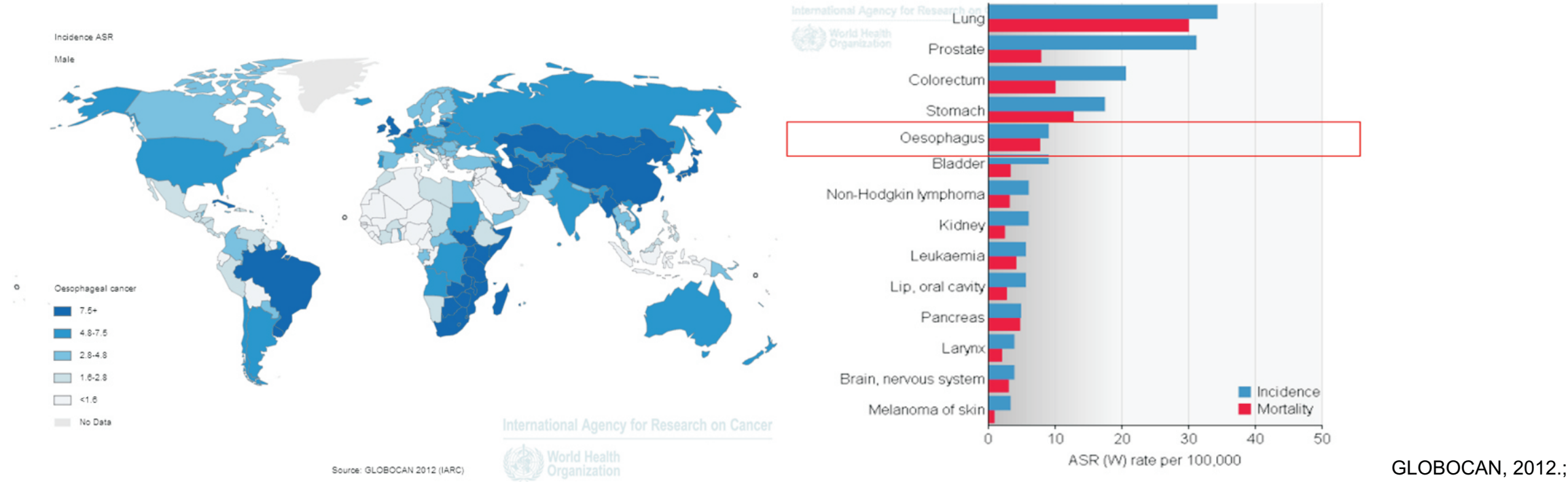


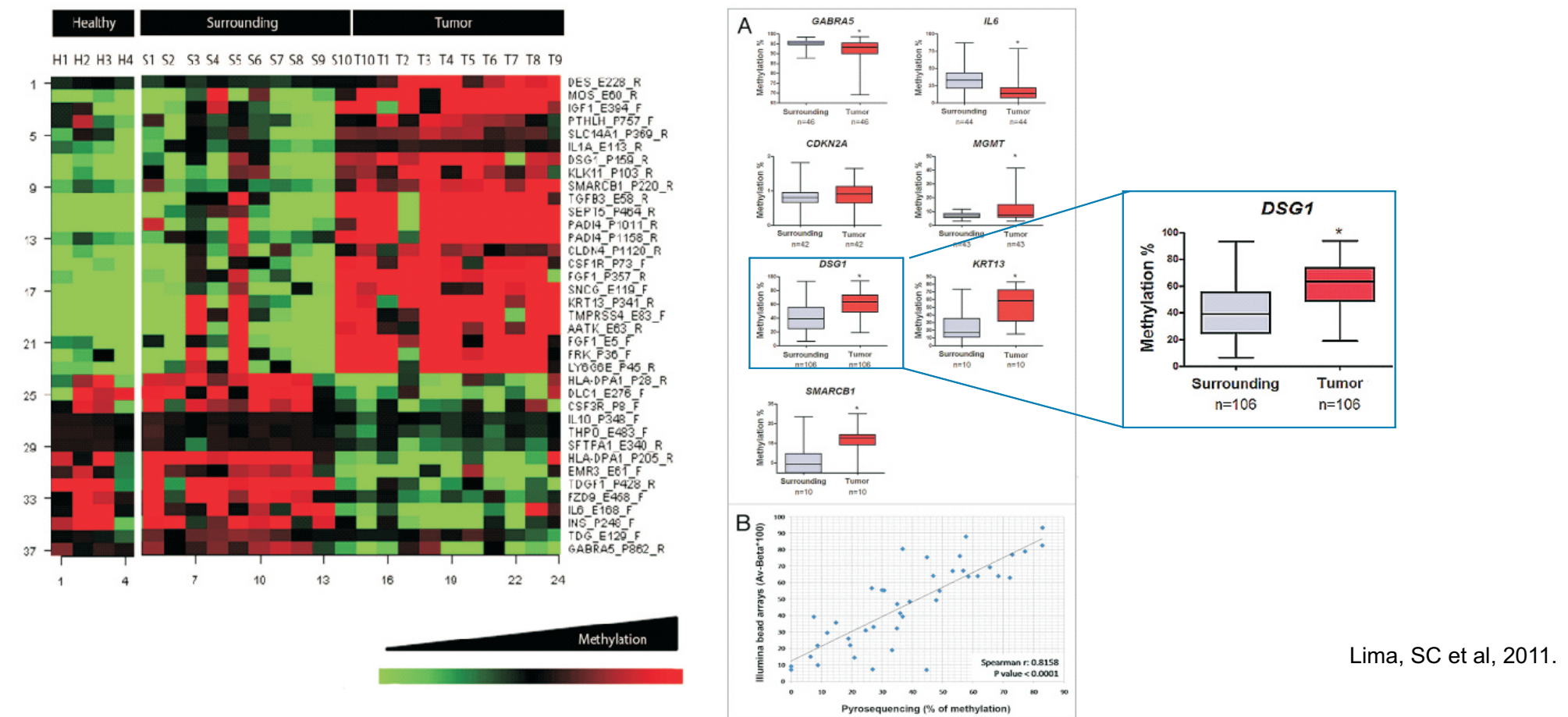
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INTRODUCTION

- Esophageal cancer (EC) is one of the ten most frequent tumors worldwide.
- EC Five-year overall survival is lower than 20% in Brazil and worldwide, what is a consequence of the lack of symptoms in the early stages of the disease, causing a late diagnosis and inefficient treatment.



- A previous study from our group identified a hypermethylation of DSG1 promoter in ESCC, in comparison with the non-tumor surrounding tissue.



- Esophageal squamous cell carcinoma (ESCC) accounts for around 80% of all EC cases.

OBJECTIVE

To evaluate the presence of *DSG1* molecular alterations in ESCC

METHODS

Imunohistochemistry; RT-qPCR; pyrosequencing; 5-Aza-2'deoxyctidine treatment.

