

Methylome Profiling of Esophageal Squamous Cell Carcinoma

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Identification of a DNA methylome signature of esophageal squamous cell carcinoma and potential epigenetic biomarkers

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Identification of a DNA Methylome Profile of Esophageal Squamous Cell Carcinoma and Potential Plasma Epigenetic Biomarkers for Early Diagnosis

Xufeng Li^{1,3*}, Fuyou Zhou^{2,3*}, Chunyu Jiang¹, Yinuo Wang³, Yanqiang Lu³, Fei Yang³, Nengchao Wang², Haijun Yang², Yanfang Zheng^{1,*}, Jiren Zhang^{1,3,*}

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Genome-wide profiling of DNA methylation and gene expression in esophageal squamous cell carcinoma

Chen Chen¹, Hao Peng², Xiaojie Huang³, Ming Zhao⁴, Zhi Li⁵, Ni Yin³, Xiang Wang¹, Fenglei Yu¹, Bangliang Yin¹, Yunchang Yuan¹, Qianjin Lu⁴

REVIEW

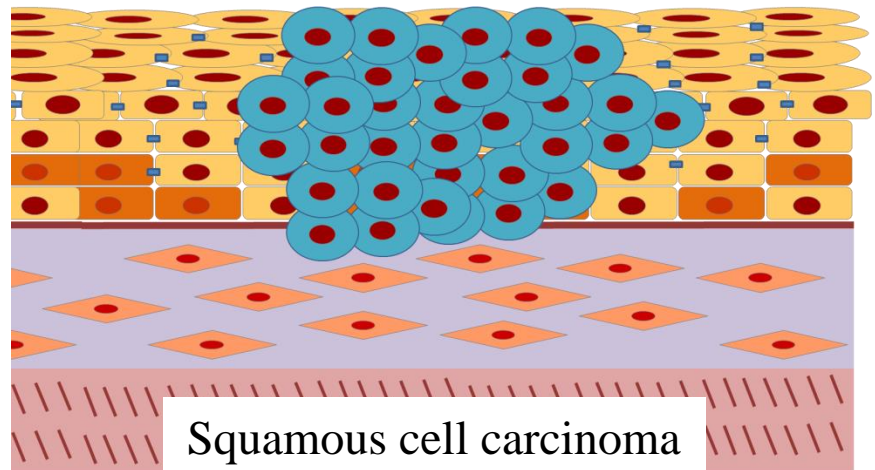
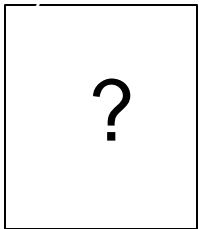
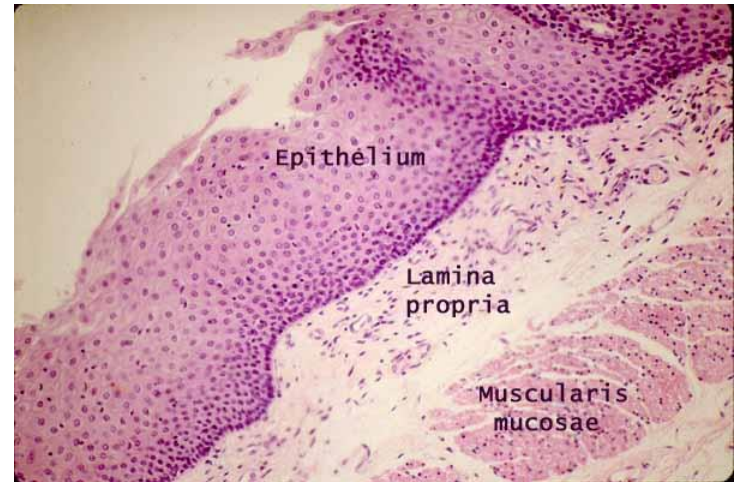
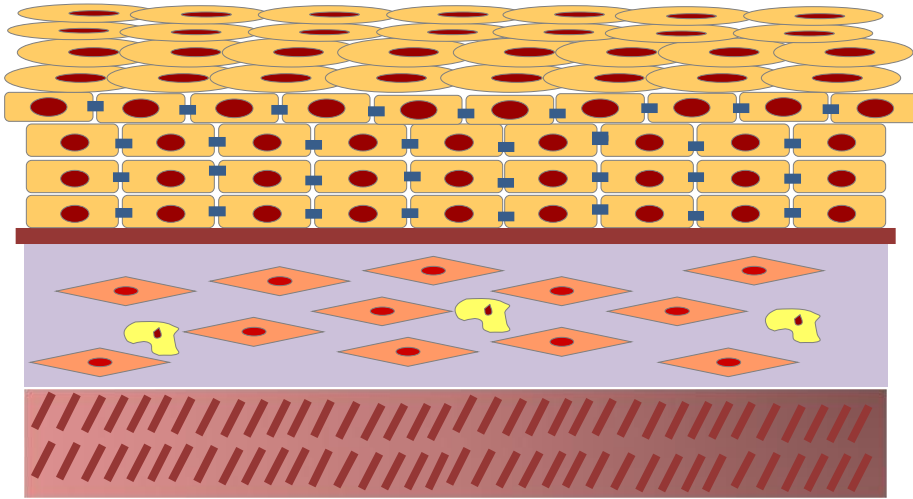
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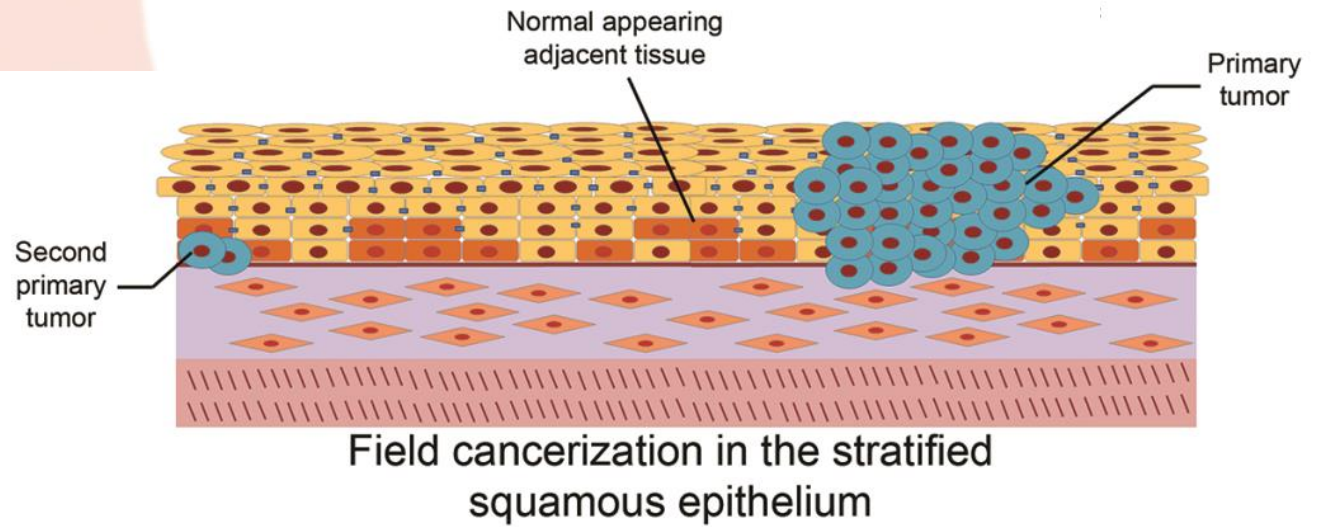
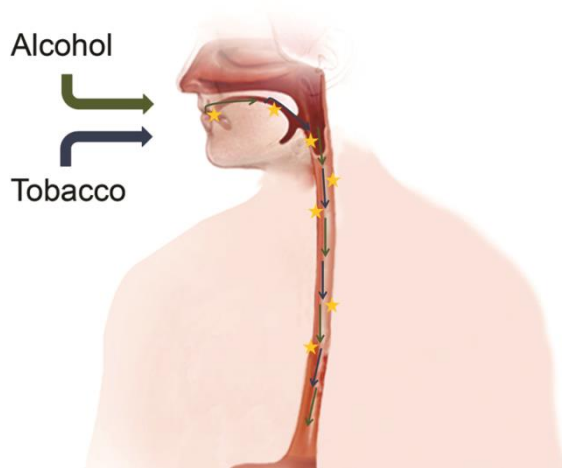
The detective, prognostic, and predictive value of DNA methylation in human esophageal squamous cell carcinoma

