SUPPLEMENTARY INFORMATION

TITLE: Overexpression of DNMT3b target genes during Enteric Nervous System development contribute to the onset of Hirschsprung disease.

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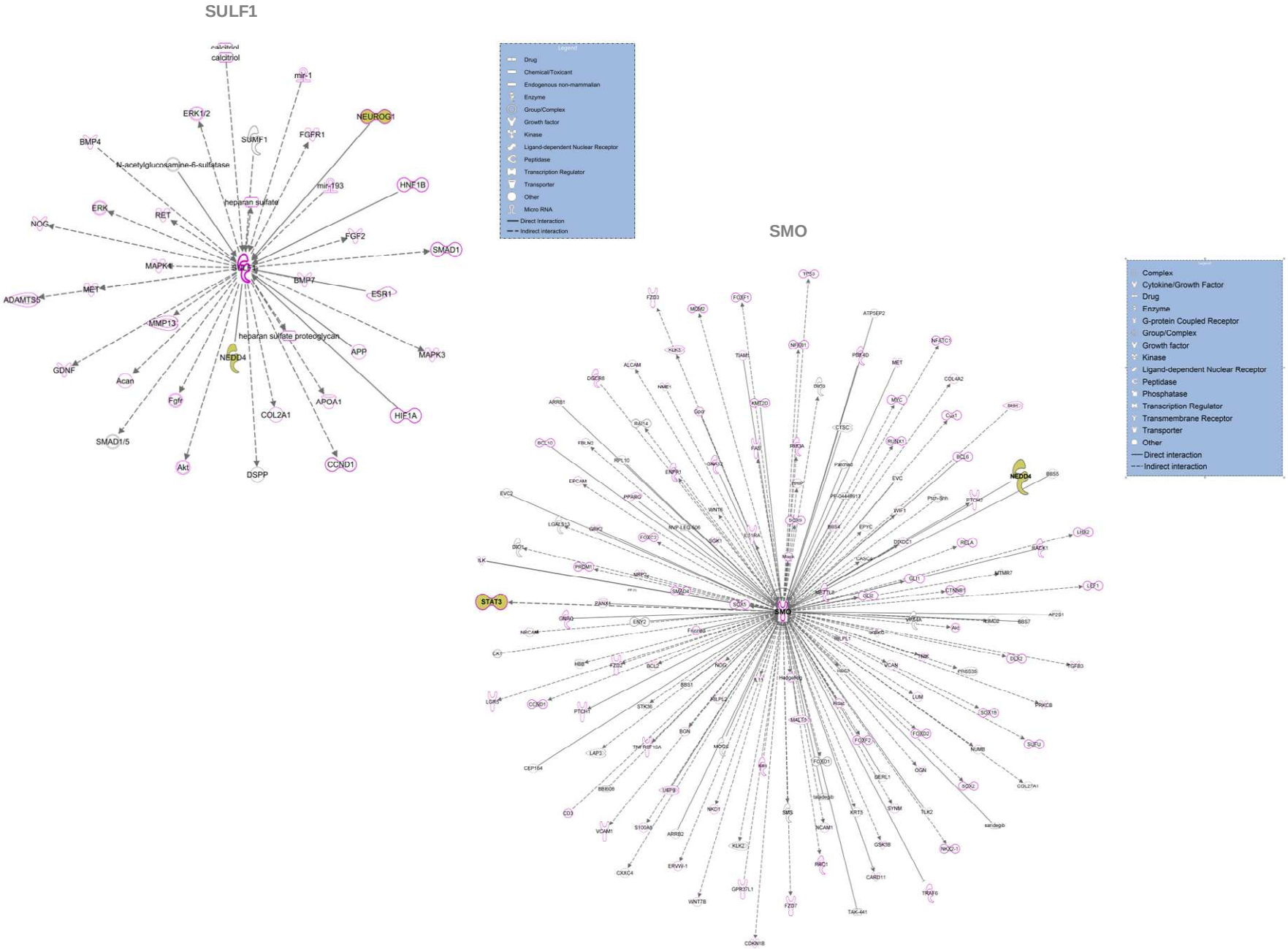
Table S1: Genes expressed in human enteric precursor cells.

