Novel Immunotherapies for Psoriasis: Clinical Research Delivers New Hope for Patients and Scientific Advances

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Immunobiologics provide the hope for safe and effective long-term management of psoriasis, a life-disabling condition. The use of targeted immunotherapies as pathogenic probes has led to scientific discoveries that help uncover new information on the pathogenesis of psoriasis and on the control of cutaneous immunity. The research described in this paper employs targeted immunotherapies as pathogenic probes of T1-mediated immune disorders, using psoriasis as the primary disease model. This approach has wide applicability to other immune-mediated inflammatory isorders. ***Keywords: Psoriasis/Immunobiologics/Cytokines/T cell activation. J Investig Dermatol Symp Proc 9:79–83, 2004***

The role of T cells in the pathogenesis of psoriasis was discovered through serendipity: the clinical use of targeted immunotherapies as pathogenic probes and, more recently, the use of SCID mouse models (Gilhar *et al*, 1997; Wrone-Smith and Nickoloff, 1996). The fact that methotrexate improves psoriatic joint and skin disease was one of the early clues that cells other than keratinocytes are pathogenic. Cyclosporine's dramatic clearing of psoriasis was first noted in the mid 1980s, when researchers observed that it inhibits mRNA transcription for a number of T cell cytokines, strongly suggesting a pivotal role for T cells in psoriasis pathogenesis (Bos *et al*, 1989; Ellis *et al*, 1991; Gottlieb *et al*, 1992). It was not conclusive proof, however, because the concentrations of cyclosporine achieved in the epidermis after oral dosing had direct effects on keratinocyte proliferation (Khandke *et al*, 1991). Not until the use of a targeted T cell toxin, denileukin diftitox, was definitive proof obtained for the role of T cells in psoriasis pathogenesis.

Denileukin diftitox is a fusion protein of IL-2 and diphtheria toxin protein fragments which specifically kills activated T cells. It has no biologic activity *in vitro* against growth factor–stimulated keratinocytes. As a single agent, denileukin diftitox clears psoriasis clinically and histologically (Gottlieb *et al*, 1995), definitively demonstrating that activated T cells are pivotal in maintaining psoriatic plaques. More recently, SCID mouse models have confirmed pathogenic roles for both CD4+ and CD8+ T cells and have suggested a potential role for NK cells (Gilhar *et al*, 1997; Nickoloff *et al*, 1995).

In general, T cells require two signals in order to be activated. The first signal is provided by antigen bound to MHC class I or II on antigen-presenting cells (APC) (e.g., Langerhans cells) interacting with surface membrane T cell receptors. In the absence of a second activating signal, however, this interaction fails to activate the T lymphocyte. The second signal can be supplied by a number of pairs of surface molecules, including LFA-1-ICAM-1, CD2-LFA3, and CD80,86-CD28-CTLA-4 (vonNoesel *et al*, 1988; June *et al*, 1990; Springer *et al*, 1987). Recent studies suggest that LFA–1-ICAM-1 interactions may be more important in anchoring the immunological synapse between T cells and APC than in actually providing a second activating signal to T cells (vanNoesel *et al*, 1988; Friedrich *et al*, 2000).

B7.1 (CD80) and B7.2 (CD86) are membrane proteins expressed primarily on activated APC and on a subset of activated T cells in psoriatic plaques. The interaction of CD28 with CD80 and CD86 delivers a "second signal" leading to T cell activation, after which CTLA-4 is upregulated on the T cell surface. In contrast to the interaction with CD28, the interaction of CD80 and CD86 with CTLA-4 leads to deactivation of the T cell and suppression of the immune response.

Soluble CTLA-4-Ig inhibits T cell activation by binding to CD80 and CD86 on APC, thus inhibiting the binding of T cell-associated CTLA-4-Ig to surface CD80 and CD86. Forty-three patients with moderate to severe plaque-type psoriasis received four intravenous infusions of CTLA-4g. Forty-six percent experienced 50% or more improvement in the Physician's Global Assessment (a clinical research tool used to measure disease activity). Clinical improvement was associated with decreased epidermal thickness and numbers of epidermal CD3+ T cells. Additionally, activated/mature dendritic cells in psoriasis lesions were reversed by B7 blockade. These results show that the stimulus for ongoing T cell activation, as well as the ongoing maturation of dendritic cells, may be sustained by B7–CD28 signaling (Abrams *et al*, 2000).

