

October 11, 1974

Dr. Francis Crick
MRC Laboratory of Molecular Biology
University Postgraduate Medical School
Hills Road, Cambridge CB2 2QH
England

Dear Francis:

I am sorry to have delayed so long in answering your letter. However, Sung-Hou Kim went to Korea to see his mother and I felt I could not reply, especially in terms of drafting a letter for publication, without consulting him. In writing my previous long letter to you, I consulted with him quite thoroughly so in a sense that letter came from both of us.

Your general criticism of our publication is unfounded. It is not true that Sung-Hou's interpretation was not sufficiently convincing for us to have published it without the stimulus of the English work. Prior to the Madison meeting we had started, and his visit to M. I. T. then was precisely for that purpose. It is quite likely that we could have been more rapid in publication if the two laboratories were not separated, but that is not the issue. Furthermore, it is not correct to say that if we saw the advantages of the revision as early as April that we should have then proceeded with publication. As I described in the earlier letter, some of the interactions were becoming definite in April, but they were not all apparent and many were tentative. It takes a long time to make sure that these interactions are correct since there were many alternative tracings to be considered. Sung-Hou found the partial structure method of value here. However, I learned in August from Robertus that in April the MRC workers had already established a number of the tertiary interactions which are in their final paper. The same question can be raised. Why did they wait until mid June to write up a paper when they already knew of these relations in April? The answer is obvious. The structure is large and complex and one has to make a number of decisions. Even so, by June it was apparent that a number of these interpretations were still tentative as shown both in our paper and in the MRC paper.

Unfortunately, the impression I get from here is that you are either not being given all of the facts or you are being misled. You were given

incorrect facts about what went on at the Gordon Conference. David Blow had incorrect notes on the Steenbock Conference, which I have been able to clear up by listening to the tape recording of the meeting. Furthermore, if it is your impression that your colleagues gave a full presentation of the structure at the Steenbock meeting, you are being grossly misled again. I have recently received a copy of the "New Scientist" article which has caused me a great deal of distress. In it the MRC group are quoted as having given a full account of their proposed model at the Steenbock meeting. This is very far from the truth. The tape transcript shows exactly what was disclosed, a slide of the wire model and an electron density map section. The wire model was chiefly useful in allowing me to point out to Jon Robertus that our revised D stem looked similar to his. However, as you know, one cannot see details in a wire model slide. In the discussion Robertus said that they have defined a large number of tertiary interactions, but unfortunately he could not show them now, but would be able to in "several weeks time." He described two of the four tertiary interactions which I had mentioned in my talk and, in response to a question, added the third one.

There are some points in your letter which I should comment on. You mention uncertainty about our incorporation of A9 into the model before the meeting. I suspect this arises from the response which Sung-Hou made at the meeting to Jon Robertus' comments about the A9 interaction. The tape transcript makes this clear. In response to a question about A9 being protected, Robertus said that this opened up "Pandora's box," as A9 was involved in a "triple base with 12 and 22." Sung-Hou's response to this, audible in the tape, was one of confusion and incredulity. I am sure that this was taken as evidence of the fact that he had not known of this interaction. In fact, A9 does not bind to either 12 or to 22; but binds to residue 23. Robertus had made an error in describing the interaction and Sung-Hou was trying to understand how he could possibly interpret that residue as interacting with both 12 and 22. Some of Robertus' confusion may have stemmed from the fact that there was an error in the diagram of the "Nature" paper which shows a tertiary interaction between A9 with both 12 and 23. In any case, if you had doubts about this interaction, all you had to do was contact Struther Arnott since he has it in his notes.

My presentation was the first one of the first day of the meeting. My comments covered our research in more or less chronological order, except at the beginning I stressed the special role of the constant bases. Near the end of the talk I presented information about the chemical modification studies and stressed the role of the constant bases in the tertiary interactions. I mentioned that we have a modified tracing with a different folding of the anticodon, different from that which we had described earlier.

I am glad that you mentioned my junior colleagues in your letter because I have been feeling very badly about them. They attended a lecture at Brandeis when Aaron was there in which Aaron more or less openly suggested that we had purloined his interpretations, repeating the charges which were in your and David's letters. This was told to me not only by my junior colleagues who attended the lecture, but also by other crystallographers in the audience. He also had apparently told this in private conversation to a number of individuals in this country because when my colleagues went to a meeting of the American Crystallographic Association at the end of August, there was considerable discussion there about the nature of these charges. Both I and my colleagues received telephone calls at that time from friends asking what was going on, as knowledge of the charges in your's and David Blow's letter seemed to be widespread. These unfounded charges have done considerable damage to our reputation. Now in the "New Scientist" publication Aaron has developed a number of additional charges which as you may imagine also distress my colleagues and myself.

