Inventory of Supporting Information

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Please complete each of the Inventory Tables below to outline your Extended Data and Supplementary Information items.

There are four sections:

- *Extended Data*
- *Supplementary Information: Flat Files*
- *Supplementary Information: Additional Files*
- *Source Data*

Each section includes specific instructions. Please complete these tables as fully as possible. We ask that you avoid using spaces in your file names, and instead use underscores, i.e.: Smith_ED_Fig1.jpg not Smith ED Fig1.jpg

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1. Extended Data

Complete the Inventory below for all Extended Data figures.

- Keep Figure Titles to one sentence only
- Upload your files as 'Figure Files' in our Manuscript Tracking system
- File names should include the Figure Number. i.e.: *Smith_ED_Fig1.jpg*
- Please be sure to include the file extension in the Filename. Note that Extended Data files must be submitted as .jpg, .tif or .eps files *only*, and should be approximately 10MB
- All Extended Data figure legends must be provided in the Inventory below and should not exceed 300 words each *(if possible)*
- Please include Extended Data *ONLY* in this table

Figure #	**Figure title** One sentence only	**Filename** This should be the name the file is saved as when it is uploaded to our system. Please include the file extension. i.e.: *Smith_ED_Fig1.jpg*	**Figure Legend** If you are citing a reference for the first time in these legends, please include all new references in the main text Methods References section, and carry on the numbering from the main References section of the paper. If your paper does not have a Methods section, include all new references at the end of the main Reference list.
Extended Data Fig. 1	**Infection and oxidative damage increase *esg>GFP+* cells in the midgut and associate with increased TTC branching**	**Tamamouna_ED_ Fig1.jpg**	**a.** Adult midgut intestinal progenitors labeled with *esg^{NP5130}-Gal4>UAS-srcGFP* were imaged in unchallenged conditions (4% sucrose) and upon oral *P.a.* infection (48hrs), and feeding with H_2O_2 (48hrs) and PQ (24hrs). DAPI (blue) in the upper panels stains all midgut nuclei. The bottom panels show the GFP-labeled progenitors separately. *P.a.* and PQ expanded the intestinal progenitors with a posterior midgut bias, whereas H_2O_2 exhibited an anterior midgut bias. **b-c.** Quantification of midgut mitosis (b, *n=10 each*) and TTC branching (c, *n=7,6*) in PQ-treated flies. **d-e.** Posterior midgut (R4) images of *btl-Gal4>UAS-srcGFP* flies in baseline conditions (sucrose) and upon PQ feeding. DAPI (blue) staining all the nuclei. Single channel images of the GFP are shown in d'-e'. **f-g.** Posterior midgut images of

			QF6>QUAS-mtdTomato flies in baseline conditions exhibit tracheal expression of the reporter. Midgut epithelial ECs with low expression of the reporter are visible is zoomed image (g). Single channel images of the Tomato are shown in f'-g'. Scale bars: 300 μm in a, 75 μm in d-g. Data are presented as mean values ± SD. Statistical significance (t-tested, two-sided for b, and U-tested for c): ns, not significant, * $0.01<p\leq0.05$, ** $0.001<p\leq0.01$ and *** $p\leq0.001$.
Extended Data Fig. 2	**The FGFR/Btl is necessary and sufficient for midgut TTC branching and ISC mitosis**	**Tamamouna_ED_ Fig2.jpg**	**a-b.** Brightfield images of the tracheae of *P.a.* infected R5 regions of the midgut in *trh-Gal4* control (a) and *trh-Gal4>UAS-btl^{DN}* (b). **c-d.** Brightfield images of the tracheae of uninfected R5 regions of the midgut in *trh-Gal4* control (c) and *trh-Gal4>UAS-λbtl* (d). **e-g.** Quantification of TTCs (e, *n=10,11,10,9,10*), TTC branching (f, *n=10,11,10,8,10*), and midgut mitosis (g, *n=8,6,10,9,6*) upon *trh-Gal4*-driven *btl* manipulation with or without *P.a*. infection. **h-i.** Brightfield images of the tracheae of *P.a.*-infected R5 regions of the midgut in *dSRF-Gal4* control (h) and *dSRF-Gal4>UAS-btl^{DN}* (i). **j-k.** Brightfield images of the tracheae of uninfected R5 regions of the midgut in *dSRF-Gal4* control (j) and *dSRF-Gal4>UAS-λbtl* (k). **l-n.** Quantification of TTCs (l, *n=10,10,8,8,11*), TTC branching (m, *n=10,10,8,8,11*), and midgut mitosis (n, *n=11,9,12,12,9*) upon *dSRF-Gal4*-driven *btl* manipulation with or without *P.a*. infection**. All** scale bars: 75 μm. Data are presented as mean values ± SD. Statistical significance (t-tested, two-sided): ns, not significant, * $0.01<p\leq0.05$, ** $0.001<p\leq0.01$ and *** $p\leq0.001$.
Extended Data Fig. 3	**Infection and oxidative damage induce *FGF/bnl* in**	**Tamamouna_ED_ Fig3.jpg**	Adult midgut *bnl*-expressing cells labeled with the reporter *bnl-Gal4>UAS-srcGFP* were imaged in unchallenged conditions (4% sucrose) and upon oral *P.a.*

