Letter to the Editor

Dear Sir,

In a recent issue of *Cytotechnology* (**24**:89–98, 1997) appeared a review article authored by A. Kadouri and R. E. Spier and entitled “Some myths and messages concerning the batch and continuous culture of animal cells”. In this article, which is meant to provide guidelines for selecting appropriate culture modes for the large-scale commercial production of proteins by recombinant animal cells, the authors unleash an unprecedented attack on our persons in order to find ground for their arguments and ideas and to justify the writing of their review paper. Because we feel that their means for supporting their opinions are unethical and unscientific, because we feel unduly attacked by the style and tone of their writing and because we regard that their paper, in the way it was written, is undeserving of publication in your otherwise distinguished journal, we are writing this letter to express our disappointment and to enlighten the unaware readers who may have been inevitably misled.

In the above-mentioned review paper, the authors single out two of our publications^{1,2} in order to “draw out...the mythology which has penetrated the literature on [the subject of choosing between batch and continuous operations]”. Already from the times of the original ancient Greek Mythology it is well known that myths propagated through the ages from generation to generation by word of mouth and were thus subject to substantial alterations. In their vast majority, myths were (and still are) completely fictional, fantastic stories with a didactic touch. There is reason to believe that A. Kadouri and R.E. Spier want to write their own “mythology” at our expense. Because the interested reader who cares to compare the points, opinions and ideas attributed to us by the authors of this review, with those really expressed in our publications, will find as much similarity as the hare has to the turtle. Indeed, one wonders if Drs. Kadouri and Spier actually read

our publications. Nowhere in our publications is it to be found, for example, the statement that “the regulatory agency for biologicals in the USA will not licence products based on processes which operate as fully continuous cultures”. This comes in direct contradiction to another statement attributed to us, namely that “it takes longer to obtain a licence for a product made by a continuous process”. If a licence for a continuous process can never be obtained then there is no point in comparing the time-to-licence of batch and continuous processes. In fact, there is no point in comparing batch and continuous processes at all. But our publications were dedicated to just this kind of comparison. We discussed batch and continuous processes with regard to safety, efficiency and economy and it was our conclusion, based on the state-of-the-art of the time (more than 5 years ago) and our extensive industrial experience, that batch is the preferred mode of operation if certain conditions are satisfied. Our publications can hardly be regarded as aphorisms of continuous processes. The complete opposite is the case. We recognized even then that¹ “the decision as to which cell culture system should be chosen, whether batch or continuous processes should be applied...is based [on several factors]”. Many of these factors are actually included in the “decision trees” that Drs. Kadouri and Spier have re-invented for the benefit of their didactic message.

In a similar fashion we read with astonishment many other “statements” attributed to us but in reality concocted by Drs. Kadouri and Spier only to be rebutted by them. For example that “a genetically engineered cell will necessarily lose the exogenous gene after it has been exposed to a period of continuous culture”, or that, “the genotype of ...cells in the bioreactor is necessarily and radically altered as a result of selective pressures...arising from the operation of a continuous process”. We invite Drs. Kadouri and Spier,

as well as the reviewers of their paper (who recommended publication) to show us where exactly in our publications are such statements made.

If Drs. Kadouri and Spier are indeed so fascinated by myths, they do not need to go through great pains to invent them. They can save time, energy and face by turning to Aesop or La Fontaine.

¹ Werner RG, Walz F, Noé W and Konrad A (1992) Safety and economic aspects of continuous mammalian cell culture. *J. Biotech.* 22: 51–68.

² Noé W, Bux R, Werner RG and Nerthold W (1992) Aspects of the continuous culture versus batch mode for animal cells in industrial processes. In: Spier RE, Griffiths JB and MacDonald C. (eds) *Developments, processes and products*, Butterworth-Heinemann, Oxford, pp 354–364.

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