Table 2 Ninety-six RET missense mutations identified from the literature and their corresponding clinical presentations

Mutation	Kind of amino acid change*	Exon	Domain†	Length of aganglionosis‡	Reference
P20L	NNP-NNP	1	SP	S	1
S32L	NP-NNP	2	CLD1	L/S‡	2, 3, 4
L40P	NNP-NNP	2	CLD1	L	5
L56M	NNP-NNP	2	CLD1	S	6
R57W	B-NNP	2	CLD1	S	7
P64L	NNP-NNP	2	CLD1	S‡	2, 3
R77C	B-NNP	2	CLD1	L‡	4, 8
G93S	NNP-NP	2	CLD1	S, TCA	1, 9
Y96C	NNP-NNP	2	CLD1	L	10
E136X	A-stop	3	CLD1	L	2
C142S	NNP-NP	3	CLD1	S	2
V145G	NNP-NNP	3	CLD1	TCA	11
C157W	NNP-NNP	3	CLD1-CLD2		7
C157Y	NNP-NNP	3	CLD1-CLD2	S	6
F174S	NNP-NP	3	CLD2	S	12
R180P	B-NNP	3	CLD2	L	13
R180Q	B-NP	3	CLD2	S	6
R180X	B-stop	3	CLD2	L	3
C197Y	NNP-NNP	4	CLD2	L	12
V202M	NNP-NNP	4	CLD2	S	14
R231H	B-B	4	CLD2	L/S	2, 9
E235K	A-B	4	CLD2	S	6
E251K	A-B	4	CLD2	L/S	2, 9
V262A	NNP-NNP	4	CLD2	L	10
D267N	A-NP	4	CLD2	L	10
R287Q	B-NP	4	CLD3	L	2
E289Q	A-NP	4	CLD3	S	9
R313Q	B-NP	5	CLD3	TCA+	13
W324C	NNP-NNP	5	CLD3	S	10
R330Q	B-NP	5	CLD3	L	1, 2, 3
R330W	B-NNP	5	CLD3	L/S	6
V331M	NNP-NNP	5	CLD3	S	15
T338I	NP-NNP	5	CLD3	L	10
R360W	B-NNP	6	CLD3	L	4
N361K	NP-B	6	CLD3	S	6
S365X	NP-stop	6	CLD3	L	5
F393L	NNP-NNP	6	CLD3-CLD4	L	2
N394K	NP-B	6	CLD3-CLD4	L	4
P399L	NNP-NNP	6	CLD3-CLD4	S	5
D469N	A-NP	7	CLD4	TCA+	16
R475Q	B-NP	7	CLD4	L	2
R475W	B-NNP	7	CLD4	S	10
E480K	A-B	7	CLD4	S	14
Y483X	NNP-stop	7	CLD4	S	11
C541X	NNP-stop	8	CYS	S	5
C570W	NNP-NNP	9	CYS	S	9
Q576P	NP-NNP	9	CYS	S	6
D584G	A-NNP	9	CYS	S	17
G588D	NNP-A	10	CYS	TCA+	16
C609W	NNP-NNP	10	CYS	S, MEN2A, FMTC	7
C609Y	NNP-NNP	10	CYS	S, MEN2A	1,6 ,9, 18
C609R	NNP-B	10	CYS	L, MEN2A, FMTC	8
C609S	NNP-NP	10	CYS	S, MEN2A	10
C611F	NNP-NNP	10	CYS	MEN2A, FMTC	7
C618R	NNP-B	10	CYS	MEN2A, FMTC	7
C618S	NNP-NP	10	CYS	L, S, MEN2A	18
C620R	NNP-B	10	CYS	S, MEN2A, FMTC	6, 13, 19
C620S	NNP-NP	10	CYS	MEN2A, FMTC	7
C620W	NNP-NNP	10	CYS	S, MEN2A	18
Q626K	NP-B	10	CYS		7
C634R	NNP-B	11	CYS	MEN2A	7
C634T	NNP-NP	11	CYS	MEN2A	7
C634G	NNP-NNP	11	CYS	MEN2A	7
A654T	NNP-NP	11	TM	L	17
S690P	NP-NNP	11	btw TM and TK	L	2
G691S	NNP-NP	11	btw TM and TK		20
R694Q	B-NP	11	btw TM and TK	S	11
T706A	NP-NNP	12	btw TM and TK	L	17
T729A	NP-NNP	12	btw TM and TK		7
E734K	A-B	12	btw TM and TK	TCA+	16
E762Q	A-NP	13	TK	L	5
S765F	NP-NNP	13	TK	L	7
S765P	NP-NNP	13	TK	L	21
S767R	NP-B	13	TK	L	2
E768D	A-A	13	TK	FMTC	22
D771N	A-NP	13	TK	TCA	14
K780X	B-stop	13	TK	L	10
L790F	NNP-NNP	13	TK		7
Y791F	NNP-NNP	13	TK	S	10, 13, 15
S795R	NP-B	13	TK	S	15
V804L	NNP-NNP	14	TK	FMTC	23
V804M	NNP-NNP	14	TK		7

R813Q	B-NP	14	TK		7
R873Q	B-NP	15	TK	L	2, 10
A884F	NNP-NNP	15	TK		7
F893L	NNP-NNP	15	TK	L	2
G894S	NNP-NP	15	TK	L	10
R897Q	B-NP	15	TK	L	10, 16, 21
K907E	B-A	15	TK	L/S	2, 6
R912Q	B-NP	16	TK	S	10
M918T	NNP-NP	16	TK		7
E921X	A-stop	16	TK	L	2, 6, 7
E921K	A-B	16	TK		7
W942X	NNP-stop	17	TK	S	2
W942C	NNP-NNP	17	TK	TCA+	16
F961L	NNP-NNP	17	TK	S	11
R969W	B-NNP	17	TK	TCA+	16
R972G	B-NNP	17	TK	L	21
P973L	NNP-NNP	17	TK	L	5, 14
M980T	NNP-NP	17	TK	S	2
R982C	B-NNP	18	TK	S	15, 19
P1039L	NNP-NNP	19	after TK		7
L1061P	NNP-NNP	19	after TK	L/S/TCA	6
M1064T	NNP-NP	20	after TK	S	2

In the text, L-HSCR (HSCR, Hirschsprung Disease) patients include those with TCA. Where both L-HSCR and S-HSCR were found to be associated with a particular mutation all presentations are listed. If one presentation predominated by greater than 2:1, the more frequent presentation is listed. These clasifications were used for all calculations in the text.

*amino acid key: NNP, neutral non-polar; NP, neutral polar; A, acidic; B, basic
†Domain key: SP, signal peptide; CLD, cadherin-like domain; CYS, cysteine-rich domain; TM, transmembrane domain; TK, tyrosine kinase domain.
‡Length of Aganglionosis key: S, short segment HSCR; L, long segment HSCR; TCA, total colonic aganglionosis; TCA+, TCA and small intestine and stomach aganglionosis; MEN2A, Multiple endocrine neoplasia type 2A; CCHS, Central congenital hyperventilation syndrome; ‡, Severe constipation observed.

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