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Microencapsulation of Living Cells and Tissues

1983 Review and Update

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Novel processes for the microencapsulation of human and mammalian cells and tissues have been developed (*1,2*). The in vitro studies of microencapsulated mammalian cells were discussed at the last International Symposium on Microencapsulation in 1979 (*2*). The report described how *in situ* microcapsular membranes were formed around living cells, such as human red blood cells, rat hepatoma cells, human sperm cells, and rat pancreatic islets, by the polysalt-bonding of polyelectrolytes of opposite charges.

Although several polyionic polymer systems have been tried with different degrees of success in the last few years, the system of polylysine alginate is still considered to be the polyelectrolyte complex system of choice, especially for in vivo applications (*2*).

Several laboratories are now utilizing this technique (*2*) to microencapsulate a wide variety of cells and biologically active materials for many kinds of applications.

After the preliminary report of Lim and Sun in 1980 (*3*) on the use of microencapsulated pancreatic islets as bioartificial endocrine pancreas,

other laboratories have also started working on the same application. Currently, my laboratory, the Islet Laboratory in Connaught Research Institute and Dr. Cochrum's laboratory in the University of California, San Francisco, all have long term (over 5 months' duration) successes of complete normalization of diabetic mice, using a single ip injection of microencapsulated rat pancreatic islets. Two other laboratories engaging in this same endeavor include one medical center in Los Angeles and another one in Philadelphia.

A new application started in 1981 by Mr. Shen, a graduate student in my laboratory, involves in vitro and in vivo studies of microencapsulated rat and cat adrenocortical cells. Results of in vitro experiments showed that the total viability of cultured adrenocortical cells was prolonged by at least 2–3 fold when microencapsulated. Microencapsulated adrenocortical cells from cats and rats have been successfully implanted intraperitoneally into adrenalectomized mice by Mr. Shen. Figure 1 is a photomicrograph of microencapsulated cat adrenocortical cells.

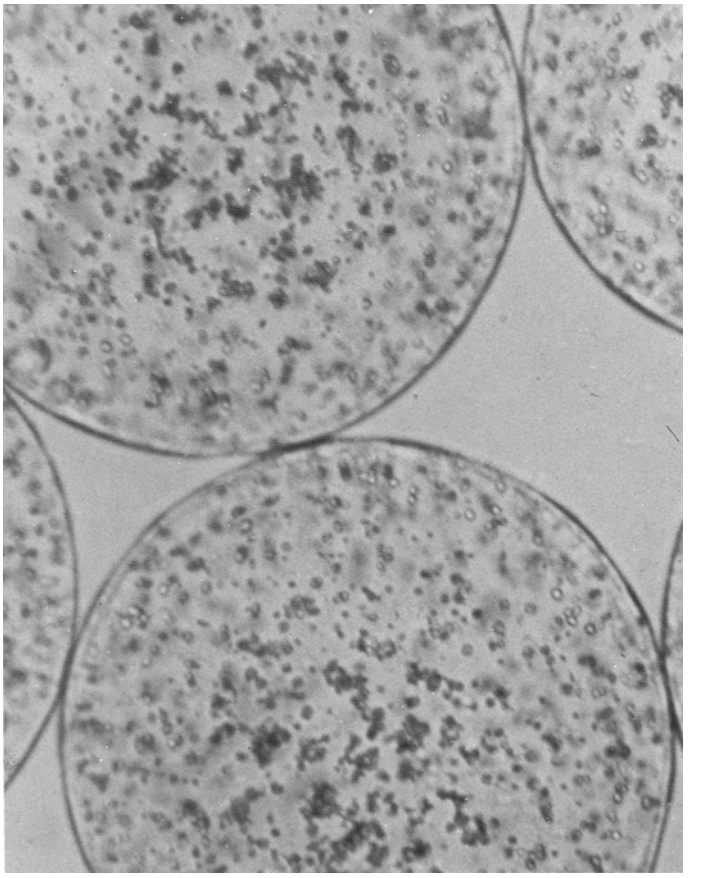


Fig. 1. Microencapsulated rat adrenocortical cells.

