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**Supplemental information**

**SPT6 loss permits the transdifferentiation  
of keratinocytes into an intestinal fate  
that resembles Barrett's metaplasia**

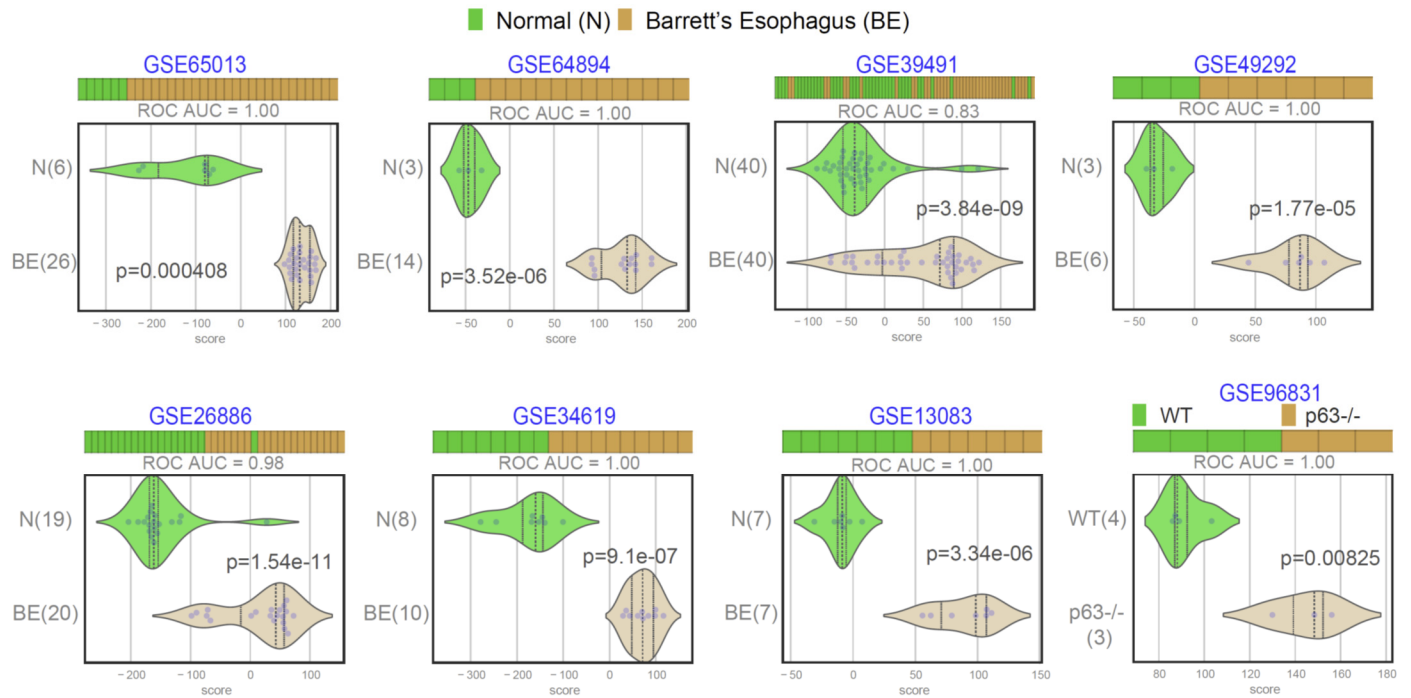
**Daniella T. Vo, MacKenzie R. Fuller, Courtney Tindle, Mahitha Shree Anandachar, Soumita Das, Debashis Sahoo, and Pradipta Ghosh**

## **SUPPLEMENTAL ONLINE MATERIALS**

### **INVENTORY OF SUPPLEMENTARY MATERIALS**

- 1. SUPPLEMENTARY TABLES**
- 2. SUPPLEMENTARY FIGURES AND LEGENDS**

## SUPPLEMENTARY FIGURES



**Supplementary Figure 1.** [Related to [Figure 1](#)]

**Differentially expressed genes (DEGs) in SPT6-depleted samples recapitulate the altered gene expression patterns seen in multiple independent cohorts of Barrett's esophagus.**

DEGs from control vs SPT6-depleted samples (Li et al., 2021) were used to rank order normal (N) from Barrett's esophageal (BE) samples across 8 publicly available independent cohorts. ROC-AUC in each case is annotated.

