Pulling the trigger on psoriasis

SIR — Psoriasis is a common inflammatory skin disease, possibly induced by a T-cell-mediated autoimmune reaction triggered by bacterial superantigens[1]. Some transgenic animal models[2] and mutations in mice[3] mimic certain aspects of psoriasis, but they do not allow study of the role of components of the immune system or exogenous stimuli, namely T cells and superantigens, in the onset of psoriatic lesions. Thus, we searched for a model in which a psoriasiform inflammation could be triggered.

Eighteen full-thickness skin grafts were transplanted from clinically uninvolved areas of three psoriatic patients onto mice with severe combined immunodeficiency (SCID), lacking B and T cells as described previously[4]. Technical manipulations (transplantation, injection) did not alter the state of the grafts as seen in controls treated with repetitive intradermal saline injections. Grafts injected with 3 μg of the bacterial superantigen exfoliative toxin showed some of the hallmarks of psoriasis (see table); these included profound epidermal thickening (akanthosis) from hyperproliferating basal keratinocytes, documented by expression of the mitosis- associated Ki-67 antigen, along with increased indentation of epidermis and dermis (papillomatosis) and focal neo-expression of the adhesion molecule ICAM-1 on basal and suprabasal keratinocytes overlying the papillary dermis. This pattern is thought to be characteristic of psoriasis[5].

When the patients' superantigen-stimulated peripheral blood mononuclear cells were simultaneously injected intraperitoneally, an epidermotropic T-cell infiltrate, positive for the cutaneous lymphocyte-associated antigen, was observed (see table). Marked T-cell epidermotropism was an exclusive feature of grafts from psoriatic donors simultaneously treated with exfoliative toxin and peripheral blood mononuclear cells. None of these phenomena was noted in 18 transplants from 3 non-psoriatic controls.

Our observations document the potential of superantigens to trigger psoriasis in a conditioned environment. This experimental approach should greatly help studies on the pathogenesis of psoriasis. In contrast to other models described so far, it allows the specific induction of psoriasiform inflammation. Moreover, this model system provides an excellent means of studying the modes of superantigen-induced (auto-)immune responses, as well as the phenomenon of lymphocyte homing in general, and epidermotropism in particular.

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1. Valdimarsson, H., Baker, B. S., Jonsdottir, I., Powles, A. & Fry, L. *Immun. Today* **16,** 145–149 (1995).
2. Wilson, J. B., Weinberg, W., Johnson, R., Yuspa, S. & Levine, A. J. *Cell* **61,** 1315–1327 (1990).
3. Sundberg, J. P., Dunstan, R. W., Roop, D. R. & Beamer, W. G. *J. invest. Derm.* **102,** 781–788 (1994).
4. Boehncke, W.-H., Sterry, W., Hainzl, A., Scheffold, W. & Kaufmann, R. *Archs derm. Res.* **286,** 325–330 (1994).
5. Nickoloff, B. J., Griffith, C. E. & Barker, J. N. W. N. *J. invest. Derm.* **94,** 151S–157S (1990).

MORPHOLOGICAL COMPARISON OF GRAFTS FROM NORMAL VOLUNTEERS AND UNINVOLVED SKIN FROM PSORIATIC PATIENTS

Source*	Normal	Normal	Normal	Psoriatic	Psoriatic	Psoriatic
Treatment	PBS	ET	ET/PBMCs	PBS	ET	ET/PBMCs
Epidermal thickness†	111 (90/123)	140 (120/168)	143 (113/166)	149 (143/165)	306 (300/417)	327 (262/450)
Papillomatosis index‡	1.2 (1.2/1.3)	1.3 (1.2/1.3)	1.2 (1.2/1.3)	1.3 (1.2/1.3)	2.2 (1.9/2.4)	2.1 (2.0/2.3)
Ki-67§	Negative	Single cells	Single cells	Single cells	Positive	Positive
ICAM-1‖	Negative	Negative	Negative	Negative	Focal	Focal
T cells	Few	Few	Few	Few	Few	Epidermotropic¶

