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Title: Increased cytotoxic T cells, CX3CR1+, γδ and IL17+ T cells in severe asthma during exacerbation

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Body: Background Asthma is a chronic inflammatory disease affecting up to 10% of the general population. In most cases, asthma symptoms are controlled by long term treatment without side effects. However, for severe asthmatics, therapy is often insufficient to gain control of the disease and symptoms progress to exacerbations. Recently, T cells populations such as cytotoxic T cells, CX3CR1+, γδ and IL-17+ T cells have been correlated to asthma severity. Our aim was to longitudinally study these cells populations in severe asthma, to better understand immune mechanism that underlies exacerbations. Methods 23 severe refractory asthmatics were enrolled in the EXPRESA study, with a longitudinal follow-up of 12 months, compring blood sampling and nasal swab. 40 exacerbations were documented. T cell phenotype was assessed by flow cytometry in samples obtained at baseline, before, during and after exacerbations. Viral colonization was also studied in nasal swab by PCR. Results We highlight increased cytotoxic T cells (CD8+perforine+), CD4+CX3CR1+ cells, γδ T cells and IL-17+ T cells ($p<0,03$) associated to increased Th2 cells (IL-5) during exacerbation. This increase in inflammatory profile is associated to decreased T regulatory population and Th1 cells (IFN-γ), which appears before exacerbation ($p<0,007$). Concerning viral colonization, the lack of virus identification failed to separate exacerbations of viral origins from others. Conclusion These results defined a T cell activation profile, specific for exacerbation outcome in severe asthma which seems to be crucial for inflammatory response which develops during exacerbation.