

This Week's Citation Classic

Foley G E, Lazarus H, Farber S, Uzman B G, Boone B A & McCarthy R E.

Continuous culture of human lymphoblasts from peripheral blood of a child with acute leukemia. *Cancer* 18:522-9, 1965.

[Children's Cancer Res. Foundation, Boston, and Dept. Pathology, Harvard Med. Sch., Children's Hosp., Boston, MA]

This communication reports the first isolation of human lymphocytic cells in useful quantities by application of the 'population dependence phenomenon'—large inocula in small-volume substrates directly in suspension culture. Cell yield was sufficient for extensive biochemical and biological studies. [The **SCI**[®] indicates that this paper has been cited over 310 times since 1965.]

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"In the 1950s, our cell culture laboratories became interested in the murine leukemias, and several were isolated in monolayer culture, wherein the attached cells were fibroblast-like, but when injected intraperitoneally in the mouse strain of origin, exhibited lymphocyte morphology. This led to similar experiments with human peripheral and bone marrow lymphocytes from patients with lymphocytic leukemia. These cells did not attach to any of several surfaces tried, but rather remained in suspension and appeared to 'want to grow,' but gradually died despite all nutritional and physical permutations. All attempts to cultivate these cells in suspension culture failed until it occurred to us to utilize the phenomenon of 'population dependence'¹—by use of large inocula in small-volume primary cultures. Final success resulted in a method (at first in homemade culture apparatus) for the quantity production of these cells for biological and biochemical studies. Improved (automatic) culture apparatus increased the yield—a 15 liter vessel, for example, produced 320×10^8 (ca 20 gm ww) of cells!

"The experiments were done in the

laboratories of microbiology and cell biology (which I organized in 1947), Children's Cancer Research Foundation, Boston, Massachusetts, perhaps better known as the Jimmy Fund Laboratories. The late Sidney Farber, director of the Foundation, and his clinical staff provided the clinical specimens and hematological and other relevant clinical data. Lazarus and Boone provided the priceless ingredient essential to any cell culture studies—'tender loving care' around the clock—in the beginning, seven days a week for nearly a year. Uzman provided the exquisite electron microscopy studies, and McCarthy provided the cytological studies. No particular problems were encountered, save assessment of the hazards (if any) inherent in the production and handling of these cells in huge quantities. We had no choice but to assume it was hazardous—thus strict containment facilities were built for the biochemical, animal, and large-scale culture work.

"A long series of publications from the Foundation on various aspects of the biochemistry, cytochemistry, cytology, biology, and nutrition of human leukemic cells as compared to nonleukemic lymphocytes resulted from these studies, as did the first successful heterotransplantation of human leukemia to an experimental animal (neonatal Syrian hamsters),² and its pathology therein,³ as well as delineation of a fundamental nutritional difference between leukemic and nonleukemic lymphocytes.⁴ However, our report attracted little attention at first—no 'awards' were received.

"We feel that our publication has become a 'classic' in its field because it indicated a direction to the isolation and cultivation of human lymphocytes which has since been modified and refined by others for many purposes. The availability of this tool, for example, enabled the development of many studies in cellular immunology."

1. Eagle H & Piez K. The population dependent requirements by cultured mammalian cells for metabolites which they can synthesize. *J. Exp. Med.* 116:29-43, 1962.
2. Adams RA, Foley G E, Uzman B G, Farber S, Lazarus H & Kleinman L. Leukemia: serial transplantation of human leukemic lymphoblasts in the newborn Syrian hamster. *Cancer Res.* 27:772-83, 1967.
3. Liknaitzky D G, Takakusu A & Adams R A. Early pathology of lymphoma developing in newborn Syrian hamsters inoculated with human leukemic lymphoblasts. *Cancer* 23:94-100, 1969.
4. Foley G E, Barell E F, Adams R A & Lazarus H. Nutritional requirements of human leukemic cells. *Exp. Cell Res.* 57:129-33, 1969.