Supplementary Information

Figure Legends

Figure S1. CAGGCreER^{TM} induces deletion in nearly all neck and zymogenic cells. ***A,*** LacZ staining after 0.75 mg of tamoxifen per 20 g mouse body weight was injected intraperitoneally into CAGGCreER^{TM};R26R mice for seven days. Around 50% of all cells were LacZ positive; however, almost all neck cells (yellow arrowhead in (middle panel)) and all ZCs (black arrowhead in (right panel)) were LacZ positive. ***B***, *Xbp1* qRT-PCR with primers specific for the loxP-flanked exon2. *Xbp1*$^{\Delta}$ stomach shows 5.2 fold less exon2 containing transcripts from control.

Figure S2. CAGGCreER^{TM};*Xbp1*$^{flox/flox}$ mice do not have defects in surface pit cell, parietal cell, and enteroendocrine cell lineages. ***A,*** Immunofluorescent staining for AAA (surface pit cell marker, magenta) and Hoechst 33258 (nucleus, blue). There was no significant difference in the number of AAA positive cells between CAGGCreER^{TM}; *Xbp*$^{flox/+}$ control (left panel) and CAGGCreER^{TM}; *Xbp1*$^{flox/flox}$ (right panel) stomachs 14 days after tamoxifen injection. ***B,*** Immunofluorescent staining for H^+/K^+ ATPase (parietal cell marker, green) and Hoechst 33258 (nucleus, blue). There was no significant difference in the number of H^+/K^+ ATPase positive cells (green) between CAGGCreER^{TM}; *Xbp*$^{flox/+}$ control (left panel) and CAGGCreER^{TM}; *Xbp1*$^{flox/flox}$ (right panel) stomachs 14 days after tamoxifen injection. ***C,*** Immunohistochemistry for Chromogranin A (enteroendocrine cell marker, brown). There was no significant difference in the number of Chromogranin A positive cells (e.g., arrowhead) between CAGGCreER^{TM}; *Xbp*$^{flox/+}$ control (left panel) and CAGGCreER^{TM}; *Xbp1*$^{flox/flox}$ (right panel) stomachs 14 days after tamoxifen injection.

Figure S3. Proliferation and apoptosis are not substantially affected by *Xbp1* deletion. *A,* Immunofluorescent staining for Brdu (red), GSII (Neck cell marker, green), and Hoechst 33258 (nucleus, blue). There was no significant difference in the number of Brdu positive cells (yellow arrow head) between wildtype control (left panel) and CAGGCreER^{TM}; *Xbp1*$^{flox/flox}$ (right panel) stomachs 14 days after tamoxifen injection.

B, Fluorescent staining for TUNEL (green), GSII (Neck cell marker, red), and Hoechst 33258 (nucleus, blue). There was no significant difference in the number of TUNEL positive cells (yellow arrow head) between wildtype control (left panel) and CAGGCreER^{TM}; *Xbp1*$^{flox/flox}$ (right panel) stomachs 14 days after tamoxifen injection.

Figure S4. *Xbp1* germline null mouse vs. control at 3 weeks old (A) and their corresponding stomachs (B).

