AB009. OA01.09: Gene expression profile reveals new biomarker for novel diagnosis and therapy in thymic and pulmonary carcinomas

Djeda Belharazem[1], Michael Kuhn[1], Berthold Schalke[2], Peter Hohenberger[3], Alexander Marx[1]

[1]Institute of Pathology, University of Medicine Mannheim, Mannheim, Germany; [2]Department of Neurology, University of Regensburg, Regensburg, Germany; [3]Department of Thoracic Surgery, University of Medicine Mannheim, Mannheim, Germany

Correspondence to: Djeda Belharazem. Institute of Pathology, University of medicine Mannheim, 68167, Mannheim, Germany.
Email: djeda.belharazem@medma.uni-heidelberg.de.

Background: Squamous cell carcinoma (SCC) is an epithelial malignancy involving many anatomical sites and is the most common cancer capable of metastatic spread. Thymic squamous cell carcinomas are rare thoracic cancers and because of their relative rarity and close histologic similarity to pulmonary squamous cell carcinomas, thymic carcinomas might be misdiagnosed as lung carcinomas involving the mediastinum. Therefore, it is important to differentiate thymic SCC from lung SCC with mediastinal extension. In this effort, comprehension of the molecular alterations is urgently needed in both malignancies in order to identify molecular marker, which could be helpful for accurate novel diagnosis and therapy of thymic and lung carcinomas.

Methods: Gene expression profiling was achieved with affimetrix microarray. Six biopsies of thymic SCC and 9 lung SCCs were studied. Differential gene expression was analysed by ANOVA (JMP Genomics, version 4; SAS, Cary, NC, USA). Array-based gene expression in tumors was re-evaluated by qRT-PCR in two independent groups of each tumor cohort. The differential expressed genes were analysed on protein level using western blot and /or immunohistochemistry. Their regulation by microRNA 204 (miR204) was investigated using miR 204 mimitic in primary thymic carcinoma cells and in 1889c cell line.

Results: Ten pathways were described in this study. All two tumor cohorts were differentially enriched by all pairwise comparisons for pathways of focal adhesion, ECM receptor interaction, and regulation of actin cytoskeleton which was significant enriched in thymic carcinomas. The transcriptional misregulation, NF-κB signaling and apoptosis pathways were more dominant in pulmonary squamous cell carcinomas. Among the differential expressed genes stem cells related gene signature PAX1, PBX3, SPIC1 and FOXG1 were significant overexpressed in thymic carcinomas, while miR204 is rather downregulated and is associated with the negative regulation of the following genes RASSF6, FXYD6 and PAX1.

Conclusions: The major finding here is the so far unreported observation of different expression profiles of stem cells related genes in thymic and pulmonary SCCs and these findings suggest that thymic carcinomas suffer from overexpression of stem cell gene signature including PAX1, SPIC, PBX3 and FOXG1, which could be used as biomarker for the histopathology to distinguish the CD117 negative thymic and lung squamous cell carcinomas and for therapy application aiming to break treatment resistance in thymic cancers. The microRNA make-up in the current study defines decreased miR204, which might act as a tumor-suppressive gene in the tumorigenesis and progression in thymic SSC.

Keywords: Thymic and pulmonary squamous cell carcinomas and diagnosis; stem cell signature; microRNA 204