Supplementary Table 1.

Systematic functional analysis of NOD2

	clone ID#	NF-kB activation overexpression	WB	NF-kB activ (-)	NF-kB activ MDP	Mutations	Region	Mouse conservativity	Notes
Point Mutants	1-89U	100.6	(+)	1.6	30.9	E13K	NC	absent	
	1-45	198.3	(+)	1.7	15.8	G25A	CARD1	absent	
	1-O04	0.6	(+)	1.9	5.3	Q31H	CARD1	+	
	1-91U	42.6	(+)	3.0	4.8	E69K	CARD1	+	
	1-84	451.0	(+)	2.2	6.8	T91I	CARD1	+	
	1-15	0.6	(+)	1.1	1.6	A106V	CARD1	E	
	1-30	0.3	(+)	1.3	1.3	L145P	CARD2	+	D.N.
	1-57	274.3	(+)	0.8	5.8	S147T	CARD2	N	
	1-77	16.1	(+)	4.6	42.0	M152L	CARD2	+	
	1-52	294.0	(+)	1.0	11.0	C167S	CARD2	+	
	1-93U	2.3	(-)	0.6	0.5	P177S	CARD2	S	
	1-6	0.8	(-)	0.7	1.3	R180K	CARD2	+	
	1-41	19.8	(+)	0.9	6.1	G194R	CARD2	+	
	1-28	309.0	(+)	1.6	33.9	L200I	CARD2	+	
	1-26	245.3	(+)	1.4	18.0	Q204R	CARD2	R	
	1-73	294.6	(+)	1.0	8.9	A216V	CARD2	+	
	1-48	ND	(-)	0.8	1.3	A232P	NOD	T	
	1-91L	54.1	(+)	1.5	35.5	L246F	NOD	+	
	1-66L	102.4	(+)	3.6	28.0	A266T	NOD	A	
	1-72	456.4	(+)	1.5	13.7	A274V	NOD	+	
	1-31	385.4	(+)	2.1	39.1	E279K	NOD	+	
	1-17	206.5	(+)	1.5	7.8	V295M	NOD	I	
	1-60L	52.2	(+)	0.4	0.6	V295E	NOD	I	
	1-88L	54.2	(+)	0.7	0.6	F327Y	NOD	+	
	1-89L	9.7	(-)	0.6	1.2	C333Y	NOD	+	
	1-O01	115.2	(+)	1.3	1.3	S344T	NOD	+	
	1-39L	65.8	(+)	0.8	30.3	R346W	NOD	+	
	1-50L	86.0	(+)	1.0	14.1	C353Y	NOD	+	
	1-O02	92.3	(+)	0.9	6.6	R373C	NOD	+	R373C is a mutation reported in CD patients (Lesage et al., 2002)
	B-box	86.7	(+)	0.8	0.9	D379A	NOD	+	
	2-7	135.9	(+)	1.3	19.5	R393C	NOD	+	
	2-n32	ND	(+)	2.9	2.0	S396Y	NOD	+	
	2-n14	ND	(+)	1.0	0.7	T401I	NOD	+	
	2-n12	ND	(+)	0.0	0.0	T401S	NOD	+	
	2-n4	ND	(+)	0.0	0.9	F408L	NOD	+	
	2-n33	ND	(+)	9.8	139.7	K421M	NOD	+	
	2-35	105.9	(+)	2.8	1.9	A429T	NOD	+	
	2-n26	ND	(+)	1.3	93.8	R439C	NOD	+	
	2-n42	ND	(+)	0.8	16.0	N443D	NOD	Q	
	2-n41	ND	(+)	7.3	93.5	I452F	NOD	+	
	2-n3	ND	(+)	1.7	17.8	R457M	NOD	+	
	2-47	97.2	(+)	2.1	11.9	R471L	NOD	Q	
	2-15	144.6	(+)	1.2	6.7	H480Y	NOD	+	
	2-O08	47.5	(+)	0.7	0.8	V492E	NOD	+	
	2-8	84.2	(+)	0.7	14.0	F521S	NOD	+	
	2-n5	ND	(+)	2.9	62.5	F521L	NOD	+	
	2-41	263.8	(+)	1.2	8.0	A525V	NOD	+	
	2-21	139.4	(+)	0.8	6.5	H549Y	NOD	+	
	2-24	120.3	(+)	1.1	5.9	G557S	NOD	+	
	2-n27	ND	(+)	7.0	78.7	M560V	NOD	+	
	2-34	128.6	(+)	1.3	14.1	V564M	NOD	+	
	2-n75	ND	(+)	1.1	7.5	Q568H	NOD	+	
