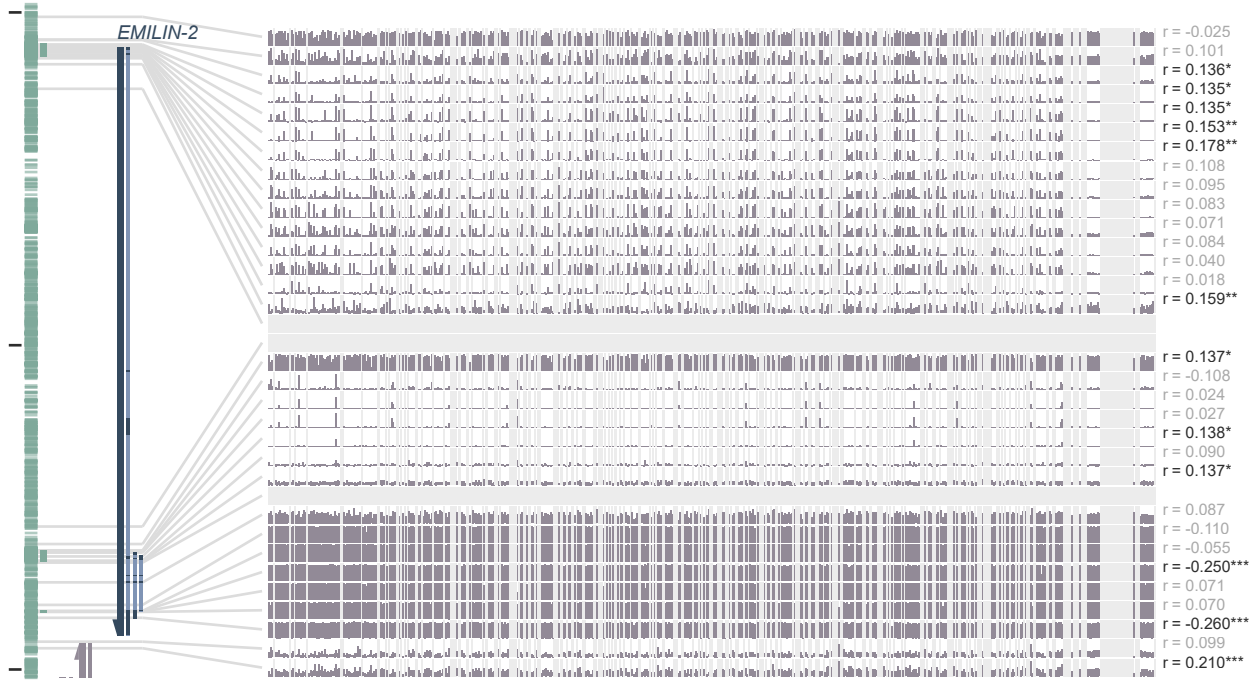
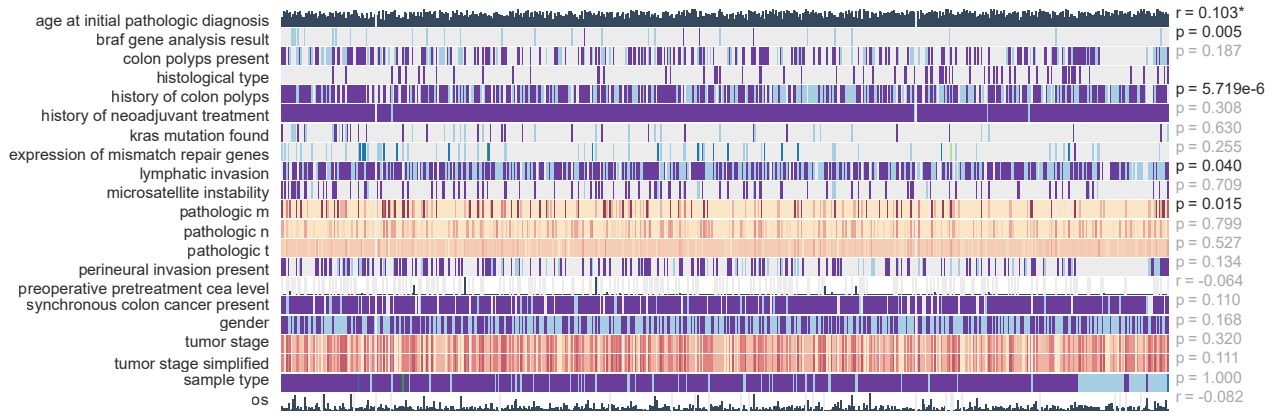
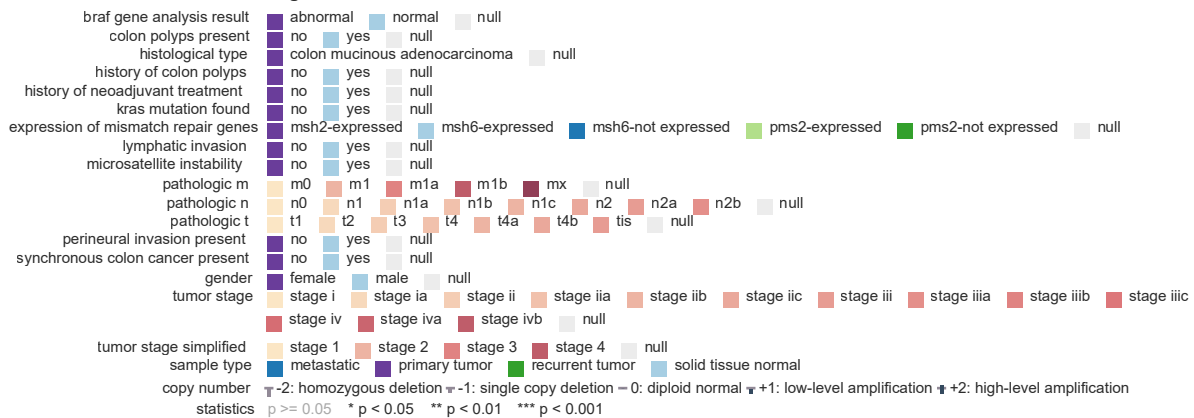