Table S1. Primer sequences

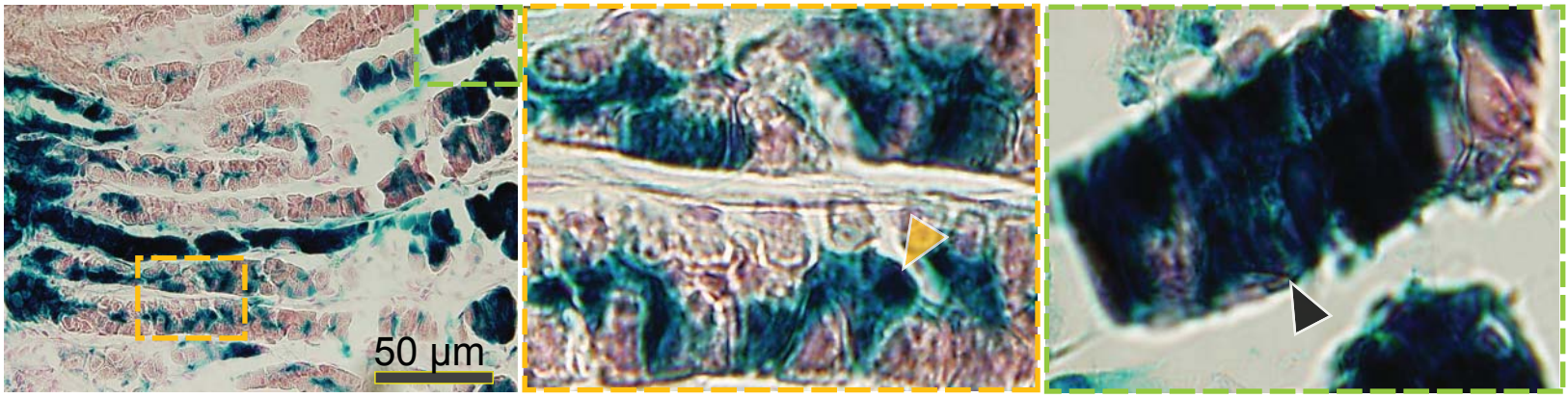
Primer	5'- Sequence – 3'	Reference
Xbp205 forward	CCT GAG CCC GGA GGA GAA	[1]
Xbp272 reverse	CTC GAG CAG TCT GCG CTG	
Mist1 forward	GCT GAC CGC CAC CAT ACT TAC	PrimerBank*
Mist1 reverse	TGT GTA GAG TAG CGT TGC AGG	
Tff1 forward	AGC ACA AGG TGA TCT GTG TCC	PrimerBank
Tff1 reverse	GGA AGC CAC AAT TTA TCC TCT CC	
H/K ATPase, α subunit forward	TCT GCT TTG CGG GAC TTG TA	This study
H/K ATPase, α subunit reverse	CGG CAT TTG AGC ACA GCA T	
Tff2 forward	TGC TCT GGT AGA GGG CGA G	PrimerBank
Tff2 reverse	CGA CGC TAG AGT CAA AGC AG	
Gkn3 forward	CCG TTG CAT TCG CTG GAG A	PrimerBank
Gkn3 reverse	AAC TGT CGC TAG TGT TCG TCA	
Pgc forward	ATG AAG AGT ATC CGG GAG ACC	PrimerBank
Pgc reverse	TGG GCT CAT AGA GTA CAC TGT AG	
GIF forward	CCC TCT ACC TCC TAA GTG TTC TC	PrimerBank
GIF reverse	CTG AGT CAG TCA CCG AGT TCT	
Edem1 forward	AGT CAA ATG TGG ATA TGC TAC GC	PrimerBank
Edem1 reverse	ACA GAT ATG ATA TGG CCC TCA GT	
Dnajb9 forward	CTC CAC AGT CAG TTT TCG TCT T	PrimerBank
Dnajb9 reverse	GGC CTT TTT GAT TTG TCG CTC	
Sec61a1 forward	GGA AGT CAT CAA GCC ATT CTG T	PrimerBank
Sec61a1 reverse	GCA TCC AGT AGA ACG GGT CAG	
Hspa5 forward	ACT TGG GGA CCA CCT ATT CCT	PrimerBank
Hspa5 reverse	ATC GCC AAT CAG ACG CTC C	
CHOP forward	CTG GAA GCC TGG TAT GAG GAT	PrimerBank
CHOP reverse	CAG GGT CAA GAG TAG TGA AGG T	
hXbp1(s) forward	TCT GCT GAG TCC GCA GCA GG	This study
hXbp1(s) reverse	CTG GCA GGC TCT GGG GAA G	
hMist1 forward	CGG ATG CAC AAG CTA AAT AAC G	PrimerBank
hMist1 reverse	CCG TCA GCG ATT TGA TGT AGT TC	
Mist1 promoter forward for ChIP	ATG GTG GCT TCC ACT CAG AC	This study
Mist1 promoter reverse for ChIP	GGC AGC ACC CTT TAA ACA TC	
Intron 4 of BmprIa forward for ChIP	GCA GCT GCT GCT GCA GCC TCC	This study
Intron 4 of BmprIa reverse for ChIP	TGG CTA CAA TTT GTC TCA TGC	

* http://pga.mgh.harvard.edu/primerbank/

Supplementary References

S1. Kaser A, Lee AH, Franke A, Glickman JN, Zeissig S, Tilg H, Nieuwenhuis EE, Higgins DE, Schreiber S, Glimcher LH, Blumberg RS. XBP1 links ER stress to intestinal inflammation and confers genetic risk for human inflammatory bowel disease. Cell 2008;134:743-56.