Kai Ma¹, Baoping Cao² and Mingzhou Guo^{2*}

The squamous epithelium

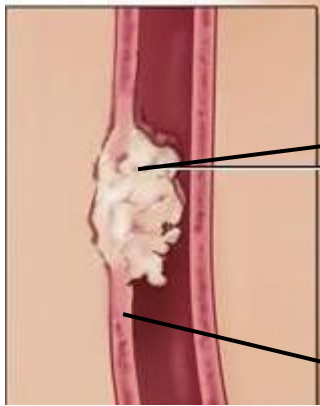


Field cancerization

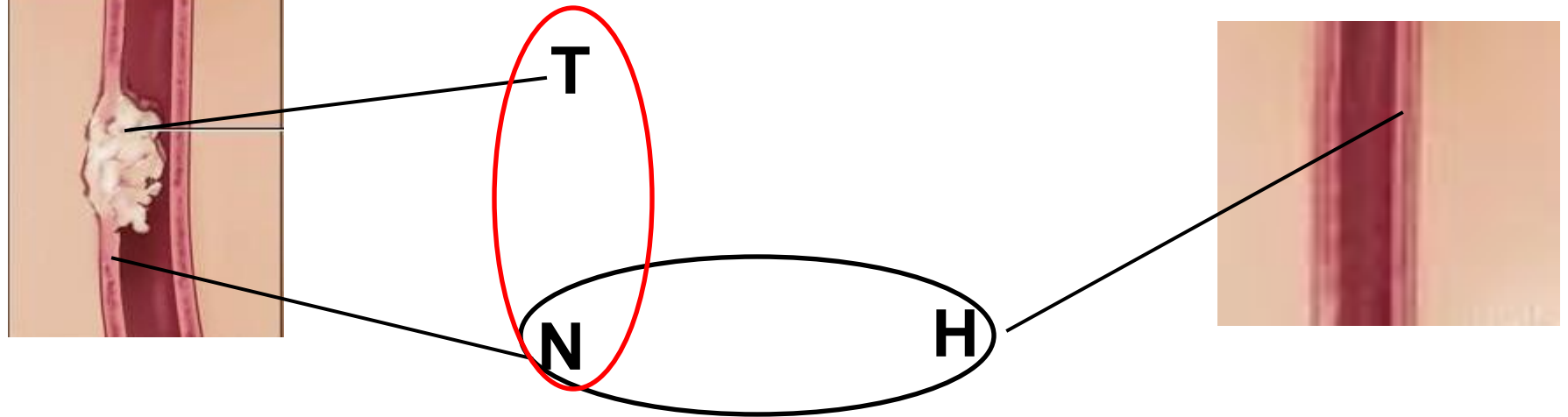


Comparisons performed

ESCC patients



Vonluteers without cancer



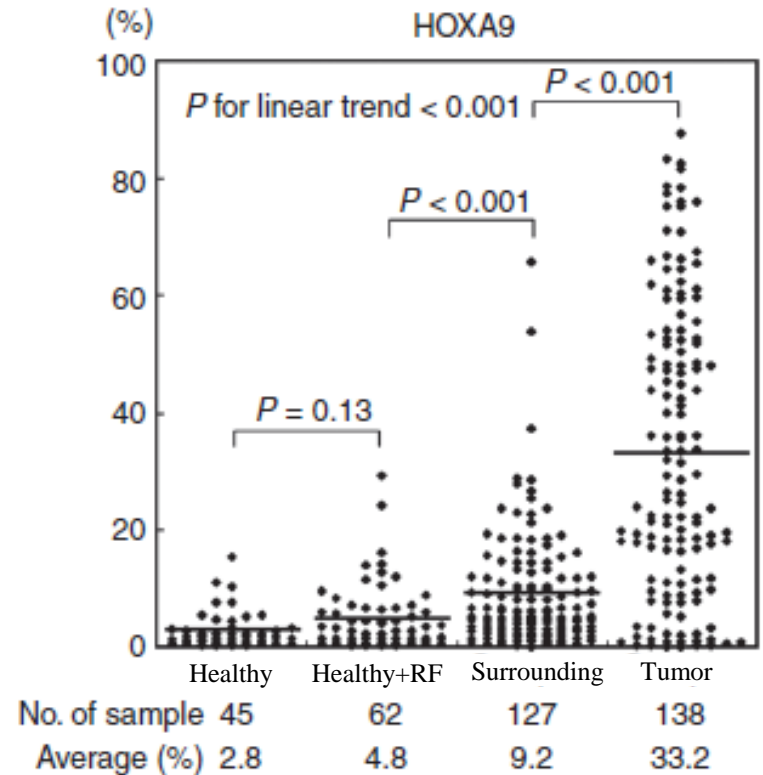
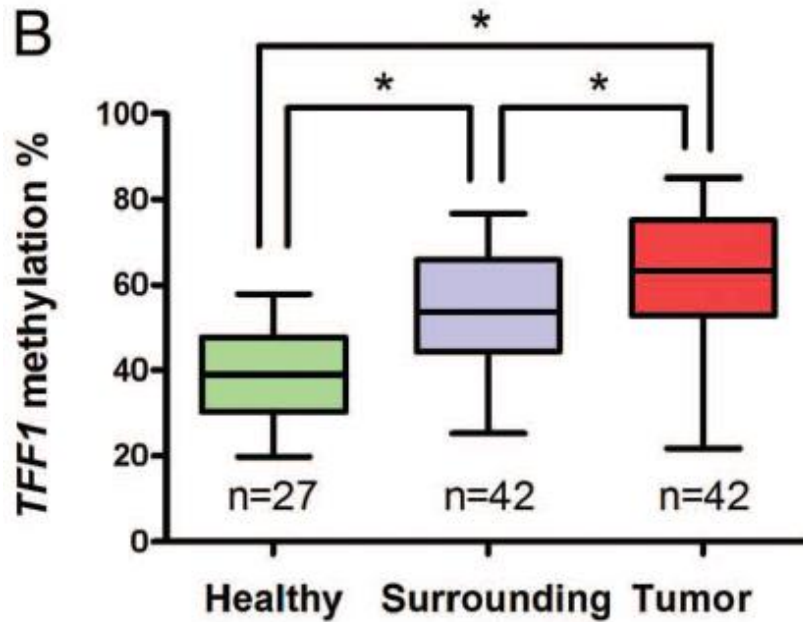
T – Tumor

N – Non-tumor adjacent tissue

H – Healthy esophageal mucosa

Field cancerization in the Esophagus

Epigenetic alterations



Objectives of genome wide methylation studies

Identify potential epigenetic drivers in ESCC

Complement genetic data on altered signalling pathways

Identify potential early diagnosis biomarkers

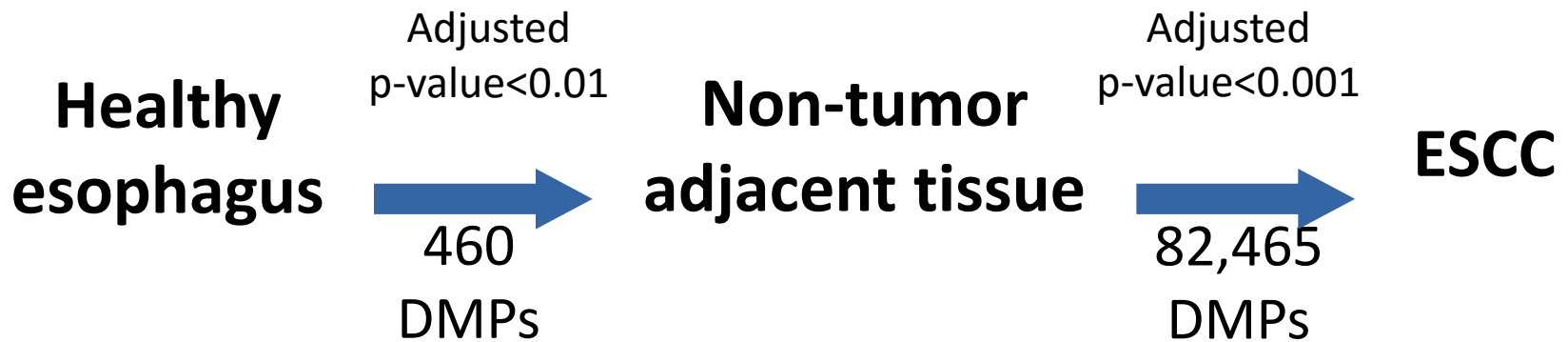
Identify novel potential druggable targets