IDEC 114 is an anti-CD80 monoclonal antibody that binds specifically and with high affinity. Significantly, it blocks the interaction of CD80 with CD28 without affecting the interaction of CD80 and CTLA-4 *in vitro*. Twenty-four patients received single intravenous infusions of IDEC 114 (Gottlieb *et al*, 2002b). Evidence of clinical and histologic activity was demonstrated.

A multiple-dose study of IDEC 114 in psoriasis was next conducted. Thirty-five patients received four intravenous infusions of IDEC 114 ranging from 2.5 to 15.0 mg/kg over a three-week to six-week period. Clinical improvement was noted in all dosage groups. Histopathological results, including reduced epidermal

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Abbreviations: APC, antigen presenting cells; ICAM, intercellular adhesion molecule; IL, interleukin; LFA, lymphocyte function-associated antigen; NFκB, nuclear factorκB; PAI, plasminogen activator inhibitor; PASI, psoriasis area severity index; TNF, tumor necrosis factor; VIP, vasoactive intestinal peptide

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CD3+ T cell counts, reduced epidermal thickness, and normalization of keratinocyte differentiation, were generally consistent with clinical outcome. With both CTLA-4-Ig and IDEC 114, however, many patients did not respond completely, suggesting that other cellular targets are important in maintaining psoriatic plaques (Gottlieb, 2002a).

CD45RO+ ("memory effector") T cells predominate in psoriasis lesions. Alefacept (LFA3TIP) is a 115-kD fusion protein that consists of the first extracellular domain of human LFA-3 fused to the hinge CH2 and CH3 sequences of human IgG1. It binds CD2 on T cells, leading to inhibition of T cell costimulation and a reversible reduction of "memory effector" (CD4+ CD45RO+, CD8+CD45RO+) T cells in peripheral blood (daSilva *et al*, 2002). In a small study, clinical response correlated with depletion of T cells from the epidermis (Springer *et al*, 1987; Friedrich *et al*, 2000; Krueger *et al*, 2002; Magilavy, 1999).

In a phase II double-blind, placebo-controlled study, 229 moderate to severe psoriasis patients were given 12 weekly intravenous doses of alefacept (0.025, 0.075, and 0.150 mg/kg versus placebo) and followed for a 12-week period. At 12 weeks, the mean reduction in the Psoriasis Area and Severity Index (PASI) was 38%, 53%, and 53% in the 0.025, 0.075, and 0.150 mg/kg groups, respectively, compared with 21% in the placebo group. Alefacept treatment required approximately three months to show dramatic clinical response. Of the 29 patients who were clear after 12 weeks, the median time until relapse (i.e., patients were no longer clear or almost clear) was 236 days. Early reduction in the number of circulating memory T cells was associated with clinical response. On a population basis, there was a correlation between reduction in the CD45RO+ (memory) T cell subset early in treatment and clinical improvement, although early reduction in memory T cell numbers was neither necessary nor sufficient for clinical response (Ellis *et al*, 2001).

Phase III trials confirmed and extended the observations made in phase II. Both intramuscular and intravenous formulations were tested. After one 12-week course of intramuscular alefacept (15 mg dosed weekly), 33% of patients achieved at least a 75% reduction in PASI. After two 12-week courses of intramuscular administration, 43% of patients achieved at least a 75% reduction in PASI (Langley *et al*, 2002). Selective reductions in memory effector (CD45RO+) T cells were related to clinical improvement (Lowe *et al*, 2002). Alefacept was recently approved by the FDA's Dermatology Advisory Panel as monotherapy for moderate to severe psoriasis.

Efalizumab (anti-CD11a, Raptiva), a non-lymphocyte-depleting, humanized monoclonal antibody against T cell lymphocyte LFA-1, has been studied as monotherapy for moderate to severe plaque psoriasis (Gottlieb *et al*, 2000; Gordon *et al*, 2002; Gottlieb *et al*, 2002a; Papp *et al*, 2001). By blocking the interaction between LFA-1 and ICAM-1, it inhibits both T cell activation and T cell emigration into skin (reviewed in Gottlieb *et al*, 2000).

