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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	%Retic	%Retic	%Retic	%Retic	%Retic	#Retic	#Retic	#Retic	#Retic	#Retic
	(%)	(%)	(%)	(%)	(%)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	1.0	2.9	2.5	2.6	3.1	62.5	164.2	145.5	145.2	180.6
RP1F02	1.3	2.1	2.1	1.9	2.1	69.0	110.4	115.7	104.0	115.2
RP1F03	1.1	2.1	2.1	2.0	2.1	63.5	110.3	114.1	110.7	121.3
RP1F04	0.8	1.9	1.5	1.3	1.7	49.8	103.6	86.0	71.4	94.1
Mean	1.1	2.3	2.1	2.0	2.3	61.2	122.1	115.3	107.8	127.8
S.D.	0.2	0.4	0.4	0.5	0.6	8.1	28.2	24.3	30.3	37.1
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	PLT					WBC				
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	375	400	392	354	369	10.60	7.29	13.02	9.06	7.93
RP1F02	510	489	476	471	472	6.66	7.24	14.79	7.27	10.63
RP1F03	252	243	248	255	237	6.90	7.45	8.05	6.46	6.76
RP1F04	337	373	399	350	358	7.74	9.14	7.82	9.34	9.15
Mean	369	376	379	358	359	7.98	7.78	10.92	8.03	8.62
S.D.	107	102	95	88	96	1.81	0.91	3.52	1.39	1.66
N	4	4	4	4	4	4	4	4	4	4

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	%Neut	%Neut	%Neut	%Neut	%Neut	%Lymph	%Lymph	%Lymph	%Lymph	%Lymph
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	39.1	33.2	50.1	52.1	35.4	57.3	62.1	46.2	44.6	60.0
RP1F02	50.1	41.3	61.3	63.9	55.1	43.8	50.5	32.4	30.3	38.1
RP1F03	23.0	23.9	27.4	38.6	25.1	71.4	71.0	68.1	55.7	70.3
RP1F04	50.1	42.6	46.2	65.7	44.4	44.0	51.2	46.8	29.8	49.3
Mean	40.6	35.3	46.3	55.1	40.0	54.1	58.7	48.4	40.1	54.4
S.D.	12.8	8.6	14.1	12.5	12.8	13.1	9.8	14.7	12.5	13.9
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	%Mono	%Mono	%Mono	%Mono	%Mono	%Eos	%Eos	%Eos	%Eos	%Eos
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	2.3	3.3	2.8	2.5	3.2	0.5	0.6	0.4	0.1	0.6
RP1F02	4.6	5.6	4.6	3.8	4.3	1.0	2.1	1.2	1.4	2.2
RP1F03	2.8	3.0	2.6	3.6	2.8	2.0	1.4	1.1	1.2	1.2
RP1F04	3.8	4.0	5.1	3.6	4.4	1.2	1.5	1.5	0.4	1.4
Mean	3.4	4.0	3.8	3.4	3.7	1.2	1.4	1.1	0.8	1.4
S.D.	1.0	1.2	1.3	0.6	0.8	0.6	0.6	0.5	0.6	0.7
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	%Baso	%Baso	%Baso	%Baso	%Baso	%LUC	%LUC	%LUC	%LUC	%LUC
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	0.4	0.2	0.3	0.3	0.3	0.4	0.5	0.2	0.4	0.5
RP1F02	0.3	0.2	0.3	0.2	0.2	0.2	0.2	0.3	0.4	0.2
RP1F03	0.5	0.3	0.4	0.4	0.2	0.4	0.5	0.4	0.5	0.4
RP1F04	0.3	0.2	0.2	0.1	0.1	0.6	0.5	0.2	0.3	0.4
Mean	0.4	0.2	0.3	0.3	0.2	0.4	0.4	0.3	0.4	0.4
S.D.	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.1	0.1	0.1
