

## **Supplementary Figure legends**

**Supplementary Figure 1. p16 immunohistochemistry thresholds.** Panels are representative of p16 quantitative analysis; % of cells with strong nuclear staining in the upper right hand corner of each panel.

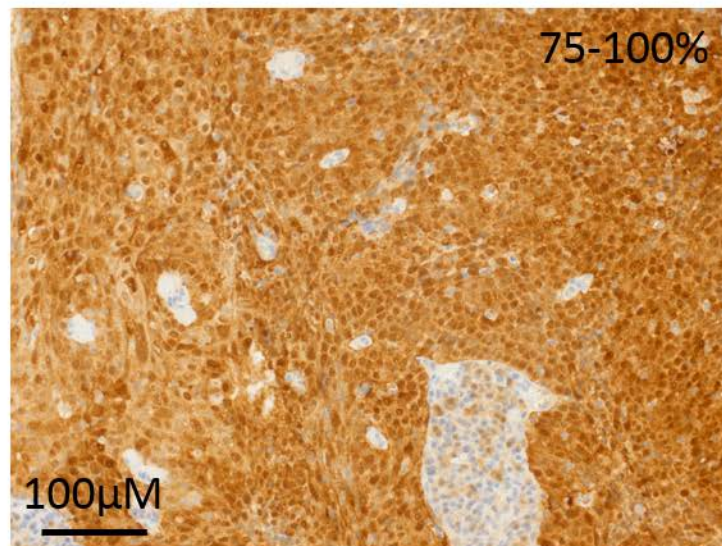
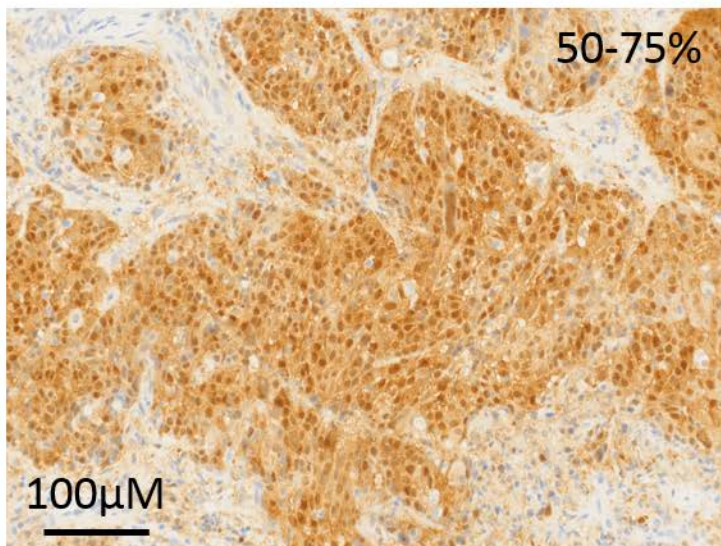
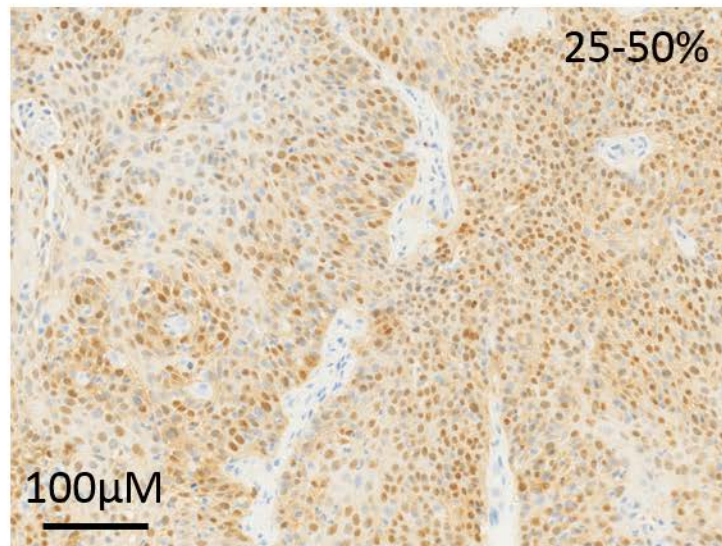
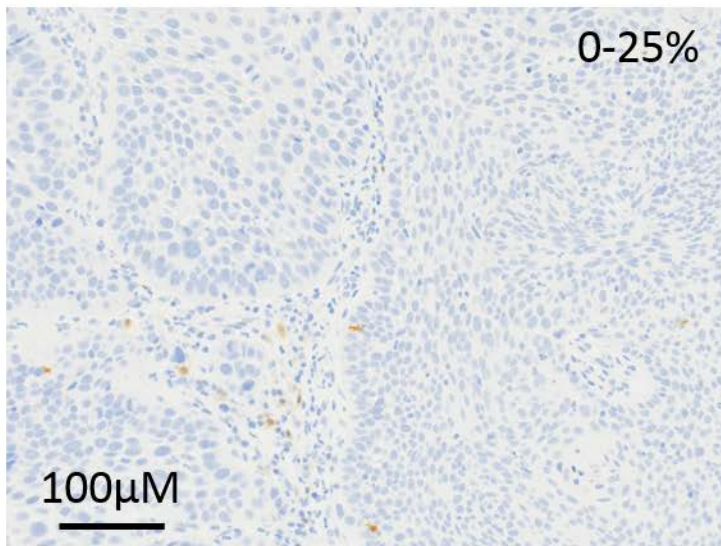
**Supplementary Figure 2. Impact of T and N classification on overall survival (OS) and disease free survival (DFS).** Analysis performed using Kaplan-Meier analysis coupled to log-rank test.