A CAGGCreER™; R26R



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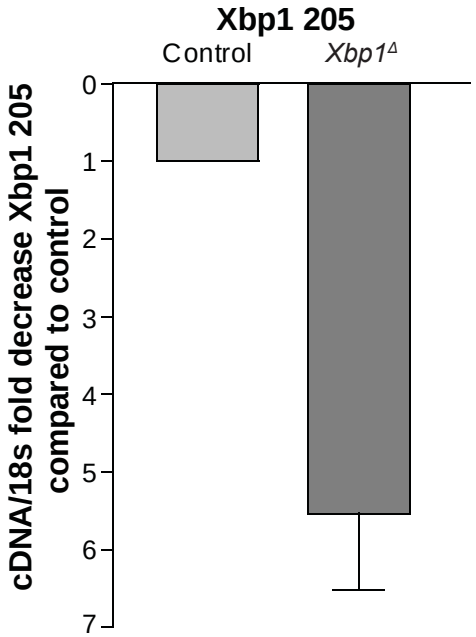
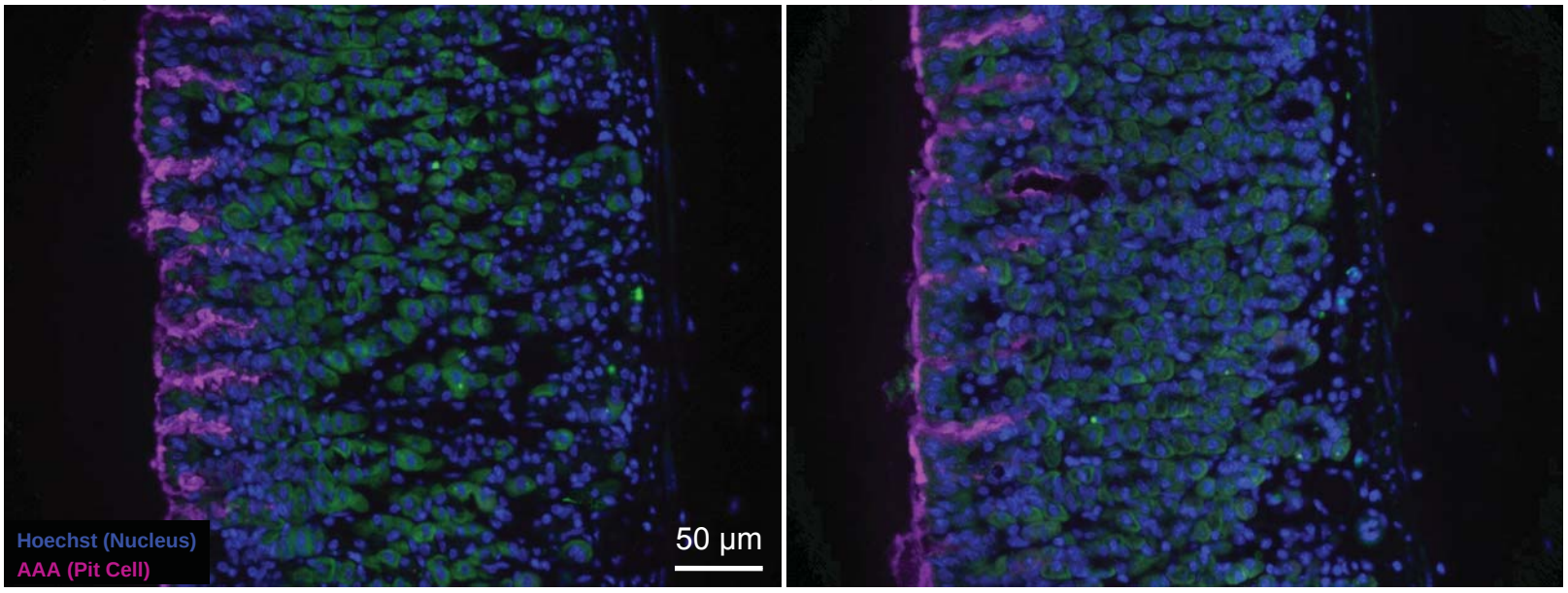


