

Supplementary Table 1 Studies using immunohistochemical methods for diagnosis of Intestinal neuronal dysplasia type B

IHQ marker	Ref.	Number of patients with IND-B	Method for IHC analysis	Histopathological findings of immunoexpression in patients with IND-B	Main conclusions
Bcl-2	Wang et al. (2016) [74]	37	Expression in ganglion cells, comparing number of cells and areas of nerve plexuses in IND-B, HD and controls.	<ul style="list-style-type: none"> - Positive expression in immature ganglion cells. - Area of myenteric plexuses significantly larger in IND-B than in control group. - Ganglion cell number significantly higher in IND-B than in control group. - Ganglion cell size smaller in IND-B. 	The method can be used with calretinin and RET as a valuable tool in the differential diagnosis between IND-B and HD.
Calretinin	Wang et al. (2016) [74]	37	Expression in nerve plexuses and muscle layers.	Positive expression in mature ganglion cells and nerve fibers in myenteric plexuses in IND-B and absence of expression in aganglionic segment in HD.	The method can be used with RET e Bcl-2 as a valuable tool in the differential diagnosis between IND-B and HD.

	Terra et al. (2017) ^[51]	29	Expression in ganglion cells and nerve fibers and number of neurons.	Positive expression in neurons of the submucosa nerve plexuses, intrinsic nerve fibers, and ectopic neurons in the mucosa. Identification of fewer neurons than H&E in quantitative analysis.	It can help in the diagnosis of IND-B, but it is not as useful as for the diagnosis of HD.
c-kit	Geramizadeh et al. (2013) ^[80]	29	Number of Cajal interstitial cells in muscle layers and myenteric plexuses in HD and controls.	Positive expression in Cajal cells in muscle layers with significantly higher numbers in IND-B compared to HD, but without significant difference with control group.	It can assist in differentiating between IND-B and HD.
	Kim et al. (2010) ^[81]	13	Number of Cajal interstitial cells in muscle layers and myenteric plexuses in IND-B and other causes of intestinal pseudo-obstruction.	Positive expression in Cajal cells in muscle layers and myenteric nerve plexuses, with no significant differences between the number of Cajal cells in IND-B and other causes of intestinal pseudo-obstruction.	No difference between IND-B and other causes of intestinal pseudo-obstruction.
	Yamataka et al. (1997) ^[82]	3	Expression in myenteric plexuses and muscle layers in IND-B and controls.	Reduction of expression in muscle layers, but not in myenteric plexuses in IND-B.	Abnormal synapse in muscle layers in IND-B.

GAP43	Kobayashi et al. (1996) [83]	14 (4 isolated IND-B and 10 IND-B associated with HD)	Expression in nerve and nerve plexuses in IND-B and controls.	- Absence of expression in muscularis mucosae and/or in the circular muscular and/or longitudinal muscular. - Positive expression in nerve plexuses.	Changes in neuromuscular junctions in IND-B.
Hu C/D	Swaminathan et al. (2015) [50]	64 IND-B associated with HD	Number of ganglion cell nuclei in submucosal plexuses.	Significant differences in the number of ganglion cells per ganglion between colonic segments with hyperplasia compared to the control group.	Validation of a quantitative histopathological criterion for the diagnosis of giant ganglia, defined by the presence of at least 7 ganglion cells.
Mast cells	Kobayashi et al. (1999) [84]	5 IND-B associated with HD	Number of mast cells in IND-B, aganglionic and ganglionic segments (HD) and controls.	A higher number of mast cells in IND-B and aganglionic segments, compared to ganglionic segments and control group.	Mast cells may be involved in the pathogenesis of HD and IND-B.
NCAM (CD56)	Geramizadeh et al. (2013)[80]	29	Number of neurons in muscle layers in IND-B, HD and controls.	Positive expression in neurons of the muscular layers, higher number of neurons in IND-B, compared to HD, but without significant differences with control group.	It can assist in differentiating between IND-B and HD.

