EXPRESSION AND CYTOKINE MODULATION OF VASCULAR CELL ADHESION MOLECULE-1 IN NORMAL AND DISEASED HUMAN SKIN. L. Seam, B. Ross, H. R. Gordon, B. MacDonald. Laboratory of Applied Dermatopathology, UMDNS, Guy's Hospital, London, UK.

Expression of adhesion molecules by vascular endothelium and other cutaneous cells is likely to be of great importance in the genesis of inflammatory skin disease. Vascular cell adhesion molecule-1 (VCAM-1) is a novel endothelial molecule with adhesive properties in vitro for lymphocytes and eosinophils. Using anti-VCAM-1 monoclonal antibodies, we have performed an immunohistochemical study of its expression in normal and inflamed skin, and have examined ways of modulating its expression in vivo.

In normal skin (n = 8) low levels of VCAM-1 were present on perivascular dendritic cells and occasional endothelial cells. In inflamed skin (allergic contact dermatitis [n = 6, 7.4–26.9 hrs], chronic atopic dermatitis [n = 6], poraldermatitis [n = 4], and lichen planus [n = 6]) VCAM-1 was upregulated on dermal endothelium and was also present on interstitial dendritic cells. Three normal volunteers underwent intradermal injection of 100U rHuTNFa and five received 500U rHuTNFa and five received 500U rHuTNFa. Following TNFa and IFNγ there was marked upregulation of VCAM-1 on dermal endothelium and dendritic cells.

Widespread expression of VCAM-1 in inflamed skin suggests that this molecule may be of importance in the initiation and maintenance of a variety of skin diseases. Both keratinocyte derived (TNFa) and lymphocyte derived (IFNγ) cytokines may be of importance in its control; interference with these pathways may be of future therapeutic benefit.

EXPRESSIOI; OF BETA-2 INTEGRIN MOLECULES ON HUMAN KERATINOCYTES IN CYTOKINE-MEDIATED SKIN DISEASES. M. Simon, J. J. Huynh; Dept. of Dermatology, University of Erlangen-Nürnberg, Erlangen, FR Germany.

Integrins are cell surface molecules of importance in a wide variety of cellular functions, including morphogenesis, cell migration, and cell matrix interactions. The beta(2) integrin subfamily, which consists of three members, each composed of a shared beta subunit (CD18) covalently associated with unique alpha subunits (CD11a, CD11b, CD11c). In the present study, we have analysed the expression pattern of B2 integrins on the surface of human keratinocytes (HKs) in biopsies obtained from healthy volunteers, from patients with tuberculosis skin tests and from the clinically involved skin of patients with acute urticaria (AU), lichen planus (LP), psoriasis vulgaris (PV), mycosis fungoides (MF) and contact dermatitis. In contrast, no specific staining of the HKs was observed with the same MABs in biopsies from healthy volunteers, from patients with AU and in the uninvolved skin specimens obtained from patients with AU and from healthy individuals. The adherence of HKs from AU patients than to control cells, This was correlated with an increased spontaneous expression of ICAM-1 on HKs in AU patients than in control HKs. These results suggest that expression of leucocyte adhesion molecules is an early response to pressure challenge in DPU although the effect of pressure challenge in normal skin of healthy subjects needs to be investigated.

TIME-COURSE, DOSE-DEPENDENCE AND DISTRIBUTION OF INTERFERON GAMMA-INDUCED ICAM-1 AND HLA-DR ON IN A HUMAN RECONSTRUCTED SKIN MODEL IN VITRO: COMPARISON OF NORMAL, HUMAN SKIN IN SHORT-TERM ORGAN CULTURE. N. Boyde, D. Caley, S.M. Robinson, M. Boucher, C. Hansey and B. Brompton. CSCR CALIFORNIA. San Diego, CA, USA.

In delayed-type hypersensitivity, the expression of class II histocompatibility antigens by keratinocytes. A crucial step in these reactions may be leukocyte retention in the epidermis by keratinocyte-expressed I ntercellular Adhesion Molecule 1 (ICAM-1), a ligand for Leukocyte Functional Antigen 1 (LFA-1); this adhesion may initiate various contact-dependent processes such as sensitization or cytotoxicity. In order to assess the stability of human-vitro models for the study of ICAM-1- and LFA-1 expression by keratinocytes and its modulation by various agents, we compared the time-course and dose-dependence of IFN Gamma-induced expression of ICAM-1 and HLA-DR in two human skin models: the human reconstructed skin model (outer root sheath cells on a keratinocyte-collagen lattice) and normal human skin in short-term organ culture. In both systems, IFN Gamma induced a strong dose-dependent ICAM-1 staining in basal, non-differentiated keratinocytes, as observed by ELISA and northern blot analysis of IFN Gamma prestained keratinocytes. Time-course experiments performed in the two models (incubation periods from 4h to 168h with IFN Gamma) induced a maximal maximal expression after 24h contact for ICAM-1, and 72h for LFA-DR. The maximal expression was observed on keratinocytes after 24h contact for ICAM-1 and 72h for LFA-DR. The maximal expression was observed on keratinocytes after 24h contact for ICAM-1 and 72h for LFA-DR. The maximal expression was observed on keratinocytes after 24h contact for ICAM-1 and 72h for LFA-DR. The maximal expression was observed on keratinocytes after 24h contact for ICAM-1 and 72h for LFA-DR. The maximal expression was observed on keratinocytes after 24h contact for ICAM-1 and 72h for LFA-DR. The maximal expression was observed on keratinocytes after 24h contact for ICAM-1 and 72h for LFA-DR. The maximal expression was observed on keratinocytes after 24h contact for ICAM-1 and 72h for LFA-DR.