Table 1. Effect of rIL-1-β on Thyrotropin-Stimulated Human Thyroid Cells.*

Amount of rIL-1-β	Experiment 1		Experiment 2		Experiment 3	
	Thyroglobulin (primary culture)	cAMP	Thyroglobulin (secondary culture)	cAMP	Thyroglobulin (primary culture)	cAMP
U/ml	percent of controls					
0.001	120	105	124	140	120	74
0.01			94	152		
0.1	79	66	96	142	143	71
1	54	75	79	136		
10	23	35	77	131	67	59
100	23	41	59	88	78	52

*The cells were cultured with thyrotropin (with and without rIL-1-β) for four days. Secondary cultures were preincubated for three to four days to allow the formation of monolayers. In cultures without rIL-1-β (controls), the mean secreted amounts of thyroglobulin and cAMP were 773 ng per microgram of DNA (range, 267 to 942) and 59 pmol per microgram of DNA (range, 10 to 106), respectively.

The findings indicate a central role of monocytes/macrophages (and possibly natural-killer cells) and their product interleukin-1 in autoimmune endocrine diseases. Moreover, low concentrations of interleukin-1 may accumulate in endocrine tissues as a result of diffusion from the blood during conditions of stress, and interleukin-1 may therefore fulfill an important physiologic role by potentiating thyroglobulin and insulin production under these circumstances.

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To the Editor: It is probably premature to exclude an action of methimazole on immunocompetent cells that modifies, albeit in a minor way, auto-aggression in the thyroid glands of patients with Graves' disease. At concentrations easily achieved in the thyroid gland (10^{-6} to 10^{-7} M), methimazole has been shown to inhibit peroxidase and to scavenge hydrogen radicals, which have deleterious effects on lymphoid-cell function.[1]

We do, however, concur that the action of methimazole on the thyroid cell is important. We have demonstrated recently that Graves' IgG strongly induces HLA-DR expression in thyroid cells in vitro, apparently through a pathway separate from that whereby γ-interferon induces DR molecules.[2] Surprisingly, methimazole inhibits Graves' IgG-induced but not γ-interferon-induced DR expression (Bodoly E, et al.: unpublished data). Our data strongly support the suggestion that methimazole also acts by modifying molecules displayed on the thyroid-cell surface and provide a mechanism for the finding that DR expression is reduced to background levels in the thyroids of patients with Graves' disease who are in remission after a course of methimazole, but not in those whose disease has not remitted.[3]

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The above letters were referred to the authors of the article and editorial in question, who offer the following replies:

To the Editor: The letter by Dr. Walfish points out that the use of two-color immunofluorescence of T cells in flow cytometry yielded results similar to those obtained in our prospective study[1] employing ultraviolet microscopical analysis. The detailed study of Chan and Walfish[2] included observations in a group of patients with untreated Graves' disease who were reported to have subnormal levels (as compared with those of healthy subjects) of activated T suppressor/cytotoxic cells ($DR^+Leu\text{-}2a^+$). This group was compared with another group of patients who, after an average of five months of therapy with propylthiouracil, had normal levels of such cells. As pointed out, the direct comparison of data from the two studies[1,2] is somewhat hampered by the different ways of expressing their results. It is clear, however, that both studies show that thyrostatic drug therapy in Graves' disease alters the balance between activated T helper ($DR^+Leu\text{-}3a^+$) and T suppressor-like cells. This is important from a biologic viewpoint.

We agree with the opinion expressed by Bendtzen et al. that monocyte products such as interleukin-1 may be important in autoimmune diseases affecting endocrine organs. Following the lead of Mandrup-Poulsen et al.,[3] we have observed a potent inhibitory effect of interleukin-1 on [^{125}I]iodide organification in porcine thyroid follicles cultured in suspension (Karlsson FA, Westermark K: unpublished data).

We agree with Farid et al. that, as we pointed out in our article,[1] a direct inhibitory effect of methimazole on immunocompetent cells is not to be excluded. However, as we also said, it is more likely that methimazole acts primarily through thyrocytes to suppress autoimmune activity. Forthcoming data cited by Farid et al. in their letter and from our laboratory (Karlsson FA, Tötter-