

## Description of Additional Supplementary Files

File Name: Supplementary Data 1

Description: CD TWAS association results for 44 imputable genes from the established IBD risk locus 2p23.3 including DNMT3A (extended region chr2:24,999kb-27,900kb to capture long range cis eQTL effects). UC TWAS association results for 44 imputable genes from the established IBD risk locus 2p23.3 including DNMT3A.

File Name: Supplementary Data 2

Description: List of significantly differentially expressed genes between WT and  $\Delta$ 3A, 3A1 and 3A2 Caco-2 cells.

File Name: Supplementary Data 3

Description: List of GO terms enriched in DEGs from in vitro experiments.

File Name: Supplementary Data 4

Description: List of differentially methylated regions (DMRs) in  $\Delta$ DNMT3A Caco-2 cells compared to WT Caco-2 cells.

File Name: Supplementary Data 5

Description: Comparison of transcription-DNA methylation correlation between *in vitro* and *in vivo*.

File Name: Supplementary Data 6

Description: List of GO terms enriched in in vitro rescued genes.

File Name: Supplementary Data 7

Description: List of differentially methylated regions (DMRs) in  $Dnmt3a^{\Delta IEC}$  compared to  $Dnmt3a^{fl/fl}$  mice.

File Name: Supplementary Data 8

Description: List of significantly differentially expressed genes between  $Dnmt3a^{fl/fl}$  and  $Dnmt3a^{\Delta IEC}$  mice.

File Name: Supplementary Data 9

Description: List of GO terms enriched in in vivo DEGs.

File Name: Supplementary Data 10

Description: List of GO terms enriched in in vivo DNAm-linked DEGs.

File Name: Supplementary Data 11

Description: List of GO terms enriched in DEGs shared between *in vitro* and *in vivo*.

File Name: Supplementary Data 12

Description: Comparison of log fold change of in vitro and in vivo DEGs.

File Name: Supplementary Data 13

Description: List of GO terms enriched in DMPs at day 5 and day 12 of DSS treatment in  $Dnmt3a^{fl/fl}$  and  $Dnmt3a^{\Delta IEC}$  mice.