# Figure S1



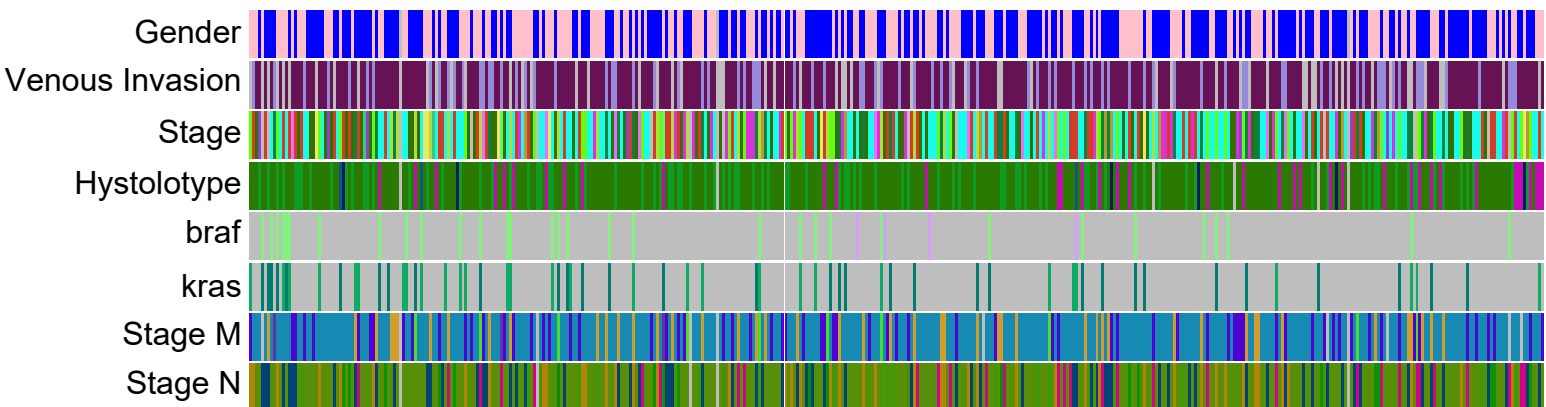
CpG dinucleotide  
 CpG island  
 gene  
 transcript