	2-33	97.6	(+)	1.2	14.5	G590S	NOD	S	
	2-54	93.7	(+)	1.5	9.9	E600Q	NOD	+	
	3-A03	118.4	(+)	18.5	131.8	P623R	NOD	V	
	3-A11	78.0	(+)	0.3	0.3	L626F	NOD	+	
	3-E2U	116.5	(+)	11.0	142.1	R634W	NOD	+	
	3-D3U	59.7	(+)	1.0	1.5	P639S	NOD	L	
	3-D07	85.8	(+)	33.9	396.2	T646M	NOD	N	
	3-H9U	98.5	(+)	2.1	19.0	C648Y	NOD	L	
	3-B09	ND	(+)	8.5	94.4	G654R	NOD	V	
	3-D4U	118.0	(+)	1.1	1.9	K655E	NOD	+	
	3-E07	107.0	(+)	7.6	108.5	V659M	NOD	E	
	3-D11	122.3	(+)	94.5	106.7	P668H	NOD	+	
	3-B11U	82.2	(+)	4.8	54.0	Q672R	NOD	+	
	3-H11	150.3	(+)	238.8	277.0	I673F	NOD	+	
	3-B5U	148.4	(+)	2.2	1.9	G680R	NOD	+	
	3-E3U	58.2	(+)	0.6	1.1	G680W	NOD	+	
	3-E04	75.9	(+)	8.9	109.1	L690M	NOD	+	
	3-B6U	124.4	(+)	0.5	1.2	L690P	NOD	+	
	3-B03	128.1	(+)	17.7	187.8	A691V	NOD	+	
	3-F02	100.8	(+)	8.6	19.9	A691T	NOD	+	
	3-O05	131.2	(+)	1.6	15.1	E692D	NOD	A	
	3-E06	57.0	(+)	0.5	1.1	S714N	NOD	+	
	3-D06	87.7	(+)	1.5	38.7	P723S	NOD	+	
	3-H7U	109.0	(+)	3.1	1.9	H734L	NOD	+	
	3-A04	161.4	(+)	6.2	2.1	E751K	LRR1	+	
	3-C6L	112.7	(+)	7.5	57.5	A759V	LRR2	V	
	3-E3L	113.1	(+)	6.6	92.7	G761S	LRR2	R	
	3-C11L	116.8	(+)	5.9	64.3	L762M	LRR2	+	
	3-B7L	124.4	(+)	1.1	1.9	G775D	LRR2	+	
	3-H4L	124.5	(+)	3.4	2.9	C779Y	LRR2	+	
	3-D4L	129.8	(+)	3.0	64.0	V793M	LRR3	+	V793M was reported in a CD patient but exhibit WT activity of NOD2 (Chamaillard et al., 2003c and present data)
	3-A01	153.8	(+)	ND	ND	A794T	LRR3	+	
	3-H7L	93.5	(+)	16.4	58.7	I805N	LRR3	V	
	3-D08	97.2	(+)	14.8	225.4	P812T	LRR3	+	
	3-H9L	130.2	(+)	4.8	25.8	D824N	LRR4	+	D824N was found in a CD and UC patient (Lesage et al., 2002) but has the activity comparable with WT Nod2
	3-E2L	115.0	(+)	0.9	1.8	D829Y	LRR4	+	
	3-B6L	117.8	(+)	4.8	2.3	G831D	LRR4	+	
	3-A10	120.6	(+)	11.3	201.6	A860G	LRR5	+	
	4-O03	134.2	(+)	1.1	12.3	L876I	LRR6	+	
	3-E10	79.1	(+)	0.1	0.1	G879R	LRR6	+	
	3-B08	91.5	(+)	1.3	1.5	T884I	LRR6	+	
	4-F11	106.8	(+)	1.3	48.3	Q889P	LRR6	E	

4-H7	106.5	(+)	0.8	1.2	**V890A**		LRR6	+	
4-G3	138.2	(+)	0.7	5.7	**L891M**		LRR6	+	
4-A11	93.1	(+)	4.3	193.1	**A892V**		LRR6	+	
4-G1	92.7	(+)	0.2	0.4	**T899A**		LRR6	+	
4-H4	137.3	(+)	0.9	25.4	**L904M**		LRR7	+	
4-A7	122.3	(+)	0.7	1.4	**W907L**		LRR7	+	
4-F1	65.2	(+)	8.1	19.6	**V911M**		LRR7	+	
4-G6	91.6	(+)	0.4	24.9	**D913V**		LRR7	+	
4-H8	102.1	(+)	1.0	0.9	**D913E**		LRR7	+	
