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Chaperone-mediated Autophagy Markers LAMP2A and HSC70 Are Independent Adverse Prognostic Markers in Primary Resected Squamous Cell Carcinomas of the Lung

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Purpose of the study: LAMP2A and HSC70 are crucial players in chaperone-associated autophagy (CMA), a process of specific, targeted, lysosome-dependent degradation of proteins. CMA is crucial to maintain cell homeostasis and is frequently upregulated in cancer. Blockage of CMA may be therapeutically exploited. We aimed to evaluate the expression patterns and any prognostic significance of LAMP2A and HSC70 in pulmonary squamous cell carcinomas (pSQCC).

Methods: LAMP2A and HSC70 were analysed by immunohistochemistry in a consecutive cohort of 336 primary resected pulmonary squamous cell carcinomas using tissue microarrays (4 TMA cores from 2 different TMA blocks). Expression levels were determined by an immunoreactivity score (IRS) generated from the staining intensity and the percentage of positive tumour cells.

Summary of results: There was no significant intratumoural staining heterogeneity across the TMA cores. Moreover, no significant correlation between the two markers was seen. There was no association of marker expression with pathological parameters (pT category, pN category, TNM staging, grading). However, high LAMP2A and high HSC70 expression levels, defined as IRS levels above the 4th quartile, were associated with worse outcome, including overall survival (p=0.012 and p=0.001) and disease free survival (p=0.049 and p=0.036). Both markers were also independent adverse prognostic factors in multivariate analysis for overall survival (LAMP2A: HR=1.772; 95%CI 0.121-2.595; p=0.003; HSC70: HR=1.955; 95%CI 1.351-2.830; p<0.001) and disease free survival (LAMP2A: HR=1.528; 95%CI 1.066-2.191; p=0.021; HSC70: HR=1.482; 95%CI 1.047-2.098; p=0.027).

Conclusions: The CMA markers LAMP2A and HSC70 are variably expressed in pSQCC, and could be evaluated as predictive biomarkers for CMA-inhibiting therapy. High expression in untreated pSQCC presents an independent adverse prognostic factor.