Two phase III clinical trials, enrolling 1095 subjects, were completed, partially evaluated, and presented at a number of national and international meetings in 2001. The clinical response to 12 weekly subcutaneous (SC) efalizumab doses was studied. The 1° (primary) endpoint was achievement of 75% or more improvement in PASI. Subjects were randomized to treatment consisting of an initial conditioning dose of 0.7 mg/kg in week 1 followed by 11 weekly doses of either 1.0 mg/kg or 2.0 mg/kg of efalizumab or placebo (Gordon *et al*, 2003).

More subjects (29.2%) treated with efalizumab (1 mg/kg) achieved at least a 75% PASI improvement in comparison to those on placebo (3.4%). Combined results from both trials show that the PASI improvement for both efalizumab groups was improved over that of placebo after only two to four doses ($p < 0.005$).

Immunohistologic studies in phases I and II demonstrated decreased T cell infiltration in plaques and normalization of keratinocyte differentiation in responding patients. Reductions in epidermal T cell number were accompanied by increases in circulating lymphocytes. On the basis of these observations, the researchers hypothesized that efalizumab inhibits T cell emigration into the skin. CD11a saturation in plaques was necessary but not sufficient for clinical clearance, as defined by the primary endpoint above (Gottlieb *et al*, 2000; Gottlieb *et al*, 1999; Papp *et al*, 2001; Gottlieb *et al*, 2002a).

The combined data with the T cell–targeting drugs tested to date suggest that other T cell surface proteins and/or other pathogenic cell types and molecular pathways are important.

PATHOGENIC CYTOKINES IN PSORIASIS

The inflammatory response in psoriatic plaques is initiated in part by activated T cells in the epidermis and dermis. T cells predominate in plaques, releasing a number of inflammatory cytokines, including tumor necrosis factor α (TNF-α). TNF-α, interferon γ (IFN-γ), interleukin 6 (IL-6), IL-8, IL-12, and other inflammatory cytokines are elevated in psoriatic lesions but not in the normal skin of psoriatic patients. TNF-α increases the synthesis of pro-inflammatory cytokines such as IL-1, IL-6, IL-8, and activates nuclear transcription factors such as NFκB. In animal models, transgenic overexpression of TNI results in arthritis, demyelinating disease, inflammatory bowel disease, and diabetes (O'Shea and Lipsky, 2002). Additionally, TNF-α increases hepatocyte synthesis of acute-phase reactants such as C-reactive protein and may, in part, account for the constitutional symptoms that severe psoriasis patients often experience (reviewed in Chaudhari *et al*, 2001; Gottlieb and Krueger, 2002; Gottlieb *et al*, 2002c; Gottlieb, 2002).

Psoriasis is an inflammatory, T cell–mediated disease; however, what causes activation of these T cells is still unknown. TNF-α has multiple activities that could increase Langerhans cell activation of T cells. It induces Langerhans cell maturation, thus allowing these cells to more efficiently present antigen and upregulate their T cell costimulatory surface molecules. After antigen exposure in the skin, Langerhans cells must exit the skin and travel to lymph nodes, where presentation of antigen to T cells takes place. TNF-α is capable of stimulating Langerhans cells to migrate from the skin to the lymph nodes. Interaction of MHC class I- or II-bound antigen with the T cell receptor, plus a second activating signal, causes T cell activation. This leads to T cell expression of surface membrane proteins, such as cutaneous lymphocyte–associated antigen (CLA), allowing them access into the skin. An additional possible method involves E-cadherin, an adhesion molecule in the epidermis that enables Langerhans cell binding to keratinocytes. Expression of E-cadherin potentially retains Langerhans cells in the epidermis, bound to keratinocytes. TNF-α decreases E-cadherin expression, which could facilitate the migration of Langerhans cells from the skin, allowing their travel to lymph nodes and subsequent T cell activation (Schuler and Steinman, 1987; Onuma, 1994; Nestle and Nickoloff, 1995; Morhenn, 1997; Kimber *et al*, 2000; De Boer *et al*, 1994).

By inducing the synthesis of adhesion molecules on endothelial cells and keratinocytes, TNF-α potentially increases cellular infiltration in skin (Gottlieb *et al*, 2002a; DeBoer *et al*, 1994; Gilhar *et al*, 1997; Nickoloff and Griffiths, 1990; Norris, 1990; Springer, 1990). Leucocyte emigration into skin could also be promoted by the induction of vascular endothelial growth factor by TNF-α (Skobe and Detmar, 2000; Xia *et al*, 2002). Vascular endothelial growth factor activity increases the number of blood vessels and may, in part, account for the Auspitz sign that dermatologists observe in psoriasis patients.