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	#Neut	#Neut	#Neut	#Neut	#Neut	#Lymph	#Lymph	#Lymph	#Lymph	#Lymph
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	4.14	2.42	6.52	4.72	2.81	6.08	4.53	6.01	4.04	4.76
RP1F02	3.34	2.99	9.07	4.65	5.85	2.92	3.66	4.79	2.21	4.04
RP1F03	1.59	1.78	2.21	2.49	1.69	4.92	5.29	5.48	3.60	4.75
RP1F04	3.88	3.89	3.61	6.14	4.06	3.41	4.68	3.66	2.78	4.52
Mean	3.24	2.77	5.35	4.50	3.60	4.33	4.54	4.99	3.16	4.52
S.D.	1.15	0.90	3.06	1.51	1.78	1.44	0.67	1.01	0.82	0.34
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	#Mono	#Mono	#Mono	#Mono	#Mono	#Eos	#Eos	#Eos	#Eos	#Eos
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	0.24	0.24	0.37	0.22	0.26	0.05	0.05	0.05	0.01	0.05
RP1F02	0.30	0.41	0.68	0.28	0.45	0.07	0.15	0.18	0.10	0.24
RP1F03	0.20	0.22	0.21	0.23	0.19	0.14	0.10	0.09	0.08	0.08
RP1F04	0.29	0.37	0.40	0.34	0.40	0.09	0.13	0.11	0.04	0.13
Mean	0.26	0.31	0.42	0.27	0.33	0.09	0.11	0.11	0.06	0.13
S.D.	0.05	0.09	0.20	0.06	0.12	0.04	0.04	0.05	0.04	0.08
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	#Baso	#Baso	#Baso	#Baso	#Baso	#LUC	#LUC	#LUC	#LUC	#LUC
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	0.04	0.01	0.04	0.03	0.03	0.04	0.04	0.03	0.04	0.04
RP1F02	0.02	0.02	0.04	0.01	0.02	0.01	0.02	0.04	0.03	0.02
RP1F03	0.03	0.02	0.03	0.03	0.02	0.03	0.03	0.03	0.03	0.03
RP1F04	0.02	0.02	0.01	0.01	0.01	0.04	0.04	0.02	0.03	0.03
Mean	0.03	0.02	0.03	0.02	0.02	0.03	0.03	0.03	0.03	0.03
S.D.	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.00	0.01
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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	PT	PT	PT	PT	PT	APTT	APTT	APTT	APTT	APTT
	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)
	-1	1	2	3	4	-1	1	2	3	4
RP1F01	9.5	9.3	9.5	9.8	9.7	22.2	22.2	22.0	22.1	22.2
RP1F02	9.8	9.9	9.8	10.1	9.8	23.9	23.4	22.2	23.8	23.2
RP1F03	9.9	9.5	9.9	9.9	9.8	25.3	25.5	25.4	25.2	25.6
RP1F04	10.7	10.3	10.5	10.5	10.8	26.5	26.2	26.6	26.4	26.4
Mean	10.0	9.8	9.9	10.1	10.0	24.5	24.3	24.1	24.4	24.4
S.D.	0.5	0.4	0.4	0.3	0.5	1.9	1.8	2.3	1.9	2.0
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	Fib	Fib	Fib	Fib	Fib
	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)
	-1	1	2	3	4
RP1F01	153.7	185.4	165.3	160.0	164.1
RP1F02	170.0	188.9	166.7	185.4	173.9
RP1F03	177.8	228.0	208.8	187.2	190.0
RP1F04	145.6	196.4	155.0	172.5	180.0
Mean	161.8	199.7	174.0	176.3	177.0
S.D.	14.7	19.4	23.8	12.7	10.9
N	4	4	4	4	4

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	RBC					HGB				
