BIC 4085

THE JOHNS HOPKINS UNIVERSITY
SCHOOL OF MEDICINE
and
THE JOHNS HOPKINS HOSPITAL

DEPARTMENT OF MEDICINE
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11th June, 1974

Dr. Seldon E. Bernstein,
The Jackson Laboratory,
Bar Harbor, Maine 04609.

Dear Seldon,

I will comment specifically on the points and suggestions made in your review of the provisional program for the Bar Harbor course. Your note of transmittal was dated May 17. I am sorry I have not gotten to respond to it sooner.

1. You suggest Hamerton as coordinator for the entire session on cytogenetics. I think there are some problems inherent in having someone who has not previously been at the course (such as Kazazian also) being the group organizer. There are, I recognize, also advantages. Borgaonkar, Gerald, Hamerton, Ruddle and I will all be in Holland at a chromosome mapping conference in July. We can put some finishing touches on the organization of the program at that time.

2. You suggest that Eicher would like to discuss "mapping of genes without recombinations." I presume that this means cell hybridization approaches as well as in situ hybridization techniques such as that of Gall. It was my thought that mapping the human genome should be postponed until the second week. I believe there is enough for one day, namely Tuesday a.m. and p.m. plus the previous evening in more conventional cytogenetics including clinical cytogenetics (see attached list). As far as Eicher taking that topic I would only point out that Ruddle is a leader in this field.

3. Yes, I think Boyer is prepared to give the discussion of primary gene action, translation etc. which is needed for the kick-off of Wednesday's session. As I had indicated by the comment in brackets I thought a lot of this could be presented within the framework of human hemoglobins. It is said that one could teach a whole course of human genetics using only the hemoglobins.

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4. I think there are problems with having Kazazian organize a session when he has not been to the course previously. Furthermore, I was much disappointed this past year by Kazazian's contributions to our medical student course. I think for various reasons we may have to leave the organization of this session in the hands of Boyer.

5. Yes, we had Scriver in mind as group leader for all the sessions on inborn errors of metabolism.

6. It will be nice to include Coleman on diabetes and obesity. We have another contribution for the inborn errors of metabolism section, namely porphyria discussed by Robin Bannerman. Robin Bannerman will be there during the two weeks of the course. He does not expect remuneration.

7. No comment.

8. Poljak and Dick Humphrey jointly have been organizing the program for Friday morning and evening. Humphrey took the course in the past and is a good man. They are bringing Bernice Schacter with them. Bernice is a very competent young lady although she is relatively new to this field. They suggested that a brief summary lecture on blood groups be left in, stating certain genetic principles. They point out, rightly I believe, that there are some genetic principles or at least genetically controlled mechanisms which are illustrated only by the blood groups, e.g., the role of an enzyme in altering immune specificity through the addition of a side chain or side group. Autoimmunity will be worked in to some extent. There is new evidence on the relationship between HL-A type and susceptibility to certain diseases which have been construed as autoimmune in nature.

9. I think it is possible that we have not allowed sufficient time for immunogenetics. The folks here (Schacter, Poljak and Humphrey) have a rather jam-packed program already planned for that Friday. I am not certain where Kaliss would be fitted in. I am sure it would be very useful to hear from him. Perhaps Kaliss could be introduced during the second week.

10. No comment.

11. I think you are right. "Mapping the human genome" can probably be adequately covered in simply the morning of Monday, even though the field is progressing with amazing rapidity. I will undertake to be the organizer for this and will attempt to keep everyone in line. I am going to a conference in Holland on mapping and can get some ideas about how to organize it there. I think it will be useful to have material on the mouse mapping for at least two reasons. One is as a contrast in methodology and Margaret Green can certainly give that and, secondly, from the point of view of the comparative map of the X chromosome because of the evolutionary conservatism of the X chromosome. The map in the mouse is of considerable interest.

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12. I would be agreeable to putting Tibby Russell on for "genetic aspects of aging" on Monday evening of the second week. Would she take the full 2 hour session? Should we put anything else on at that time? for example, would Harrison like to talk on aging at that time and use Tuesday morning for developmental genetics? See my comment about Murphy and longevity in man (below).

13. I suspect we don't need to worry about a transition between aging and development. Probably Tibby will provide that for us on Monday evening. She should plan to do that.