A *Xbp1*$^{\Delta/+}$ 14d 7Mo

Xbp1$^{\Delta}$ 14d 7Mo



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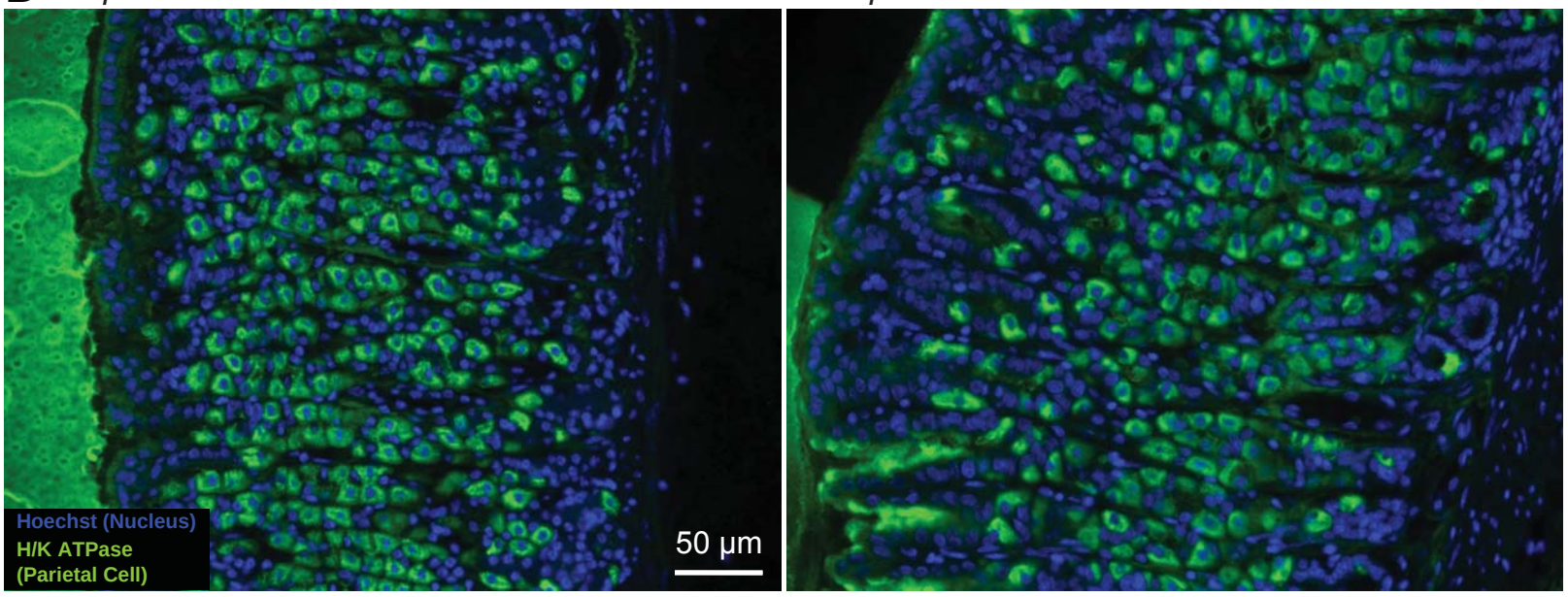

