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Farias R N, Bloj B, Morero R D, Sineriz F & Trucco R E. Regulation of allosteric membrane-bound enzymes through changes in membrane lipid composition. *Biochim. Biophys. Acta* **415**:231-51, 1975. [Inst. Química Biológica, Fac. Bioquímica, Química y Farmacia, Univ. Nacional de Tucumán and Lab. Microbiología Industrial, Facultad de Farmacia y Bioquímica, Univ. Buenos Aires, Argentina]

This paper discussed 15 reports from our research group on the effect of membrane lipids over the cooperative membrane-bound enzymes and on the methodological importance of cooperative transitions of membrane-bound enzymes for evaluating changes in situ of membrane conformation. Furthermore, it showed that such cooperative changes may have significant physiological consequences in the biological control of membrane enzymes. [The *SCI*® indicates that this paper has been cited in more than 355 publications.]

Membrane-Bound Enzyme Regulation

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In 1966, we made the marginal observation that erythrocyte ATPase from rats fed with a commercial diet showed a lesser degree of cooperation for inhibition by P compared with animals fed a diet prepared in the laboratory, in which all dietary components were defined.[1] The first step was to supplement the commercial diet with the components of the defined diet (I.e., salts, vitamins, fat, and others). Only the fat supplementation was effective for the recovery of the enzyme cooperation. These observations elicited our first publication.[2] The second step was to search for the root of these observations, feeding the rats with five different natural fats or oil-supplemented diets—one with the commercial diet and another with fat-free diet. Results indicated that neither the essential fatty acid nor the nonessential ones were particularly involved in the cooperative phenomena evaluated with the inhibition by F*.[3] An important observation here was taken from the doctoral dissertation of Bernabe Bloj, who died in a laboratory accident in February 1987. We named our institute in his honor.

The fact that cooperative enzymes from mammalian and bacterial membranes correlated with the membrane fatty acid fluidity raised the possibility of evaluating hormone-induced changes in membrane fluidity through changes in Hill coefficient. This experimental approach was used to investigate whether the interaction between hormones and membranes could result in the modification of membrane fluidity.[4] The interaction of insulin with the membrane receptor is now a subject of general interest.

The frequent citation of this paper can perhaps be traced back to the link it represented between the ideas expressed in the model of J. Monod, J. Wyman, and J.P. Changeux, for the cooperative behavior of soluble enzymes, and membrane enzyme regulation. At that time, the investigation on membrane structure and function was in explosive development, as reflected in the fluid-mosaic model formulated by S.J. Singer and G. Nicolson.

The first stage of this series was developed at the Universidad de Buenos Aires (1966-1968) and, later on, at the Universidad de Cordoba (1968-1971), while the last stage took place at the Universidad de Tucuman (1971-1975). The two latter universities are 600 km and 1,300 km, respectively, northwest of Buenos Aires. We note this to emphasize that (a) the structure of the research group* changed with place and time, and (b) the political situation in Argentina was involved in the course of these changes. Many of us remember well the hard days of Horco Molle—the university living quarters, hidden in the natural beauty of the "Cerros Tucumanos" foothill—where a sense of togetherness and stamina was deeply rooted. All doctoral candidates contributing to this subject went abroad for a postdoctoral study period, but they eventually returned to Argentina. And this was good!

The research group was formed by A.L. Goldemberg, H. Moreno, A.G. Gaio, E. Martinez de Melian, E. Massa, B. Bloj, F. Sineriz, R.D. Morero, *0.* de Mendoza, and L. Unates.

1. **Farías R N.** Metabolismo de fosfato en gldbulos rojos de conejo en deficiencia de vitamina E (alfa-tocoferol) (Phosphate metabolism in red corpuscles of rabbits with vitamin E (alpha-tocopherol) deficiency). Doctoral dissertation. Universidad Buenos Aires. 1967.
2. **Farías R N, Goldemberg A L** *&* **Trucco R E. The** effect of fat deprivation on the interactions of sodium and potassium with the ($Na^+ + K^+$)-activated ATPase from rat erythrocyte. *Lift Sci.* **7**:1177-81, 1968.
3. **Bloj B, Morero R D, Fan'as R N & Tnicco R E.** Membrane itpid fatty acids and regulation of membrane-bound enzymes. Allosteric behavior of erythrocyte (Mg^{++})-ATPasc. ($Na^+ + K^+$)-ATPase and acetylcholinesterase from rats fed different fat-supplemented diets. *Biophys. Biochim. Acta* **311**:67-9, 1973. (Cited 145 times.)
4. **Farías R N.** Membrane cooperative enzymes as a tool for the investigation of membrane structure and related phenomena. *Advan. UpidRes.* **17**:251-82, 1980.

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