To the Editor:

We thank Dr. Case for adding his important series to the literature. The pathogenesis of Felty's syndrome may be heterogeneous, and this may be reflected in the variability of the granulocyte response to lithium carbonate. Although all eight patients responded in the original report of Gupta and colleagues, one should note that there was great variability among the patients in terms of both absolute and relative increments of circulating neutrophils. Other failures and marginal successes of neutrophil response to lithium carbonate therapy in Felty's syndrome were discussed at the 1979 Eagle River meeting on "The Effects of Lithium on Granulopoiesis and Immune Function."

We wonder if Dr. Case's patient 5 had a qualitative disorder of granulocyte function that was corrected with lithium carbonate and associated with clinical improvement despite continuing granulocytopenia. Lithium-mediated improvements of qualitative granulocyte abnormalities, especially defective chemotaxis, have recently been reported in humans as well as in the homozygous beige mouse with Chediak-Higashi syndrome.

An international collaborative effort (at least a registry) is needed to determine the ultimate role of lithium carbonate in all forms of neutropenia.

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To the Editor:

In a recent review1 F. W. Ruscetti and E. C. Gallo pointed out the possible relevance of T lymphocyte growth factor (TCGF) as a regulatory molecule for the growth and function of T lymphocytes. They also discussed the theoretical advantages of agar T-cell colonies as an approach for the clonal analysis of T lymphocytes. As mentioned by the authors, the cloning of T cells in agar, which we believe was indeed initiated by Bujadoux et al.,2 has readily expanded following studies from Rozenstajn et al.3 Quite a short time later, these studies were simultaneously confirmed by others and, we believe, extended by ourselves,4 since to the best of our knowledge, we presented the first evidence that colony formation does not require any cell preincubation with PHA in liquid culture. Subculture experiments4 together with kinetic studies5,6 lead us to suspect that in vitro agar T-cell colony formation requires some interaction between a T colony-forming cell (TCFC) and at least two populations of "cooperating cells" (CC). CC mediate their effect through soluble factor(s),7 which we proposed to refer to as "colony-promoting activity" (CPA) since we were able to show that CPA not only enhances T-cell colony growth but represents a true promoting factor that is perquisite for requirement for T-cell colony formation.8 Obviously the requirement of both PHA and CPA to induce TCFC proliferation into agar colonies bears some analogy with the need of TCGF for long-term proliferation of PHA-activated T cells in liquid culture. However, we have accumulated recent indications that both systems might differ in at least four respects:

1. Preliminary evidence would suggest that CPA (in contrast to TCGF) sensitizes TCFC to some mitogenic effect of PHA,4 whereas TCGF has been shown to require preactivation of T cells by PHA or alloantigens in order to exert its mitogenic effect.7
2. High CPA levels are found in the supernatant of nonadherent non-T, B-enriched cell cultures stimulated with PHA6; in contrast, most evidence indicates that TCGF is a T-cell-derived factor probably produced under the inductive effect of monocyte mediated by interleukin-1.
3. TCGF and CPA appear also to differ in their kinetics of production as indicated by the recovery of substantial CPA levels in the supernatants of 4-day peripheral blood mononuclear cell cultures stimulated with PHA,8 whereas TCGF levels have been reported to reach a peak in 24-48 hr cultures and usually to fall to undetectable values in 4-day cultures supernatants.
4. Finally and perhaps of major importance has been the recent demonstration that T-cell colonies may derive from mature E-rosette-forming (E-RFC) T cells but are obtained with a much higher plating efficiency from immature T-cell precursors (OKT3+, Ia+, E-RFC-) that are found in the bone marrow9 as well as in peripheral blood.10

Studies in our laboratory are now under way in order to further explore these avenues of research. Nevertheless, we believe that the T-cell colony assay should also provide some interesting insights in order to clarify earlier steps of T-cell differentiation in the future.

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