	Kim et al. (2010) [81]	13	Expression and distribution of nerve fibers in muscle layers, lamina propria, and muscularis mucosa in IND-B and other causes of intestinal pseudo-obstruction.	Positive expression in nerve fibers in muscle layers and mucosa, reduced expression in nerve fibers in external longitudinal muscle layer in IND-B, compared to other causes of intestinal pseudo-obstruction.	Abnormalities in neuromuscular junctions in IND-B.
	Kobayashi et al. (1996) [83]	14 (4 isolated IND-B and 10 IND-B associated with HD)	Expression in nerve fibers and nerve plexuses in IND-B and controls.	- Absence of expression in muscularis mucosae and/or in circular muscular and/or in longitudinal muscular. - Positive expression in nerve plexuses.	Changes in neuromuscular junctions in IND-B.
	Nogueira et al. (2011) [85]	11 (2 isolated IND-B, 8 IND-B associated with HD and 1 IND-B associated with hypoganglionosis)	Expression in nerve trunks in IND-B, HD and controls.	Increased expression in nerve trunks in IND-B.	IND-B cannot be attributed to changes the neuromuscular junction.
NGF	Kobayashi et al. (1999) [84]	5 IND-B associated with HD	Expression of mast cells in IND-B, aganglionic and ganglionic segments (HD) and controls.	Expression of mast cells close to ganglia in IND-B and close to hypertrophied nerve trunks in HD.	Mast cells may be involved in the pathogenesis of HD and IND-B.

NO synthase	Bosmann et al. (2001) ^[86]	17	Expression in ganglion cells in IND-B and controls.	Increase in the number of NO synthase positive ganglion cells, compared to the control group.	Increase in local NO production in IND-B.
NSE	Kim et al. (2010) ^[81]	13	Expression and distribution of nerve fibers in muscle layers, lamina propria, and muscularis mucosa in IND-B and other causes of intestinal pseudo-obstruction.	Positive expression in nerve fibers in the muscle layers and mucosa, without significant differences compared other causes of intestinal pseudo-obstruction.	Difference in NSE expression between IND-B and other causes of intestinal pseudo-obstruction.
Peripherin	Bosmann et al. (2001) ^[86]	17	Number of ganglion cells.	Increase in number of NO synthase positive ganglion cells compared to control group.	Increase in local NO production in IND-B.
	Szabolcs et al. (1996) ^[87]	3 IND-B associated with HD	Density of ganglion cells in submucosal and myenteric nerve plexuses.	Markedly high ganglion cell density in IND-B associated with HD compared to HD and control group.	Can be useful in the diagnosis of different forms of malformations of the enteric nervous system.

PGP9.5	Geramizadeh et al. (2013) ^[80]	29	Number of neurons in inner and outer muscle layers in IND-B, HD and controls.	Positive expression in neurons of the inner intestinal muscle layer, with a significantly higher number of neurons in patients with IND-B, compared to HD, but without significant differences when compared to the control group.	It can assist in differentiating between IND-B and HD.
	Kramer et al. (1994) ^[88]	1	Specific marker of nervous system.	Positive expression in enlarged nerve trunks, hyperplastic nerve ganglia, and heterotopic nerve cells.	IND-B can be diagnosed using this immunohistochemical method.
PTEN	O'Donnell & Puri (2011) ^[89]	10	Expression in myenteric and submucosal plexuses in IND-B, HD and controls.	Significantly reduced expression in submucosal and myenteric nerve plexuses.	IND-B may be related to lower PTEN expression.
RET	Bosmann et al. (2001) ^[86]	17	Number of ganglion cells.	RET-IHQ showed only a few ganglion cells.	Not useful in the diagnosis of IND-B.

