Immunological Features of Psoriasis

Effects of Ro-109359, Concanavalin A, Pokeweed Mitogen, and Methotrexate on Cultivated Lymphocytes

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Summary. Isolated peripheral mononuclear cells of psoriasis patients with different disease characteristics, e.g. head-localised, quiescent guttata, confluent active widespread and erythrodermic, were cultured in a modified Mishell-Dutton system. Using the plaque-forming cell (PFC) assay, single cell antibody formation was studied, and class distribution monitored, adding pokeweed mitogen (PWM), concanavalin A (ConA), methotrexate (MTX) or Ro-109359/31, as well as autologous sera to the culture. PFC-estimation vs. sheep red blood cells (SRBC) and burro red blood cells (BRBC) revealed a distinct suppression of primarily IgG-PFC in some of the PWM-treated patients' cultures; ConA maximally reduced PFC by only 50%, compared to 100% for normal immune cells. Ro-109359/31 reduced mainly IgG-PFC in the co-cultures with PWM or autologous sera. MTX resulted in a reduction of IgG-PFC and IgM-PFC equally. The results were compared with cultured immune cells from normal individuals. The two antigenically different indicators, the partial abolition of ConA induced suppression, broad-based immunoglobulin elevation in the sera, and the mainly IgG-formation hint at the role of polyclonal B-cell activation in the perpetuation of psoriasis, which can be specifically reduced by Ro-109359/31. Suppressor cell dysfunctions remain to be discussed.

Key words: Psoriasis — Ro-109359 — ConA — PWM — MTX — Cultivated lymphocytes

Zusammenfassung. Die hier durchgeführten Untersuchungen erfolgten an mononukleären Zellen von Patienten, die an einem frischen Schub einer Psoriasis vulgaris bzw. einer psoriatischen Erythrodermie litten. Die peripheren mononukleären Zellen wurden mit Hilfe einer Dichtegradientenzentrifugation isoliert und anschließend einer 6-Tage-Kultur mit Pokeweed-Mitogen (PWM), Concanavalin A (ConA), Methotrexat (MTX) und dem Retinoidabkömmling

Schlüsselwörter: Psoriasis - Ro-109359 - ConA - PWM - MTX - Lymphozytenkulturen

Recently, retinoic acid analogs have been demonstrated to act on immune functions and influence some forms of cancer at the intracellular level of transformed cells (Fig. 1). Retinoic acid analogs exert substantial effects on immunological parameters [1,2] and subsets of lymphocytes [3]. Mostly, however, reports deal with the reduction of hyperplasia and metaplasia in the development of several forms of cancer [4–6]. Selective inhibition of cell transformation by viruses [7], protection of cells against chemical agents, such as carcinogenic phorbol esters [8], asbestos-induced hyperplasia and metaplasia [9] or nitrosureas [10], methylcholanthrenes [11] and polycyclic aromatic hydrocarbons [12, 13] have been claimed. Thus, possible prevention from EBV-infection has also been reported [7] and, in addition, retinoic acid binding to transforming cells has been demonstrated [14]. Some kind of competitive inhibition of retinoic acid analogs with transforming agents as well as more general effects on cell division and DNA synthesis have been postulated [15].

Clinical investigations have led to wide-spread use of retinoic acid analogs for therapeutic trials of patients with neoplastic and dermatological disorders, e.g. some forms of eruptive psoriasis [16, 17]. The causes of this disease complex are not known, but recently certain alterations of immune functions and quantitative aberration of T, B, and Null cells as well as monocytes have been suggested [18, 19]. Deficient or dysfunctioning subsets of T cells have been made responsible for a decrease in lymphocyte transformation tests with ConA, PHA, PPD and PWM-responses in such patients. An important feature of previous investigations into the pathogenesis of this disease is the demonstration of a wide variety of various autoantibodies towards stratum corneum, surface IgG on lymphocytes and the nuclei of basal cells [37, 38, 41]. Also, delayed hypersensitivity-type (DTH) immune reactions appear reversibly impaired during the acute stage of the disease [20]. Experimentally, DTH is known to involve lymphokines and may be blocked by MTX [21], a drug that is also frequently applied to patients with severest degrees of psoriasis. Although the described mechanisms are complex and not well under-