TNF-α increases keratinocyte proliferation *in vitro* (Gottlieb *et al*, 2002c). It has been found to increase type I vasoactive intestinal peptide (VIP) receptor mRNA in keratinocytes. Subsequent binding of VIP to its receptor promotes keratinocyte proliferation and stimulates synthesis of pro-inflammatory cytokines such as IL-6, IL-8, and RANTES (Kakurai *et al*, 2001). TNF-α increases plasminogen activator inhibitor type 2 (PAI-2), a serine

proteinase inhibitor, which is thought to protect cells from apoptosis (Wang and Jensen, 1998). The prevention of apoptosis by this or other mechanisms could lead to increased longevity of keratinocytes and consequently to a thickened epidermis.

TNF-α is found at particularly high concentrations in the skin lesions and plasma of patients with psoriasis (Ettehadi *et al*, 1994). In psoriatic arthritis, the concentrations of cytokines secreted by activated monocytes/macrophages (TNF-α, IL-1, LI-6, and IL-8) are raised in the synovial fluids and membranes. As well as being involved in inflammatory processes, TNF-α is associated, both directly and indirectly, with bone and cartilage destruction, a feature of psoriatic arthritis (Mease *et al*, 2000). Thus, it potentially contributes to the clinical and histologic phenotype that is characteristic of psoriasis.

INFLIXIMAB

Infliximab is a chimeric IgG1 anti-TNF-α monoclonal antibody that binds to transmembrane-bound and soluble TNF-α with high specificity, affinity, and avidity (Scallon *et al*, 1995). Neutralizing transmembrane-bound TNF-α on the cells that synthesize it—for example, APC, keratinocytes, mast cells, and activated T cells (Scallon *et al*, 1995)—infliximab acts like a "sponge" to absorb soluble circulating TNF-α. It competes with the TNF receptor for receptor-bound ligand on target cells, such as lymphocytes, APC, endothelial cells, and keratinocytes, and has the potential to kill cells bearing surface TNF-α by both complement-mediated and antibody-dependent cell-mediated cytotoxicity. Infliximab induces apoptosis of activated T cells *in vitro* (tenHove *et al*, 2002).

Although not currently indicated for psoriasis, infliximab is indicated for moderate to severe Crohn's disease (for the reduction of signs and symptoms and closure of enterocutaneous fistulas) and moderate to severe rheumatoid arthritis (for reduction of signs and symptoms and inhibition of progression of structural damage) (Chaudhari *et al*, 2001; Scallon *et al*, 1995; Maini *et al*, 1999; Oh *et al*, 2000; Present *et al*, 1999; Targan *et al*, 1997; VanOosten *et al*, 1996).

In psoriasis, the TNF story started with a 57-year-old female with recalcitrant, severe psoriasis and Crohn's disease who was treated for refractory inflammatory bowel disease with infliximab. The patient had a 15-year history of Crohn's disease with dependence on high-dose prednisone (up to 60 mg/day), and a 20-year history of moderate to severe psoriasis treated with topical corticosteroids. Two weeks after a single infusion of infliximab (5 mg/kg), dramatic improvement in the patient's psoriasis was demonstrated (Oh *et al*, 2000). The PASI measured at baseline, two weeks post-infliximab infusion, and four weeks post-infusion were 34.1, 19.9, and 12.1, respectively. By 16 weeks post-infusion, the patient's PASI had gradually returned to baseline values of 34.3. The patient received a second dose of infliximab (5 mg/kg) 16 weeks following the first dose. As with the first dose, her psoriasis and Crohn's disease followed a similar course of clinical improvement in follow-up examinations (Oh *et al*, 2000).

On the basis of this observation, a study of the clinical benefit and safety of infliximab monotherapy in the treatment of moderate to severe plaque-type psoriasis was executed (Chaudhari *et al*, 2001). An additional aim of this study was to use infliximab as a targeted therapeutic probe to determine the role of TNF-α in psoriasis pathogenesis. Thirty-three patients with moderate to severe plaque psoriasis were randomized to receive placebo or infliximab 5 or 10 mg/kg infusions at weeks 0, 2, and 6. Patients were assessed at week 10 for the primary endpoint determination. Of 11 patients, 9 (81.8%) and 8 (72.7%) had at least 75% improvement in the PASI in the 5- and 10-mg/kg dosing groups, respectively, compared to 2 of 11 (18.2%) in the placebo group ($p < 0.05$ for each infliximab group versus placebo). There were no serious adverse events, and infliximab was well tolerated. The fact that a targeted anti-TNF agent clears psoriasis in 80% of patients suggests that for most patients TNF-α plays a pivotal role in the pathogenesis of this condition (Chaudhari *et al*, 2001).

