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Title: The role of the regulated retrotransposon transcriptome in asthma

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Body: Rationale: Genetic studies identified over 200 asthma susceptibility genes that associate with the asthmatic pathology. In the light of the novel functions for mobile DNA elements, we propose that complex diseases, such as asthma, may result from transposed and transposable elements (TEs) which integrate in asthma susceptibility genes or in their regulatory elements. Objectives: To investigate whether TEs may cause asthma. Therefore, we performed (i) in-silico analysis of TEs in selected asthma susceptibility genes which could potentially function as transcription modulators; (ii) establish CAGE libraries (cap analysis of gene expression) using human lung tissue of asthma patients and of healthy controls; and (iii) analyze the transcriptome of the lung tissue CAGE libraries. Methods: The gene sequence of twelve asthma susceptibility genes (DPP10, CYFP2, HLAG, GPRA, SFRS8, PHF11, ADAM33, PCDH1, CH13L1, ORMDL3, PDE4D, DENN1B) were analyzed in silico for the presence of TEs. In addition, we analyzed the 100'000 5'-upstream bp region in order to localize TEs that can potentially act as alternative promoters/enhancers. Results: In silico analysis showed that the TE content in the 12 analyzed gene ranged from 8% (ADAM33) to 49% (GPRA). Within the 12 genes we observed a significant gene-specific distribution of the TE types (SINE, LINE, LTR). The analysis of the upstream 5'-regions showed that the TE content ranged from 28% to 58%. Outlook: DNA sequencing of the named genes will reveal differences in TE content in asthma vs. control. CAGE analysis will enable us to compare the retrotransposon transcriptome of asthma and controls.