DEFECTS IN MICELLE CORE INDUCED BY *ESCHERICHIA COLI* DHODH

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Electron Spin Resonance (ESR) is a powerful technique that uses either transition metal ions or spin probes (stable nitroxide radicals) to monitor changes in the probe vicinity. Some advantages of spin-labeling ESR experiments are the possibility of employing a selective probe presenting simple ESR spectra and their high sensitivity to molecular motions. Changes in nitroxide surroundings can be related to a variety of biologically-relevant processes such as protein conformational changes, lipid-protein interactions, and to the dynamic structure of biological membranes. We use ESR to monitor changes in the neighborhood of spin-labeled phospholipids incorporated into a membrane model system induced upon *Escherichia coli* DHODH (EcDHODH) addition. DHODH catalyzes the fourth step in the *de novo* pyrimidine nucleotide synthesis pathway. In rapidly proliferating mammalian cells, the pyrimidine salvage pathways are insufficient to overcome deficiencies in the *de novo* pathway for nucleotide synthesis. As certain parasites lack salvage enzymes, the inhibition of DHODHs has turned out to be an efficient way to block pyrimidine nucleotide biosynthesis. EcDHODH is a class 2 DHODH, which are membrane associated through an N-terminal extension. We address the main goal of investigating the effect of EcDHODH binding to phospholipid/detergent micelles. The use of specific simulation routines allows us to characterize the ESR spectra in terms of changes in polarity and mobility around the spin-labeled phospholipids. To the best of our knowledge, this is the first report showing direct evidences concerning the binding of class 2 DHODH to membrane systems and its implication in protein function.