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Toll-like receptor expression in severe asthma with chronic rhinosinusitis

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Background

We have in an epidemiological study identified a group of individuals with multiple asthma symptoms (MSA) that reflect a more severe and uncontrolled disease. An altered innate immunity and adaptive immunity, and effects of microorganisms may play a role in the development of both CRS and asthma. The innate immune system use Toll-like receptors (TLRs) to recognize microbes and activate defense mechanisms within minutes of microbial invasion which is followed by an antigen-specific response by the adaptive immune system. Thus, innate and adaptive immune cells are sequentially activated and reciprocally regulate one another. Glycogen synthase kinase-3β (GSK3β) has been demonstrated as a regulator of both innate and adaptive immunity. GSK3β was shown to modulate inflammatory responses through TLR-mediated production of pro-inflammatory cytokines and inactivation of GSK3β (phosphorylated GSK3β) lead to a reduced IL-12 production, which was suggested to skew the balance towards a Th2 response.

Aim

To determine the degree of expression of TLRs 2, 4, 7 and 9 on monocytes as well phGSK3β using flow cytometry. We hypothesize that the co-existence of CRS in patients with asthma and especially patients with MSA has an increased TLR expression involved in the innate immune system.

Method

Participants were selected from an epidemiological cohort, the West Sweden Asthma Study. Clinical parameters as well as fresh peripheral blood cells were obtained from one group of non-asthmatic subjects with CRS (CRS) and four different groups of asthmatics: 7 subjects with MSA (MSA), 7 subjects with other asthma (OA), 7 subjects with MSA and CRS (MSA/CRS) and 9 subjects with OA and CRS (OA/CRS). These five groups were compared to a control group consisting of 10 healthy subjects without asthma or CRS.

Results

Individuals with MSA or CRS only, showed significantly increased TLR2, TLR7 and TLR9 expression (rMFI) on $CD14^+$ monocytes compared to controls as well as the expression of phGSK3β and CD14. Individuals in the combined MSA/CRS group showed increased expression of CD14 and TLR2, but increased expression of TLR4 was only found in the CRS group.

Conclusion

The upregulated expression of TLRs in the MSA group compared to control group suggest a higher susceptibility towards an altered immune response that might reflect the degree of severity. Furthermore, the increased phosphorylation of GSK3β may indicate a switch in the immune response from a pro-inflammatory to a dysregulated Th2 response.

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