4-H9	56.1	(+)	1.2	1.0	**G915E**		LRR7	+	
4-B5	105.7	(+)	0.9	15.7	**A920T**		LRR7	+	
4-A8	101.5	(+)	2.8	8.2	**V935M**		LRR8	+	
4-H5	108.3	(+)	5.2	45.6	**A944V**		LRR8	+	
4-G10	124.8	(+)	0.7	24.4	**L947M**		LRR8	+	
4-E4	92.6	(+)	3.4	62.0	**L949V**		LRR8	+	
4-H6	106.8	(+)	0.4	30.8	**L949M**		LRR8	+	
4-B12	92.6	(+)	5.7	42.5	**M956T**		LRR9	S	
4-C3	117.1	(+)	0.9	1.6	**E959K**		LRR9	+	
4-G2	54.7	(+)	0.2	1.6	**L960V**		LRR9	+	
4-B11	83.4	(+)	1.5	62.8	**Q968H**		LRR9	C	
4-E11	62.0	(+)	1.5	11,9	**G978E**		LRR9	+	G978E was reported in a CD patient (Lesage et al., 2002)
4-H3	137.0	(+)	1.1	22.5	**S984T**		LRR10	T	
4-D7	119.2	(+)	2.3	174.2	**K986I**		LRR10	+	
4-C9	54.2	(+)	0.9	1.2	**K989E**		LRR10	+	
4-A12	97.2	(+)	0.8	2.3	**S991F**		LRR10	+	
4-A9	122.7	(+)	0.9	1.7	**G999R**		LRR10	+	
4-A5	ND	(+)	5.0	123.4	**A1002S**		LRR10	+	
4-O02	105.1	(+)	1.3	2.1	**N1010S**		LRR10	+	
4-E8	92.7	(+)	3.4	55.8	**T1012I**		LRR11	A	
4-G8	106.0	(+)	0.6	8.7	**T1012S**		LRR11	A	
4-F12	54.8	(+)	4.6	104.3	**G1032C**		LRR11	S	
4-E2	127.8	(+)	1.8	39.3	**L1038F**		LRR11	+	
1-51U	392.8	(+)	7.1	76.4	G25S	V208F	NC,CARD2		
1-92	321.4	(+)	1.5	9.2	L19I	V256I	NC,NODs		
1-59	227.8	(+)	0.8	7.6	A112G	W123R	CARD1		
1-40	19.6	(+)	1.3	21.9	G48E	E361G	CARD1,NOD		
1-42	64.6	(+)	2.8	15.3	A140T	A211D	CARD2		A140T was reported in CD and UC patients (Lesage et al., 2002)
1-65	189.7	(+)	1.0	10.6	V203A	I251T	CARD2,NOD		
1-80	622.0	(+)	1.8	11.5	P213S	A224T	CARD2,NOD		
1-16	147.2	(+)	2.1	17.3	R15K	V149M	CARDs		
1-69U	119.9	(+)	1.3	87.9	G48E	A131V	CARDs		
1-96U	150.4	(+)	6.9	76.6	G96C	L214M	CARDs		
1-54L	70.2	(+)	1.1	34.1	L288I	V328I	NOD		
1-96L	55.9	(+)	1.3	44.0	T284S	M339K	NOD		
2-27	83.0	(+)	1.5	11.4	T546S	W556R	NOD		
2-37	109.1	(+)	0.8	10.7	L516M	K589T	NOD		
2-n49	ND	(+)	3.1	49.5	**R393C**	R587W	NOD		
2-n40	ND	(+)	1.5	83.4	L472P	V591I	NOD		
3-A07	133.1	(+)	13.5	496.4	L629F	N637I	NOD		
3-B01	91.7	(+)	2.3	83.3	K698M	L701F	NOD		
3-B02	98.2	(+)	3.3	71.2	C608Y	Q650H	NOD		
3-C10	64.2	(+)	2.1	13.3	F606Y	L701H	NOD		
3-B10	82.8	(+)	12.8	143.5	E697D	R830Q	NOD,LRRs		
3-C04	54.0	(+)	8.4	132.8	N631I	I836V	NOD,LRRs		
3-H9	113.1	(+)	0.3	24.4	**C648Y**	**D824N**	NOD,LRRs		
3-B7U	112.9	(+)	2.5	27.2	A725T	A726T	NOD		A725G was a mutation found in CD (Lesage et al., 2002)
