

Actin-Associated Gene Expression is Associated with Early Regional Metastasis of Tongue Cancer

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Introduction & Objectives

■ Regional metastasis of Oral cancer

- In oral cancer, 6% to 85% of cases are known to have regional metastasis.
- Since the presence and extension of **neck lymph node metastasis** are the **most significant prognostic factors**, biopsy of sentinel lymph node, elective neck dissection, radiation therapy, and observation are possible treatment option for clinically node negative oral cancer.

■ Limitation of DOI

- Several clinicoradiologic parameters are suggested and one of the most important prognostic parameters is the **depth of invasion** of the primary tumor.
- However, the limitation of using the depth of invasion cutoff is the **difficulty in obtaining this information preoperatively**.
- Elective neck dissection has been part of the treatment of patients with clinically node negative squamous cell carcinoma of the oral tongue

■ Objectives

- We aimed to analyze the **genetic difference** between **early and late cervical lymph node metastasis** in oral tongue cancer patients and to suggest genetic background for **choosing eligible patients for elective neck dissection**.

Materials and Methods

■ TCGA Data Analysis

- **All genomic data** for Head and Neck Squamous Cell Carcinoma(HNSCC) from oral tongue were obtained from **The Cancer Genome Atlas (TCGA)** Data Portal
- **Gene-level gene expression** data from mRNA sequencing were included in the analyses.
- **Clinical data** for TNM stage were included. According to the T and N stage, following two groups
- Group 1: T1/2 and N2/3 (n = 41)
- Group 2: T4 and N0 (n = 65).

■ Differentially Expressed Gene Analysis and Gene Ontology Enrichment/KEGG Pathway Analysis

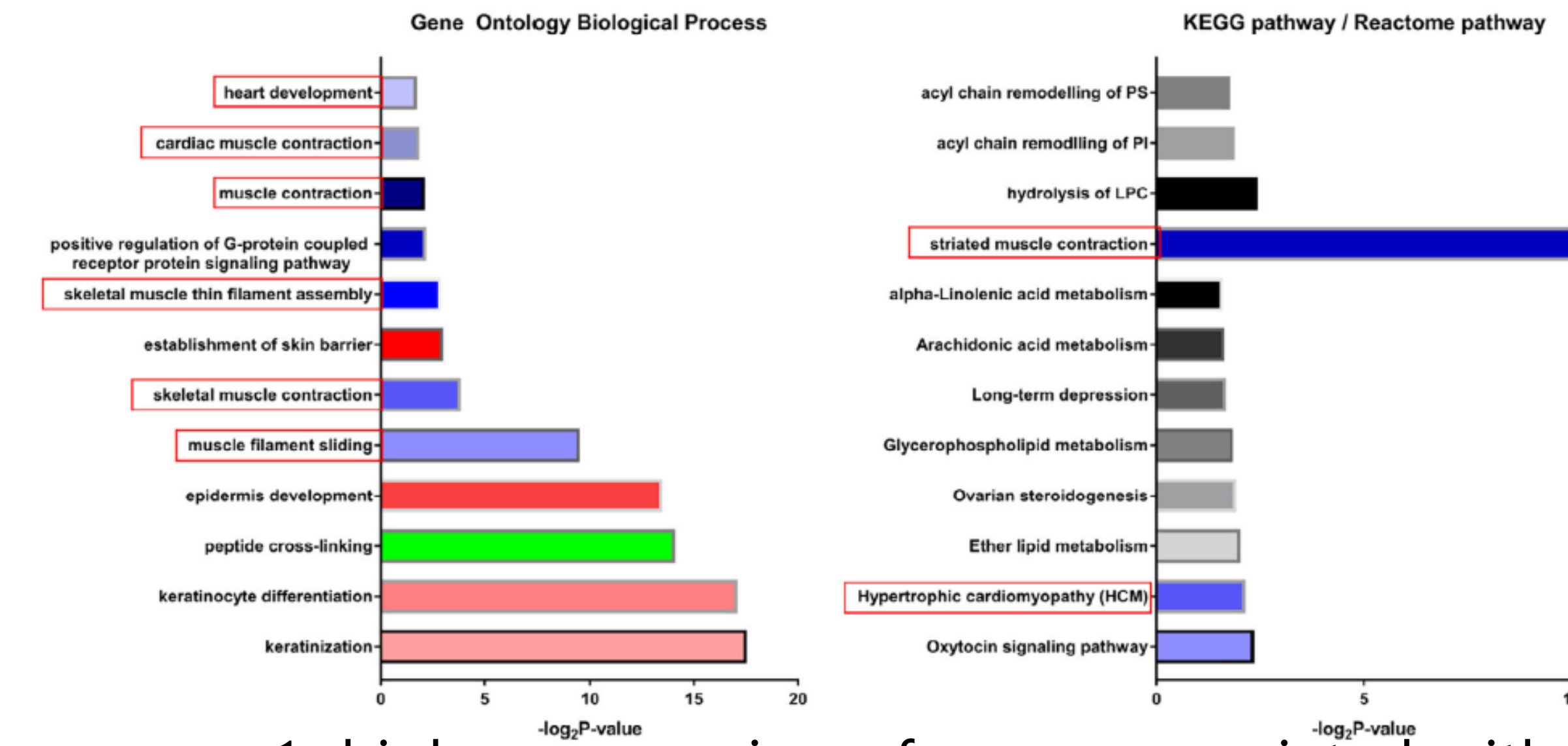
- R package
- **Differentially expressed genes** (DEGs) between the **N0** and **N+** groups were identified
- The Database for Annotation, Visualization, and Integration Discovery (**DAVID**) web-based program
- gene ontology (GO) enrichment analysis
- **KOBAS 3.0** software
- KEGG pathway analysis and functional annotation for DEGs