**Supplementary Figure 3. Impact of tobacco exposure on overall survival (OS), disease free survival (DFS) and locoregional control (LRC).** Analysis performed using Kaplan-Meier analysis coupled to log-rank test.

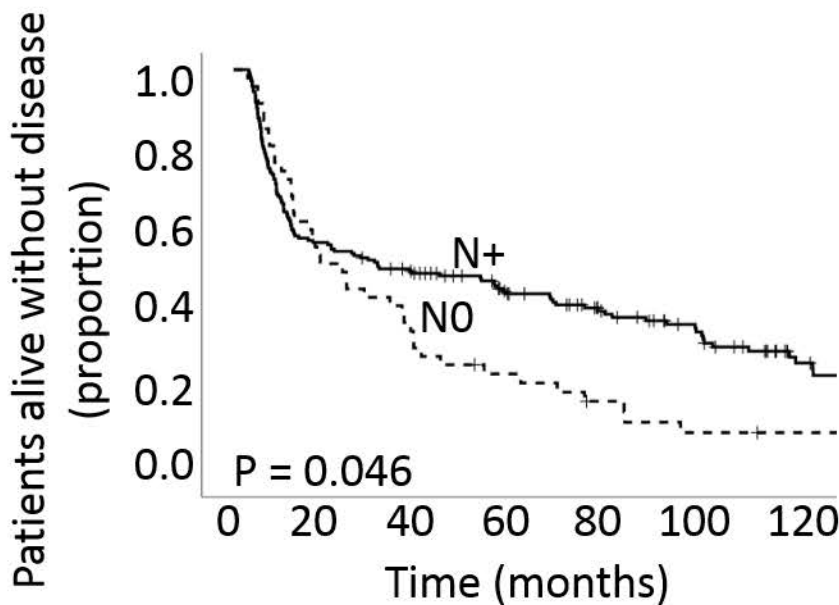
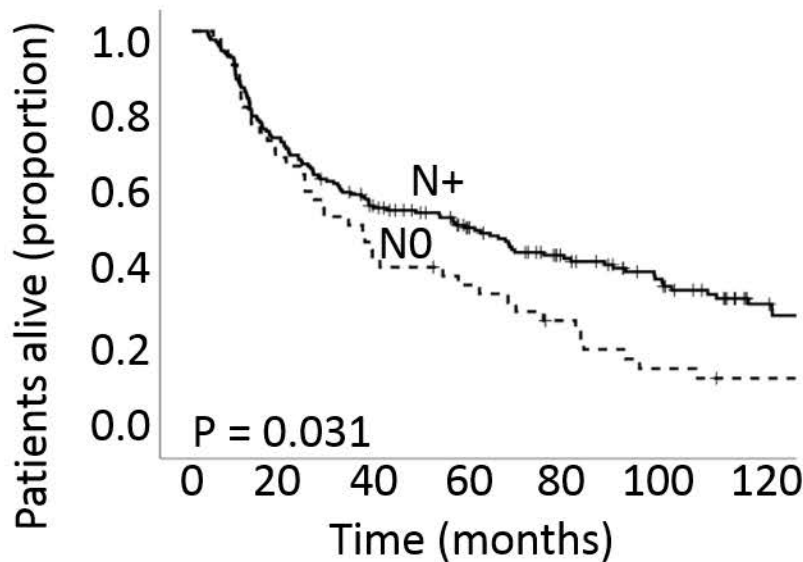