Analyse potential etiological specific associated methylation signatures

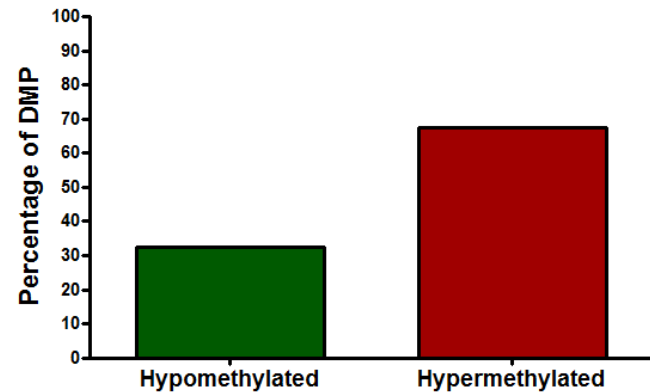
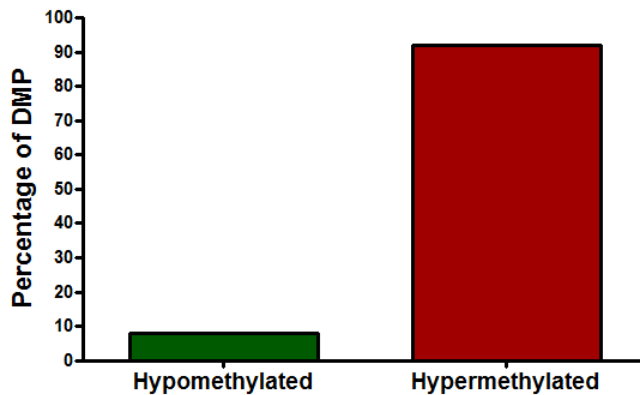
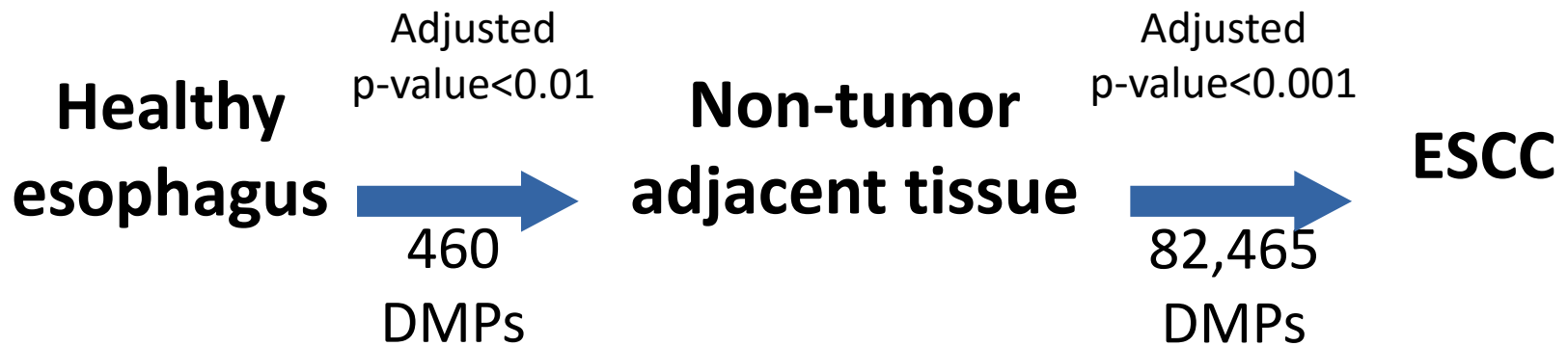
Profile of the individuals included in the study

	Healthy Individuals	ESCC patients
Healthy mucosa	7	
Non-tumor adjacent tissue		17
Tumor		24
Gender		
Female	4 (57%)	21 (87%)
Male	3 (43%)	3 (13%)
Age		
Median	54.5	56
Minimum	38	39
Maximum	63	77