3-H1U	90.7	(+)	1.1	35.0	L662S	A725T	NOD		
3-O04	133.5	(+)	1.6	6.7	V785M	C833S	LRRs		
4-A2	124.2	(+)	2.5	101.5	V955F	L1038V	LRRs		V955I was reported in CD and UC patients exhibit WT activity of NOD2 (Chamaillard et al., 2003c)
4-C6	74.1	(+)	0.9	47.4	A946S	A1000T	LRRs		
e	0.6	(+)	0.5	48.0	K953N	**G1032C**	LRRs		
3-E03	73.4	(+)	10.2	109.4	**G680W**	**G761S**	NOD,LRR	*	
3-C11U	75.2	(+)	1.1	19.1	S683T	A735V	NOD,LRR	*	
1-86	224.5	(+)	1.4	11.8	F282I	Q323K	NOD		
2-n1	ND	(+)	1.4	9.8	T389R	**R393C**	NOD		
2-n46	ND	(+)	1.0	9.8	I580N	G590D	NOD		
2-n50	ND	(+)	1.5	37.7	**H480Y**	L599M	NOD		
2-n2	ND	(+)	1.2	3.6	E392D	M513V	NOD		
1-43U	293.1	(+)	1.3	7.2	Q79L	V208I	CARDs		
4-A10	87.0	(+)	6,5	43.5	L929M	R930G	LRRs		
3-D10	109.0	(+)	45.1	55.0	F719I	K731R	NOD		
3-C09	64.8	(+)	44.3	30.3	**G680R**	C710Y	NOD		
3-H5	96.0	(+)	111.5	115.5	N637I	A725V	NOD		
2-n74	ND	(+)	0.4	0.6	S493P	P598H	NOD		
2-n57	ND	(+)	0.7	0.5	L515M	**V564M**	NOD		
3-A8U	128.1	(+)	0.3	2.5	W687L	R702Q	NOD		R702W was reported to be associated to CD (Hugot et al., 2001 and Ogura et al., 2001)
1-47L	19.2	(+)	0.6	2.1	V256I	N289Y	NOD		N289S was reported in CD patients (Lesage et al., 2002)
1-5	6.2	(+)	1.1	4.3	**R180K**	N193K	CARD2		
4-F2	87.8	(+)	0.6	0.4	A888S	L985M	LRRs		
4-D8	77.4	(+)	0.8	0.7	A1006V	G1032D	LRRs		
3-H7	103.5	(+)	0.4	0.7	**H734L**	**I805N**	LRRs		
3-B5L	136.3	(+)	1.9	1.9	**C779Y**	N872K	LRRs		
3-C1L	115.1	(+)	2.1	0.6	L782V	**A759V**	LRRs		
4-B10	81.9	(+)	1.3	0.8	Q945P	L1039W	LRRs		
4-E5	96.3	(+)	0.9	1.2	A948T	L975F	LRRs		
4-E6	111.6	(+)	0.9	1.1	K989T	L1031F	LRRs		
4-G12	92.0	(+)	1.1	1.3	S928R	**V935M**	LRRs		
4-H10	84.7	(+)	1.7	1.4	W907S	D925Y	LRRs		
4-O04	121.7	(+)	0.7	0.7	E958K	N993K	LRRs		
2-n59	ND	(+)	0.3	0.4	L407P	G481D	NOD		
3-G11	113.0	(+)	0.2	0.5	A707V	S714C	NOD		
3-F11	123.7	(+)	6.2	5.6	A675G	K834M	NOD,LRRs		
1-23	107.5	(+)	1.0	2.2	E72K	A266V	CARD1,NOD		
1-78	238.5	(+)	0.7	1.6	**M152L**	Y165N	CARD2	*	
1-3	63.2	(+)	1.2	1.2	P213S	K305N	CARD2,NOD		
1-1L	42.6	(+)	0.7	0.6	D290E	G302C	NOD		
1-4L	52.2	(-)	0.4	0.4	S272T	Q323H	NOD		
1-51L	39.9	(+)	0.8	0.7	T284I	C354R	NOD		
1-55L	67.6	(+)	0.8	2.1	R311Q	L349F	NOD		R311W was reported in a CD patient (Lesage et al., 2002) but exhibits WT Nod2 activity.