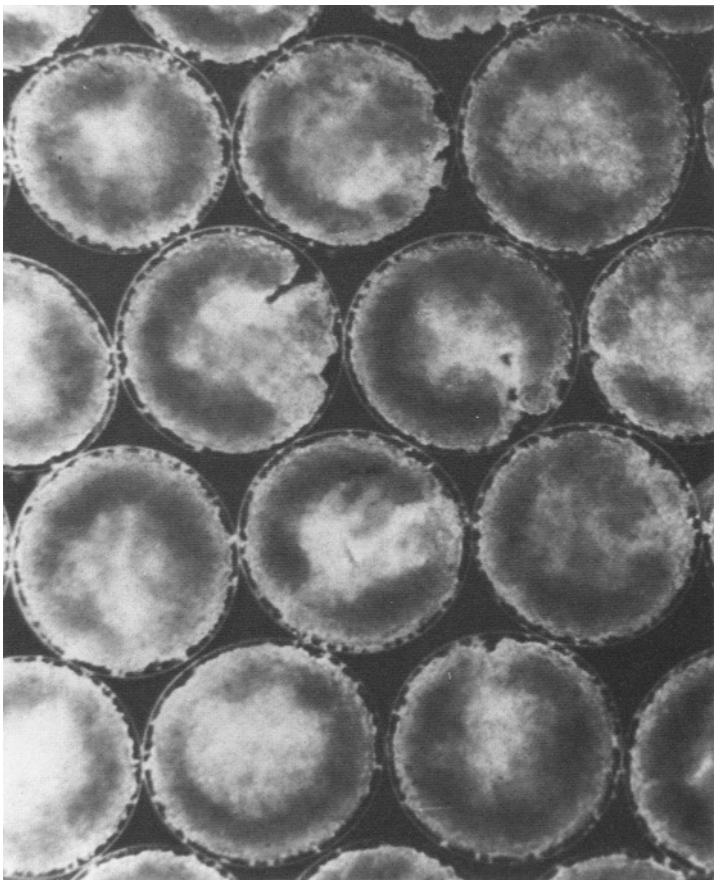
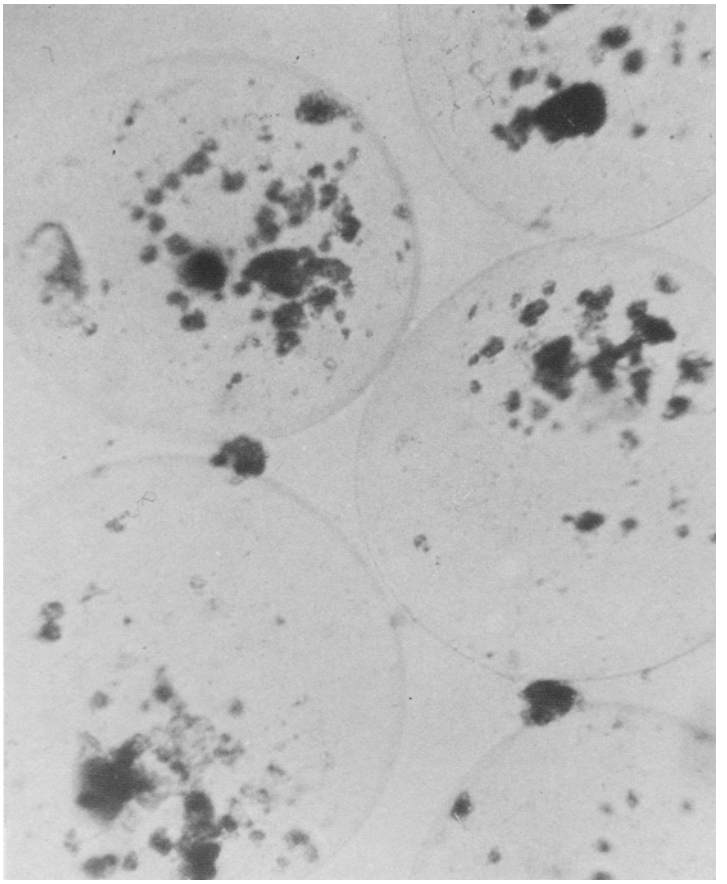


Fig. 2. Microencapsulated mouse–mouse hydridoma cells.

Damon Biotech, Inc. is now routinely mass-culturing microencapsulated hybridoma cells for the convenient and high-efficiency production of monoclonal antibodies. A microscopic picture of microencapsulated mouse–mouse hybridoma cells is shown in Fig. 2. A 40–50-fold increase in both the concentration and the purity of the harvested monoclonal antibody over that of conventional cell culture procedures is generally obtained. This impressive advantage results mainly from the natural trapping and isolation of the immunoglobulin molecules within the microcapsules.

Work has been in progress at the Dairy Science Department of Virginia Polytech Institute by Nebble and Saacke on the in vitro and in vivo application of microencapsulated bovine sperm cells. A novel and convenient way of artificial insemination in animal breeding is anticipated to derive from this new application of cell microencapsulation.

Another useful application of this new process of microencapsulation is the long-term maintenance of tumor cell lines. An example is a feline breast carcinoma cell line that has been maintained in culture in



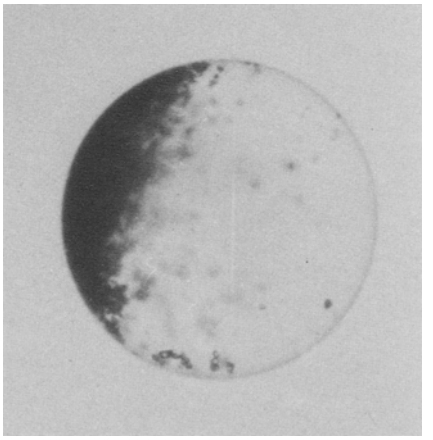


Fig. 4. Microencapsulated crystalline insulin.

our laboratory for more than 1 yr (Fig. 3). The same tumor cells without the benefits of microencapsulation failed to survive in culture in less than 3 months. Without microencapsulation it is virtually impossible to maintain feline tumor tissue cultures on a long-term basis.

In spite of the exciting and encouraging early experience with the in vitro studies of microencapsulated rat liver cells (4), no one has taken up this very important application at present.

Finally, this same system of polyelectrolyte complex microcapsules has been developed into carriers for the controlled release of bioactive materials with essentially zero-order kinetics of release. Figure 4 shows microcapsules containing crystalline insulin.

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