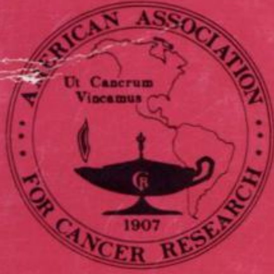

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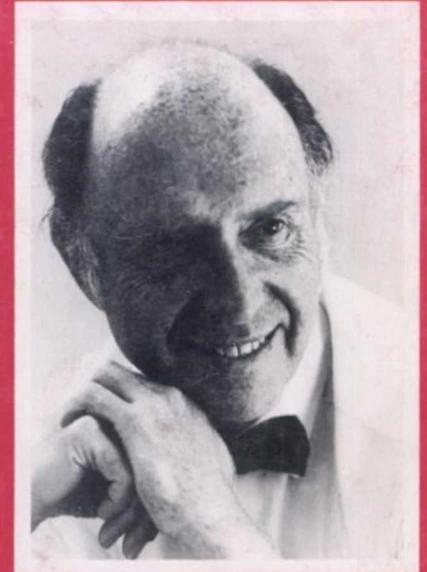

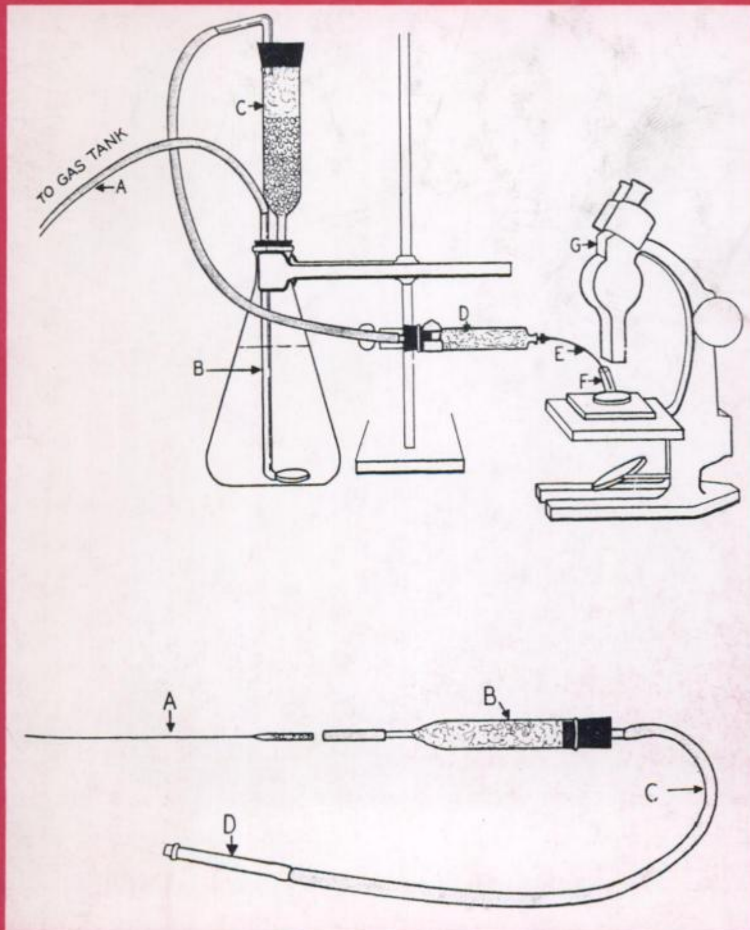

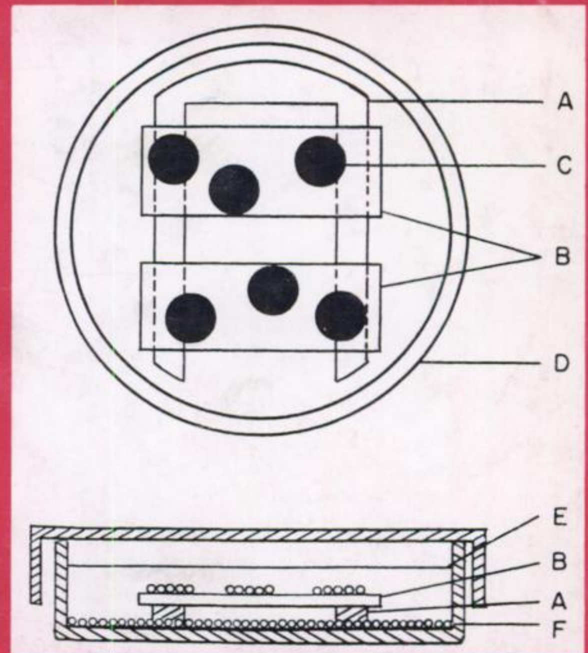

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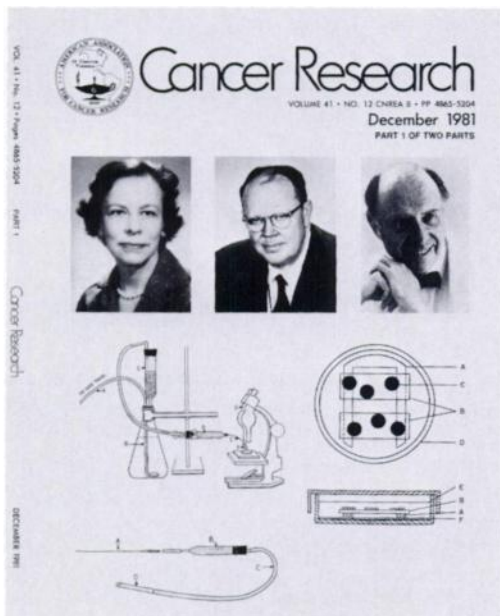

Mammalian cloned cell populations in culture have been of great value in many aspects of experimental cell biology.

Interest in creating colonies from individual mammalian cells, or clones, goes back to over 50 years ago. However, single cells that were isolated failed to grow because of the culture media and techniques then available. In 1935, Johannes K. Moen (J. Exp. Med., *61:* 247, 1935) applied the bacteriological plating technique to individual mononuclear cells of the guinea pig. The first successful growth from a single isolated mammalian cell of a fixed tissue origin was achieved in 1948 by the tissue culture group working at the National Cancer Institute, K. K. Sanford, W. R. Earle, and G. D. Likely (J. Natl. Cancer Inst., *9:* 229, 1948). Success was attributed to improvements in tissue culture media techniques and to the creation of a restricted environment in which the single cells could adjust to the culture medium and begin to divide. The original procedure maintained single cells in capillary tubes for the first few cell divisions, from which the colony migrated out into the flask to establish a clone culture. The method was altered a decade later (Exp. Cell Res., *23:* 361, 1961) and subsequently simplified [See P. F. Kruse and M. K. Patterson (eds.), *Tissue Culture Methods and Applications,* p. 237. New York: Academic Press, Inc., 1978]. The 1961 paper includes a history of cloning mammalian cells.