1-69L	60.8	(+)	0.5	0.7	P285L	L288F	NOD		
2-O03	41.2	(+)	0.5	2.4	L406M	G464R	NOD		

2-O10	53.9	(+)	0.5	0.8	P486L	G534C					NOD		
2-36	54.2	(+)	0.8	0.9	G446S	H524Y					NOD		
2-n15	ND	(+)	0.8	1.9	N409K	L535M					NOD		
3-C1U	ND	(+)	0.7	0.6	Q607H	L663R					NOD		
3-C6U	78.4	(+)	0.6	0.6	L629F	G677W					NOD		
3-B06	94.1	(+)	11.0	22.9	**L690P**	**G831D**					NOD,LRR		
3-E02	75.0	(+)	0.4	0.4	R634W	**D829Y**					NOD,LRR	*	
1-71	0.2	(+)	1.0	0.7	V46A	V56I					CARD1		
1-88U	0.6	(-)	0.5	0.8	S30C	W123L					CARD1		
1-91	0.5	(+)	0.9	1.4	E69K	L246F					CARD1,NOD	*	
1-1U	0.7	(+)	0.5	0.4	V142A	C167S					CARD2		
1-76	0.7	(+)	0.8	0.9	F175I	T253V					CARD2,NOD	*	
1-O08	0.7	(-)	0.6	0.2	F161I	E324D					CARD2,NOD		
1-12	0.7	(+)	1.1	0.3	G96E	Q135P					CARDs		
1-74	0.9	(+)	1.0	1.2	C29F	A156P					CARDs		
3-A8L	126.1	(+)	ND	ND	D798E	Q809H					LRRs		
2-n10	ND	(+)	ND	ND	T526I	S566P					NOD		
1-10	336.9	(+)	1.1	21.8	G25C	H83R	Q108H				NC,CARD1		
3-E05	135.2	(+)	7.9	78.8	T646M	S658R	H669Y				NOD		
1-55U	279.4	(+)	1.7	56.3	S55N	Q108H	C219Y				NC,CARDs		
1-90	221.0	(+)	1.3	11.1	Q37L	P117H	D262N				CARD1,NOD		
1-25	97.6	(+)	1.3	21.8	L187I	G319A	L367I				CARDs,NOD		
1-11	203.1	(+)	1.0	16.4	P269A	K341R	R346W				NOD		
2-n21	ND	(+)	2.5	12.5	L434I	R468H	P528L				NOD		
3-D02	66.3	(+)	3.7	25.0	N631I	A707T	V816L				NOD,LRRs		
2-n72	ND	(+)	5.9	49.0	T405I	G504R	A525T				NOD		
3-A08	98.8	(+)	20.5	147.3	W687L	R702Q	D798E				NOD,LRR	R702W was reported to be associated to CD (Hugot et al., 2001 and Ogura et al., 2001)	
3-B07	107.1	(+)	4.5	58.6	A725T	A726T	G775D				NOD,LRR		
3-C01	43.7	(+)	8.4	57.8	Q607H	L663R	L782V				NOD,LRR		
3-A05	189.3	(+)	13.8	196.6	S618N	L767F	S773G				NOD,LRRs	*	
3-B11	83.9	(+)	4.0	44.5	Q672R	T770R	I805N				NOD,LRRs	*	
3-B05	94.5	(+)	13.6	114.9	G680R	C779Y	N872K				NOD,LRRs	*	
3-C11	106.7	(+)	1.1	19.1	S683T	A735V	L762M				NOD,LRRs	*	
3-H1	58.5	(+)	0.4	32.9	L662S	A725T	D824N				NOD,LRRs	*	
1-87	370.3	(+)	1.9	13.4	A105D	E215D	H287R				CARDs,NOD		
4-D3	103.2	(+)	3,1	30.8	Q927H	A946V	V955I				LRRs	V955I was reported in CD and UC patients (Lesage et al., 2002)	
3-G08	109.3	(+)	518.8	454.4	A616I	L769V	I836F				NOD,LRRs		
3-F01	98.0	(+)	0.4	1.2	S732N	E778K	P792R				NOD,LRRs	*; E778K was reported in a CD patient and was shown to be a loss-of-function mutation (Chamaillard et al., 2003c)	
4-D11	86.9	(+)	1.2	0.9	A922D	K989N	G1020W				LRRs		
3-E12	116.1	(+)	0.3	0.4	P668S	G738R	R790Q				NOD,LRRs	R790Q was reported in CD but exhibits WT Nod2 activity (Chamaillard et al., 2003c)	
1-27L	81.4	(+)	0.6	0.9	L276M	V328F	L336M				NOD		
1-22	0.7	(+)	1.0	4.8	V46A	A140V	R143W				CARDs	A140T was reported in CD and UC patients (Lesage et al., 2002)	
1-54U	0.6	(+)	0.4	0.8	P24Q	L199H	T228S				NC,CARD2,NOD		
1-7U	0.5	(+)	0.9	0.4	L57R	H75R	A110T				CARD1		
1-88	0.6	(-)	0.7	1.1	S30C	W123L	**F327Y**				CARD1,NOD	*	
1-50U	1.0	(+)	0.5	0.8	R138L	A196G	S234Y				CARD2,NOD	R138Q was reported in a CD patient and was shown to be a loss-of-function mutation (Chamaillard et al., 2003c)	
