Conclusions: Neutrophils in ulcerative colitis are attracted to the intestine by steroid-sensitive chemotactic factors, activated locally, and kept alive by mainly GM-CSF.

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The molecular heterogeneity of eosinophil cationic protein; studies by SELDI-TOF MS

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Background: Eosinophil cationic protein (ECP) is a highly heterogeneous protein produced in the granules of eosinophil granulocytes. The heterogeneity is dependent both on polymorphisms in the ECP gene such as the coding 434(G>C) polymorphism and also post-translational modifications (PTMs) of the protein. The aim was to study the heterogeneity of ECP further. Hence, an affinity capture assay based on an antigen-antibody interaction with the surface enhanced laser desorption/ionization- time of flight mass spectrometry (SELDI-TOF MS) technology was developed.
Materials and methods: MS analysis of ECP was performed by affinity capture with SELDI-TOF MS, using monoclonal anti-ECP antibodies coupled to PS20 arrays. Eosinophil extracts from purified eosinophils of single individuals and ECP purified from buffy coats were analyzed. Also, ECP from buffy coats was deglycosylated by a variety of enzymes and analyzed.
Results: Several molecular species of ECP was detected in each eosinophil extract. One anti-ECP antibody used, clone 614, could distinguish the genetic variants of the ECP 434(G>C) gene polymorphism. MS analysis of ECP purified from buffy coats revealed up to 10 different molecular species. This heterogeneity was to the major extent due to N-linked oligosaccharides, on which sialic acid, galactose and acetyl-glucoseamine were positioned.
Conclusions: The SELDI-TOF technique is a convenient tool to study protein heterogeneity; by means of this technique both genetic and post-translational causes of the molecular heterogeneity of the eosinophil cationic protein could be detected.

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Identification of a novel phospholipase B activity in human neutrophils

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Background: The identification and characterization of novel proteins in human neutrophils is important to understand the functions of human neutrophils. In searching for novel proteins, we found a protein (a product of a gene FLJ22662) which has an amino acid sequence similarity with Dictyostelium phospholipase B (PLB), suggesting a putative PLB.
Materials and methods: The putative PLB was purified from organelle extracts of normal human granulocytes using Sephadex G-75 chromatography, Mono-S cation exchange chromatography and hydroxyapatite chromatography.
Results: The molecular weight of the protein was estimated to be about 130 kDa by gel filtration and 25 kDa and 45 kDa by SDS-PAGE. The residues from the 25 kDa band were found towards the N-terminus of the full length protein, while the residues from the 45 kDa band were found toward the C-terminus of the protein. The putative PLB needed molecular processing to acquire its deacylation activity. In addition to phosphatidylcholine, the enzyme also displayed activity against phosphatidylinositol and phosphatidylethanolamine. Positional specificity of the enzyme revealed a phospholipase B (PLB) nature. The enzyme is active at a broad pH range with an optimum at 7·4. Immunoblotting using antibodies against the fragment of 45 kDa indicated a neutrophil origin of the PLB.
Conclusions: The existence of the novel PLB in neutrophils and its enzymatic activity against phospholipids suggest a role in defence against invading microorganisms and in the generation of lipid mediators of inflammation.

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Human monocyte Fcgamma receptors expression: synergy of rimonabant and statins

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Background: Macrophage Fcg receptors (FcgRs) are relevant in inflammation and the pathophysiology of atherosclerosis. The anti-inflammatory actions of statins contribute to the success of these drugs in the prevention of cardiovascular events. An effect more potent than the projected benefit based upon their LDL-cholesterol lowering properties. Preliminary data suggest that, rimonabant (an endo-cannabinoid receptor CB1 antagonist) posses anti-inflammatory actions that, may add to its beneficial metabolic effects in the prevention of atherosclerosis.
Objectives: We have assessed whether treatment with rimonabant plus statins has synergistic effects regulating peripheral blood monocyte FcgRs expression.
Methods: The surface expression of the human FcgRs, FcgRI, FcgRIIa, FcgRIIb, and FcgRIII was determined by FACS analysis with specific monoclonal antibodies in peripheral blood monocytes (PBM) obtained from patients treated with rimonabant (20 mg/day) plus atorvastatin (20, 40, or 80 mg/day) during at least 6 months.
Results: Enhancement of the surface expression of PBM-FcgRIIb in patients treated with rimonabant plus atorvastatin (52 ± 5%) was superior to that of patients treated with either, rimonabant (27 ± 2%) or atorvastatin (23 ± 1·6, 31 ± 3, and 39 ± 3·5% for 20, 40 and 80 mg/day, respectively) alone ($P < 0·005$). The expression of both, PBM-FcgRIII and PBM-FcgRIII was significantly decreased by treatment with either rimonabant, atorvastatin, or both ($P < 0·01$). Decreased expression of PBM-FcgRIIb was associated with increased plasmatic levels of adiponectin ($r = 0·773$, $P < 0·005$), and with decreased plasmatic levels of C reactive protein ($r = 0·708$, $P = 0·027$).
Conclusions: Treatment with rimonabant plus statins has synergistic effects regulating peripheral blood monocyte FcgRs expression. This synergistic immunoregulatory action of the treatment with rimonabant plus statins may contribute to their benefit in the prevention of cardiovascular events.

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Treatment with a cannabinoid receptor CB1 antagonist regulates monocyte Fcgamma receptors expression

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Background: Macrophage Fcgamma receptors (FcgRs) have an important role in the pathophysiology of atherosclerosis and inflammation. Preliminary data suggest that, rimonabant (an