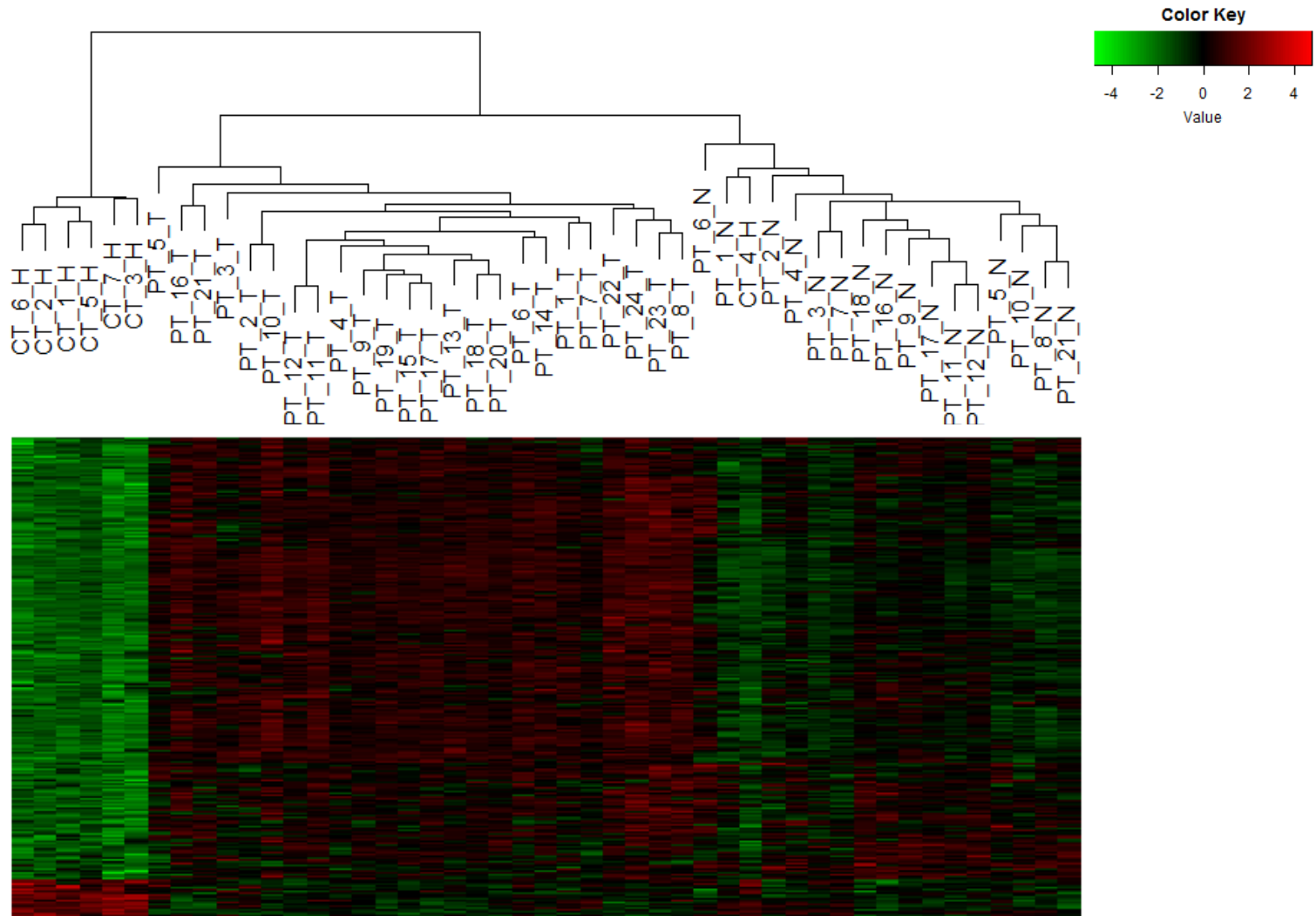
Number of differentially methylated probes in each comparison



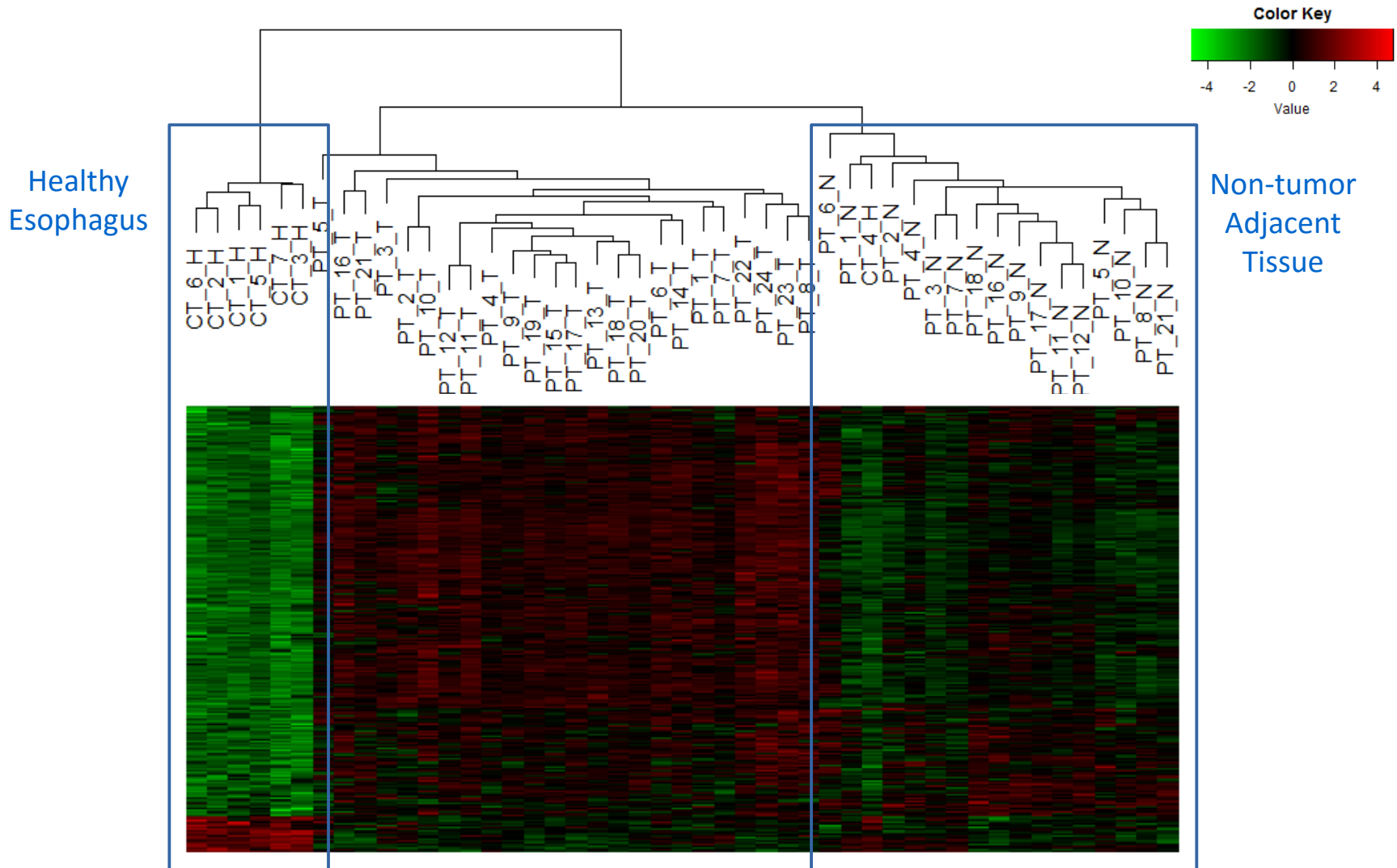
Number of differentially methylated probes in each comparison