Transplantations were done as described previously[4]. Six full-thickness skin grafts were prepared from the inner aspect of the forearm of each of three healthy volunteers and from clinically uninvolved skin at the same location from three psoriatic patients. Two grafts of each individual received a similar treatment: intradermal injection with PBS; with ET diluted in PBS; or with ET diluted in PBS and simultaneous intraperitoneal injection of the donor's PBMCs. Intradermal injections consisted of 100 μl PBS with or without 3 μg ET (Toxin Technology, Florida). Intraperitoneal injections contained 2×10^6 of the donor's PBMCs in 100 μl PBS. PBMCs were stimulated in supplemented RPMI 1640 medium containing 100 ng ml^{-1} ET 48 h before injection at a density of 1×10^6 cells per ml. Injections were given at days 28, 31, 34 and 37 after transplantation; mice were killed at day 40. Grafts were handled for immunoperoxidase and immunofluorescence staining as reported previously[4]. ET, exfoliative toxin; PBMCs, peripheral blood mononuclear cells; PBS, phosphate-buffered saline.

*Each cohort consists of six grafts from three different individuals. Experiments were done one individual at a time, and so this table summarizes the data from six independent experiments.

†Median (minimum/maximum), indicated in μm.

‡Length ratio of dermo-epidermal border to skin surface; medians (minimum/maximum) are indicated.

§Staining pattern of basal keratinocytes.

‖Staining was observed on keratinocytes overlying the papillary dermis only.

¶Most intra-epidermal $CD3^+$ cells were also positive for the cutaneous lymphocyte-associated antigen.

RIP for viruses

SIR — Many plants contain ribosome-inactivating proteins (RIPs) with *N*-glycosidase activity, which depurinate large ribosomal RNA from sensitive ribosomes, thus arresting protein synthesis[1]. All RIPs so far tested inhibit the replication of plant and animal viruses[2]. The exact role of these proteins in plants is unclear, but it has been proposed that they exert a defensive, antiviral function[3]. We report here that viral infection induces the expression of two single-chain RIPs (beetin 27 and beetin 29) in sugar beet (*Beta vulgaris*). A similar expression was obtained by treating beet leaves with hydrogen peroxide or salicylic acid, two mediators of plant acquired resistance[4].

Two proteins, beetin 27 (relative molecular mass 27,000) and beetin 29 (M_r 29,000), were isolated from leaves of sugar beet infected with beet mild yellowing virus, by a procedure used to purify single-chain RIPs[5]. Beetins displayed several properties of RIPs: beetin 27 (the more abundant) inhibited cell-free protein synthesis and promoted the release of the

1. Barbieri, L., Battelli, M. G. & Stirpe, F. *Biochim. biophys. Acta* **1154,** 237–282 (1993).
2. Battelli, M. G. & Stirpe, F. in *Antiviral Proteins in Higher Plants* (eds Chessin, M., DeBorde, D. & Zipf, A.) 39–64 (CRC Press, Boca Raton, 1994).
3. Irvin, J. D. in *Antiviral Proteins in Higher Plants* (eds Chessin, M., DeBorde, D. & Zipf, A.) 65–94 (CRC Press, Boca Raton, 1994).
4. Chen, Z., Silva, H. & Klessing, D. F. *Science* **262,** 1883–1886 (1993).
5. Arias, F. J. *et al. Planta* **186,** 532–540 (1992).
6. Taylor, S. *et al. Pl. J.* **5,** 827–835 (1994).
7. Barbieri, L., Gorini, P., Valbonesi, P., Castiglioni, P. & Stirpe, F. *Nature* **372,** 624 (1994).
8. Lodge, J. K., Kaniewski, W. K. & Tumer, N. *Proc. natn. Acad. Sci. U.S.A.* **90,** 7089–7093 (1993).
9. Citores, L. *et al. J. exp. Bot.* **45,** 513–516 (1994).