	(10 ⁶ /μL)	(10 ⁶ /μL)	(10 ⁶ /μL)	(10 ⁶ /μL)	(10 ⁶ /μL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	5.49	5.18	5.30	5.20	5.38	14.0	13.2	13.4	13.0	13.5
RP2F02	5.34	4.93	5.18	4.87	4.83	13.4	12.2	12.9	12.1	11.9
RP2F03	6.50	6.16	6.29	6.03	6.07	14.1	13.1	13.6	13.1	13.2
RP2F04	6.00	5.74	5.66	5.63	5.63	13.3	12.7	12.4	12.5	12.4
Mean	5.83	5.50	5.61	5.43	5.48	13.7	12.8	13.1	12.7	12.8
S.D.	0.53	0.55	0.50	0.51	0.52	0.4	0.5	0.5	0.5	0.7
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	HCT					MCV				
	HCT	HCT	HCT	HCT	HCT	MCV	MCV	MCV	MCV	MCV
	(%)	(%)	(%)	(%)	(%)	(fL)	(fL)	(fL)	(fL)	(fL)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	43.8	40.3	41.6	42.2	44.1	79.8	77.9	78.5	81.2	81.9
RP2F02	44.7	43.0	44.2	42.8	41.9	83.8	87.3	85.3	87.9	86.8
RP2F03	51.3	47.1	49.3	48.2	48.0	78.9	76.4	78.4	80.0	79.1
RP2F04	44.2	41.8	41.0	41.6	42.6	73.6	72.9	72.5	73.9	75.7
Mean	46.0	43.1	44.0	43.7	44.2	79.0	78.6	78.7	80.8	80.9
S.D.	3.6	2.9	3.8	3.0	2.7	4.2	6.2	5.2	5.7	4.7
N	4	4	4	4	4	4	4	4	4	4

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	MCH	MCH	MCH	MCH	MCH	MCHC	MCHC	MCHC	MCHC	MCHC
	(pg)	(pg)	(pg)	(pg)	(pg)	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	25.5	25.5	25.2	25.0	25.1	31.9	32.7	32.2	30.8	30.7
RP2F02	25.1	24.8	24.8	24.9	24.7	30.0	28.4	29.1	28.3	28.5
RP2F03	21.7	21.3	21.6	21.7	21.8	27.5	27.9	27.5	27.1	27.6
RP2F04	22.1	22.1	21.9	22.2	22.1	30.0	30.3	30.2	30.1	29.2
Mean	23.6	23.4	23.4	23.5	23.4	29.9	29.8	29.8	29.1	29.0
S.D.	2.0	2.0	1.9	1.7	1.7	1.8	2.2	2.0	1.7	1.3
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	%Retic	%Retic	%Retic	%Retic	%Retic	#Retic	#Retic	#Retic	#Retic	#Retic
	(%)	(%)	(%)	(%)	(%)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	0.7	1.7	0.9	2.9	1.1	36.0	86.3	46.9	153.1	61.7
RP2F02	1.1	5.0	3.2	3.0	2.9	57.7	248.4	163.3	144.6	142.0
RP2F03	0.7	1.6	1.5	1.6	1.3	46.1	99.4	92.6	95.3	77.4
RP2F04	1.1	1.3	1.5	1.6	1.9	66.9	74.5	83.5	89.8	107.8
Mean	0.9	2.4	1.8	2.3	1.8	51.7	127.2	96.6	120.7	97.2
S.D.	0.2	1.7	1.0	0.8	0.8	13.5	81.5	48.7	32.8	35.5
N	4	4	4	4	4	4	4	4	4	4

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	PLT					WBC				
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	506	547	514	413	407	7.40	6.14	8.81	3.69	7.54
RP2F02	469	493	508	456	438	8.98	7.88	8.69	8.40	9.42
RP2F03	382	378	416	350	324	11.23	7.55	6.76	12.12	6.98
RP2F04	368	340	336	313	312	10.26	7.37	10.63	7.49	8.94
Mean	431	440	444	383	370	9.47	7.24	8.72	7.93	8.22