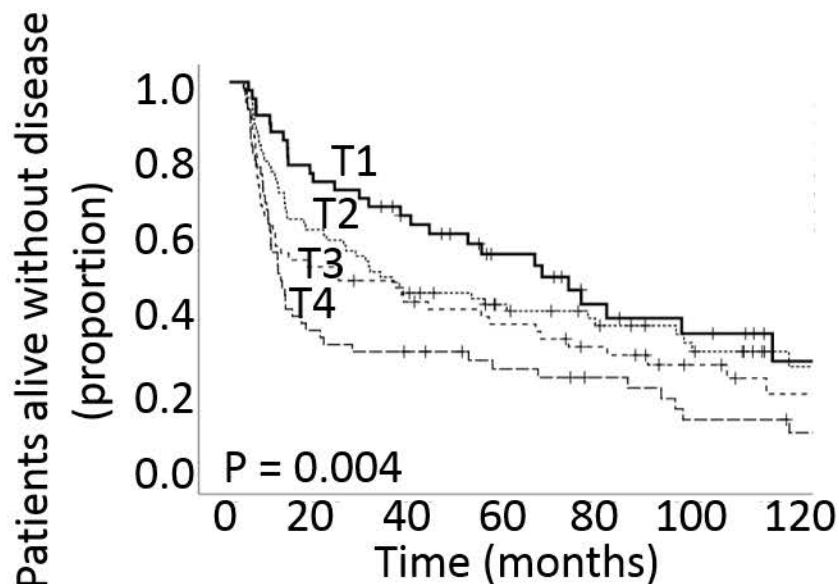
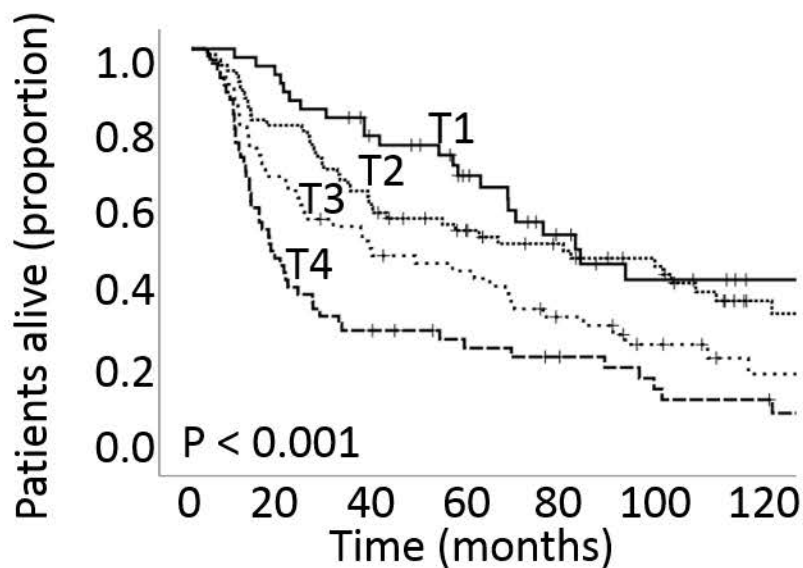
**Supplementary Figure 4. Temporal shifts in overall survival (OS) and locoregional control (LRC).** Analysis performed using Kaplan-Meier analysis coupled to log-rank test.

