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Title: The proteasome subunits PSMA5 and PSMB4 are potent markers to discriminate between typical and atypical carcinoid tumors of the lung

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Body: Introduction: 40S proteasome is an important player in tumorigenesis, cancer-induced immunoreaction and apoptosis. Differences in different expression levels of PSM subunits, especially of the catalytic chains, might be also important for drug sensitivity/resistance and is a potential drugable therapeutic target. A study was designed to test the expression levels of PSM subunit in different pulmonary tumors with neuroendocrine features, potentially resulting in a feasible predictive or diagnostic marker. Material and methods: 80 pulmonary tumors with neuroendocrine features (20 typical carcinoides, 20 atypical carcinoides, 20 LCLC, 20 SCLC) were tested for gene expression levels of PSMA1, PSMA5, PSMB4, PSMB5 and PSMD1. As internal reference genes, ACTB and GAPDH were used. Expression was determined by commercial available TaqMan-Assays (AoD). Results: All tested enzymes showed a strong correlation in expression pattern to each other ($p < 0.01$). No correlation to clinical data (age, gender) could be determined except PSMB4/sex ($p = 0.022$). PSMB4 seems to have the power to divide all different entities ($p = 0.043$), PSMA5 ($p = 0.024$ with exact "Wilcoxon Mann-Whitney Rank Sum Test") and PSMB4 ($p = 0.050$ with exact "Wilcoxon Mann-Whitney Rank Sum Test") show statistical significance to discriminate between typical and atypical carcinoid tumors. Conclusion: PSMA5 and PSMB4 seem to be powerful diagnostic tools to differentiate the aggressive and the non-aggressive neuroendocrine pulmonary carcinoids from each other. This may result in a useful diagnostic marker, lacking in the nowadays pathology.