## Legend

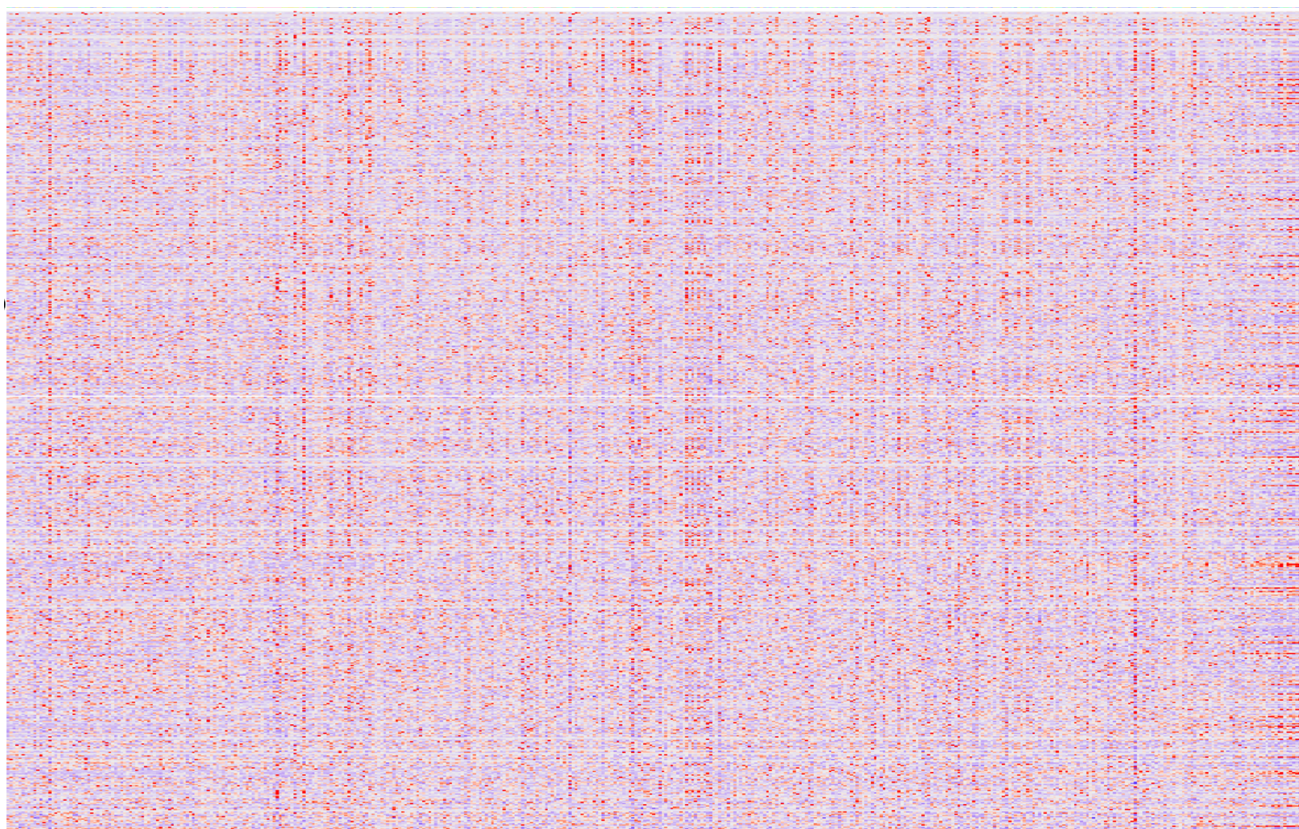


**Figure S1. The *EMILIN-2* gene is methylated in CRC.** Epigenetic landscape of the *EMILIN-2* gene and clinical and molecular parameters characterizing the COAD cohort (477 colorectal cancer patients) from the Cancer Genome Atlas (TCGA), as assessed by MEXPRESS (accessed on 12 March 2021). The analyses are in relation to the levels of *EMILIN-2*. The Pearson correlation coefficients are reported on the right and highlight a significant correlation between the expression of the *EMILIN-2* gene, the methylation probes, and the corresponding clinical parameters.

Figure S2



2000 most variable genes



Gender  
No  
Yes

Venous Invasion  
NA  
No  
Yes

braf  
NA  
Mutated  
Not mutated

kras  
NA  