An open-label extension was next implemented to assess the ability of infliximab monotherapy to maintain the clinical benefit achieved following an initial induction regimen. Additionally, the safety database for infliximab monotherapy in patients with moderate to severe plaque psoriasis was expanded. In the open-label extension, patients received a three-dose induction regimen of infliximab 5 or 10 mg/kg at weeks 0, 2, and 6. During weeks 10 through 26, patients were evaluated for loss of response (defined as loss of at least half of the improvement in the PASI score achieved at week 10) and were retreated with open-label infliximab 5 or 10 mg/kg as needed. Twenty-nine subjects participated. At week 10, 77% of infliximab-treated patients achieved at least 75% improvement from baseline in the PASI score. Among the 19 patients who continued in the trial through week 26, 58% maintained at least 50% improvement and 48% maintained at least 75% improvement in the PASI score as compared to the baseline score (Gottlieb *et al*, 2002e). There were no serious adverse events, and infliximab was well tolerated.

The pharmacodynamic response to infliximab was next investigated through immunoperoxidase analysis of lesional (weeks 0, 2, 10) and nonlesional (week 0) biopsies for changes in epidermal CD3+ T cell number, epidermal keratin K16 expression (a marker of abnormal keratinocyte differentiation), aberrant keratinocyte ICAM-1 expression, and epidermal thickness (Gottlieb *et al*, 2002c). Correlation analyses between histology and clinical efficacy measures were performed using the Spearman correlation test. Rapid and marked decreases in epidermal T cell infiltration, in epidermal thickness, and in keratinocyte adhesion molecule expression, along with normalization of keratinocyte differentiation, were demonstrated in infliximab-treated psoriatic plaques. Decreases in epidermal T cell infiltration were highly correlated with decreases in epidermal thickness. The observed infliximab-induced, histologic changes preceded achievement of the clinical endpoints and showed a high degree of correlation with the clinical scoring systems utilized (Gottlieb *et al*, 2002c). The combined clinical and immunohistologic data again demonstrate a pivotal role for TNF-α in the pathogenesis of psoriasis.

ETANERCEPT

Etanercept is a fusion fragments of protein of two TNF receptor p75 extracellular domains with one IgG1 Fc region. It is FDA-approved for rheumatoid and psoriatic arthritis. Sixty patients with psoriatic arthritis were enrolled in a double-blind, placebo-controlled study that compared etanercept (25 mg subcutaneously twice a week) with placebo when dosed for 12 weeks (Mease *et al*, 2000). The American College of Rheumatology criteria for improvement (ACR 20) (Mease *et al*, 2000) were used to assess the clinical response of psoriatic arthritis. In those patients with 3% or greater body surface area involvement with psoriasis, PASI and target lesion assessments were done. Forty-seven percent of patients in both the etanercept and placebo groups were on concurrent methotrexate therapy. Twenty percent in the etanercept group and 40% in the placebo group were on systemic corticosteroids.

The ACR 20 was achieved by 73% of etanercept patients as compared with only 13% of placebo patients at 12 weeks. In those patients evaluable for psoriasis activity, 26% in the etanercept group achieved 75% or greater improvement in PASI (Frederiksson and Pettersson, 1978) as compared with 0% in the placebo group. Median target lesion improvement was 50% and 0%, respectively, in the two groups. Etanercept was well tolerated, with injection site reactions being the most common adverse event observed (Mease *et al*, 2000).