**Supplementary Figure 5. Biological signature of OPSCC.** A) Common DEGs shared by tumors as a function of p16, tobacco exposure and multinucleation. B) Common DEGs shared by tumors as a function of MN and SpaTIL algorithm defined risk categories. LR= low risk by specific feature, p16 positivity or tobacco exposure; HR= high risk by specific feature, p16 negativity or tobacco exposure

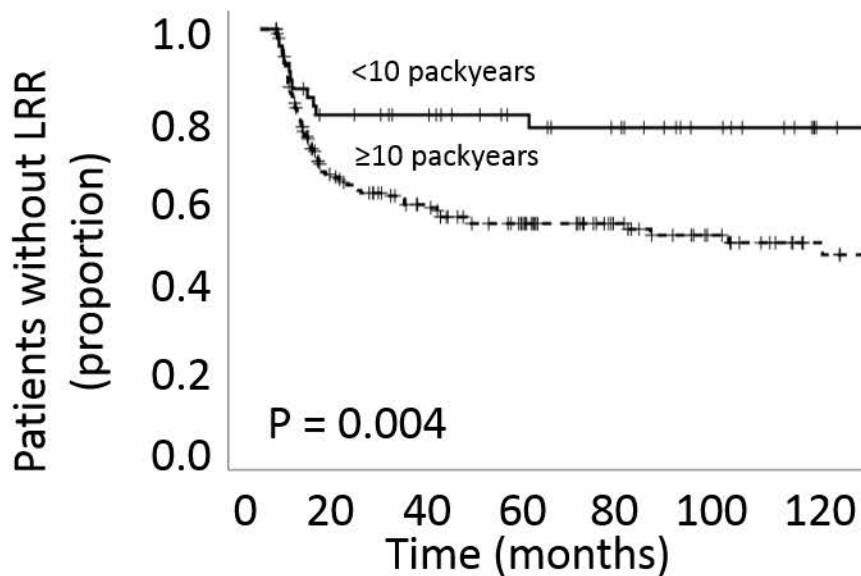
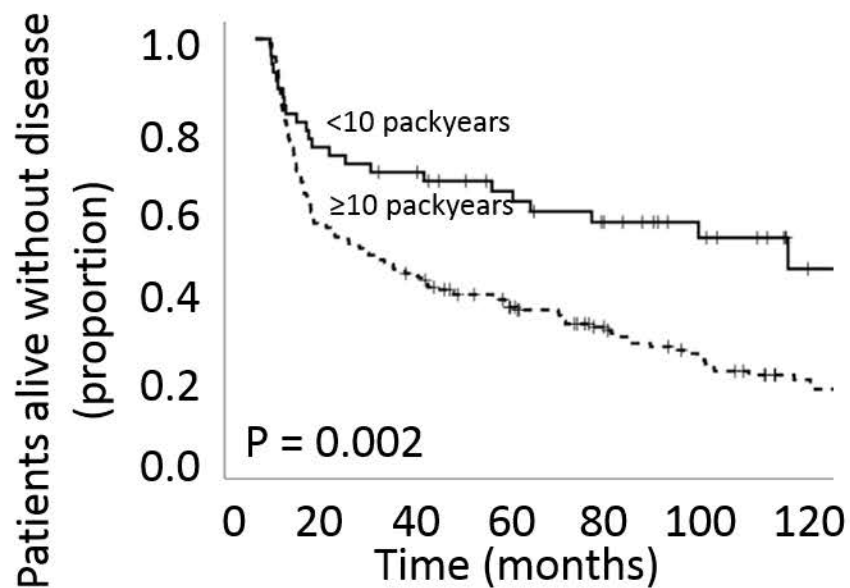
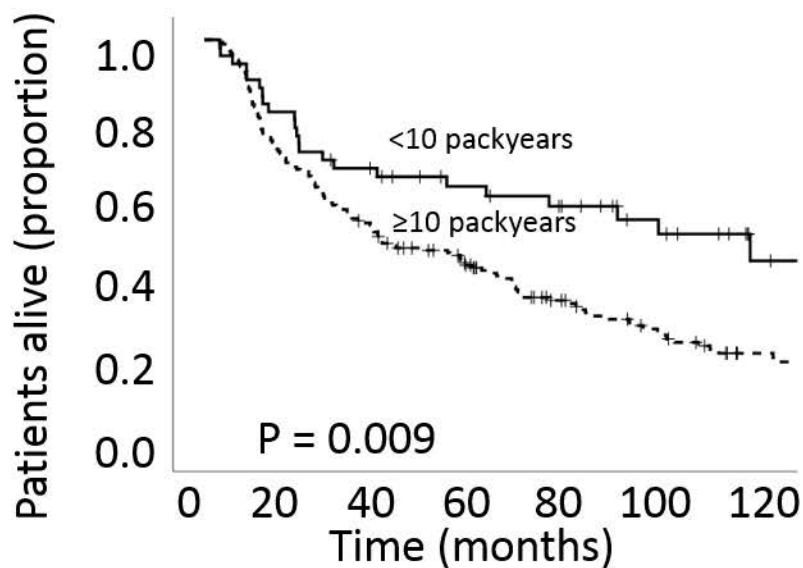
# Supplementary figure 1