Mutated  
Not mutated

Stage  
Discrepancy  
I  
IA  
II  
IIA  
IIB  
IIC  
III  
IIIA  
IIIB  
IIIC  
IV  
IVA  
IVB

Stage M  
NA  
M0  
M1  
M1a  
M1b  
MX

Stage N  
NA  
N0  
N1  
N1a  
N1b  
N1c  
N2  
N2a  
N2b  
NX

Hystological type  
NA  
Discrepancy  
Colon Adenocarcinoma  
Colon Mucinous adenocarcinoma  
Rectum Adenocarcinoma  
Rectum Mucinous adenocarcinoma

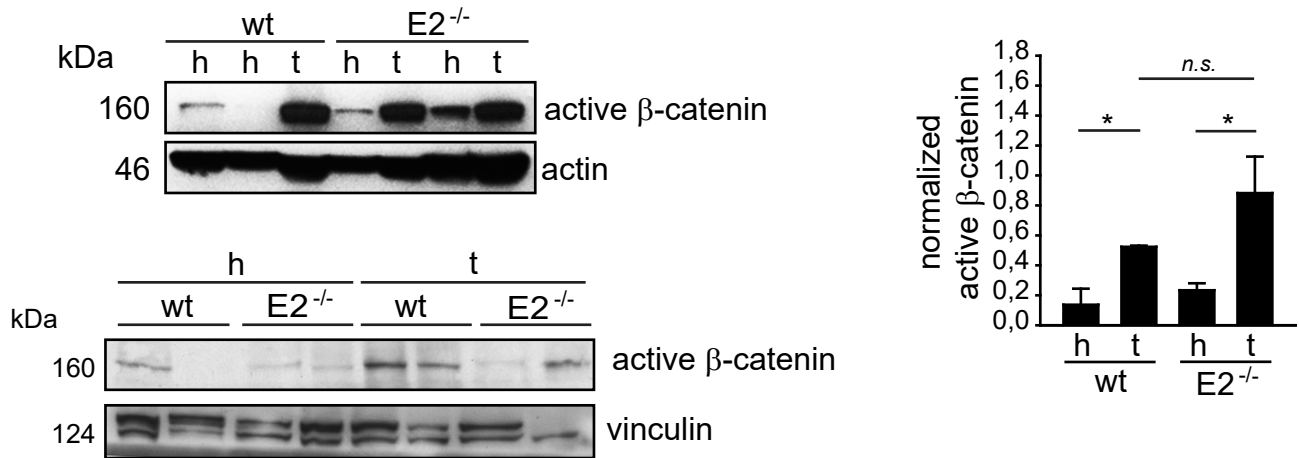
Gene expression  
4  
2  
0  
-2  
-4

**Figure S2. The expression of EMILIN-2 is variable among CRC patients.** Stratification of the patients of the TCGA COAD cohort based on the EMILIN-2 protein levels; molecular and clinical parameters are indicated and detailed on the bottom. The heat map shows the levels of the 2000 most variable genes.