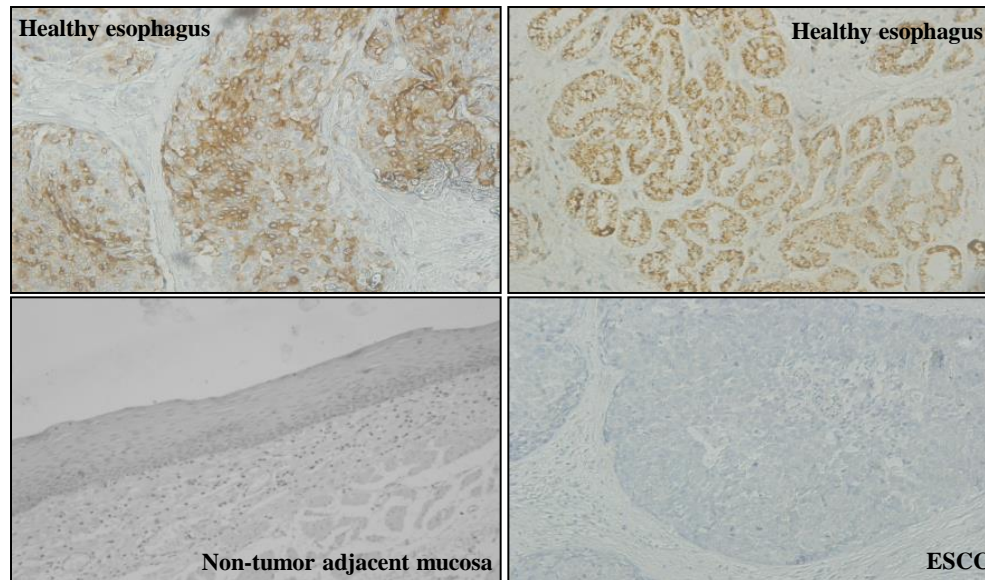
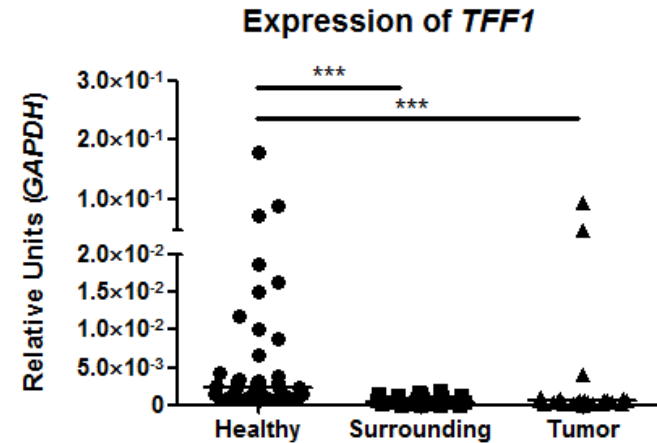
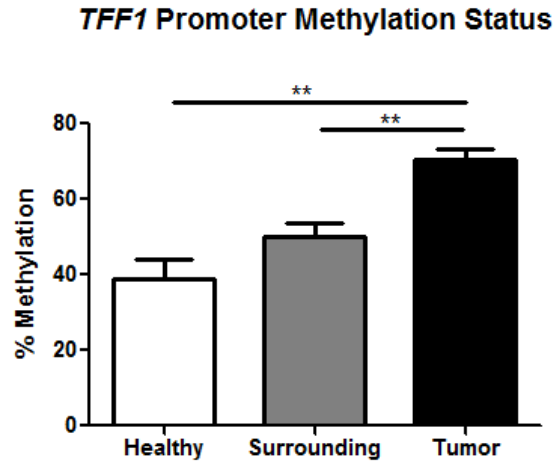
Healthy vs Non-tumor Adjacent Tissue