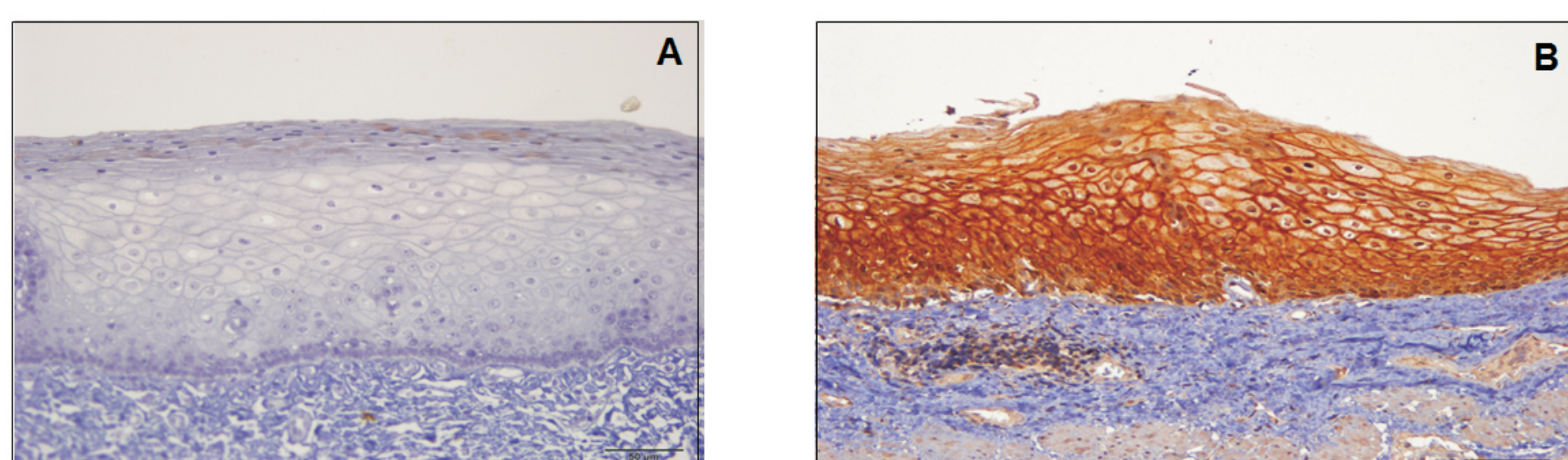
RESULTS

Characteristics of the individuals included in this study

	FFPE	Fresh tissue
Total number	25	36
Age	Median: 57 (39 - 74)	Median: 58,7 (39 - 77)
Gender	M - 14 (58,3%) F - 10 (41,7%) MD - 1	M - 27 (75%) F - 9 (25%) MD - 0
Differentiation	<i>In situ</i> and Well - 1 (4%) Moderately - 19 (76%) Poorly - 5 (20%)	<i>In situ</i> and Well - 0 (0%) Moderately - 26 (72,2%) Poorly - 10 (27,8%)
Tumor stage	I and II - 3 (30%) III and IV - 7 (70%) MD - 15	I and II - 2 (11,8%) III and IV - 15 (88,2%) MD - 19
Analyses performed	IHQ - 25 RT-PCRq - 0 Pyrosequencing - 0	IHQ - 0 RT-PCRq - 36 Pyrosequencing - 36

