Differentiation of a cultured cell refers generally to a change in the expression of some peculiar functions specific to this cell. Generally differentiation involves only a modification of some biochemical properties of the cell such as synthesis of melanin by melanocytes (KREIDER et al., 1975) or synthesis of collagen by bone fibroblasts (MANNER and KULEBA, 1974) or tendon cells (SCHWARTZ et al., 1976). However, differentiation is sometimes characterized by a net change in the cell morphology which accompanies the biochemical changes as for example with myoblasts.

Few works have been devoted to the changes that occur in lipid during cell differentiation. Most of them concern gangliosides and other glycolipids, localized mainly in the plasma membrane, probably on its outer part (see for review CRITCHLEY and VICKER, 1977), analysing the possible relations between these lipids and the observed changes of the cell morphology.

EPITHELIOID CELLS

When treated with butyrate some epithelioid cells undergo a striking morphological differentiation (GINSBURG et al., 1973). HeLa cells are normally round or polygonal. When short chain fatty acids (C3-C5) are added to the culture medium, the cells stop growing and become more fibroblastic, developing extended processes. Concomitant with this change, a specific increase of the GM3 ganglioside is observed. Extensive studies of this type of differentiation have been performed on HeLa cells by the group of FISHMAN and BRADY (FISHMAN 1Chargé de Recherche au CNRS.
et al., 1974, 1976; SIMMONS et al., 1975) and on KB cells by MACHER et al., 1978). The main properties of the short chain fatty acids induced differentiation are summarized below;

(a) The best results are obtained with butyrate. Propionate and valerate are also active.

(b) Only GM3 increases. No changes occur in the other glycolipids.

(c) Specific INDUCTION of the CMP-NeuAc lactosylceramide neuraminyltransferase is observed. No changes in the activity of the other glycolipid synthesizing enzymes are reported.

(d) After withdrawal of the inducer from the culture medium, the lactosylceramide neuraminyltransferase decreases and the normal morphology of the cells reappears.

(e) The morphological differentiation and the increase of the GM3 are not consequences of the stop of the cell growth occasioned by butyrate, as thymidine does not induce any differentiation. However, butyrate added to cells arrested by thymidine, induces a morphological change and an increase in the synthesis of GM3.

(f) Inhibitors of the cytoskeleton polymerisation like colcemid inhibit, in the presence of butyrate, the morphological change but are without effects on the increase of the GM3 synthesis.

(g) Addition of GM3 to the medium of undifferentiated cells does not induce a morphological change.

NEUROBLASTOMA CELLS

A comparison of neuroblastoma cells grown in either suspension or in monolayer, in the same medium, has been done by YOGEESWARAN et al. (1973). When grown in suspension these cells are round. After they are plated on a solid support, they flatten and become polygonal. Some cells show small processes. Despite the great disparity in their morphology, no differences in the ganglioside were found between the two kinds of cells. However, we now know that this morphological change does not correspond to a differentiation. Furthermore, the morphology of neuroblastoma cells growing in monolayer in normal medium, remains very different from that of normal neurons. A study of neuroblastoma cells after differentiation induced, either by withdrawing the serum from the culture medium or by adding to this medium inducers such as dibutyryl cyclic AMP (dbcAMP) or bromodeoxyuridine (BrdU) was performed in our laboratory (REBEL et al., 1973; CIESIELSKI et al., 1977). After such treatments cells developed numerous long processes and seemed similar to neuronal cells.