	the midgut epithelium		infection (48hrs), feeding with H_2O_2 (48hrs) and PQ (24hrs). DAPI (blue) in the upper panels stained all midgut nuclei. The bottom panels show the GFP-labeled *bnl* expressing cells separately. *P.a.* and PQ induced the reporter throughout the midgut, whereas H_2O_2 exhibited an anterior midgut bias. Scale bar: 300 μm.
Extended Data Fig. 4	**Btl/Bnl signaling in the epithelial cells is necessary for efficient tracheal remodeling and mitosis in response to infection**	**Tamamouna_ED_ Fig4.jpg**	**a-b.** Quantification of TTC branching upon progenitor- (a) and EC-specific (b) silencing of *bnl* (bnl^{RNAi3}) and *btl* (btl^{RNAi}) (a, *n=10,8,5,10,7,7* and b, *n=10,7,9,10,9,8*). **c-d.** Quantification of midgut mitosis upon progenitor- (c) and EC-specific (d) silencing of *bnl* (bnl^{RNAi3}) (c, *n=6,8,12,12* and d, *n=9,9,11,13*). **e.** Quantification of *esg*+ progenitors as a percent of total number of cells in the posterior regions of the midgut upon progenitor-specific knockdown of *btl* (btl^{RNAi}) and *bnl* (bnl^{RNAi3}) (*n=12,15,15)*. **f-g.** Quantification of midgut mitosis upon progenitor- (f) and EC-specific (g) silencing of *btl* (btl^{RNAi}) (f, *n=8,13,11,13* and g, *n=12,11,11,16*). **h.** Quantification of *esg*+ progenitor cells/total number of cells in the posterior midgut upon progenitor-specific knockdown of *btl* (btl^{DN}, *n=9,9*). Data are presented as mean values ± SD. Statistical significance (t-tested, two-sided): ns, not significant, * $0.01<p\leq0.05$, ** $0.001<p\leq0.01$ and *** $p\leq0.001$.
Extended Data Fig. 5	**Infection and oxidative damage activate Hif-1α/Sima in the midgut epithelium and the visceral TTCs**	**Tamamouna_ED_ Fig5.jpg**	Hif-1α/Sima activation was monitored via the *ldh-Gal4>UAS-nlsGFP* reporter expression in the adult midgut epithelium and the intestinal trachea of the R5 region in unchallenged flies (sucrose) and upon *P.a.* and PQ treatment (a, c, e), and of the R2 region in unchallenged flies (sucrose) and upon H_2O_2 feeding (b, d). Epithelial sections (a-d) and trachea surface sections (a'-d') of the same midguts were imaged. DAPI (blue) in a-d and a'-d' stains all the nuclei. a''-d'' and a'''-d'''