In 1955, Theodore Puck and P. I. Marcus, of the University of Colorado, Denver (Proc. Natl. Acad. Sci. U. S. A., *41:* 432, 1955), described a method of plating human cancer cells (HeLa) over a layer of nondividing irradiated "feeder" cells. A year later, the technique was evolved obviating the "feeder" requirement (J. Exp. Med., *103:* 273, 1956).

More recently, these techniques have been replaced by plating cell suspensions with aid of soft agar, plastic films, or nylon cloth (see *Methods in Cell Biology.* New York: Academic Press, Inc., 1979; *e.g.,* Vol. 22, pp. 237 and 247). However, these represent colony isolates and not clones from rigidly established single cells.

Pictured are Drs. Katherine K. Sanford on the *left,* Wilton R. Earle (1902–1964), center, and Dr. Theodore T. Puck on the *right.* The figures on the *left* diagram the original procedure of Sanford *et al.,* 1948. Single cells were picked from the floor of the flask by means of a micropipet. During cell isolation, the culture was gassed with 5% CO_2 in air to maintain the correct pH of the medium. A section of the capillary with the select cell was then cut and inserted into a flask. The figures on the *right* diagram the arrangement used to grow clones of HeLa cells (*C*) over a layer of "feeder" cells (*F*), immersed in liquid medium at *Level E* (from Puck and Marcus, 1955).

We are indebted to Drs. Sanford and Puck for the material and photographs.

M.B.S.