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[54] **LIVING CELLS ENCAPSULATED IN CROSSLINKED PROTEIN**

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[58] **Field of Search** 435/174, 177, 178, 182, 435/240, 241; 424/36, 94, 93; 252/316

[56] **References Cited**

U.S. PATENT DOCUMENTS

2,889,252	6/1959	Valentine	424/36 X
3,137,631	6/1964	Soloway	424/36 X
3,516,942	6/1970	Scarpelli	252/316
3,642,978	2/1972	Ogawa	424/37
3,664,963	5/1972	Pasin	252/316
3,691,090	9/1972	Kitajima et al.	252/316
3,714,065	1/1973	Kitajima et al.	252/316
3,780,195	12/1973	Balassa	426/350
3,838,007	9/1974	Van Velzen	435/177 X
3,937,668	2/1976	Zolle	252/316
4,024,233	5/1977	Winchell	424/1
4,094,965	6/1978	Layne et al.	252/316 X
4,107,288	8/1978	Oppenheim et al.	424/22
4,147,767	4/1979	Yapel, Jr.	424/36 X
4,187,285	2/1980	Meeks et al.	424/1
4,251,387	2/1981	Lim et al.	424/94 X
4,255,411	3/1981	Lim et al.	424/1
4,257,884	3/1981	Lim	435/182 X
4,324,683	4/1982	Lim et al.	424/94 X
4,352,883	10/1982	Lim	435/182 X
4,353,888	10/1982	Sefton	435/240 X

OTHER PUBLICATIONS

Chang, T. M. S., Encapsulation of Enzymes, Cell Contents, Cells, Vaccines, Antigens, Antiserum, Cofactors, Hormones and Proteins, Biomedical Applications of Immobilized Enzymes and Proteins, vol. 1, Plenum Press, 1977 (pp. 69, 83–88 & 151–153).

Chang, T. M. S., Semipermeable Microcapsules, Science, vol. 246, 1964 (pp. 524–525).

Business Week: Jan. 11, 1982, pp. 122–123.

Genetic Engineering News, "At Damon, Microencapsulated Monoclonal Antibodies", Mar./Apr. 1982 (pp. 24–25).

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[57] **ABSTRACT**

Living cells are encapsulated by: (a) dispersing living cells in an aqueous solution of a capsule wall-forming protein; (b) forming aqueous droplets of the cell containing dispersion in an aqueous-immiscible, cell compatible continuous processing medium; and (c) crosslinking the protein with a crosslinking agent which is soluble in the continuous processing medium but substantially insoluble in the aqueous droplets. The resultant capsules containing living cells may be treated with a capsule wall degrading enzyme to enlarge pores of the capsules. The encapsulated cells may be used for administration of cells to an animal for growing the cells in the animal or for delivery to the animal of a substance produced by the cells. By the cells being encapsulated, the cells are not destroyed by the aminal immune system and immune response by the animal may be minimized.

26 Claims, No Drawings