1-35	1.3	(+)	0.8	1.4	G52A	A110T	Y165N				CARDs		
1-58	0.4	(+)	0.9	0.9	M28I	S47P	A188V				CARDs		
1-83U	0.5	(+)	1.1	0.9	G96R	T97A	N151I				CARDs		
3-F04	107.7	(+)	ND	ND	V659M	L840M	Y882H				NOD,LRRs		
3-C06	48.4	(+)	ND	ND	L629F	G677W	A759V				NOD,LRR	*	
3-F05	101.1	(+)	ND	ND	M749I	E751G	E778Q				LRRs	*; E778K was reported in a CD patient and was shown to be a loss-of-function mutation (Chamaillard et al., 2003c)	
2-42	126.2	(+)	0.5	4.6	R393C	A428D	D512V	L553V			NOD		
1-2	63.7	(+)	1.0	15.9	A16V	L57M	L155M	R159L			NC,CARDs		
1-21	57.8	(+)	1.6	14.7	A36E	S116P	K221T	D291E			CARDs,NOD	D291N was reported in a CD patient and was shown to be a loss-of-function mutation (Chamaillard et al., 2003c)	
1-24	358.3	(+)	1.9	27.9	P117T	V208A	A264S	P371S			CARDs,NOD		
1-32	107.1	(+)	1.4	27.8	G6D	M28K	P177S	L276M			CARDs,NOD		
3-H4U	89.3	(+)	4.2	73.6	A619V	C648G	Q664K	R716H			NOD		
1-96	ND	(+)	4.5	41.1	G96C	L214M	T284S	M339K			CARDs,NOD	*; Loss of NF-kB activation in overexpression studies was confirmed at least in four experiments	
4-B6	80.4	(+)	1.2	7.1	V942M	L967P	R968P	E1001K			LRRs		
2-n58	ND	(+)	1.0	1.5	E383D	R393P	L415V	C561S			NOD		
1-51	86.3	(+)	1.0	1.3	G25S	V208F	T284I	C354R			NC,CARD2,NOD		
1-39	217.4	(+)	0.9	1.5	Q37H	M152I	L226R	R346W			CARDs,NOD		
1-83L	31.1	(+)	0.6	0.5	A266D	T275S	S306N	R346W			NOD		
2-4	26.1	(+)	0.5	1.5	L410H	S431L	R439C	I517V			NOD	S431L was reported in a CD patient but exhibits WT activity of Nod2 (Chamaillard et al., 2003c)	
1-66U	1.3	(+)	0.4	0.6	R15T	S47T	W93C	R138W			NC,CARDs	*; R138Q was reported in a CD patient and was shown to be a loss-of-function mutation (Chamaillard et al., 2003c)	
1-7	0.3	(+)	0.9	0.6	L57R	H75R	A110T	A261P			CARD1,NOD	*	
1-1	0.3	(+)	1.0	1.2	V142A	C167S	D290E	G302C			CARD2,NOD	*	
1-50	0.5	(+)	1.2	0.9	R138L	A196G	S234Y	C353Y			CARD2,NOD	*; R138Q was reported in a CD patient and was shown to be a loss-of-function mutation (Chamaillard et al., 2003c)	
1-60U	1.3	(+)	0.5	1.5	E43D	R86S	I174V	A188P			CARDs		
1-13	0.6	(-)	1.0	1.5	L84M	L88I	I174N	Q323H			CARDs,NOD		
1-69	1.5	(+)	0.9	1.0	G48E	A131V	P285L	L288F			CARDs,NOD		
1-34U	1.9	(+)	0.6	0.9	C29Y	G78C	R138W	R235H			CARDs,NOD	R138Q and R235C were reported in a CD patient and was shown to be a loss-of-function mutation (Chamaillard et al., 2003c	
3-F10	89.0	(+)	ND	ND	A660G	A726V	V774L	S828L			NOD,LRRs		
2-n79	ND	(+)	ND	ND	R393C	R468H	G481S	L570I					
1-14	40.5	(+)	1.5	11.7	L20F	P213H	V230L	C247Y	H313L		CARDs,NOD		
3-A06	70.7	(+)	5.4	94.6	L602I	T646M	Q704R	K757M	A783T		NOD,LRRs		
3-A09	109.0	(+)	4.0	52.4	V807L	L822S	L835F	N852K	A868V		LRRs		
2-n56	ND	(+)	0.7	1.0	S425T	R439H	E475A	F584I	G590D		NOD		
1-47U	56.7	(+)	0.7	0.3	R15K	A112S	Q135H	E169G	A197V		NC,CARDs		
1-55	40.3	(+)	0.5	0.8	S55N	Q108H	C219Y	R311Q	L349F		CARDs,NOD	*; R311W was reported in a CD patient but exhibits WT Nod2 activity (Chamaillard et al., 2003c).	