■ Validation Study

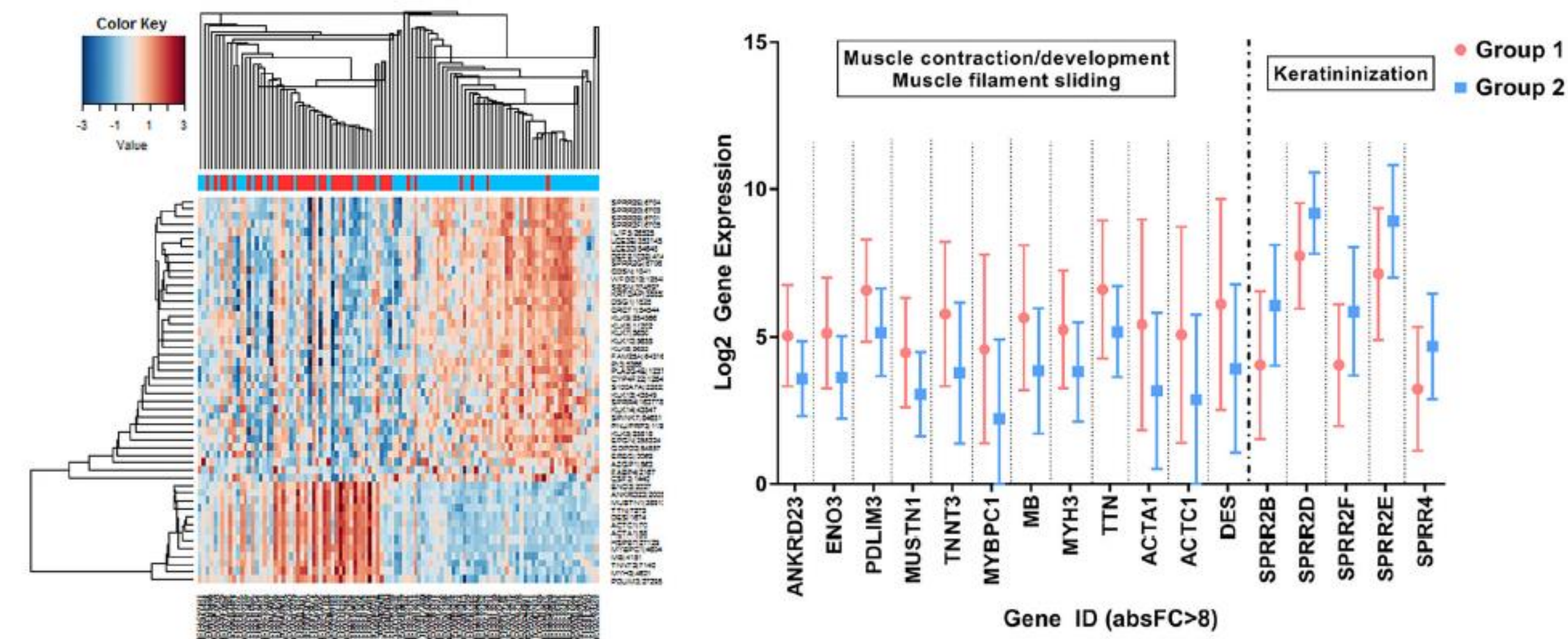
- Retrospective review the pathological data
- 285 patient diagnosed with SqCC of mobile tongue
- **Group 1: T1/2 and N2/3 (n = 36)**
- **Group 2: T4 and N0 (n = 25)**
- Formalin-fixed paraffin embedded (FFPE) block was subjected into immunofluorescence and immunohistochemical analysis