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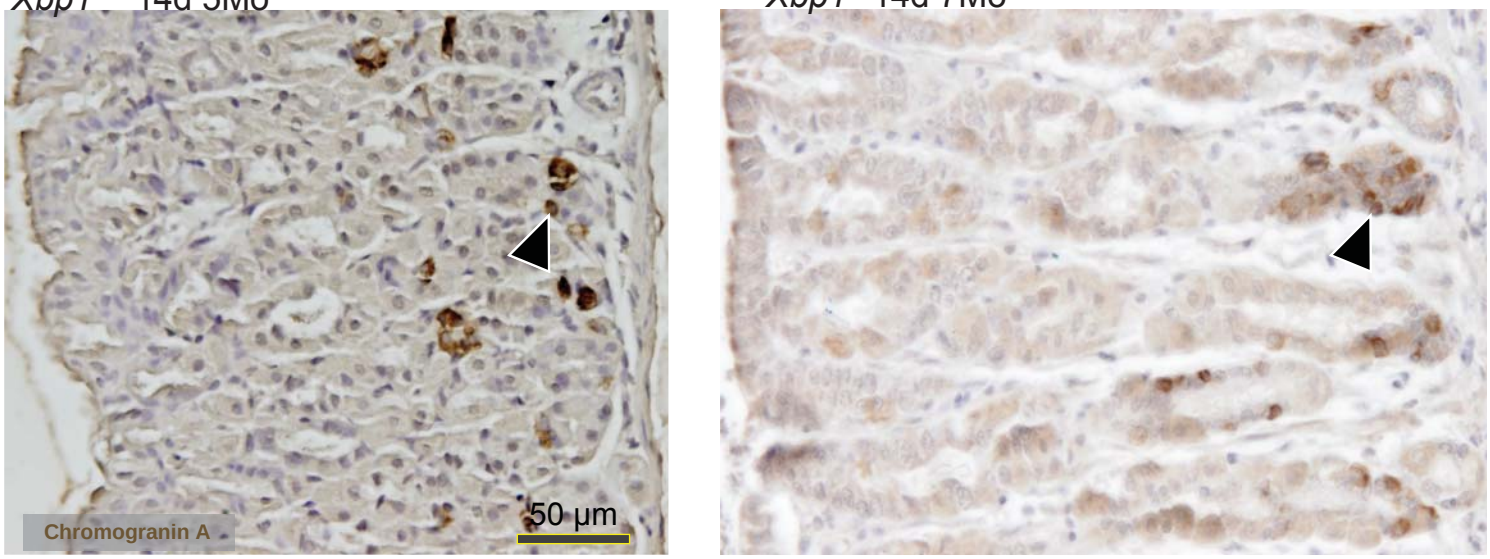

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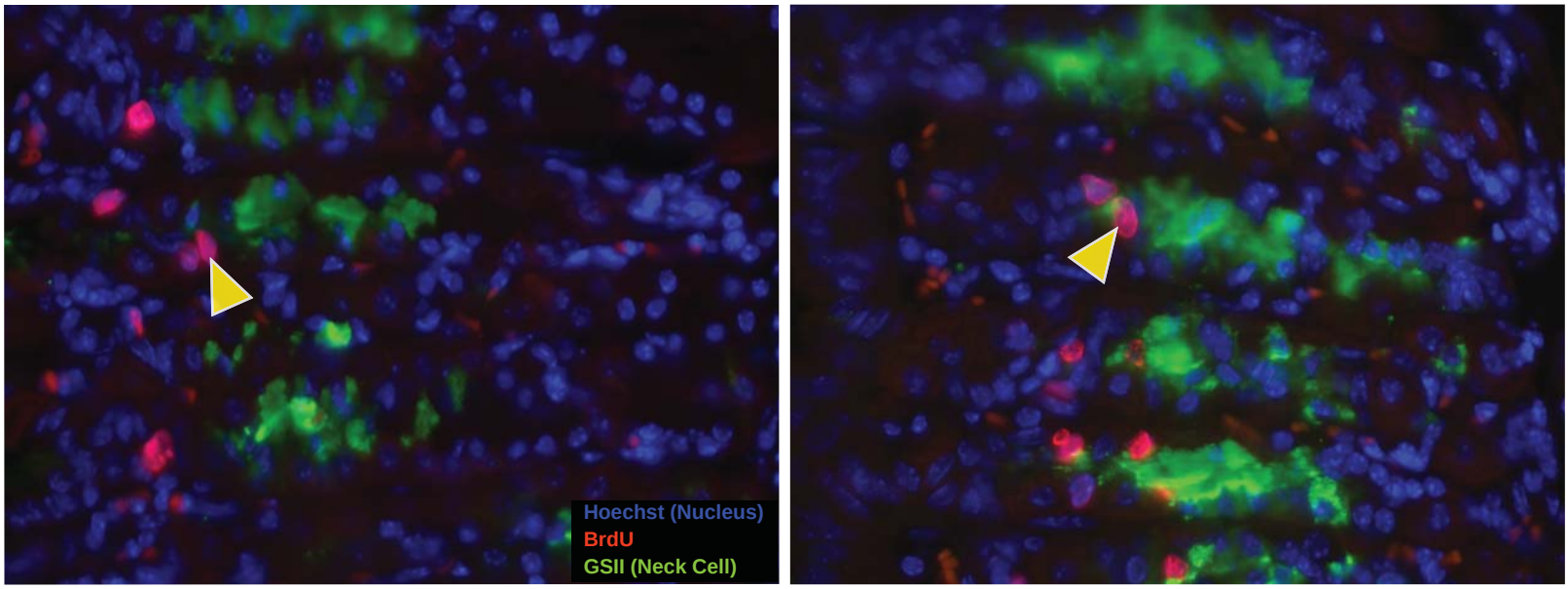
Xbp1$^{\Delta}$ 14d