**Supplementary Table 1 [Related to Figure 1D-G]**

**Barrett's Metaplasia Gene Signature [PMID: 16449976]**

Ref: <https://www.nature.com/articles/1209357/tables/1>

<b>UP Genes</b>		<b>DOWN Genes</b>		
TNFRSF10C	AZGP1	MAL	FDXR	NEDD9
LTA	CREB3L1	LGALS7	CDA	ANXA8
ARPC3	FOXA3	RELN	GPX3	SERPINB3
GAL5	TCEAL1	ANXA1	CBR3	SPRR2C
TSPAN-1	NR0B2	ARS	SULT2B1	CSTA
LAMC2	CXCL3	EMP1	PAX9	LY6G6C
TS4SF8	GDF15	VAT1	RARG	S100A2
CRIP1	PDGFA	ALOX12	TRIM29	TPD52L2
TM4SF3	GJB1	KRT6A	CRABP2	CSTB
KRT8	INSR	ST3GAL4	MAFG	KIAA0657
COL4A2	PNPLA2	KRT4	NFRKB	PPL
SERPINH1	AGR2	PGD	ECM1	
LYZ	AADAT	KRT1	INI1A	
CYBA		FDXR	ARF4L	
HGD		CDA		
PSMB8		GPX3		

**Supplementary Table S1 [Related to Figure 1D-G]**

**Tissue-derived Barrett's Metaplasia Gene Signature.**

Differentially expressed genes (DEGs) from Barrett's esophagus (BE) vs. normal esophageal mucosa (NE) (Wang et al., 2006) used to rank order control and SPT6-depleted samples (Li et al., 2021) in Figure 1D-G. The p-value was <0.001 between BE vs. NE in analysis of variance (ANOVA). The FDR was <0.001 in significance analysis of microarray (SAM) with more than two-fold changes.

<b>Supplementary Table 2 [Related to Figure 1K]</b>		
<b>GSM ID</b>	<b>GSE ID</b>	<b>Correlation Matrix ID</b>
<b>GSM4634684</b>	GSE153129	CTLi-1
<b>GSM4634685</b>	GSE153129	CTLi-2
<b>GSM4634681</b>	GSE153129	SPT6i-1
<b>GSM4634682</b>	GSE153129	SPT6i-2
<b>GSM3415805</b>	GSE120795	Colon-1
<b>GSM3415821</b>	GSE120795	Colon-2
<b>GSM3415854</b>	GSE120795	Brain-1
<b>GSM3415888</b>	GSE120795	Brain-2
<b>GSM3415810</b>	GSE120795	Ski mus-1
<b>GSM3415864</b>	GSE120795	Ski mus-2
<b>GSM3701297</b>	GSE129153	Adipocyte-1
<b>GSM3701298</b>	GSE129153	Adipocyte-2
<b>GSM4483226</b>	GSE148818	Trachea-1
<b>GSM4483228</b>	GSE148818	Trachea-2
<b>GSM1423129</b>	GSE58963	BE-1
<b>GSM1423130</b>	GSE58963	BE-2

**Supplementary Table 2 [Related to [Figure 1K](#)]**

**Datasets used for comparing the SPT6i keratinocyte transcriptome with that of other adult human tissues.**

Selection of GSM and GSE IDs used to generate the correlation matrix in Figure 1K including SPT6-depleted and control samples, colon, brain, skeletal muscle, adipocytes, trachea and Barrett's metaplasia.

<b>Supplementary Table 3 [Related to Figure 2A-C]</b>	
<b>Metaplasia-specific and intestine-specific geneset [PMID: 21703447]</b>	
Source: <a href="https://doi.org/10.1016/j.cell.2011.05.026">https://doi.org/10.1016/j.cell.2011.05.026</a>	
<b>Metaplasia-Specific Genes:</b>	<b>Intestine-specific Genes:</b>
Cyp2f2	Nr5a2
Krt6a	Muc3
Pax9	Tinag
Adh7	Afm
Upk2	Hnf4a
Muc4	Muc2
Sox1	Cdx1
Gapbrp	Isx
Upk1a	Tff3
Ceacam1	Lgals2
Cxcl17	Cdx2
Car4	Alpi
Krt31	Apob
Runx2	Fabp2
Krt7	Lct
	Apoc3

**Supplementary Table 3 [Related to Figure 2A-C]**

**Genes that distinguish the metaplastic BE epithelium from the normally differentiated intestinal epithelium.**

Metaplasia-specific and intestine-specific genes used to perform GeneSet Enrichment Analysis (GSEA) on human Barrett's esophagus (BE) vs. small intestine tissue in Figure 2B and SPT6 KO vs. small intestine-derived organoids in Figure 2C.