ISTITUTO DI PATOLOGIA GENERALE E BATTERIOLOGIA
DELLA UNIVERSITÀ DI GENOVA
Direttore: Prof. LUIGI MICHELAZZI

Viale Benedetto XV
Telef. 31.421

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Prof. Joshua Lederberg
Department of Genetics
College of Agriculture
University of Wisconsin
Madison (Wisconsin)

Dear Professor Lederberg,

many thanks for your letter of January 9 and for the kind advices which are contained.

Your observations are essentially right. In effects, it cannot be excluded, a priori, that the induction of new biochemical activities which I have obtained in my strains is a consequence of an adaptive rather than of a mutative phenomenon. In this case, however, it should be necessary to admit that desoxyribonucleic acid has the ability to stimulate and to orient the adaptive processes, because the untreated original strains, which were not able to attack the sugars at the beginning of the experiment, maintained this property at the end. I will however call your attention on the fact, which is described at page 165 of my italian work, that the strain of Proteus OX 19, which did not produce adaptive enzymes for the oxidation of xylose and fructose even after 45 passages on media added with the sugars, was able to acquire the oxidative ability after a treatment with the NP pf Proteus OX 2. In this case it seems very difficult to think to an adaptive phenomenon.

It cannot be excluded also that NP provides the most favorable conditions for the overgrowth of the variant cells. Nevertheless, it should be necessary to admit that not all the NP fractions have this ability: in effects, the acquisition of the new properties did not occur after treatment with NP from all used bacteria (e.g. with NP from Coli 10).

In regards to the determinative technique which was employed, the manometric technique was choosed because it offers the possibility to measure also the little differences, which are not detected by cultural methods. In a second step of my research, the biochemical activities were tested also with

cultural methods,in media of agar-bromothymol-blue -sucrose(virage to pH 6.0-7.6):it was observed that Coli UQ is a good fermenter(I agree with you on this point),while the strains SG and I(SG-I6)are less good fermenters and Coli I is a non-fermenter:these properties,in our media, are now maintained at present. If you consider the values of attack which are reported in the Tables I and 2 of my italian work,you can see that a great correspondence exists among these data.

In regards to the acquisition of new enzymes,it results from the experiments of Avery and al. and of Boivin and al. that a rearrangement of the enzymatic equipment must take place during the transformative phenomena:in effects,the production of a new capsular polysaccharide must be related to a rearrangement of the enzymes which are responsible for therr synthesis. Acquisition of M protein by mutation directed by DNA in pneumococci was recently described by Macleod and Austrian :it seems likely;from these researches,that also the proteins can be acquired in consequence of a directed mutation :the enzymes also are presumably proteins/.

At present I am studying on the possibility of directed mutation in Staphylococci:I have found some differences,probably of mutative origin,in the oxidative attack of methionine and of cystine by treatment of a Staphylococcus with the NP fractions from other Staphylococci. Anyhow,further researches in the direction which you have suggested will be performed.It will be my duty to inform you on the eventual results,either positive or negative.

I shall look forward to hearing from you again.

Thanking you very much for your interest and for your very kind advices,I am

Yours sincerely

Mario U.Dianzani,M.D.,
Pharm.D.