			correspond to separated channels for reporter expression in the epithelium and the intestinal trachea, respectively. The *ldh-Gal4>UAS-nlsGFP* reporter was expressed in cells of the midgut epithelium and in the midgut TTCs in baseline conditions in the anterior (R2 in b, b') and posterior (R5 in a, a') midgut. *P.a.* (c, c'), H_2O_2 (d, d') and PQ (e, e') induced the reporter in the epithelium and the trachea at varying degrees. All images were acquired at the same confocal settings as their respective controls. Scale bar: 75 μm.
Extended Data Fig. 6	**Hif-1a/Sima is necessary in the intestinal epithelium and the trachea for TTC branching**	**Tamamouna_ED_ Fig6.jpg**	**a-b.** Brightfield images of the midgut TTCs (R5 region) upon trachea-specific (via *btl-Gal4*) *sima* knockdown in the background of heterozygous *simaKG* in baseline conditions. **c-d.** Bright-field images of the midgut TTCs (R5 region) upon EC-specific (via *Myo1A-Gal4*) *sima* knockdown in the background of heterozygous *simaKG* in baseline conditions. **e-f.** Bright-field images of the midgut TTCs (R5 region) upon trachea-specific (via *btl-Gal4*) *sima* knockdown in the background of heterozygous $sima^{KG}$ in *P.a.*-infected conditions. g-h. Bright-field images of the midgut TTCs (R5 region) upon EC-specific (via *Myo1A-Gal4*) *sima* knockdown in the background of heterozygous $sima^{KG}$ in *P.a.*-infected conditions. The images correspond to examples of those quantified for Fig. 4e,i. Scale bar: 75 μm.
Extended Data Fig. 7	**Time-course analysis of $Notch^{DN}$ progenitor-derived midgut tumors**	**Tamamouna_ED_ Fig7.jpg**	**a-d.** The R4a region of control (reared for 4 days at 18^0C) (a) and tumorous midguts (reared for 4, 7 and 10 days at 29^0C) (b-d) of the *esg-Gal4 UAS-eGFP tub-*$Gal80^{ts}$*>UAS-*$Notch^{DN}$ genotype with concomitant expression of *QF6>QUAS-mtdTomato* (red) to label the trachea. DAPI (blue in a-d) is used to label all midgut nuclei and Prospero (a''-d'') labels the EEs. a'-d', a''-d'' and a'''-d''' correspond to the individual channels for

			eGFP, Prospero and Tomato-labeled trachea, respectively. Scale bars: 75 μm. **e-g**. Quantification of TTC branching in the R4a of control (*Notch^{DN}* uninduced) and *Notch^{DN}*-expressing midguts (e, *n=4,8,4,6,4,7*), in the *Notch^{DN}* tumor-region vs. neighboring non-tumor area on the same image (f, *n=6,6,4,4,6,6*), and midgut mitosis of control (*Notch^{DN}* uninduced) and *Notch^{DN}*-expressing midguts (g, *n=20 each*) during a time-course analysis at 4, 7, and 10 days post-tumor induction. Scale bar: 75 μm. Data are presented as mean values ± SD. Statistical significance (t-tested, two-sided): ** $0.001<p\leq0.01$ and *** $p\leq0.001$.
Extended Data Fig. 8	**Time-course analysis of *Ras^{V12}* progenitor-derived midgut tumors**	**Tamamouna_ED_ Fig8.jpg**	**a-d.** The R5 region of control *esg-Gal4 UAS-eGFP tub-Gal80^{ts}* (reared for 1 day at 29^{0C}) and *esg-Gal4 UAS-eGFP tub-Gal80^{ts}>UAS-Ras^{V12}*-tumor bearing midguts (reared for 1, 3 and 5 days at 29^{0}C) with concomitant expression of *QF6>QUAS-mtdTomato* (red) to label the trachea. DAPI (blue in a-d) was used to label all midgut nuclei. a'-d' and a''-d'' correspond to the individual channels for the eGFP and the Tomato-labeled trachea, respectively. Scale bar: 75 μm.

Delete rows as needed to accommodate the number of figures (10 is the maximum allowed).

2. Supplementary Information:

A. Flat Files

Complete the Inventory below for all additional textual information and any additional Supplementary Figures, which should be supplied in one combined PDF file.

- **Row 1:** A combined, flat PDF containing any Supplementary Text, Discussion, Notes, Additional Supplementary Figures, Supplementary Protocols, simple tables, and all associated legends. Only one such file is permitted.
- **Row 2:** Nature Research's Reporting Summary; if previously requested by the editor, please provide an updated Summary, fully completed, without any mark-ups or comments. **(Reporting Summaries are not required for all manuscripts.)**

Item	**Present?**	**Filename** **This should be the name the file is saved as when it is uploaded to our system, and should include the file extension. The extension must be .pdf**	**A brief, numerical description of file contents.** **i.e.:** ***Supplementary Figures 1-4, Supplementary Discussion, and Supplementary Tables 1-4.***
Supplementary Information			
Reporting Summary	Yes	Tamamouna et al nr-reporting-summary.pdf	

B. Additional Supplementary Files

Complete the Inventory below for all additional Supplementary Files that cannot be submitted as part of the Combined PDF.

