March 26, 1975

Dr. Shiro Kato
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Dear Dr. Kato,

Thank you very much for your letter of March 14, 1975; the information it contained is useful to us. In reviewing my correspondence with you, I find to my embarrassment that I have never actually explained our research. Please let me do so now.

We have prepared radioactive DNA complementary to the region of the avian sarcoma virus genome which is deleted when transformation-defective segregants are formed during propagation of the virus. This c-DNA represents the entirety of the deleted region; we therefore assume that at least part of it represents genetic information required for sarcomagenesis and transformation of fibroblasts. We have found that all independent isolates of avian sarcoma virus contain these same nucleotide sequences, whereas the sequences are all missing from independent isolates of avian leukosis viruses and from all transformation defective variants. Homologous sequences are present in the DNA of normal chicken, quail, pheasant, and turkey cells but are not transcribed into RNA; however, they are transcribed into RNA in sarcomas induced in quail by methylcholathrene. Since these sarcomas are producing no detectable virus, we think they are not infected but that the methylcholanthrene has induced the expression of the endogenous "transforming" sequences. We cannot say that this induction is responsible for oncogenesis, but it appears that the expression of the nucleotide sequences in question is correlated with oncogenesis. As a result of recent work, we now know that the same nucleotide sequences are also transcribed into RNA in the MSB-1 cells, which you established. This could either be due to the presence of the same nucleotide sequences in the DNA of Marek's virus or to the induction of expression of the sequences in the chicken genome by infection with Marek's virus. We doubt that the sequences are present in the genome of Marek's virus because, to date, we have found them only in avian sarcoma viruses. But we have not yet tested Marek's disease virus DNA, and, until we do so, we cannot interpret the results with MSB-1 cells. Incidentally, the endogenous virus of chickens - RAV-0 - does not contain the "trans-
forming" nucleotide sequences in its genome; hence, expression of the transforming nucleotide sequences is apparently an independently regulated event.

I hope that these remarks make our work clear. If you have any questions, please let me know. I would be happy to correspond with you further about these matters. In any event, I think you can understand now why the MSB-1 cell line is so important to our purposes and why we are so happy that you originally isolated it.

Sincerely yours,

J. Michael Bishop, M.D.
Professor of Microbiology