	Wang et al. (2016) [74]	37	Expression in ganglion cells, number of cells and areas of nerve plexuses in IND-B, HD, and controls.	<ul style="list-style-type: none"> - Expression present in mature and immature ganglion cells. - Area of myenteric plexuses significantly larger in IND-B than in control group. - Ganglion cell number in the myenteric plexus significantly higher in IND-B than in control group. - Identification of ectopic myenteric plexuses in IND-B. 	Can be used together with calretinin and Bcl-2 in the differential diagnosis between IND-B and HD.
S100	Bosmann et al. (2001) [86]	17	Number of ganglion cells	S100 IHQ showed only a few ganglion cells.	Not useful in the diagnosis of IND-B.
	Geramizadeh et al. (2013) [80]	29	Number of neurons in muscle layers and myenteric plexuses, in IND-B, HD and controls	Expression in neurons of the muscle layers and myenteric nerve plexuses, with a significantly higher number of neurons in IND-B, compared to HD, but without significant differences with control group	It can assist in the differential diagnosis between IND-B and HD.

	Kim et al. (2010) [81]	13	Expression and distribution of nerve fibers in muscle layers, lamina propria and muscularis mucosa in IND-B and other causes of intestinal pseudo-obstruction.	Expression in nerve fibers in the muscular layers and mucosa, without significant differences between IND-B and other causes of intestinal pseudo-obstruction.	Not useful in the differential diagnosis between IND-B and other causes of intestinal pseudo-obstruction.
Synaptophysin	Bosmann et al. (2001) [86]	17	Number of ganglion cells	Synaptophysin showed only a few ganglion cells.	Not useful in the diagnosis of IND-B.
	Geramizadeh et al. (2013) [80]	29	Number of neurons in muscle layers and myenteric plexuses, in IND-B, HD and controls	Expression in neurons of the muscle layers and myenteric nerve plexuses, with a significantly higher number of neurons in IND-B, compared to HD, but without significant differences with control group.	It can assist in the differential between IND-B and HD.
	Kobayashi et al. (1996) [83]	14 (4 isolated IND-B and 10 IND-B associated with HD)	Expression in synaptic vesicles in the plexuses and nerve fibers in IND-B and controls	- Absence of expression in the muscularis mucosa and/or muscularis propria - Positive expression in nerve plexuses.	Change in neuromuscular junctions in IND-B

	Kobayashi et al. (1997) ^[90]	5 (3 isolated IND-B and 2 IND-B associated with HD)	Expression in synaptic vesicles in plexuses and nerve fibers in IND-B and HD	Strong expression in myenteric ganglion and reduction in muscle layers.	The method is applicable in intraoperative evaluation to assess the distribution of synapses in myenteric plexuses and intestinal muscle layers.
	Nogueira et al. (2011) ^[85]	11 (2 isolated IND-B, 8 IND-B associated with HD and 1 IND-B associated with hypoganglionosis)	Expression in nerve trunks in IND-B, HD and controls	Increased expression in nerve trunks in IND-B, irregularly distributed in the mucosa, muscularis mucosa, and muscularis propria.	IND-B cannot be attributed to changes in the neuromuscular junction
	Yamataka et al. (1997) ^[82]	3	Expression in myenteric plexuses and muscle layers.	Reduced expression in the muscle layers, but not in the myenteric plexuses in IND-B	In association with decreased expression of c-kit, it can demonstrate the role of Cajal cells in the pathophysiology of IND-B.
SMA (1a4)	Kim et al. (2010) ^[81]	13	Expression and distribution in muscularis mucosa and muscle layers in IND-B and other causes of intestinal pseudo-obstruction.	Expression in muscle fibers from muscular layers and muscularis mucosa, without differences between IND-B and other causes of intestinal pseudo-obstruction.	No differences between IND-B and other causes of intestinal pseudo-obstruction.

	Rolle et al. (2003) ^[91]	16 isolated IND-B and 11 IND-B associated with HD	Expression in submucosa vasculature of IND-B and controls.	Increased filaments around the submucosa vessels compared to control group.	Abnormal vasculature may aid in the diagnosis of IND-B.
Sox10	Liu et al. (2019) ^[60]	32	Number of Sox10 + glial cells and nerve cells of plexuses in IND-B, HD and controls.	High proliferation of glial cells and nerve cells in nerve plexuses in IND-B.	A negative correlation between Sox10 IHC expression and blood Sox10 methylation, which may be related to IND-B etiopathogenesis.