SP0092 REGULATION OF NEUTROPHIL APOPTOSIS DURING ACUTE INFLAMMATION – A ROLE FOR THE BCL-2 FAMILY OF APOPTOSIS-ASSOCIATED GENES

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Introduction The life-span of circulating polymorphonuclear neutrophils (PMN) is relatively short when compared to other leukocytes but it can be further shortened by accelerating apoptosis. This is thought to be critical for the control of acute inflammation since apoptosis allows the “silent” elimination of emigrated PMN and thereby prevents uncontrolled tissue damage. This study was undertaken to elucidate the mechanisms which determine the life-span of emigrated PMN during acute inflammation.

Methods Apoptosis of isolated human PMN was investigated by (1) analysis of DNA content, (2) detection of DNA degradation, (3) analysis of nuclear morphology, and (4) measurement of CD16 expression on the cell surface. Gene expression was analysed by semi-quantitative RT-PCR and western blotting technique. Intraperitoneal thioglycollate injection in mice was used as an *in vivo* model for acute inflammation.

Results Leukocyte adhesion molecules of the $\beta 2$ integrin family (CD11/CD18) which are critically involved in the recruitment of PMN to sites of inflammation were found to potentiate TNF α -induced apoptosis of human PMN within 4 h and 8 h after stimulation. The effect required aggregation of the $\beta 2$ integrin Mac-1 (CD11b/CD18) and was independent of Fc receptors. An enhancement of apoptosis was also observed after migration of PMN through an endothelial cell monolayer which stained positively for ICAM-1, the ligand for the $\beta 2$ integrins LFA-1 (CD11a/CD18) and Mac-1 (CD11b/CD18) suggesting that PMN emigration promotes apoptosis. This was confirmed using an *in vivo* model of acute inflammation in mice. Moreover, inflammatory, i.e. emigrated PMN showed a differential expression of apoptosis-associated genes of the bcl-2 family when compared to circulating PMN: Whereas the pro-apoptotic factor bax-alpha was up-regulated, the expression of the anti-apoptotic bcl-XL was down-regulated in emigrated PMN. Since the bcl-2 family plays an important role in the regulation of apoptosis, this shift of balance between anti- and pro-apoptotic factors may be responsible for the enhancement of apoptosis in inflammatory PMN.

Conclusions The present study suggests a physiologically relevant mechanism for the control of acute inflammation by promoting the turnover of previously emigrated PMN. This mechanism which involves the bcl-2 family of apoptosis-associated genes may be critical to subside local inflammatory processes *in vivo*.

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SP0093 JUNCTIONAL ADHESION MOLECULE-2 (JAM-2) IS LOCALISED AT INTERCELLULAR JUNCTIONS AND PLAYS A ROLE IN LYMPHOCYTE TRANSMIGRATION

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We identified a novel Junctional Adhesion Molecule by a selective RNA display method. The protein was named JAM-2 based on its 30–40% homology to JAM and VE-JAM. The three JAMs define a novel subset of immunoglobulin superfamily molecules which will be referred to as JAM-1 (JAM), JAM-2 and JAM-3 (VE-JAM). JAM-2 is highly expressed by HEVs and lymphatic endothelial cells in lymphoid organs, suggesting that it may play a role in lymphocyte recirculation. The role of JAM-2 in inter-endothelial junctions has been addressed using endothelial cells over-expressing JAM-2 protein. These cells have an increased ability to sustain lymphocyte transmigration in agreement with the pattern of expression found *in vivo*. Transfected cells are also more permeable to FITC-dextran. Furthermore, an antibody directed against the extracellular domain of JAM-2 is able to partially block the transmigration. Our findings suggest that JAM-2 may facilitate lymphocyte extravasation across HEVs by rendering the inter-endothelial junctions more leaky. The role of JAM-2 in inflammatory processes will be discussed.

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SP0094 RHEUMATOLOGY DEVELOPMENT: HOW TO REACH THE EQUALLY AND HIGH STANDARD EDUCATED AND TRAINED HEALTH PROFESSIONAL THROUGHOUT EUROPE

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The health-related outcome for all with musculoskeletal conditions (MSC) in Europe should be equal which requires similarities in their care. This is dependent on financial and human resources, a key one being the competency of the health professional which will be determined by their training and CME. The integrated multidisciplinary team need suitable training which must be harmonised throughout Europe to ensure the outcome of care is similar for all. Learning objectives must be established for all the professional groups relevant to their contribution to the management of MSC which may vary between countries. From this a curriculum can be developed. Different methods of teaching may be used but the tendency is towards problem-based learning integrating basic with clinical knowledge and linking all those involved in the management of similar problems. The assessment should be based on the curriculum. Standards for rheumatology have been developed in Europe for undergraduates, specialist training and CME. Similar standards need to be developed for other health professionals in rheumatology. These must reflect the educational needs which will depend on their roles in clinical practice in different countries. The ultimate measure of the quality of training of all HPs in rheumatology is the clinical outcomes achieved within the constraints of financial resources and priority given to their care.

SP0095 WHAT NEW SKILLS SHOULD A RHEUMATOLOGIST ACQUIRE?

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