

Correlation of changes of CHO-K1 cells metabolism to changes in protein expression in camp differentiation

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We focused our studies on the Chinese hamster ovary (CHO) mammalian tumor cell line, a good model to study the cell differentiation, namely reverse transformation. We started from the data known in literature, including the results obtained in our laboratory some years ago indicating that CHO-K1 cells are sensitive to the presence of FCS in growth medium and that in presence of cAMP the shape of cells changes from polygonal to elongated. It is known indeed that cyclic 3',5'-monophosphate adenosine (cAMP) transforms CHO cells, *in vitro*: they lose characteristics associated with malignancy and adopt characteristics of normal fibroblasts.

A correlated investigation of cell metabolism and protein expression of Chinese hamster ovary cells (CHO) under different growth conditions was then performed by ¹H Nuclear Magnetic Resonance, Mass Spectrometry and biochemical assays. CHO-K1 cells metabolism is probed by ¹H-NMR and biochemical assays in different experimental conditions, namely growth in normal medium, in medium enriched by 10% FCS and after reverse transformation by cAMP. In order to obtain complementary informations and to study different aspects of cells we related these results with those independently obtained by MS analysis of nuclear proteins. CHO fibroblasts have shown different metabolic products when grown in different media and when differentiation is stimulated by adenosine 3',5' cyclic monophosphate (cAMP). In particular, while addition of Fetal Calf Serum causes an increase in the glucose metabolism correlated to changes in lipid composition of the membrane observed by ¹H-NMR, differentiation induced by cAMP causes biochemical differences in glucose and lipidic metabolism uniquely correlated both to the specific changes in the composition of nuclear proteins, revealed by mass spectrometry, and to the differences in metabolism, determined by NMR.

In conclusion, the combined utilization of ¹H-NMR, biochemical assays and Mass Spectrometry shed new light in our understanding of cell metabolism and protein composition during reverse transformation. Other studies are in progress to better understand the complexity of such processes that regulate cell metabolism and protein expression.

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