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Dr. Alfred E. Mirsky
The Rockefeller University
New York, New York 10021

Dear Dr. Mirsky:

I am deeply grateful for the interest you have shown in the draft of my Daedalus paper and the extensive comments which you have sent to me. I am sure that taking your comments into account will greatly improve the quality of my effort. I will certainly eliminate the ungracious phrases that you did not "bother" to mention the base ratio equivalence (which, incidentally, did not later become known as "base pairing" but is an analytical datum which, in part, led to the discovery of base-pairing; there is base pairing in some nucleic acids for which the equivalence rule does not hold) and that you were "willing to grant" that DNA is part of the transforming principle. I assure you that I did not mean to give offense.

As far as the discovery of DNA is concerned, I thought that the idea of the equivalent hereditary contribution of egg and sperm to the offspring was known in the 1860's, as well as the equality of nuclear and inequality of cytoplasmic mass of male and female gametes. Hence I believed that the inference was then made that the nucleus is the "ideoplasm." But I now see that the term "ideoplasm" was not used until the 1880's. In any case, on rereading Miescher's paper I agree that he nowhere mentions heredity. However, on p. 152 Miescher writes "Ein aus reinen Zellen bestehendes Material, wie das vorliegende, musste vor Allem dazu einladen, die Frage nach der chemischen Constitution der Zellkerne ernstlich in Angriff zunehmen." Hence I think that the (conventional textbook) assertion that he undertook to establish the chemistry of the nucleus is not all that far off the mark. The source of my apparently mistaken information that Altmann was a pupil of Miescher's is, I am embarrassed to admit, Borek's "The Code of Life." Anyway, I shall correct all these errors to which you so kindly drew my attention.

But I regret that my views on the later history of molecular genetics are evidently very different from your own. To be sure,

the facts that genes were known to be located on chromosomes, that chromosomes were known to be nucleoproteins, that the nucleolus was found to contain RNA, that X-rays, UV and certain chemicals were found to cause mutations, showed that the gene has some material existence. But the gene concept (based on the character difference, as you must know) did remain devoid of any material content until the notion of the cistronic nucleotide sequence had been formulated. I would be grateful if you could supply some examples to me which would falsify my assertion that the success of the theories and experiments of classical geneticists does not depend on the knowledge of structures at the submicroscopic, or molecular level where the genes lie. The very cases which you cite in your letter, namely the early efforts to learn about the nature of the gene by X-rays and chemical mutagens, did not lead anywhere because the "classical" genetic experiments which were carried out in connection with these studies did not have the level of fine structure resolution necessary to make critical tests of events at the molecular level.

Thank you also for sending me a copy of your exchange of letters with Luria in the Scientific American. I had already read this correspondence with great interest, and it will not surprise you to learn that my sympathies are rather on Luria's side. In fact, I am just now finishing the manuscript of a textbook on molecular genetics, which, I regret to say, is giving short shrift to all organisms other than E. coli and its phages. My justification for this procedure is not that E. coli is a "model" system for anything, nor that it is simple, but that it is the one single organism with which a coherent, global story can be told. My teaching experience in both elementary as well as advanced biology courses has convinced me of the pedagogical value of restricting the choice of organisms to the absolute minimum, and I assure you that if it had been possible to present the story of molecular genetics based on experiments with man I would have preferred to do so.

Thanking you once more for your help, I remain

Sincerely yours



Gunther S. Stent