Gene	Ct	Function
MYDGF	26	It is associated with several biological processes such as angiogenesis stimulating endothelial cell proliferation.
CDK5RAP2	30	It is essential for a correct mitotic cell cycle.
DRG1	29	It has a potential role in proliferation and/or cell differentiation during development of nervous system.
EED	32	It is major component of Polycomb repressive complex 2, this is a epigenetic regulator that methylates histone H3 at lysine 27, controling neural crest gene expression during neural crest development
KPNA1	31	It plays a key role in the nuclear transport of signal transducer and activator of transcription 3 (STAT3) and STAT1 transcription factors.
LITAF	27	Its main functions are inflammatory response and apoptosis.
RAB10	30	It is implicated in vesicle trafficking. These events mediated vesicle trafficking by Rab10, are essential for axon development which is essential for proper neurons morphogenesis and thus for correct neuronal migration, and for dendrite growth and morphogenesis which is necessary for connectivity between neurons and to capture information from the environment.
STAT3	30	It mediates the expression of a variety of genes in response to cell stimuli, and thus plays a key role in many cellular processes such as cell growth and apoptosis.
SULF1	32	It controls the neuronal and glial generation during ventral neural tube development. Also it is essential for normal migration of neural crest cells.
BBX	28	It has been associated with maintaining neural stem cells, neural crest cells development and progenitor cell selfrenewal.
PPP2R2B	31	It is widely expressed in embryonic mouse brain. At the cellular level it is limited to neurons and it plays a role in neuronal cell during brain development
RNA45s5	29	It is a non coding RNA which serves as the precursor for the 18S, 5.8S and 28S

Figure S1


SULF1
calcitriol
mir-1
ERK1/2
NEUROG1
BMP4
SUMF1
FGFR1
N-acetylglucosamine-6-sulfatase
mir-193
HNF1B
heparan sulfate
ERK
RET
NOG
FGF2
SMAD1
MAPK1
SULF1
BMP7
ESR1
MET
ADAMTS5
MMP13
heparan sulfate proteoglycan
APP
MAPK3
NEDD4
GDNF
Acan
APOA1
Fgf8
COL2A1
HIF1A
SMAD1/5
CCND1
Akt
DSPP
Drug
Chemical/Toxicant
Endogenous non-mammalian
Enzyme
Group/Complex
Growth factor
Kinase
Ligand-dependent Nuclear Receptor
Peptidase
Transcription Regulator
Transporter
Other
Micro RNA
Direct Interaction
Indirect interaction
SMO
SMO
STAT3
NEDD4
Complex
Cytokine/Growth Factor
Drug
Enzyme
G-protein Coupled Receptor
Group/Complex
Growth factor
Kinase
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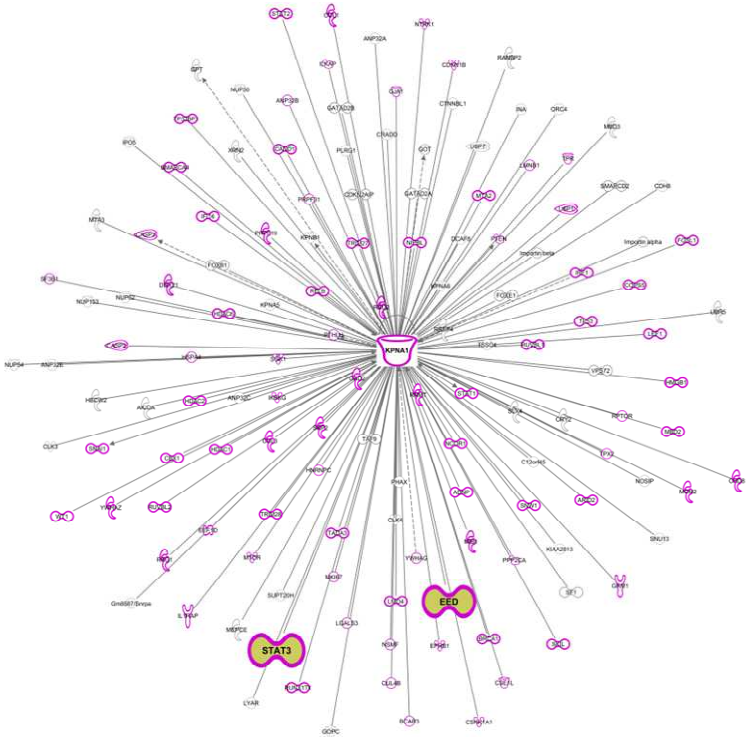
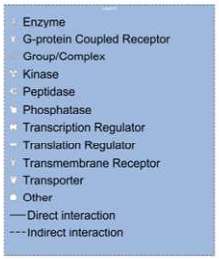
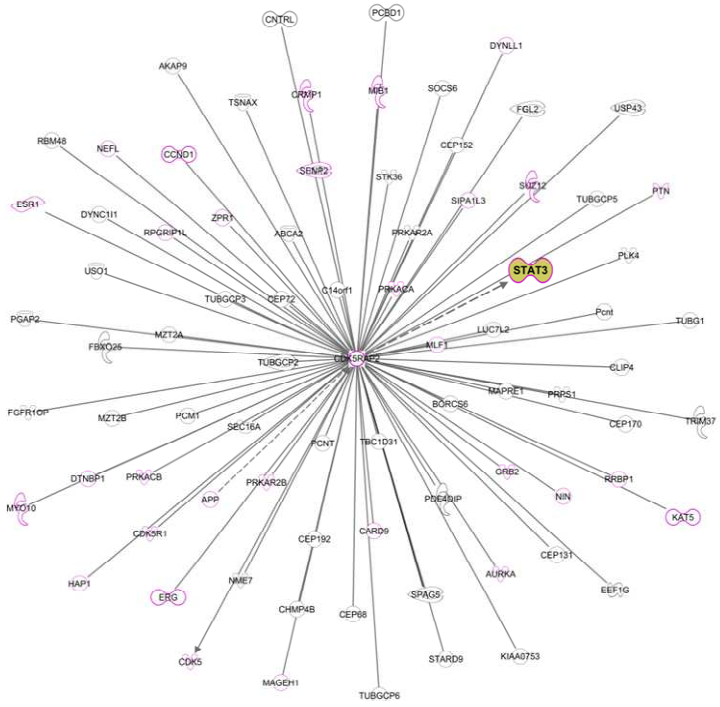
Peptidase
Phosphatase
Transcription Regulator
Transmembrane Receptor
Transporter
Other
Direct interaction
Indirect interaction