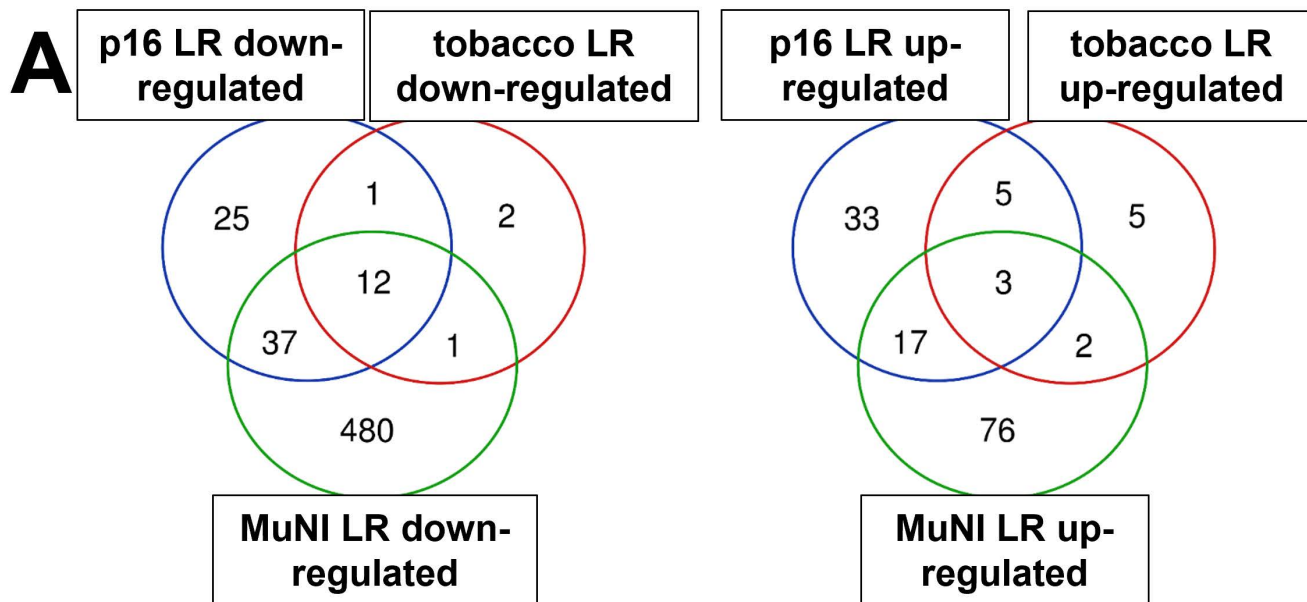
## Supplementary figure 2



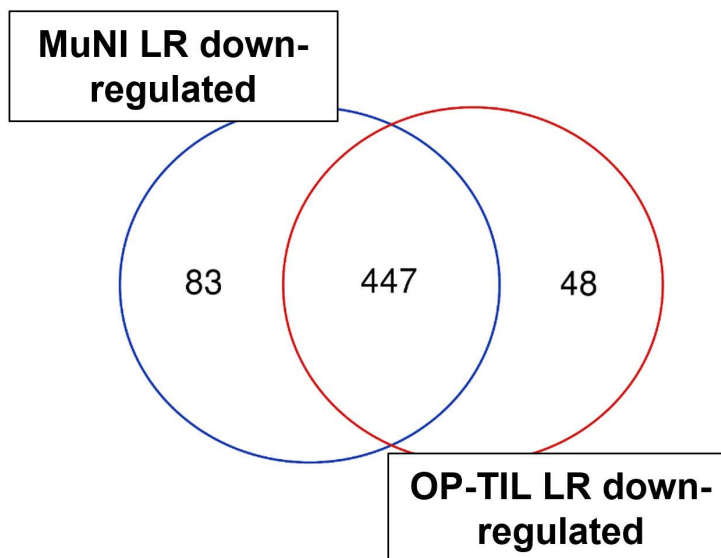
# Supplementary figure 3



# Supplementary figure 5



**B**



## Supplementary figure 4