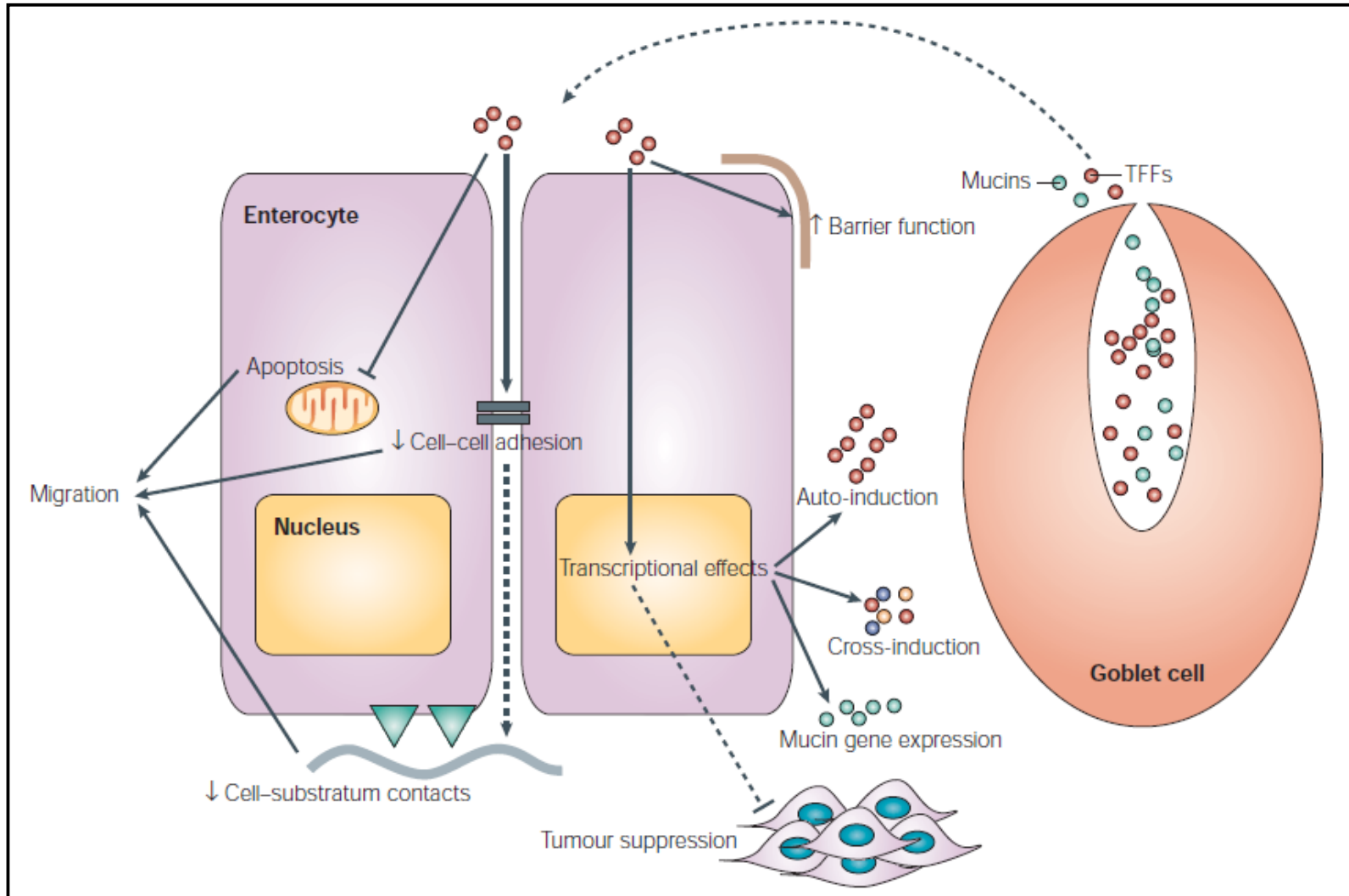
Healthy vs Non-tumor Adjacent Tissue



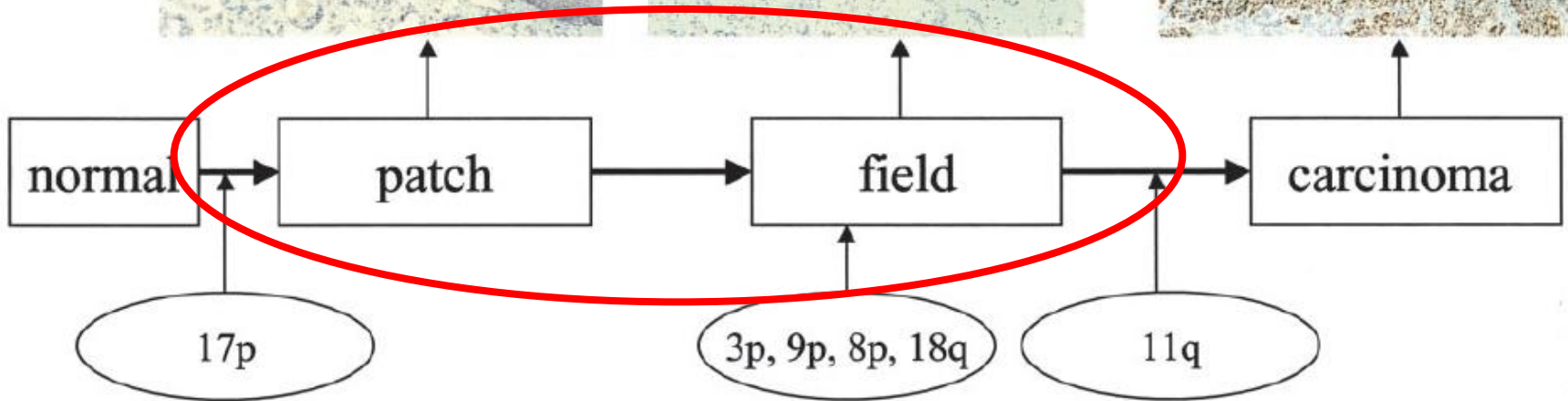
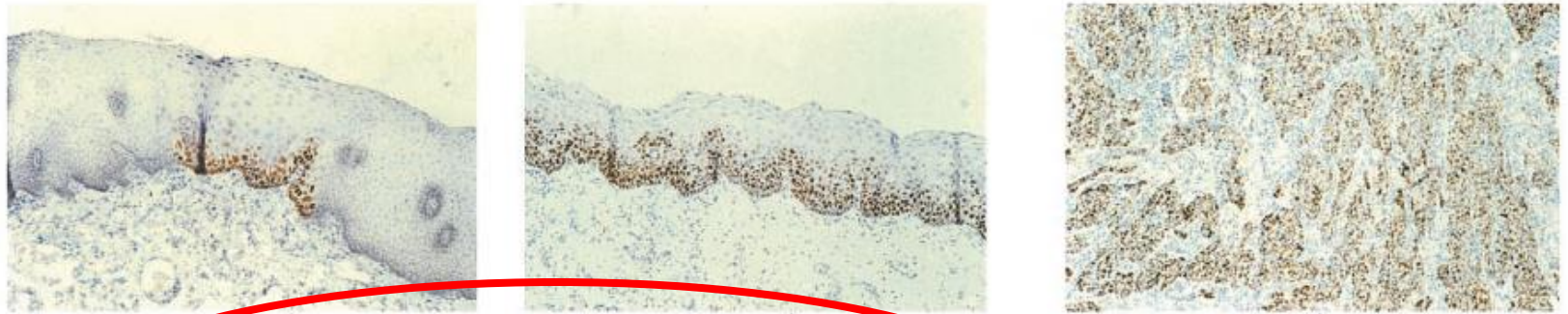
TFF1 alterations in non-tumor adjacent mucosa and ESCC



