7	44.57 \pm 7.0
	IL6	392.88 \pm 2.8	390.24 \pm 7.4	{2.64} \pm 7.9

10 aM concentration (~60 target molecules)

Target	Probe	Hybridization \pm s.d	Mean background \pm s.d.	Signal \pm s.d
IL2	F508C	398.28 \pm 3.0	388.44 \pm 2.7	{9.84} \pm 4.0
	IL2	444.05 \pm 5.8	420.25 \pm 6.7	{23.80} \pm 8.9
	IL6	428.70 \pm 4.3	418.40 \pm 5.2	{10.30} \pm 6.7
IL2	F508C	441.29 \pm 4.9	431.58 \pm 6.0	{9.71} \pm 7.8
	IL2	411.33 \pm 3.1	399.00 \pm 5.1	{12.33} \pm 6.0
	IL6	423.81 \pm 6.8	417.44 \pm 5.5	{6.37} \pm 8.7
IL2	F508C	271.78 \pm 3.3	267.20 \pm 1.4	{4.58} \pm 3.6
	IL2	261.04 \pm 4.5	250.63 \pm 1.0	{10.41} \pm 4.6
	IL6	302.85 \pm 5.3	297.28 \pm 4.2	{5.57} \pm 6.8

Average fluorescent intensity and background of 1 fM, 100 aM, and 10 aM **IL6** target concentrations hybridized to the multiplexed array. Bracketed signals are less than 3X the signal standard deviation and are below the signal-to-noise range. Each probe correctly identified its complementary target except for the 10 aM concentrations, where no signal was acceptable.

1fM concentration (~6000 target molecules)

Target	Probe	Hybridization \pm s.d	Mean background \pm s.d.	Signal \pm s.d
IL6	F508C	373.01 \pm 4.0	358.77 \pm 5.0	{14.24} \pm 6.4
	IL2	393.33 \pm 6.5	375.80 \pm 3.2	{17.53} \pm 7.2
	IL6	494.88 \pm 12	405.63 \pm 5.0	89.25 \pm 13
IL6	F508C	549.93 \pm 9.4	524.01 \pm 4.0	{25.92} \pm 10
	IL2	454.28 \pm 11	426.39 \pm 4.2	{27.79} \pm 12
	IL6	86.35 \pm 6.0	297.38 \pm 2.7	86.35 \pm 6.6
IL6	F508C	406.46 \pm 6.9	381.01 \pm 5.3	{25.45} \pm 8.7
	IL2	377.27 \pm 9.3	355.84 \pm 2.6	{21.43} \pm 9.7
	IL6	382.24 \pm 6.5	322.22 \pm 3.9	60.02 \pm 7.6

100 aM concentration (~600 target molecules)

Target	Probe	Hybridization \pm s.d	Mean background \pm s.d.	Signal \pm s.d
IL6	F508C	299.32 \pm 7.6	286.15 \pm 7.5	{13.17} \pm 11
	IL2	264.39 \pm 6.7	248.35 \pm 2.9	{16.04} \pm 7.3
	IL6	284.43 \pm 4.2	262.77 \pm 2.3	21.66 \pm 4.8
IL6	F508C	262.69 \pm 3.8	248.05 \pm 3.1	{14.64} \pm 4.9
	IL2	243.05 \pm 3.3	228.59 \pm 4.5	{14.46} \pm 5.6
	IL6	337.09 \pm 2.7	310.01 \pm 4.1	27.08 \pm 4.9
IL6	F508C	262.40 \pm 3.8	246.31 \pm 3.9	{16.09} \pm 5.4
	IL2	242.34 \pm 2.7	233.35 \pm 4.9	{8.99} \pm 5.6
	IL6	351.25 \pm 5.3	314.49 \pm 1.3	36.76 \pm 5.5

10 aM concentration (~60 target molecules)

Target	Probe	Hybridization \pm s.d	Mean background \pm s.d.	Signal \pm s.d
IL6	F508C	259.09 \pm 3.4	253.19 \pm 0.65	{5.90} \pm 3.5
	IL2	238.54 \pm 5.6	231.78 \pm 2.7	{6.76} \pm 6.2
	IL6	330.74 \pm 2.1	320.31 \pm 3.9	{10.43} \pm 4.4
IL6	F508C	265.93 \pm 2.5	257.46 \pm 2.4	{8.47} \pm 3.5
	IL2	258.22 \pm 3.8	248.91 \pm 4.2	{9.31} \pm 5.7
	IL6	303.99 \pm 6.4	283.47 \pm 4.6	{18.23} \pm 8.4
IL6	F508C	256.12 \pm 3.0	248.24 \pm 1.0	{7.88} \pm 3.2
	IL2	231.12 \pm 0.32	225.18 \pm 2.7	{5.94} \pm 2.7
	IL6	327.78 \pm 7.1	317.63 \pm 6.4	{10.15} \pm 9.6