

August 1m 1959

Dear Dr. Sterzl:

Thank you for your interesting letter of July 23, just received.

Perhaps Miss O'Connor at Ciba/London will have been able meanwhile to send you a copy of my written reply as submitted for the symposium publication. Let me say first how important I think your experiment is, since it does represent almost the only quantitative evaluation of cellular performance. At the same time I would not become too frantic over its implications until some of the indicated numbers were more explicitly confirmed.

If we accept your calculations, which are perhaps favorably biased, we may then come to the main issue, the potential productivity of a single antibody-forming cell. You quote Berenblum at 6×10^{-12} g/day but I wonder if this is not too small. Dixon calculated a yield about 10^{-10} g per cell (J Exp Med 102:379)(he writes γ g, by the way, for m g): this figure would be based on every cell being active; on the other hand, it does not take account of possible proliferation. In any case, I would assume that a plasma cell has a weight of about 10^{-9} g., and would expect it to be capable of producing a major fraction of its own weight in antibody. It will, of course, be important to get precise values for this parameter, as should be possible before long. In rabbits, a globulin pool of about 1 gm is turned over in 5 days by 5-10 gms. of lymphoid cells. This would give a basal rate of about 2×10^{-11} gm ab/cell/day and I would think this would be much higher in specially stimulated and mature plasma cells.

I do not have Berenbaum's paper close at hand; our medical school library is preparing to be moved to a new building on the campus here-- where I hope to have some opportunity to show you around before too long.

Turning to your calculations, I would read $2^8 \times 40 = 10,240$ cells., after 4 days. But the total number of cell-days will be your figure ~ 5000 . I do not know what to think of the expected rate of division; I agree that you are probably not underestimating it, but these cells may well do better, for a time, than Puck's tissue cultures. I do not think 5000 (Talmage's figure) is unrealistic for the ratio of (total antibody species)/(antibody species reacting with your antigen), which is the relevant figure. Perhaps, as we discussed, the ratio is even smaller in your particular case owing either to past experience of the donor rabbits with cross-reacting antigens, or to a genetically determined preference that would have had some adaptive value in evolution.

I will of course be very pleased to hear of the progress of your experiments along these lines. Thank you for sending me the comment, and please do let me know (when the right time comes) how I can facilitate your visiting us. I am not now planning to visit Europe next year, but I will likewise keep you informed of any useful opportunity. Dr. Nossal is arriving in a few weeks to continue our collaboration. You will doubtless see him in 1961 (I hope sooner) if he can arrange to return to Australia via Central Europe.

Yours cordially,

Joshua Lederberg