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A meeting review

1st International Conference on Cutaneous Lupus Erythematosus Düsseldorf, Germany, September 1–5, 2004

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The "1st International Conference on Cutaneous Lupus Erythematosus" has taken place in Düsseldorf, Germany, September 1–5, 2004, in cooperation with the American College of Rheumatology (ACR) Response Criteria Committee on SLE.

The Organizing Committee was formed by A. Kuhn, T. Ruzicka, and M. Schneider (Düsseldorf, Germany), P. Lehmann (Wuppertal, Germany), and R.D. Sontheimer (Iowa, USA).

The idea which originally inspired the Organizing Committee was gathering the world's most representative experts about lupus erythematosus (LE) to focus on the cutaneous manifestations of the disease from different points of view.

Abbreviations: ACLE, acute cutaneous lupus erythematosus; ACR, American College of Rheumatology; ADCC, antibody dependent cell-mediated cytotoxicity; aPL, antiphospholipid antibodies; APS, antiphospholipid syndrome; BlyS, B lymphocyte stimulator; CAMs, cellular adhesion molecules; CLE, cutaneous lupus erythematosus; CCLE, chronic cutaneous lupus erythematosus; CQ, chloroquine; CTD, connective tissue diseases; DEGs, differentially expressed genes; DLE, discoid lupus erythematosus; HCQ, hydroxychloroquine; ICAM-1, intercellular adhesion molecule 1; iNOS, inducible NO synthase; LE, lupus erythematosus; LFA-1, lymphocyte function associated antigen 1; LET, lupus erythematosus tumidus; LTR, lichenoid tissues reaction; NOD, nonobese diabetic; NZB, New Zealand Black; NZW, New Zealand White; NLE, neonatal lupus erythematosus; NO, nitric oxide; SCLE, subacute cutaneous lupus erythematosus; SCID, severe combined immunodeficient; SEGRAs, selective glucocorticoid receptor agonists; SLE, systemic lupus erythematosus; TCR, T cell receptor; TDT, transmission disequilibrium testing; UCTD, undifferentiated connective tissue disease; UVR, ultraviolet radiation; VCAM-1, vascular adhesion molecule 1.

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During the conference, the "European Society of Cutaneous Lupus Erythematosus (EuSCLE)" and the "Interdisciplinary Study Group of Lupus Erythematosus (ISGLE)" were founded, and at the end, a meeting of the "American College of Rheumatology Response Criteria Committee on SLE" took place. Besides the conference hours, the Local Organizing Committee arranged a beautiful boat-trip on the river "Rhein" and a farewell dinner party with a very impressive piano and soprano concert.

1. The pathogenesis of lupus erythematosus: what we know

David A. Norris (Denver, USA) summarized recent data on the **pathogenesis of cutaneous lupus erythematosus** (CLE) and addressed the questions: where are we now and where are we going? In the past decades, extensive investigations have been performed in the field of photoimmunology, and it has become evident that ultraviolet radiation (UVR) exposure can significantly compromise the immune system. The implications of the immunosuppressive properties of UVR are manifold, because UV-induced immunosuppression not only is responsible for the inhibition of protective cell-mediated immunity but also contributes to the initiation, development, and perpetuation of several skin disorders, such as connective tissue diseases (CTD). These effects include induction of inflammation, production of antibodies, and keratinocyte and endothelial cell death. It has been evaluated by which mechanisms UVR releases inflammatory mediators and cytokines, suppresses immunity, and induces adhesion molecules in the epidermis and dermal vessels. The link between apoptosis and the development of autoantibodies has further been shown in vitro by demonstrating that during UVB-induced keratinocyte apoptosis, intracellular antigens including SSA/Ro, ribosomes, calreticulin, and phospholipid complexes, are translocated to two distinct blebs on the cell surface (Casciola-Rosen et al. J Exp Med, 179:1317–1330, 1994). Interestingly, during apoptosis, these antigens could be structurally modified by granzyme B, ICE-like proteases, and reactive oxygen intermediates to produce cryptic epitopes that can bind to MHC II molecules and produce an antibody response. However, it has also been shown that binding of IgG from anti-Ro/SSA-positive sera enhanced by UVR, heat, and ionophores does not require apoptosis; it can be observed in cells dying by necrosis (Norris et al., Photochem Photobiol 65:643–646, 1997). Further recent studies suggest that predisposing factors to subsequent development of systemic autoimmunity may be the incomplete induction of tolerance to apoptotic antigens, potentially through abnormal apoptotic signaling and effector pathways, decreased apoptotic cell clearance, or abnormal signaling thresholds on responding lymphocytes. In summary, UVR-induced apoptosis of keratinocytes is believed to be a key factor in photosensitive LE, and deficiencies in molecules involved in removal of apoptotic cells appear to promote the development of this disease. The role of TNF-α polymorphism in inducing apoptotic keratinocytes in response to UVR needs to be further investigated.

Fukumi Furukawa (Wakayama, Japan) gave an overview on **animal models of LE**, which are commonly used to study the genetic, environmental, and pathogenic aspects of autoimmune diseases. Regarding experimental autoimmune diseases, these models can be divided into several broad groups: (1) inbred mice that spontaneously develop a disease similar to human systemic lupus erythematosus (SLE); (2) chronic graft-vs-host diseases induced in F1 hybrid mice injected with lymphoid parental cells; (3) UVR-irradiated mice immunized with some components of DNA; (4) immunodeficient mice, such as severe combined immunodeficient (SCID) mice and nude mice inoculated or engrafted with immunocompetent cells or tissues; (5) gene-manipulated mice, such as transgenic or knockout mice; and (6) drug-induced lupus erythematosus-prone mice. There are different inbred strains of SLE-prone mice, including New Zealand Black (NZB), F1 hybrids of NZB×New Zealand White (NZW; B/W F1), MRL/Mp-lpr/lpr (MRL/lpr), and BXSB mice. Compared with B-lupus strains, such as NZB, B/W F1, and BXSB mice, the MRL/lpr mouse has some unique features, such as rheumatoid arthritis, inflammatory changes in their salivary glands (e.g., Sjogren's syndrome), and arteritis. Macroscopic skin lesions are also observed in MRL/lpr mice. In addition, several transgenic and knockout mice with LE-associated phenotypes have been described, such Bcl-2, Fli-1, CD19, IL-4, etc.,