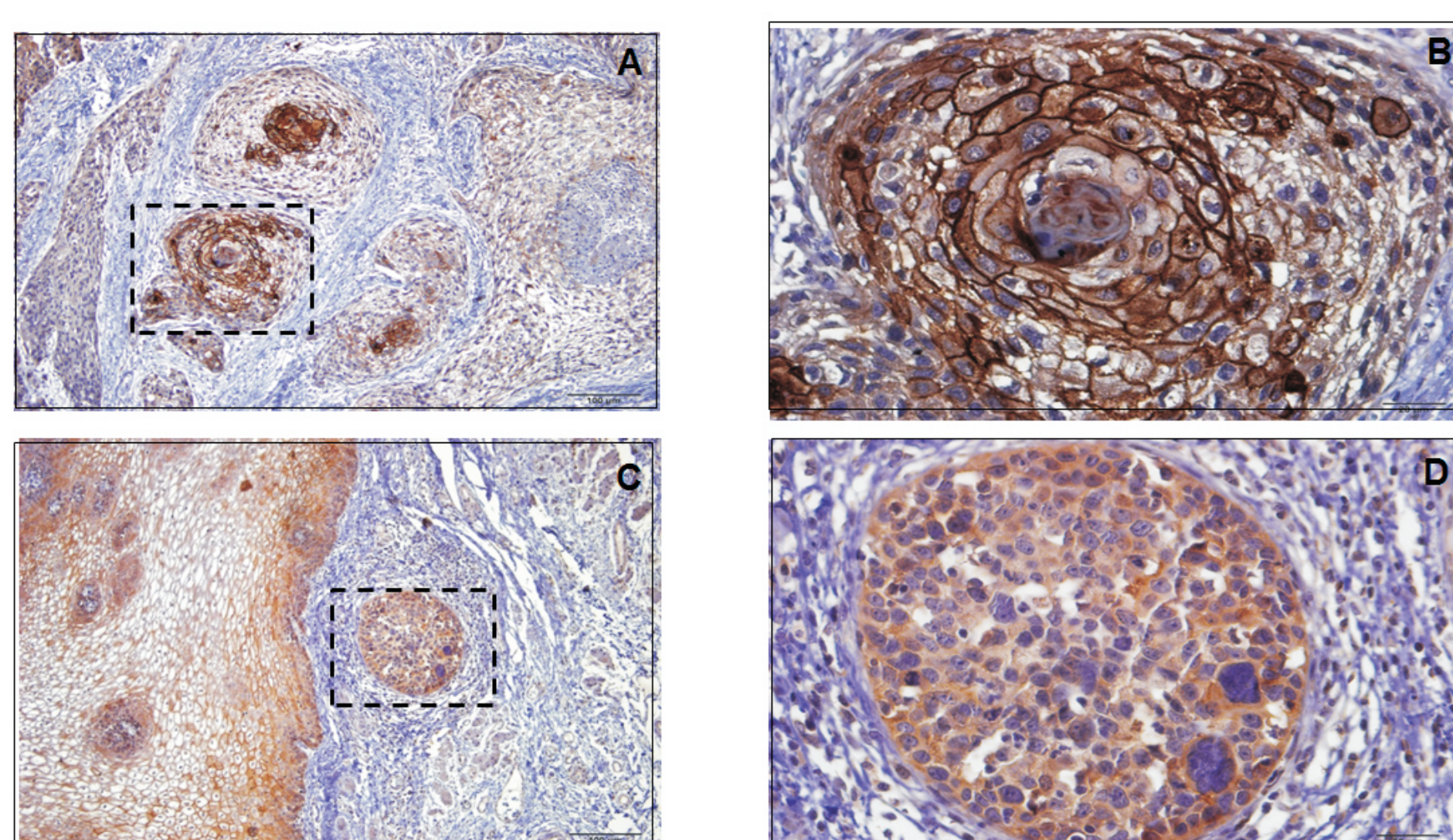
Note: MD: Missing data; The percentages were calculated considering only the patients with available information.

DSG1 protein expression in healthy individuals



DSG1 protein expression in healthy esophageal tissue. (A) Negative control; (B) Positive control with cytoplasmic staining in the basal layer, membrane and cytoplasmic staining in the suprabasal layers and membrane staining in the apical layers.