Phase III studies have confirmed the clinical results seen in the phase II studies of psoriatic arthritis (PsA) patients: 205 patients with PsA were enrolled; 101 received etanercept and 104 received

placebo. Patients received 25 mg etanercept or placebo twice weekly (SC) for 24 weeks. Concomitant therapy with methotrexate, oral corticosteroids, and nonsteroidal anti-inflammatory drugs was permitted. The primary arthritis endpoint was ACR 20 at 12 weeks. Psoriasis improvement was measured by target lesion score and, in a subset of patients with psoriasis involvement $\geqslant 3\%$ ($n = 66$ for etanercept; $n = 62$ for placebo), by the PASI. Arthritis was significantly improved with etanercept treatment. ACR 20 was achieved by 59% of the etanercept group and 15% of the placebo group at 12 weeks ($p < 0.0001$). Significant improvement in arthritis was maintained with continued etanercept treatment through the end of the study at 24 weeks. AC 70 was achieved in 11% of the etanercept-treated patients versus 0% of the placebo-treated patients at 12 weeks. Psoriatic target lesions were also significantly improved with etanercept treatment; median improvement at 24 weeks was 33% in etanercept patients and 0% in placebo patients ($p < 0.0001$). PASI measurements confirm this result. Etanercept was well tolerated in this patient population (Mease *et al*, 2001) and is FDA approved for psoriatic arthritis.

The next study examined the efficacy of etanercept as monotherapy in patients with psoriasis. In a 24-week multicenter, blinded, randomized study, patients received etanercept 25 mg or placebo by SC injection twice weekly. The primary endpoint was achievement of at least a 75% improvement in PASI (PASI 75) at 12 weeks. One hundred and twelve patients enrolled in the study. Groups ($n = 57$ for etanercept; $n = 55$ for placebo) were well-matched for patient age, psoriasis duration, and disease intensity. The percent of patients achieving PASI improvement of at least 75% at 12 weeks was significantly higher in the etanercept group versus the placebo group (30% and 2%, respectively; $p < 0.0001$). Efficacy continued to improve with longer treatment, with 54% of etanercept-treated patients and 5% of placebo-treated patients reaching PASI 75 at 24 weeks ($p < 0.0001$). Statistically significant improvements in patient global, physician global, and target lesion assessments and DLQI (a quality of life questionnaire) confirmed the efficacy of etanercept therapy. Etanercept was well tolerated, with numbers of patients reporting adverse events similar between groups (70% for etanercept, 67% for placebo). The rates of adverse events (4.49 per patient-year for etanercept, 5.66 per patient-year for the placebo group) were also similar. Mild injection site reactions were observed in 9% of the etanercept-treated patients versus 0% of the placebo-treated patients. This study provided further evidence that etanercept as monotherapy for psoriasis is efficacious and well tolerated (Gottlieb *et al*, 2002d).

The accumulated data point to a key role for TNF-α in the pathogenesis of psoriasis and psoriatic arthritis, rheumatoid arthritis, and Crohn's disease. Additionally, both infliximab and etanercept have demonstrated efficacy in ankylosing spondylitis, suggesting that this disorder, too, is at least partially mediated by TNF-α. There are case reports and small series of patients with other immune-mediated inflammatory diseases treated successfully with TNF-targeting immunotherapies (infliximab). These include uveitis, Sjögren's syndrome, giant cell arteritis, graft versus host disease, sarcoidosis, hidradenitis suppurativa, and pyoderma gangrenosum (Chaudhari *et al*, 2001; Oh *et al*, 2000; Braughman and Lower, 2001; Botros *et al*, 2000; Braun *et al*, 2002; Cambell and Ghosh, 2001; Couriel *et al*, 2000; De Clercq, 1987; Fabrizio *et al*, 2001; Gorman *et al*, 2002; Martinez *et al*, 2001; Schothorst *et al*, 1991; Smith *et al*, 2001; Steinfeld *et al*, 2001; Tan *et al*, 2001). Rather than considering these disorders as separate and localized to nonoverlapping therapeutic areas, perhaps we should group these diseases by common pathogenesis.

The IL-10 and IL-11 cytokines have been demonstrated in small clinical trials to shift cytokine expression in psoriatic plaques of responding patients toward a more normal T1/T2 cytokine expression ratio (Asadullah *et al*, 1998; Trepicchio *et al*, 1999). In larger, double-blind, placebo-controlled trials, however, risk/benefit ratios were unsatisfactory. The utility of cytokine deviation strategies is therefore still an open question. It is possible that IL-4 may be a more successful candidate to pursue (Thomas, 2001).

CONCLUSION

Although there is more work to be done, immunobiologics provide the hope for safe and effective long-term management of life-disabling psoriasis. The use of targeted immunotherapies as pathogenic probes has led to scientific discoveries that help uncover new information on the pathogenesis of psoriasis and on the control of cutaneous immunity.

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