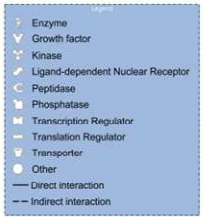
KPNA1



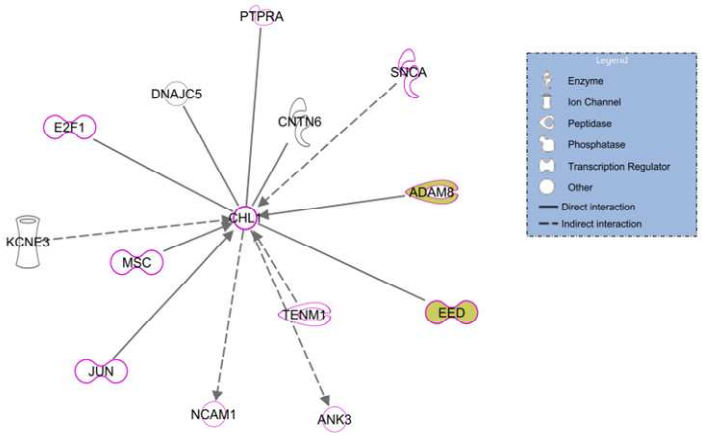


CDK5RAP2

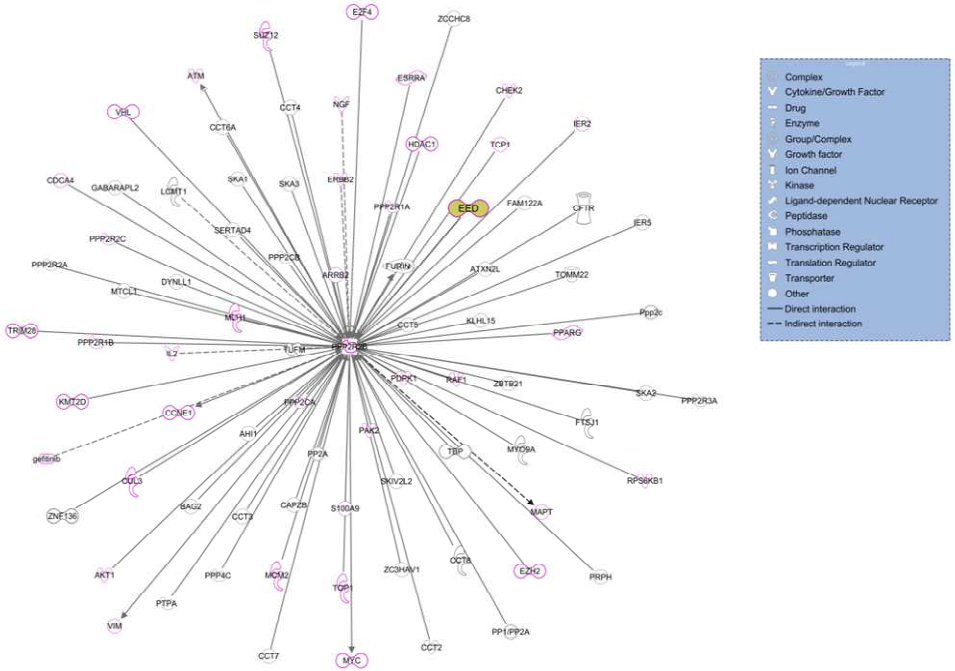




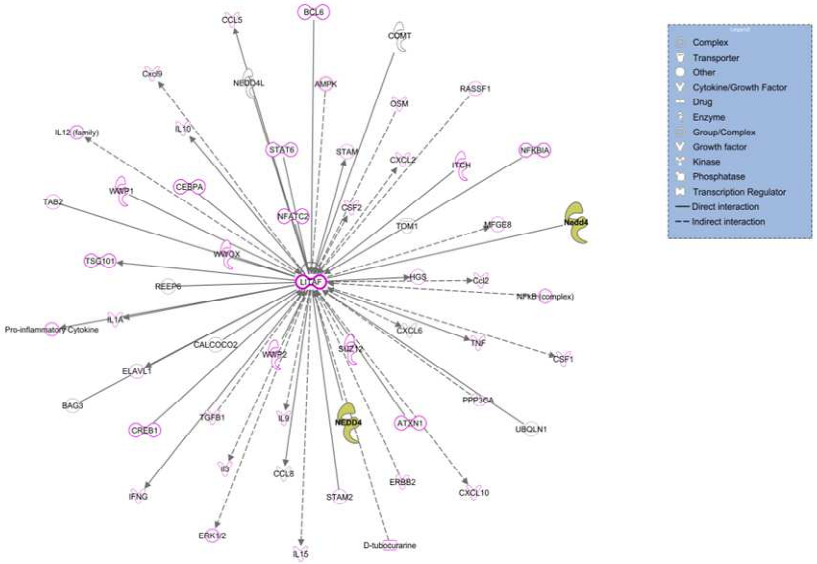
CHL1



PPP2R2B



LITAF



BBX

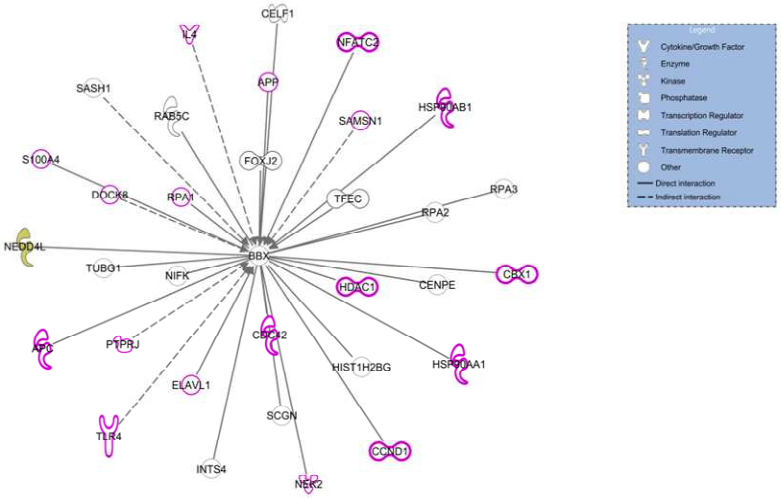


Figure S1: Gene interaction of DNMT3b target genes. Images obtained by the IPA tool. Relationships shown by straight lines represent; chemical-chemical interactions, chemical-protein interactions, correlation, protein-protein interactions and RNA-RNA interactions: non targeting interactions. Relationships shown by arrows represent; activation, causation, expression, localization, membership, modification, molecular cleavage, phosphorylation, protein-DNA interactions, protein-RNA interactions, regulation of binding and transcription, and the direction of the effect caused. The genes highlighted by IPA with category "cellular development" are labeled in pink and the genes selected by us are labeled in yellow.