DSG1 protein expression in CEE



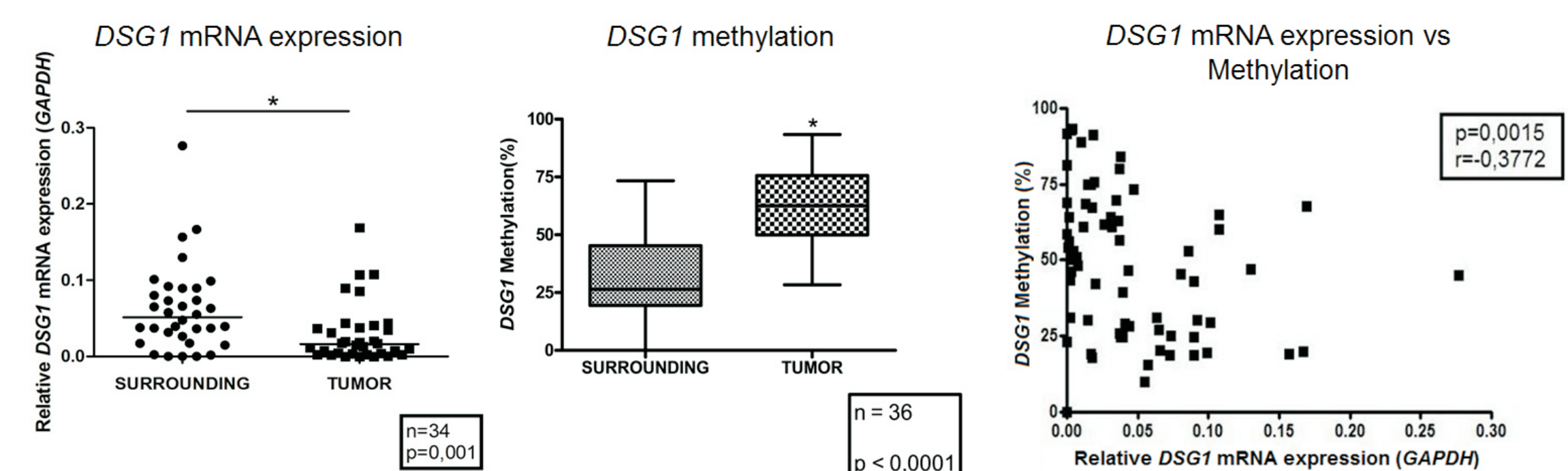
DSG1 protein expression in ESCC. (A) Tumor with heterogeneous staining; (B) Tumoral island with different staining patterns, depending on the cellular differentiation; (C) Epithelial tissue with invasion area, homogeneous membrane staining pattern on most of the tumoral area; (D) Tumoral invasion showing cytoplasmic staining and cellular atypia;