2-10	33.9	(+)	1.1	1.0	F384V	Q412E	T510N	H549Y	L570F		NOD		
1-60	0.7	(+)	0.9	1.0	E43D	R86S	I174V	A188P	**V295E**		CARDs,NOD		
1-66	0.5	(+)	0.8	1.4	R15T	S47T	W93C	R138W	A268T		NC,CARDs,NOD	R138Q was reported in a CD patient and was shown to be a loss-of-function mutation (Chamaillard et al., 2003c)	
1-54	0.4	(+)	0.8	0.7	P24Q	L199H	T228S	L288I	V328I		NC,CARD2,NOD		
3-H4	123.9	(+)	ND	ND	A619V	C648G	Q664K	R716H	**C779Y**		NOD,LRRs		
3-F08	108.8	(+)	ND	ND	E752D	R753W	R791L	N853S	D857Y		NOD,LRRs	R791Q and N853S were reported in a CD patient respectively (Lesage et al., 2002)	
1-67	25.0	(+)	0.9	3.4	H75Q	S127W	Q164R	V263M	L288F	T347I	CARDs,NOD		
1-4U	0.8	(+)	0.5	0.5	P24R	M28I	A107T	A112V	I141A	P177A	NC,CARDs		
1-47	0.6	(+)	0.9	0.9	R15K	A112S	Q135H	E169G	A197V	V256I	N289Y C,CARDs,NOD	N289S was reported in a CD patient and was shown to be a loss-of-function mutation (Chamaillard et al., 2003c)	
Truncation mutants													
1-37	5.0	(+)	1.5	31.7	E3stop	T228S	L309M				NC,NOD		
1-68	0.5	(-)	0.9	1.4	E13K	C29stop					CARD1		
1-29	1.0	(-)	1.5	1.6	A16T	F34delT					CARD1		
1-56	1.6	(-)	0.7	1.0	G25D	F34delT					CARD1		
1-38	1.2	(-)	1.1	0.9	**V56delT**						CARD1		
1-49	1.0	(-)	0.9	1.0	**E72stop**						CARD1		
1-53	1.1	(-)	0.9	1.2	**W98stop**						CARD1		
1-O03	0.7	(-)	0.5	0.3	L88I	Q108stop					CARD1		
1-94	0.8	(-)	1.2	1.1	**Q135stop**						CARD2		
1-46	0.6	(-)	0.7	0.5	**L172delT**						CARD2		
1-36	1.5	(-)	1.0	1.5	H146N	Q179stop					CARD2		

	1-81	0.8	(-)	0.8	0.8	A140V	Q201stop				CARD2	A140T was reported in CD and UC patients (Lesage et al., 2002)
	1-18	3.1	(-)	1.1	1.0	**A106V**	A217G	W260stop			NOD	
	1-34	0.8	(-)	1.1	1.5	C29Y	G78C	R138W	R235H	Q335stop	NOD	R138Q and R235C were reported in a CD patient and was shown to be a loss-of-function mutation (Chamaillard et al., 2003c
	1-34L	115.9	(-)	0.6	0.5	**Q335stop**					NOD	
	1-93L	96.5	(-)	1.3	0.6	D262N	C354stop				NOD	
	1-93	164.7	(+)	0.9	2.4	P177S	D262N	C354stop			NOD	*
	1-43L	76.3	(-)	0.6	0.7	G299R	Q365stop				NOD	
	1-43	45.2	(-)	0.6	0.6	Q79L	V208I	G299R	Q365stop		NOD	*
	2-31	130.1	(+)	1.5	1.2	**L376delT**					NOD	
	1-8	181.8	(+)	1.2	0.8	S136I	P285L	P342S	T377delA		NOD	*
	1-8U	99.0	(+)	0.4	0.9	P285L	P342S	T377delA			NOD	
	2-n48	ND	(+)	0.4	0.7	G413S	P427delT				NOD	
	2-22	91.3	(+)	0.9	2.0	**G505delG**					NOD	
	2-25	103.3	(+)	0.8	1.3	C483Y	G505delG				NOD	
	2-n80	ND	(+)	ND	ND	H394N	P397T	A419G	L485V	S506delC	NOD	
	2-51	139.3	(+)	ND	ND	**Y514stop**					NOD	
	2-n17	ND	(+)	0.7	1.6	T401S	M513I	T526delC			NOD	
	2-n9	ND	(+)	ND	ND	S396F	T526insC	C561S			NOD	