TFFs: protectors of the mucosa



Putative pathways involved in esophageal carcinogenesis

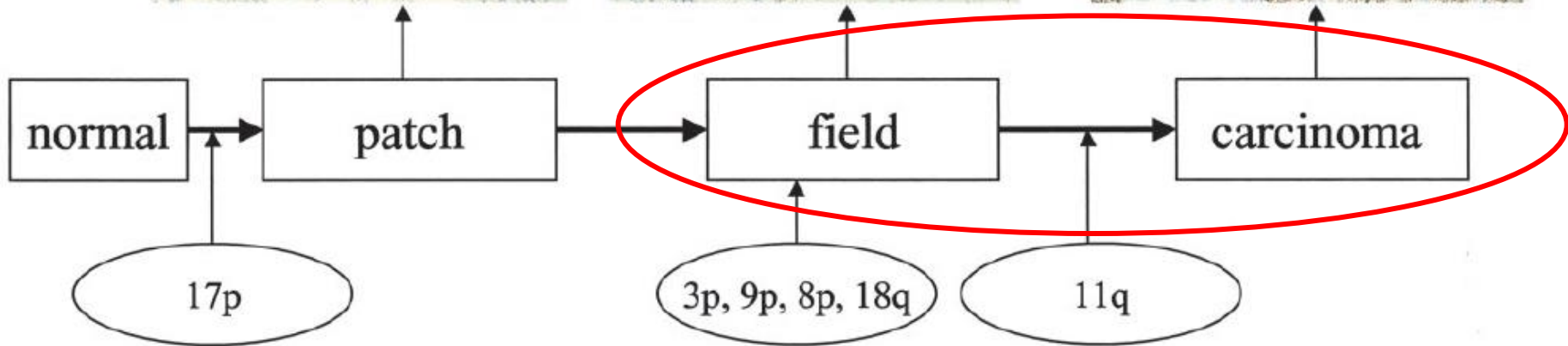
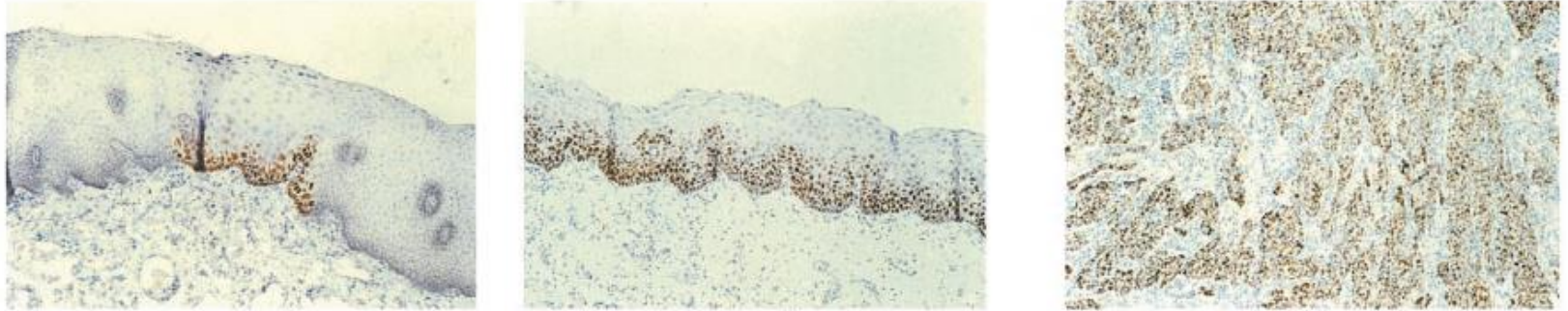


***TFF1* promoter hypermethylation
BCL3 gene body hypermethylation**



**Loss of mucosa protection
Resistance to apoptosis**

Putative pathways involved in esophageal carcinogenesis



***IL6* promoter hypermethylation**
***DSG1* promoter hypermethylation**
***FBXL7* gene body hypomethylation**



Inflammatory stimuli to proliferation and survival
Loss of cell adhesion/differentiation
Resistance to apoptosis/Induction of cell proliferation

Questions and difficulties

Are there epigenetic drivers in ESCC?

What is the intra-tumor methylation heterogeneity in ESCC?

Are most of methylation alterations produced by etiological factor transitory or permanent?

Can we perform an unique and large Genome Wide Methylation Study with different ESCC patients exposed to different etiological factors?
(Unique protocols, funding, etc...)

Can we identify etiological specific associated methylation profile in ESCC?

Can we use methylation data to develop non-invasive early diagnosis biomarker and adjuvant epigenetic therapy?

Thank you

Obrigado