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Regulatory role of micro RNA in severe asthma

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Allergic asthma is a chronic inflammatory disease characterized by an airway hyper-responsiveness and a deregulated inflammation in response to allergens. Available treatments are mainly symptoms-driven and do not interfere with the natural history of the diseases. Severe asthma constitutes a challenging problem for the healthcare system. Its heterogeneity complicates the management of the disease. There is a significant need to understand the pathogenesis of severe asthma. Bronchial epithelium is considered a key player in coordinating airway wall remodeling. While in mild asthma, the epithelium is damaged and fails to proliferate and to repair in severe asthma the epithelium was reported to be highly proliferative and thicker. This may be due to different regulatory mechanisms. We studied microRNAs profile and evaluated their role in regulating proliferation of bronchial epithelial cells obtained from severe asthmatic subjects in comparison to cells obtained from mild asthmatics and healthy controls. We found that in mild asthma epithelial cells produce high amount of TGF β_1 and express high level of TGF β_1 -RI and phosphorylated-Smad3 indicating that TGF β_1 signalling is up-regulated. In severe asthma, this pathway was down-regulated. Thus, in epithelial cells from severe asthmatics compared to mild asthma and controls, miR-19a, a member of the miR-17~92 cluster is up-regulated and increases proliferation. Knockdown of miR-19a in epithelial cells reduces significantly their proliferation through targeting TGF- β downstream signaling. Our study uncovers a new regulatory pathway involving miR-19a that is critical to the severe phenotype of asthma and indicates that down-regulating miR-19a expression could be explored as a potential new therapy to modulate the epithelium repair in asthma.

Biography

Jamila Chakir is a Full Professor, Department of Medicine at Laval University and Institut Universitaire de Cardiologie et Pneumologie de Québec. She obtained a PhD degree in Immunology in France. She received Postdoctoral Research Training at Laval University and McGill University, Canada in inflammation and remodeling in asthma. Her research focuses on cellular and molecular mechanisms of airway remodeling. She has published more than 200 papers, communications and book chapters in the respiratory and immunology field and holds grants from Canadian agencies. She is a member of different national and international scientific committees and has received several awards from national and international organisms.

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