Score	Membrane staining (percentage of cases)	Cytoplasmic staining (percentage of cases)
0	28%	0%
1	32%	12%
2	20%	8%
3	12%	20%
4	8%	60%
Total	100%	100%

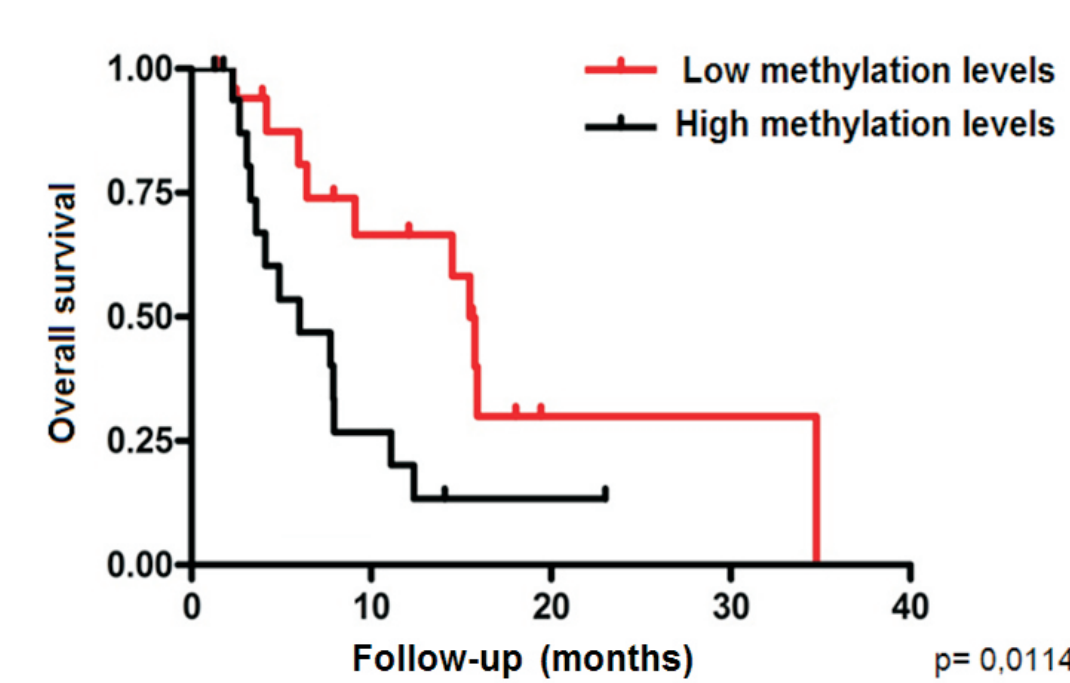
CONCLUSION

- This is the first study to show that the downregulation of *DSG1* expression might be a consequence of its promoter hypermethylation in ESCC and might be associated with cellular differentiation.

