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Title: Notch signalling in human basophils

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Body: Notch signalling plays a key role in the development of the immune system. Recently, Notch was found to induce lung allergic responsiveness in CD4+ T-cells and regulate eosinophil function. As basophils play a key role in allergic reactions, our aim was to analyse, whether basophils express Notch-1 or Notch-2 and whether Notch signaling has an impact on basophil function. Human basophils were isolated from venous blood of healthy donors via magnetic cell sorting (MACS®). RNA and protein of basophils and PBMC were extracted. Notch-1 and Notch-2 expression was determined by RT-PCR and Western Blot. To explore Notch functionality, basophil migration towards Jagged-1 [10^{-4} – 10^{-14} M] and fMLP [10^{-8} M] was evaluated in Boyden chambers. In a second setting basophils migrated towards fMLP [10^{-8} M] after preincubation with the specific gamma secretase inhibitor DAPT [10^{-6} – 10^{-12} M]. Migration depth was analysed by microscopy. Furthermore, basophils were stimulated with plate-bound Jagged-1 for 24 h before histamine release was measured by ELISA. The RT-PCR and Western Blots revealed basophils to express both, Notch-1 and Notch-2. In comparison to PBMC, human basophils were found to express Notch-1 to a greater extent, whereas Notch-2 expression was lower than that in PBMC. With regards to functionality we found that Jagged-1 [10^{-8} M] most significantly induced chemotaxis in basophils and DAPT [10^{-6} - 10^{-8} M] most effectively blocked basophil migration ($p< 0.0001$). Furthermore, after Jagged-1 stimulation an increase of histamine concentration by 8.67 fold could be determined. We could show for the first time that human basophils express Notch-1 and Notch-2 and that the Jagged-1/Notch signalling pathway is involved in basophil functions.