	2-n81	ND	(+)	ND	ND	R459C	T526delC	A572P			NOD	
	2-n86	ND	(+)	ND	ND	H460N	T526delC				NOD	
	2-n65	ND	(+)	1.1	1.2	T526del	Q568L				NOD	
	2-n62	ND	(+)	0.9	1.3	T526del	L585M				NOD	
	2-26	35.4	(+)	1.0	1.3	**P527delC**					NOD	
	2-n37	ND	(+)	2.0	2.7	R420L	P528delC				NOD	
	2-n29	ND	(+)	1.2	0.9	G451A	G534delG				NOD	
	2-n71	ND	(+)	0.7	1.4	**Q568stop**					NOD	
	2-1	126.1	(+)	0.9	0.9	**583insA**					NOD	
	3-G05	160.3	(+)	233.6	224.1	**Q664stop**					NOD	
	3-O01	106.1	(+)	ND	ND	**W687stop**					NOD	
	3-F07	67.4	(+)	80.2	140.4	**W709stop**					NOD	
	3-F03	65.0	(+)	11.6	24.5	**W741stop**					LRR1	
	3-O09	116.1	(+)	42.1	55.8	**K768stop**					LRR2	
	3-D05	97.1	(+)	31.7	45.4	**L795insC**					LRR3	
	3-G04	92.3	(+)	93.4	81.9	**Y821stop**					LRR4	
	3-G10	106.1	(+)	283.4	295.5	**K854delA**					LRR5	
	3-D3L	147.3	(+)	3.7	4.1	**L855stop**					LRR5	
	3-D03	68.8	(+)	ND	ND	**P639S**	L855stop				LRR5	
	4-C10	93.7	(+)	1.2	1.4	**W907stop**					LRR7	
	4-B9	101.1	(+)	2.9	4.3	G894E	E921K	W931stop			LRR8	
	4-D4	80.6	(+)	1.2	1.2	**E964stop**					LRR9	
	4-D10	106.3	(+)	1.0	1.1	**E958stop**					LRR9	
	4-F9	86.9	(+)	0.9	0.9	**K953stop**					LRR9	
	4-C4	67.1	(+)	1.4	2.0	**N965delA**					LRR9	
	4-H2	111.6	(+)	0.8	0.9	L901V	C973stop				LRR9	
	4-C1	67.5	(+)	0.6	0.7	**G978delG**					LRR9	
	4-F10	104.2	(+)	0.6	0.7	**I987delA**					LRR10	
	4-G9	118.9	(+)	2.1	1.2	**I987insA**					LRR10	
	4-D6	92.6	(+)	0.9	0.8	V890M	A922T	E963Q	E1001stop		LRR10	
Controls	positive		(+)	4.0	55.0							
	negative	0.0	(-)	1.8	1.3							

Abbreviations and colour code

WB	Western Blot
*	Derived mutant clone from our present mutagenesis analysis
D.N.	Dominant negative mutant
NC	Region N-terminal to CARDs
(-)	No protein was detected by Western Blot analysis using anti-Nod2 polyclonal antibody (epitope located between amino acids 354 and 376)
(+)	Protein was detected by Western Blot analysis using anti-Nod2 polyclonal antibody
BS	Blau syndrome
CD	Crohn's Disease
ND	Not determined
*	NF-kB activation results represent mean of normalised values from triplicate cultures as described in methods

coloured high lights

	ability to respond to synthetic MDP is retained
	ability to respond to MDP is lost or partially lost (less than 25% of the wild-type response) but mutant can activate NF-kB in overexpression studies
	ability to activate NF-kB in overexpression condition is lost
	constitutive NF-kB activation

coloured letters

blue	deletional, insertional or nonsense mutation
orange	also found in mutants with ability to respond to MDP
bold	also found in mutants with a single amino acid substitution