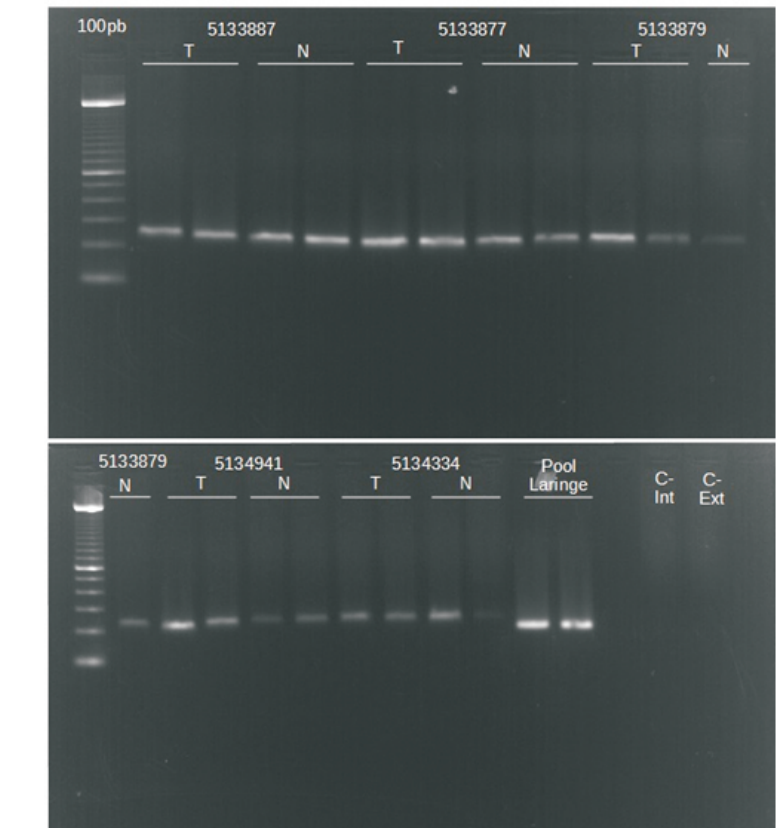
DSG1 gene expression and promoter methylation in ESCC



