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WISCONSIN

1st September 1958

Dr. E. S. Russell
Jackson Laboratory
Bar Harbor, Me.

Dear Ed:

Notwithstanding all the rumors to the same effect, I am accepting appointment at Stanford, moving out sometime next year. The post will be a Department of Genetics (sic) in the medical school which is moving to the main campus from San Francisco. My lab will be adjacent to Art Kornberg's Biochemistry group, and not far from Henry Kaplan. The new appointments in Biology — Clifford Grobstein and Ch. Yanofsky — add substantially to the prospects for an exciting concentration of interest in experimental genetics and development.

We hope to round this out in the Genetics Department by at least one sound appointment in cytol. mammalian genetics. I would be especially anxious to be joined by a colleague whose interests were appropriate to the elaboration of the "genetics of somatic cells", as might be typified either in transplantation or implantation research. As the distractions away from research are minimal, and we should have a uniquely favorable setting for genetic research, this should be an excellent opportunity. The terms of appointment would be commensurate with the experience and promise of the appointee at any rank; my own preference would perhaps be for an appointment suitable for an associate professorship, but don't let this factor weigh too heavily.

I am writing you, of course, to solicit your advice and help in canvassing the field and I would be very grateful to you for the effort. I would prefer that you concentrate on thinking who might best profit (and why not?) from a liaison with the existing programs (bacteria [Cavalli & myself]; phage [Dale Kaiser]; neurospora [Yanofsky & Pittendrigh]; DNA enzymology [Kornberg & Co.]; carcinogenesis etc. [Kaplan]... and leave presumed availability as a hurdle for us to cope with. It would help us define our objectives just to think of the personal embodiments of indicated virtues! Will you help us?

Our third appointment in Genetics may well be a human geneticist with experimental leanings. Despite his biometrical inclinations, Jim Crow would have been ideal but he has decided to stay at Madison and take over my post in medical genetics, — as a sideline, I suppose, to his many other doings! (I am looking forward to strong developments in genetics in the "applied" (i.e. clinical) departments too. Genetics itself is committed to a basic science program essentially parallel to Biochemistry.) Any suggestions from you in this area would be welcome too.

To turn to a more interesting domain: George Klein and I had some time together in Stockholm and we were discussing possible approaches to mutation and segregation in normal tissues. Two ideas came up, both pertinent to your own work on hematopoiesis. They are based on the supposition of selection for more effective genotypes of hematopoietic stem cells: (1) under treatment with anti-leukemic drugs which also affect the marrow, and (2)

in your W series of mutants. Have you given any thought to this yourself — it seems a logical extension of your transplantation therapy experiments. (By the way, my recent collection must be deficient — where are these published?). (1) would be a matter of mutation to drug resistance if this is true in leukemic cells; (2) has two aspects: (a) a simple mutation, e.g. $WW \rightarrow Ww$, and (b) segregation as might occur, not obviously so easily selected for, but say $WW' \rightarrow W'W'$. In any case, I would be interested to hear what you think of the quantitative aspects of such experiments: can you devise situations apt for the detection of small numbers of, say, w — cells? If so, you may already have at hand the system needed to detect somatic ~~eg~~ combinations, e.g., $WW\ H_2^a H_2^a \times ww\ H_2^b H_2^- \rightarrow Ww\ H_2^a H_2^-$ as might be selectively detected in a $WW\ H_2^a H_2^a$ recipient. The basic design of all such experiments would be pretty much the same: to look at the hematopoietic tissues of surviving animals by retransplantation in series in, say, WW hosts.

Do you think the exceptional cases you have already reported of long term survival of Ww genotypes might have been due to ~~ww~~ mutation? (or chromic contamination for that matter)?

Yours sincerely
Joshua