# Editorial

The development of decisive therapeutic interventions for hematopoietic and solid tumor neoplasms has in the past been hampered by the lack of a detailed understanding of the molecular and functional defects in the neoplastic cells. During the past five years, the molecular analysis of leukemia cells has generated an exciting array of discoveries about the abnormalities in the growth stimulatory and inhibitory pathways within the abnormal cells themselves, which provide possible explanations for why leukemic cells are accumulating in increased numbers in the peripheral blood and marrow of these patients.

Chronic myelogenous leukemia (CML) was the first neoplastic disorder associated with a single and specific chromosomal abnormality, the Philadelphia chromosome translocation (1). A chimeric fusion gene, the *bcr-abl*, which coded for the p210 tyrosine-specific protein kinase, was found to be created by this translocation (2). The critical molecular interactions between the $p210^{bcr\text{-}abl}$ protein and the intracellular signal transduction elements such as Grb-2 (3) are still being worked out.

Gordon et al. (4) were the first to go outside of CML cells to study how these cells interact with other cells which might regulate myelopoiesis in vivo, the stromal cells. They reported a defect in cellular adhesion to the stromal cells to be present in CML myeloid cells, which is presumed to play a role in the regulation of myeloid cell growth (4). In vitro culture of CML and normal hematopoietic cells on stromal monolayers showed a selective in vitro growth advantage for the normal versus the CML cells presumably based on the ability of the normal cells to bind to and be supported by stromal cells (5). $\alpha$-interferon, which generates a complete cytogenetic response in 20% of CML patients (6 and 7), restores the adhesion of CML cells to stromal cells (4).

In this issue of *The Journal* Bhatia et al. (7) extend this work by showing that the $\alpha$-interferon induced correction of an adhesion defect between myeloid cells and stromal cells is inhibitable by monoclonal antibodies to the $\alpha_4$, $\alpha_5$, and $\beta_1$ integrin molecules. Because they were unable to demonstrate a change in the levels of these membrane proteins on CML lineage positive cells after exposure to interferon, they conclude that interferon corrects the functional defect which is associated with CML. Similar techniques in the past were used to show that a regulatory interaction exists between normal T cells and myeloid cells mediated by the surface proteins CD2 and LFA-3; that this interaction does not occur in CML myeloid cells due to decreased LFA-3 surface expression; and that this defect was correctable by $\alpha$-interferon (8). The present studies of Bhatia et al. (7) show that the $\alpha_4$, $\alpha_5$, and $\beta_1$ integrin molecules are involved in the alpha-interferon induced correction of the adhesive defect in CML. A detailed analysis of this issue in cells at different stages of myeloid maturation (LTCIC, CFUGEMM, CFUGM), and in different hematopoietic lineages, may clarify the precise mechanism through which this occurs. The studies of Bhatia et al. (7) identify another of a growing list of neoplastic diseases in which the interaction of the abnormal cells and other cells or proteins present in the tissue of origin play a major role in the development of the disease. Clearly, cancer and hematopoietic neoplastic diseases arise not only from signals from within the neoplastic cells (the seed), but also from the interaction of the seed with the soil (in this case, the stroma). Recognition of the importance of this new dimension of human neoplastic disease is already having an impact on the development of effective therapy for these diseases (9).

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J. Clin. Invest.

0021-9738/94/07/0003/01 $2.00
Volume 94, July 1994, 3