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Dear Gus,

In order to close, if possible, the chapter in history of science : who invented first " the hemolytic plaque technique", the following resumes what I know for certainty (being a personal witness). The fact that Niels invented also the plaque technique, independently, in 1962, and published it in 1963 (with Nordin) makes no doubt in my mind. This phenomenon is well known in the history of science and technology : Poincaré and Einstein for general relativity ; Bell (who asked for the patent of telephone in the morning, which T. Edison did it in the afternoon of the same day) and Edison, etc.

1. In 1958, Joe Ingraham, working in Taliaferro's laboratory, at the University of Indiana, tried the detection of individual antibody producing cells by a hemolytic plaque technique. Joe suffered (as is often the case) of knowing too much ; did not want to use agar as the gel medium knowing its anticomplementary activity. He had thought of different gelifying media and, finally, chose carboxy-methyl-cellulose (C.M.C.), well suited for the purpose, non toxic for the cell and easily buffered at physiological PH.

You know all this, naturally, as well as myself, but, if I write this, it is for a third party (if you need it), not for you who has been intimately involved in the CMC plaque technique. Joe's model was lymph node cells of rabbits immunized with S.R.B.C. He got the first hemolytic plaque in 1958 and, later on (probably in 1962), showed them to me (and put them earlier in a progress report). They were not beautiful but all proper controls had been made (absence of C, use of rabbit red blood cells, etc.) showing that he was indeed in presence of rabbit lymphoid cells producing hemolytic antibody.

2. In 1960, investigating where he could spend a sabbatical year, Joe wrote to Talmage proposing him, as research program, the development of the plaque forming cell (PFC) technique. Talmage rejected this program and suggested another program. This may be proven by looking in the archives of Talmage or in the NIH bursaries program.
3. At the end of 1961 or beginning of 1962, Joe wrote to me asking if I could accept him in my lab with the same program on PFC. (I do not have this letter in my hand since my own archives are at the Institut Pasteur, but it could be found). I accepted this proposal and Joe presented a formal request to the NIH, with his research program, in 1962. It was formally accepted by the NIH and the Institut Pasteur administration. I guess that all these administrative documents could be found in the archives of these administrations, with the history of PFC.

The only way, greatly improbable, by which Niels could have known anything about PFC's before his work in 1962, would be by possible discussion with David

Talmage whom he certainly knew and met, but I doubt about this. So, the final conclusion is that Niels was the first to publish a technique for PFC, slightly before Joe, but that Joe is probably the first to have done experimental work on plaque formation.

Anyway, the first independant published technical demonstration of the feasibility of plaque technique was due to Niels Jerne and Nordin. For this, he got the Nobel Prize in 1984. Naturally, as very often, the justification for Nobel Prizes, is very ambiguous. I feel that the prize for Niels goes much above the Nobel ! His influence on the whole field of immunology, from 1950 to 1980 was enormous and I wish that the prize should be given always as rightly !

Now, a little funny note. I just recently renewed correspondence with Mel Cohn and discovered that he, himself, had the idea and experimented the plaque technique in 1955. (see Ann.Rev.Immunol. 1994 (12) p 16) :

"We divided the work : Lennox investigated the microdrop approach and I, the plaque assay. I immunized rabbits in the footpad with sheep erythrocytes, and at various times made a cell suspension from the popliteal lymph node that I plated with sheep erythrocytes and complement in a soft agar layer analogous to the phage plaque assay. No plaques were visible ; yet; in suspension culture, the cells secreted large amounts of hemolytic antibody. The failure was quickly pinpointed ; the agar was a very anti-complementary and we had no clue as to how to solve that problem. The two solutions that appeared years later were to find another gelling medium and to neutralize the anti-complementary activity of agar with DEAE-dextran ; neither the reagents nor the know-how was available to us in 1955...."

So, as we well know "nothing new under the sun..."

If I wrote to you this fairly long letter, it is because I thought that, after the long and fruitful meetings we had so often and the friendly connections we established between your family and mine, you were aware of the details regarding the history of the plaque technique invention...

If you want to communicate the essence of these information to a third party, feel free to do it. I rely on your judgment to do this properly. Anyhow, I feel that this question is of little importance except, maybe, to the historians of science, as a model of simultaneous independent inventions or discoveries.

Anyway, I am more interested by what is going now in the world and what will be on future ! On this, my expectations are very gloomy !

Please let me know if I will have the joy of meeting you and Lynn in the distant future. Do not wait too long since my life expectancy becomes small (I am 86 now !).

Yours as ever.