S.D.	67	97	85	64	62	1.66	0.76	1.58	3.46	1.15
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	%Neut	%Neut	%Neut	%Neut	%Neut	%Lymph	%Lymph	%Lymph	%Lymph	%Lymph
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	51.7	32.5	40.9	40.0	31.5	45.1	63.2	53.4	56.3	63.0
RP2F02	45.0	35.7	31.1	53.5	37.0	48.5	58.9	63.0	42.3	57.9
RP2F03	42.7	26.4	21.7	61.0	24.2	51.7	66.6	71.0	34.3	68.8
RP2F04	61.6	47.1	55.8	49.2	42.0	33.8	46.7	38.8	46.1	52.6
Mean	50.3	35.4	37.4	50.9	33.7	44.8	58.9	56.6	44.8	60.6
S.D.	8.5	8.7	14.6	8.8	7.6	7.8	8.7	13.8	9.1	6.9
N	4	4	4	4	4	4	4	4	4	4

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	%Mono					%Eos				
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	2.5	3.5	4.7	2.8	4.6	0.1	0.3	0.4	0.2	0.4
RP2F02	4.4	3.7	3.9	3.0	3.0	1.2	1.0	1.1	0.6	1.1
RP2F03	3.9	5.5	5.3	3.6	4.5	0.9	0.8	1.1	0.5	1.8
RP2F04	3.5	4.8	4.5	3.6	4.0	0.6	0.7	0.4	0.5	0.8
Mean	3.6	4.4	4.6	3.3	4.0	0.7	0.7	0.8	0.5	1.0
S.D.	0.8	0.9	0.6	0.4	0.7	0.5	0.3	0.4	0.2	0.6
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	%Baso	%Baso	%Baso	%Baso	%Baso	%LUC	%LUC	%LUC	%LUC	%LUC
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	0.4	0.2	0.2	0.3	0.2	0.2	0.3	0.3	0.3	0.3
RP2F02	0.4	0.3	0.3	0.3	0.3	0.5	0.4	0.6	0.3	0.6
RP2F03	0.4	0.3	0.4	0.3	0.3	0.4	0.4	0.6	0.4	0.3
RP2F04	0.3	0.2	0.2	0.2	0.3	0.2	0.4	0.3	0.4	0.4
Mean	0.4	0.3	0.3	0.3	0.3	0.3	0.4	0.5	0.4	0.4
S.D.	0.0	0.1	0.1	0.1	0.0	0.2	0.1	0.2	0.1	0.1
N	4	4	4	4	4	4	4	4	4	4

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	#Neut	#Neut	#Neut	#Neut	#Neut	#Lymph	#Lymph	#Lymph	#Lymph	#Lymph
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	3.83	1.99	3.61	1.47	2.37	3.34	3.88	4.71	2.08	4.75
RP2F02	4.04	2.81	2.70	4.49	3.49	4.36	4.64	5.48	3.56	5.45
RP2F03	4.80	1.99	1.47	7.39	1.69	5.81	5.03	4.80	4.15	4.81
RP2F04	6.32	3.47	5.93	3.68	3.75	3.47	3.45	4.12	3.45	4.70
Mean	4.75	2.57	3.43	4.26	2.83	4.25	4.25	4.78	3.31	4.93
S.D.	1.13	0.72	1.88	2.45	0.96	1.14	0.72	0.56	0.88	0.35
N	4	4	4	4	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	#Mono	#Mono	#Mono	#Mono	#Mono	#Eos	#Eos	#Eos	#Eos	#Eos
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	0.19	0.21	0.42	0.10	0.35	0.00	0.02	0.04	0.01	0.03
RP2F02	0.39	0.29	0.34	0.26	0.29	0.11	0.08	0.09	0.05	0.11
RP2F03	0.44	0.41	0.36	0.43	0.31	0.10	0.06	0.07	0.06	0.12
RP2F04	0.35	0.36	0.47	0.27	0.36	0.06	0.05	0.05	0.04	0.07
Mean	0.34	0.32	0.40	0.27	0.33	0.07	0.05	0.06	0.04	0.08
S.D.	0.11	0.09	0.06	0.13	0.03	0.05	0.03	0.02	0.02	0.04
N	4	4	4	4	4	4	4	4	4	4