

cultures originating from the same strain. To illustrate: after the first series of experiments had been carried in the flasks under this treatment for about twelve days, it was noticed that the cells of one of the cultures belonging to a strain of fibroblasts derived from muscle had very suddenly given rise to a broad band of macrophages. A few days later a culture of the same age, but belonging to a strain of heart fibroblasts, behaved similarly. Less than two weeks later a third culture showed the same phenomena. This third culture, which had been treated for twenty-eight days in the flask when the transformation occurred, had been made from a strain of fibroblasts originating from bone periost, a strain which had been carried for twelve passages before the experiment was made. It was therefore quite obvious that the phenomenon was not limited to any one cell type. It is interesting to note that Carrel and Ebeling,<sup>3</sup> Fischer<sup>4</sup> and Ephrussi and Hughes<sup>5</sup> have reported the occasional occurrence *in vitro* of similar transformations, although the factors responsible for the changes have never been clearly defined.

After these and many similar observations had been made, new experiments were set up in an endeavor to duplicate as closely as possible every step in the treatment of these cultures in the hope that the changes might recur. And since this proved to be the case, we had a better opportunity for studying the predisposing conditions. Since, also, but a limited number of the cultures comprising the various experiments showed the phenomena, it was possible to make a comparative study of the general condition and rate of growth of cultures which had transformed and of those which had not. It was found that those cultures which had not transformed fell into two groups, namely, cultures which responded very favorably to the plasma treatment, as evidenced by the condition of the cells and their rate of proliferation, and those which could not adapt themselves to the new medium and very early succumbed when deprived of the abundant food substances which they had received before being placed under the conditions of the experiments. When transformation did occur, it seemed to take place at some critical period in the life of a culture in which the degeneration process was already quite evident, but was advancing at a relatively gradual rate.

These cells have been referred to as macrophages because they appeared identical with macrophages both in form and behavior. They were quite independent, very active, and showed no tendency to form

a tissue. They also possessed the typical undulating membrane. Their origin was very easily ascertained. They were invariably budded off from the fibroblast-like cells at the periphery of a culture which showed unmistakable signs of degeneration. The cells from which the macrophages were derived were always very heavily granulated and distended. Several macrophages were usually pinched off from a single fibroblast, until finally nothing was left of it but a small remnant packed with the globules and granules of the original cell. When the transformation process had once begun, it continued with great rapidity. The macrophages wandered out into the medium at a uniform rate from the entire periphery, and, inasmuch as plasma is the optimal medium for their multiplication, they eventually covered an area which was, in some cases, twelve times as great as that finally covered by the colony of fibroblasts from which they were derived. The identity of the macrophages was further borne out by certain reactions, typical of blood and tissue macrophages, to alterations in the chemical constitution of the medium.

It seems reasonable to conclude that the macrophage and the fibroblast represent functional variations of the same cell type. The extent to which a cell changes its form depends, however, upon its physiological condition at any one moment and upon the chemical and physico-chemical properties of the medium. In order to determine the nature of such properties as may be responsible for these changes, it now becomes necessary to study the effect upon the cells of various constituents of the medium employed.

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### BOOKS RECEIVED

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<sup>3</sup> A. Carrel and A. H. Ebeling, *J. Exp. Med.*, 44, 261, 1926.

<sup>4</sup> A. Fischer, *Arch. f. exper. Zellforschung*, 3, 345, 1926.

<sup>5</sup> B. Ephrussi and Y. Hughes, *C. R. de la Soc. de biol.*, 105, 697, 1930.