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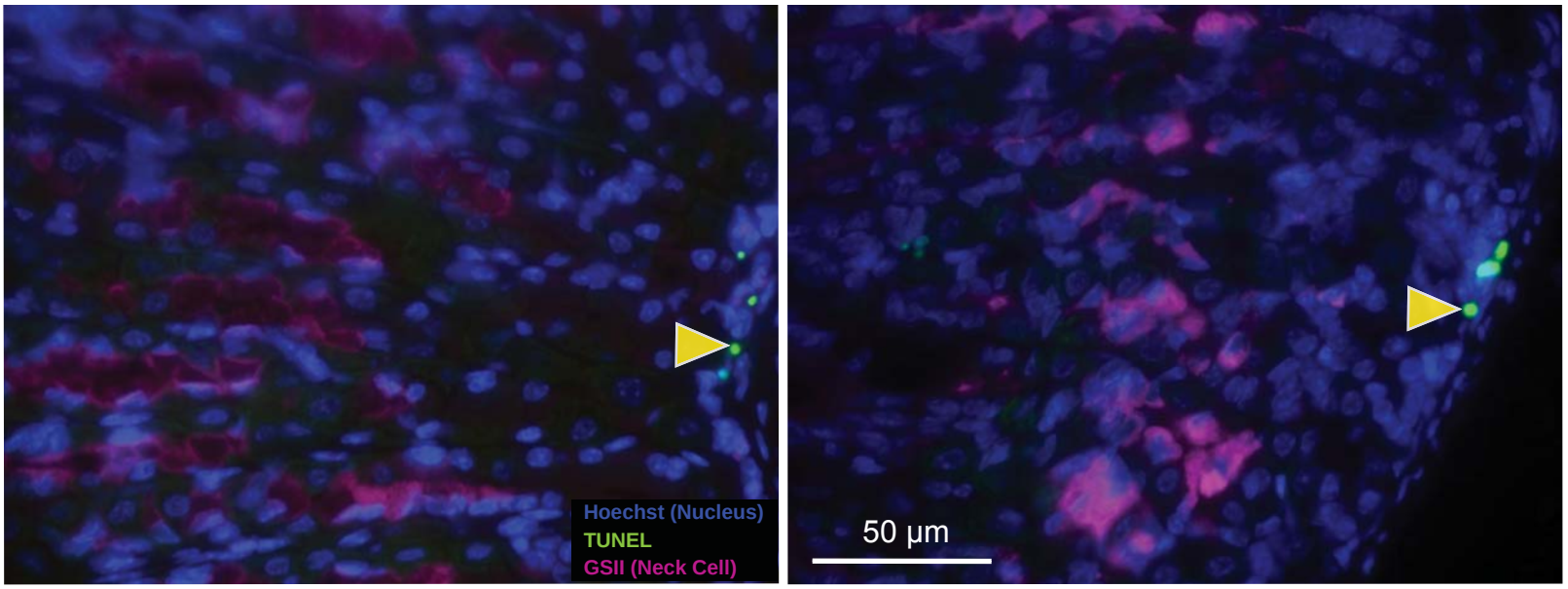

A

B