14. In connection with the Mouse Clinic I think it would be very useful if you could let me know what mutant mice Margaret Green et al would plan to present. What I would like to do is to have some medical members of the faculty and perhaps of the student body prepared to discuss the medical condition in comparison with the condition in the mouse. Eva Eicher's hypophosphatemic rickets would certainly be of great interest. I believe that you have a sideroblastic anemia in the mouse (perhaps more than one) which would be of great interest also because the sideroblastic anemias in man are being increasingly recognized. Robin Bannerman has expressed a willingness to help with the Mouse Clinic. As you know, he has recently written a long review on animal models of hematologic disorders in man.

15. I think we could plan to organize the morning on lysosomal diseases as follows:

Background 8.30 - 9.15 George Thomas
Sphingolipidoses 9.15 - 10.15 Dr. Schneider
Coffee 10.15 - 10.45
Mucopolysaccharidoses 10.45 - 11.30 Dr. McKusick
Mucolipidoses 11.30 - 12.15 Dr. Kelly

17. I believe that a very good morning's program could be worked up for Thursday of the second week from miscellaneous short papers by staff and by students. You mention in your notes a number of short contributions from the Bar Harbor group which may be difficult to fit in anywhere else.

The topics you suggest for that Thursday morning are <u>per se</u> good ones, but I am not certain we have anyone on board who is particularly expert in those areas.

I would be perfectly willing to leave the organization of that Thursday morning until the first week of the course, at least the final decision on it. I suppose we should inform the "students" that theyshould bring material including slides for possible presentation, and possible participants at Bar Harbor would like to know that they might be presenting.

Incidentally, I am rather taken, I mustsay, with the organization which runs through Friday evening and feel that we should do that and not worry about fall-off in attendance.

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18. I suspect that Boyer would not plan to cover geographic and racial distribution of inherited diseases. The ethnic distribution of disease has been a special hobby-horse of mine and I will bring some slides along on this which might be shown in relation to Boyer's talk.

Comments on your general comments: I think it is defensible to put the talk on the genetics of sex abnormalities in the second week. It is much more of a developmental genetics topic in its present development than cytogenetics pure and simple. There is fascinating work, as you know, coming out of a study of testicular feminization both in the mouse and in man and there is additional very interesting work on mendelian sex abnormalities in man. Mapping the human genome should, I feel, come in the second week because of the need of a bit of statistical background for the family study aspects thereof.

I think that it would be perfectly superb if you would talk on phenocopies, mimicry and gene environment interactions in phenotype.

You know, it occurs to me in looking over the program that we might move the Mouse Clinic to Thursday morning. This will decongest Tuesday morning, leaving the possibility of adding some other persons such as Bernstine and Stevens. On Thursday morning we could make the Mouse Clinic a paired-up operation between a "mousologist" and an M.D. discussing diseases from a comparative point of view and pointing up by implication the usefulness of mouse models.

I think the best time for you to talk on phenocopies etc. would be on the morning of Tuesday of the second week, in the section on developmental genetics.

I would like to feel free to call on either students or faculty to discuss the Mouse Models from the medical point of view. I think we could work up a very good program.

I have heard from Scriver and he is willing to organize the inborn errors of metabolism session. He is also willing to talk both on treatment and on screening on the final Friday. He would propose to confine his screening discussion to screening for heterozygotes and the usefulness of using more than one test to improve the signal-to-noise ratio.

For the Monday evening program of the second week (genetic aspects of aging) it would be worthwhile, I believe, to have Tony Murphy present results from a study which we have been doing here in Baltimore on the genetics of longevity in man. This is a follow-up study which was initiated by Raymond Pearl in the 1920's and has considerable interest.

I would appreciate it greatly if you and I could have an arrangement whereby you were always present for the beginning of the morning session at 8.30 a.m. and the beginning of the evening session at 7.30 p.m. so that if I have trouble getting from our cottage on Echo Lake the show would still get on the road. With family responsibilities and transportation problems I suspect it may be important to have this sort of back up.

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I think we should ask people to give us an outline of their lectures by July 10th.

Attached is a xerox copy of a list of topics which Borgaonkar has suggested should be covered in the section on cytogenetics, Monday evening and all day Tuesday of the first week.

I would like to hear from you and the other Jax folks soon about the topics for the Mouse Clinic. I am enthusiastic about the idea of devoting the whole of the second Thursday morning to this and to having discussions in fair depth between a Jax person and an M.D.

Things seem to be coming along very well. Let me know your reactions to the thoughts I have expressed here. I would like to make up another somewhat mature program no later than Monday, June 24.

Very best regards.

Sincerely,

Victor A. McKusick, M.D.

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