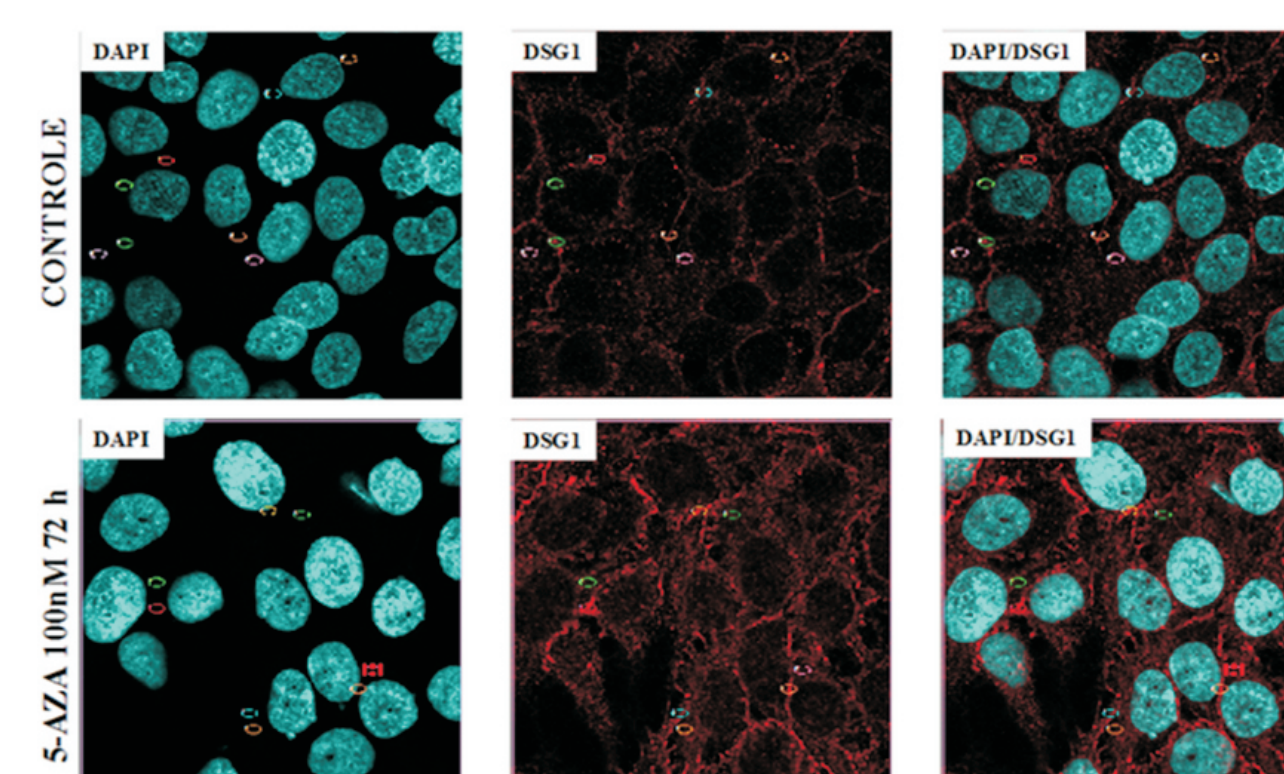
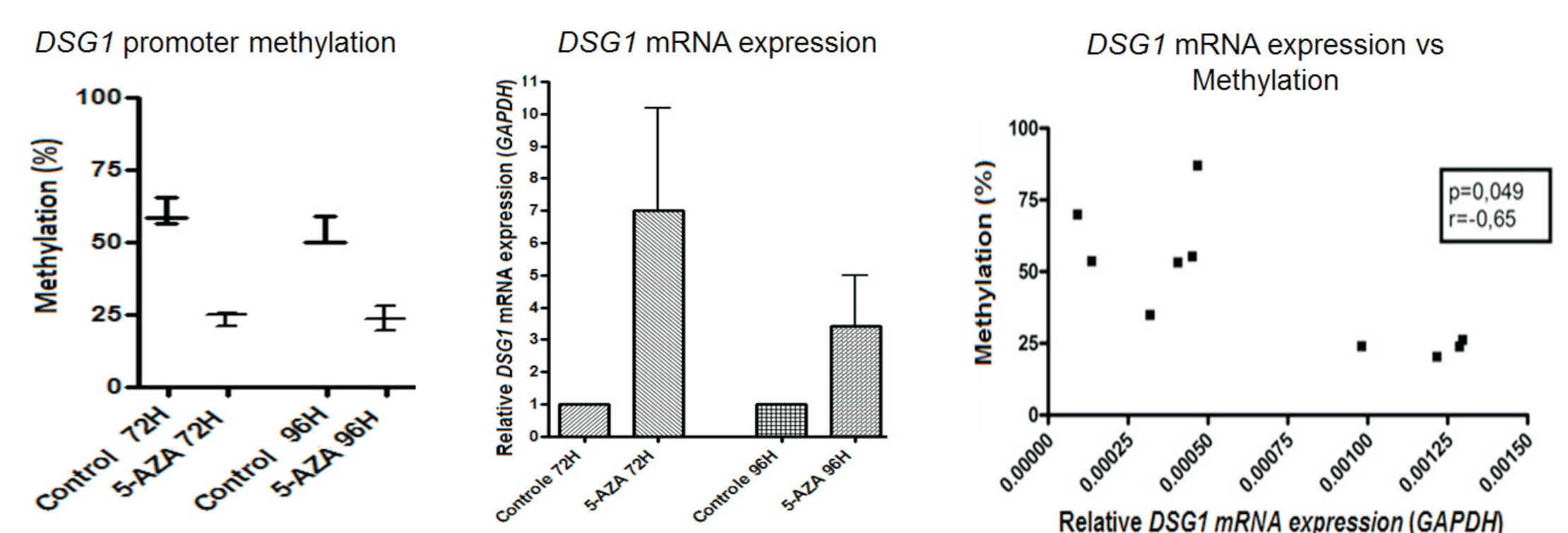
DSG1 methylation and survival



mRNA expression of DSG1 isoform



5-aza-2'deoxyctidine treatment in CEE cell line



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