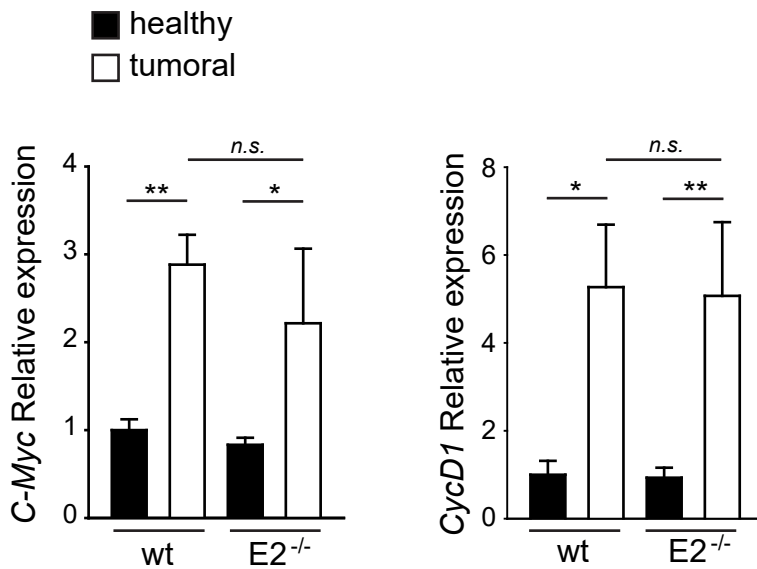


**Figure S3**

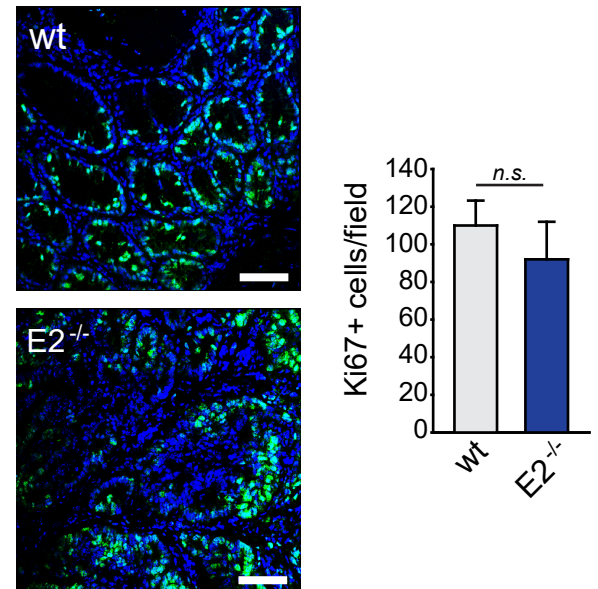
**A**



**B**



**C**



**Figure S3. The higher tumor rate in  $Emilin-2^{-/-}$  mice does not hinge on the activation of the Wnt/ $\beta$ -Catenin pathway.** **A**, Representative Western blot analyses (left) and quantification (right) of  $\beta$ -catenin activation in the healthy (h) and tumoral (t) colonic mucosa of *wild type* (wt) and *Emilin-2<sup>-/-</sup>* ( $E2^{-/-}$ ) mice; n=3. **B**, Relative expression levels of c-Myc (left) and Cyclin D1 (CycD1, right) in the healthy and tumoral colonic mucosa of *wild type* (wt) and *Emilin-2<sup>-/-</sup>* ( $E2^{-/-}$ ) mice. **C**, Representative images (left) and quantification (right) of the Ki67 stainings performed on adenomas developed in *wild type* (wt) and *Emilin-2<sup>-/-</sup>* ( $E2^{-/-}$ ) mice. Blue: nuclei; green: Ki67, scale bar=50  $\mu$ m. Graphs represent the mean  $\pm$  SD of at least three independent experiments; in A and B, *P* values were obtained using the one-way ANOVA test and in C the paired Student's t-test; \**P*<0.05, \*\**P*<0.01, n.s.: *P*>0.05.