■ Differentially Expressed Gene Analysis and Gene Ontology Enrichment/KEGG Pathway Analysis

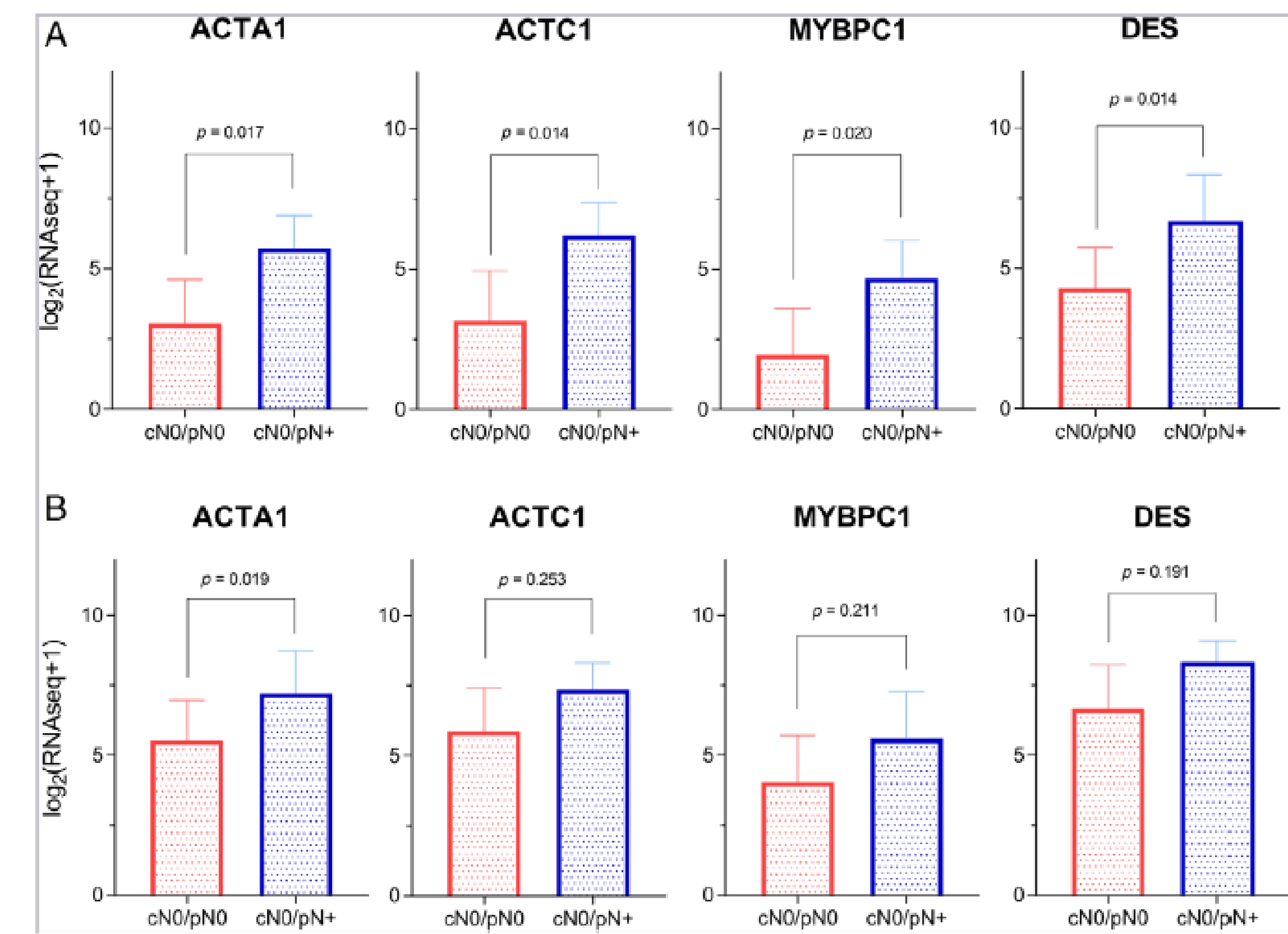
- biological process associated with keratinization, keratinocyte differentiation, muscle contraction and peptide cross-linking was highly expressed.



