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[WCBIP] Biomarker analysis using bronchoscopic samples

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**Background.** 5-10% of asthma patients cannot be adequately controlled despite the use of all currently available therapeutic approaches. Selected miRNAs, including let-7a, miR-21 and miR-223 are emerging as important biomarkers and regulatory molecules involved in the pathogenesis of asthma. Further, the role of let-7a in lung inflammatory processes by modulation of TH2 responses, mainly by targeting IL-13 and IL-6, has been described in mouse models and several cell lines. Overexpression of let-7a reduces airway inflammation and airway hyper-responsiveness in lungs of induced mouse model of asthma. We therefore wanted to find out whether let-7a, miR-21 and miR-223 are differentially expressed in bronchial biopsies of severe asthmatics.

**Methods.** Twenty-four asthmatics treated at the University Clinic Golnik (2010-2012) were included. We divided them into two subgroups according to the asthma severity (GINA guidelines), 12 in mild asthmatic group and 12 in severe uncontrolled asthmatic group. They were in a stable phase of a disease, with no evidence of exacerbation in the past four weeks. As controls we used 10 patients with no known chronic disease, in six of them bronchoscopy was indicated because of prolonged cough that was finally attributed as a consequence of gastro-esophageal reflux disease (GERD) and four of them had hemoptysis with normal radiologic, endoscopic and lung function findings.

Bronchial biopsies were taken with flexible bronchoscope during diagnostic procedures and were immediately formalin fixed and then paraffin embedded using standard procedures. Total RNA was extracted from 10 FFPE tissue sections 5 mcm thick using the miRNeasy FFPE Kit following the manufacturer's instructions. Quantitative PCR was used to analyze the expression of selected miRNAs (let-7a, miR-21, miR223).

**Results.** We found significantly reduced expression of let-7a in patients with severe asthma in comparison to both, patients with mild asthma as well as to the control group ( $p < 0,05$ ). When comparing the entire group of asthma patients to the controls we didn't observe any difference in expression of let-7a (Figure 1). No significant differences in miR-21 and miR-223 expression were found between different groups analyzed.

**Conclusion.** Reduced let-7a levels in bronchial biopsies of patients with severe, therapy resistant asthma, could not only be used as a potential biomarker to discriminate between different asthma phenotypes, but also might be a potential novel therapeutic for rapid and fine tuned modulation of response at the inflammatory site for a group of patients that are most affected and still lack the efficient treatment.

