

Goodwin J S, Messner R P, Bankhurst A D, Peake G T, Saiki J H & Williams R C, Jr. Prostaglandin-producing suppressor cells in Hodgkin's disease. N. Engl. J. Med. 297:963-8, 1977.
[Dept. Medicine. Div. Rheumatology. Univ. New Mexico Sch. Medicine, Bernalillo County Medical Center, Albuquerque, NM]

Monocytes from six patients with untreated Hodgkin's disease produced fourfold more prostaglandin E₂ (PGE₂) than did controls. Either physical removal of the monocytes by adherence to glass or blockade of prostaglandin production by the addition of indomethacin partially restored the depressed *in vitro* mitogen reactivity of the Hodgkin's disease lymphocytes. [The SCI® indicates that this paper has been cited in over 430 publications since 1977.]

James S. Goodwin
Division of Gerontology
Department of Medicine
University of New Mexico
School of Medicine
Albuquerque, NM 87131

September 21, 1984

In 1974, I left the National Institutes of Health (NIH) for New Mexico to finish my internal medicine training and to escape the East Coast. After my residency, I applied to stay in New Mexico for a rheumatology/immunology fellowship with Ron Messner and Ralph Williams. Ralph suggested that I apply to the Arthritis Foundation for funding. He suggested that I write a grant proposal on prostaglandin control of immune function, since he was under the impression that I had worked on prostaglandins at NIH (I had not). I knew then, as I know now, that it is dangerous to attempt to disabuse Ralph of his opinions, so I studied up on prostaglandins and wrote a grant proposal.

The most important work at that time was by Plescia showing that prostaglandins produced by a tumor could "subvert" attempts by the immune system to reject the tumor.¹ Also important was work by Dave Webb in mice showing that glass-adherent splenic T cells produced prostaglandins that sup-

pressed the proliferation of nonadherent splenic T cells.^{2,3} I found roughly the same system in human peripheral blood, except that the adherent cell that produced the prostaglandins was almost certainly a monocyte. The prostaglandin E (PGE) that was produced suppressed mitogen-stimulated proliferation of human T cells. Ron and I termed this system the "prostaglandin-producing suppressor cell" demonstrating that our combined skills in marketing equaled and perhaps exceeded our skills in immunology.⁴

We then set out to look for diseases in humans where an overactivity of this prostaglandin-producing suppressor cell might be responsible for depressed cellular immune function. Hodgkin's disease was our first choice because Twomey and his associates in Houston had already shown that monocyte suppressor cells were important in the depressed mitogen reactivity in that disease.⁵ In the first six untreated patients that we studied, we showed that their monocytes produced fourfold more PGE per monocyte and that much of the depressed mitogen response could be reversed *in vitro* by adding a cyclo-oxygenase inhibitor, such as indomethacin.

Since this was my first paper in immunology, I spent a few nervous months waiting for someone to reproduce our findings. Over the next few years, many groups confirmed the overproduction of PGE by Hodgkin's disease monocytes, but most investigators found a less complete restoration of the *in vitro* mitogen response with the addition of indomethacin. Over the past six years, there have been more than 100 articles on the role of the prostaglandin-producing suppressor cell in various human diseases (reviewed in reference 6). The example of Hodgkin's disease would still appear to be the most clear-cut.

1. Plescia O J, Smith A H & Grlawich K. Subversion of immune system by tumor cells and role of prostaglandins. *Proc. Nat. Acad. Sci. US* 72:1848-54, 1975. (Cited 215 times.)
2. Webb D R & Osheroff P L. Antigen stimulation of prostaglandin synthesis and control of immune responses. *Proc. Nat. Acad. Sci. US* 73:1300-9, 1976. (Cited 160 times.)
3. Webb D R & Nowowiejski I. Mitogen-induced changes in lymphocyte prostaglandin levels: a signal for the induction of suppressor cell activity. *Cell. Immunol.* 41:72-85, 1978. (Cited 125 times.)
4. Goodwin J S, Bankhurst A D & Messner R P. Suppression of human T-cell mitogenesis by prostaglandin: existence of a prostaglandin-producing suppressor cell. *J. Exp. Med.* 146:1719-34, 1977. (Cited 430 times.)
5. Twomey J J, Laughter A H, Farrow S & Douglass C C. Hodgkin's disease: an immunodepleting and immunosuppressive disorder. *J. Clin. Invest.* 56:467-75, 1975. (Cited 235 times.)
6. Goodwin J S & Ceuppens J. Regulation of the immune response by prostaglandins. *J. Clin. Immunol.* 3:295-315, 1983.