- group 1: higher expression of genes associated with muscle contraction / lower expression of keratinization than group 2

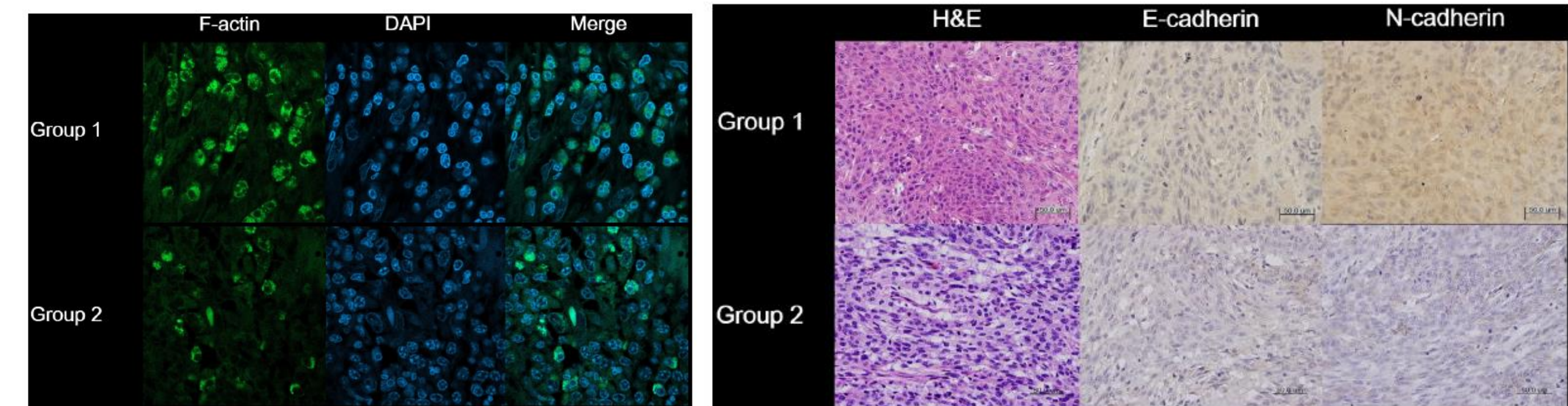


- Chosen 4 genes: ACTA1, ACTC1, MYBPC1, DES
- Comparison 2 groups: cN0/pN0 and cN0/pN+
- cN0/pN+ → T1-4 tumors: ACTA1, ACTC1, MYBPC1, DES overexpression
- T1-2 tumors: ACTA1 overexpression



■ Validation Study

- Immunofluorescence analysis. Phalloidin was highly expressed in group 1 than group 2
- Immunohistochemical analysis. There was no significant difference in E-cadherin and N-cadherin expression in groups 1 and 2.



Conclusion

Genes associated with cytoskeleton, especially ACTA1, is over-expressed in tongue cancer with early regional metastasis. The gene can be the surrogate or adjunctive marker for selecting elective neck dissection of clinically N0 tongue cancer patients.

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