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Meeting abstract

Protein kinase C-ζ is involved in the inhibition of eosinophil migration

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Background

The accumulation of eosinophils in lung tissue is a hallmark of asthma, and it is believed that eosinophils play a crucial pathogenic role in allergic inflammation. Therefore, eosinophils are currently considered a major therapeutic target in allergic diseases. Prostaglandin (PG) E_2 exerts anti-inflammatory and broncho-protective mechanisms in asthma, but the underlying mechanisms have remained unclear. We have shown previously that PGE_2 and the EP_2 receptor agonist butaprost inhibit eosinophil trafficking *in vitro* and *in vivo* [1].

Methods

Human eosinophils were purified by negative magnetic selection from peripheral blood. Chemotaxis was determined in 48-well microBoyden chambers and migrated eosinophils were enumerated by flow cytometry.

Results

The chemotaxis of human eosinophils towards the chemoattractant eotaxin was attenuated by PGE_2 and the selective EP_4 agonist ONO-AE1-329 in a concentration-dependent manner. Pretreatment of eosinophils with the adenylyl cyclase inhibitor SQ-22536, the protein kinase A inhibitor H-89 or the p38 MAP kinase inhibitor SB-202190 did not prevent the inhibitory effect of PGE_2, while the phosphatidyl inositol 3-kinase (PI3K) inhibitor LY-294002, triciribine, a specific inhibitor of Akt phosphorylation, and a myristoylated pseudosubstrate of protein kinase (PK) C-ζ (mPS), partially or completely reversed the inhibitory effect of PGE_2 and ONO-AE1-329 on the migration of eosinophils towards eotaxin.

Conclusion

Protein kinase C is an increasingly diverse family of enzymes that has been implicated in a range of cellular functions within the eosinophil. The present data show that the PI3K/Akt/PKC-ζ pathway is involved in the negative regulation of the migration of human eosinophils mediated by EP_2 and EP_4 receptor activation.

References

1. Sturm EM, Schratl P, Schuligoi R, Konya V, Sturm GJ, Lippe IT, Peskar BA, Heinemann A: **Prostaglandin E_2 inhibits eosinophil trafficking through E-prostanoid 2 receptors.** *J Immunol* 2008, **181:**7273-7283.