Let me cite a specific example which leads me to believe that you are not completely informed about what was going on. The point I wish to raise stems from the statement in your first letter that we gave no indication that we were planning to publish material based on what we had said at the Steenbock meeting. This is quite untrue, for not only did your colleagues understand that we were publishing a paper, but they acted in accordance with this. Let me cite the following facts:

Fact 1: The original version of the "Nature" paper, which Robertus sent us a preprint of on August 5 makes only passing reference to chemical modification experiments, involving only residues 16, 17 and 20. This was despite the fact that a large experimental effort had been carried out dealing with the study of the pyrimidine modifications of yeast tRNA^{phe}. The studies were completed well before the Steenbock meeting as Brian Clark reported on them there. I suspect that a general statement was not made in the "Nature" paper because of residual uncertainty about the interpretation of certain parts of the electron density map.

Fact 2: During my presentation at the Steenbock meeting, I laid great emphasis on the chemical modification studies. I showed a slide listing the purines that are unreactive and reactive for yeast tRNA^{phe} and also discussed the analogous studies of Chang on other tRNA's for pyrimidine modifications. It was clear that the slide which I showed was prepared for publication and indeed it was an earlier version of

Figure 1 of our publication. This was noted by your colleagues. I made a statement, repeated twice, that we have a tertiary folding in our model which accounts for the chemical modification data.

Fact 3: Immediately after the Steenbock meeting your colleagues prepared an unusual paper for the journal "Nucleic Acid Research" which presents very little experimental data, but essentially says that the model is entirely in agreement with chemical modification studies. This paper was prepared in a great rush and special pressure was put on the Editors to publish the paper quickly. An Editor of this journal informed me that the rule of the journal is that papers received and refereed by the 21st of the month go into the next month's issue. Their paper was received on the 28th of June and it appeared in about two weeks time. In fact, it appeared in such a rush that a figure was included in it with an incorrect twisting of the T ψ C loop. They would never have rushed so and published a paper with so little data except they knew we were to publish. Furthermore, nowhere in that paper is there any reference to the fact that I had clearly stated at the Madison meeting that our molecular model agreed with the chemical modification data. In addition, they describe the T54-A58 interaction with more confidence than in the "Nature" paper, and it was one of the tertiary interactions described by me in my talk.

Fact 4: When the "Nature" paper was revised some two weeks later, a sentence was added saying that the model is in good accord with chemical modification data.

All of this occurred of course before my preprint arrived in Cambridge and it is quite clear to an outsider that it was done in response to my presentation at the Steenbock meeting. In short, the interpretation of their electron density map was not sufficiently convincing for them to have ^{made} a broad statement about chemical modification without the stimulus of my presentation at the Steenbock meeting. I rather suspect that you know nothing about this, but the facts speak for themselves. Under these circumstances, do you think that a public statement from your colleagues might be appropriate?

Let me say how much I deeply resent this whole business. Aaron sent two junior colleagues to a meeting with instructions: They were to say they had sent a manuscript in, but were not prepared to disclose the contents except in a superficial fashion. When we then joined in this cat-and-mouse game of not telling all, a hue and cry arose from the MRC, when we sent you our paper, with a large number of false charges flying about. The information on which these charges were leveled was

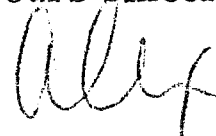
completely unreliable, based on inferences obtained in the context of discussions at a meeting in which we adopted Aaron's ground rules, i. e. , tell only a minimum of what you have been doing. Aaron then proceeded to publicize these initial charges without attempting to verify them, and when these were shown to be false, he then proceeded to invent new charges dealing with the interactions between Kim and myself, again with no factual basis whatsoever. On top of this, he made false statements to the "New Scientist," and again strongly implied publicly that we had purloined his interpretations. Minimal effort was made by him or others at Cambridge to ascertain the factual basis of any of these charges. Having carried out a very complete public character assassination of me and my colleagues, he poses as the injured party.

The "New Scientist" is widely read here and several friends have asked me about the charges it contains. It seems to me that Aaron has been leaking selective portions of our correspondence in such a way as to cast me in a very bad light. In view of this I do not see how we can make a simple public statement along the lines suggested in David Blow's or your letter without responding to the various charges aired in the "New Scientist" article. I have been in touch with the editors of "Science" who have read the "New Scientist" piece, but they have informed me that they are strongly disinclined to publish anything on this matter either from me or the MRC. So at the present time I am pondering what would be an appropriate course of action. I feel that Aaron has behaved very badly in making a number of public charges both in lectures here and in statements to the "New Scientist" and I am now debating whether a lengthy and detailed reply to the "New Scientist" would be an appropriate forum for setting the facts straight.

On the scientific side I agree entirely with your comments concerning the desirability of proving the structure. In the present state of our analysis we regard many of the interactions as tentative as indicated in our paper; however, judging from the description of the MRC fourier as published in the "Nature" article, I believe there are some small, but perhaps significant differences in the structures found in the monoclinic and the orthorhombic forms. However, this will only come out in the long run with further work.

With best regards.

Yours sincerely,



Alexander Rich