- Do not list Supplementary Figures in this table (see section 2A)
- Where possible, include the title and description within the file itself
- Spreadsheet-based tables & data should be combined into a workbook with multiple tabs, not submitted as individual files.
- Compressed files are acceptable where necessary. ZIP files are preferred.
- Please note that the *ONLY* allowable types of additional Supplementary Files are:
    - Supplementary Tables ○ Supplementary Audio ○ Supplementary Videos ○ Supplementary Software
    - Supplementary Data, for example: raw NMR Data, Cryo-EM Data, Computational Data, Crystallographic Data, etc.

Type	**Number** **If there are multiple files of the same type this should be the numerical indicator. i.e. "1" for Video 1, "2" for Video 2, etc.**	**Filename** **This should be the name the file is saved as when it is uploaded to our system, and should include the file extension. i.e.: *Smith_ Supplementary_Video_1.mov***	**Legend or Descriptive Caption** **Describe the contents of the file**
Supplementary Table	1-3	Tamamouna_ED_Tables.xlsx	*Supplementary Table 1.* *Drosophila* and *Pseudomonas* strains used in this study. Supplementary Table 2. Reagents and Antibodies used

			in this study. Supplementary Table 3. Primer sequences used in this study.

Add rows as needed to accommodate the number of files.

3. Source Data

Complete the Inventory below for all Source Data files.

- Acceptable types of Source Data for Main Figures and Extended Data Figures are:
  - Statistical Source Data
    - Plain Text (ASCII, TXT) or Excel formats only
    - One file for each relevant Figure, containing all source data
  - Full-length, unprocessed Gels or Blots
    - JPG, TIF, or PDF formats only
    - One file for each relevant Figure, containing all supporting blots and/or gels
- 'Source Data' is only allowed for Main Figures and Extended Data Figures.
  - Include Unprocessed Gels or Blots for Supplementary Figures as additional Supplementary Figures.
  - Include Statistical Source Data for Supplementary Figures as 'Supplementary Data' files and list them in section 2B.
  - Please see this example of Source Data in a publication.

Parent Figure or Table	**Filename** **This should be the name the file is saved as when it is uploaded to our system, and should include the file extension. i.e.: *Smith_SourceData_Fig1.xls,* or *Smith_ Unmodified_Gels_Fig1.pdf***	**Data description** **i.e.: Unprocessed Western Blots and/or gels, Statistical Source Data, etc.**
Source Data Fig. 1	Tamamouna_SourceData_Fig1.xlsx	Numerical Source Data for Figure 1

Source Data Fig. 1	Tamamouna_Additional_Images_Figure1.pdf	Additional Images for key experiments of Figure 1
Source Data Fig. 2	Tamamouna_SourceData_Fig2.xlsx	Numerical Source Data for Figure 2
Source Data Fig. 3	Tamamouna_SourceData_Fig3.xlsx	Numerical Source Data for Figure 3
Source Data Fig. 4	Tamamouna_SourceData_Fig4.xlsx	Numerical Source Data for Figure 4
Source Data Fig. 5	Tamamouna_SourceData_Fig5.xlsx	Numerical Source Data for Figure 5
Source Data Fig. 5	Tamamouna_Additional_Images_Figure5.pdf	Additional Images for key experiments of Figure 5
Source Data Fig. 6	Tamamouna_SourceData_Fig6.xlsx	Numerical Source Data for Figure 6
Source Data Fig. 7	Tamamouna_SourceData_Fig7.xlsx	Numerical Source Data for Figure 7
Source Data Fig. 7	Tamamouna_Additional_Images_Figure7.pdf	Additional Images for key experiments of Figure 7
Source Data Fig. 8	Tamamouna_SourceData_Fig8.xlsx	Numerical Source Data for Figure 8
Source Data Extended Data Fig. 1	Tamamouna_SourceData_ED_Fig1.xlsx	Numerical Source Data for ED Figure 1
Source Data Extended Data Fig. 2	Tamamouna_SourceData_ED_Fig2.xlsx	Numerical Source Data for ED Figure 2
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Source Data Extended Data Fig. 4	Tamamouna_SourceData_ED_Fig4.xlsx	Numerical Source Data for ED Figure 4
Source Data Extended Data Fig. 5		
Source Data Extended Data Fig. 6		
Source Data Extended Data Fig. 7	Tamamouna_SourceData_ED_Fig7.xlsx	Numerical Source Data for ED Figure 7
Source Data Extended Data Fig. 8		