1 Inhibition of IFN-γ as a Method of Treatment of Various Autoimmune Diseases, Including Skin Diseases

B. Skurkovich, S. Skurkovich

1.1 Introduction ................................................. 2
1.2 Treatment of Th-1-Mediated Autoimmune Diseases ........ 4
1.2.1 Rheumatoid Arthritis .................................. 5
1.2.2 Multiple Sclerosis .................................... 5
1.2.3 Corneal Transplant Rejection .......................... 6
1.2.4 Type I Diabetes ...................................... 6
1.2.5 Uveitis .................................................. 7
1.3 Treatment of Th-1-Mediated Autoimmune Skin Diseases Using Anti-IFN-γ ....................................... 7
1.3.1 Psoriasis Vulgaris ................................... 7
1.3.2 Alopecia Areata ....................................... 9
1.3.3 Vitiligo ................................................. 10
1.3.4 Acne Vulgaris ....................................... 11
1.3.5 Herpes Simplex Virus Type 1 ........................... 11
1.4 Genetic Skin Diseases in Which Cytokines May Be Involved ............................................ 12
1.4.1 Dystrophic Epidermolysis Bullosa (DEB) ................. 12
1.5 Other Th-1-Mediated Skin Diseases in Which Testing of Anticytokine Therapy Is Warranted .......................... 13
1.6 Beneficial Effect of Anti-IFN-γ in Possibly Non-Th-1-Mediated Skin Diseases .......................... 14
1.6.1 Herpes Simplex Virus Type 2 ........................... 14
Abstract. We pioneered anticytokine therapy (ACT) for autoimmune diseases (ADs). In 1974, we proposed that hyperproduced interferon (IFN) can bring AD and anti-IFN can be therapeutic. In 1989, we proposed removing tumor necrosis factor (TNF)-α together with certain types of IFN to treat various ADs. We found IFN in patients with different ADs and conducted the first clinical trial of ACT in 1975. Anti-IFN-γ and anti-TNF-α work in similar ways, but the latter brings serious complications in some patients. We obtained good, sometimes striking, therapeutic effects treating many different Th-1-mediated ADs with anti-IFN-γ, including rheumatoid arthritis, multiple sclerosis (MS), corneal transplant rejection, and various autoimmune skin diseases such as psoriasis, alopecia areata, vitiligo, acne vulgaris, and others. Anti-IFN-γ was in some ways superior to anti-TNF-α, which was ineffective in MS. Anti-IFN-γ therapy holds great promise for treating many Th-1 ADs, especially skin diseases.

1.1 Introduction

Anticytokine therapy was pioneered by S. Skurkovich, who in 1974 published in Nature the proposal that the hyperproduction of interferon (IFN) (a cytokine) can bring autoimmune disease and that neutralization of IFN could be therapeutic (Skurkovich et al. 1974). This proposal was based on data describing the mechanism of IFN action (Skurkovich et al. 1973). It was postulated that IFN production was a part of the immune response and that any disturbance of IFN production could lead to immune system dysregulation and vice versa (Skurkovich et al. 1973, 1982). In other words, a disturbance of IFN synthesis can bring disease. In 1975, IFN was found in the blood of autoimmune patients and the first anticytokine therapy was tested (Skurkovich and Eremkina 1975).

Many years ago, it was proposed that anticytokine therapy could be beneficial in treating a wide variety of autoimmune diseases and diseases of supposed autoimmune genesis, in which disturbed IFN synthesis is a common mechanism of pathology; these included prolongation of skin allografts, collagenoses, rheumatism, hemolytic anemia, immune form