

May 16, 1936

Dear Dr O'Brien

In putting forward, in 1934, the scheme for research in serological genetics at the Galton Laboratory I gave general reasons for the supposition that many genetic factors, distinguishable serologically, were probably as yet undiscovered in man, and urged that, if this were so, the following three aims ought to be pursued: -

"1. Some of the genes causing human anomalies may themselves possess serological reactions, and be thereby capable of unequivocal detection. Persons of genotypes normally anomalous in whom the anomaly is suppressed or obscured could thus be recognised, and the study of inheritance facilitated. Anomalies appearing more or ^{less} late in life could be detected in childhood.

"2. Some genes which are recessive in their clinical manifestation and are propagated largely by heterozygous carriers may yet have serological effects, and so be capable of recognition.

3) The genes responsible for anomalies, even in the absence of all serological effects specific to them, must certainly be linked with other genes situated in the same chromosomes. As there are only 23 pairs of autosomal

the prospect, chromosomes in man, with an increasing number of recognisable serological reactions, of finding at least one, and probably more, linked with those responsible for a given defect or anomaly is not a remote one, provided the means are available for carrying out a systematic research in pedigrees showing anomalies."

Since Dr Taylor's establishment as a member of the Galton Laboratory in October 1935 he has found abundant evidence that the unknown, but recognisable, reactions of human blood corpuscles are extremely numerous. Indeed he has scarcely examined any animal serum without finding constant reactions distinguishing different ^{human} individuals, not referable to the spontaneous O, A, B series, or to Landsteiner's M and N allelomorphs. During the initial period of exploration it has not been possible to follow up all the promising indications of this sort which have appeared, though we think that one factor (T) found in pig serum can now be used with the same confidence as any of the standard reactions.

It is in pig serum also that Dr Taylor has detected, and repeatedly confirmed, a very remarkable series of reactions of the blood of patients in institutions for the mentally deficient, reactions which it has not been possible, so far, to parallel using the blood of normal persons. This was first observed last March in the blood of a series of patients from Stoke Park being tested for the new factor T, and was absent in the majority of cases when the sera used had been exhausted

in their responses to the blood of any mentally deficient patient; that is to say, the difference between the reactions of the cells was paralleled and confirmed by differences between the corresponding supernatant sera.

This discovery suggested the extremely important possibility that the reaction was due to a genetical factor commonly diffused among mentally deficient patients, though rare in the general population. A further batch of defectives, this time from Colchester, was immediately tested with sera prepared specially to bring out the supposed effect, and a second time the difference between the blood of patients and that of normal persons was definitely confirmed. Since then a third batch, also from Colchester, has been examined, and has given positive reactions.

The reactions, however, are not simple, and it would be at least premature to assume that only a single genetical factor is at work. It is indeed certain that much work will have to be done, both on sera from other sources and on the conditions of preparation and preservation of the cells needed to give the most reliable results, before any definite genetical interpretation should be attached to them. It is, indeed, the potential importance of this discovery, and the variety of the subordinate questions which its elucidation requires, that is the reason for my now writing to you, since Dr Taylor and Miss Prior alone

cannot possibly hope to bring their work under this head to fruition without entirely abandoning the important exploratory programme which they had commenced, and, even so, it is to be feared that progress would be unduly delayed.

Within the existing Rockefeller grant, which the Medical Research Council administers, we are able at once to increase our equipment, i.e., in particular our capacity for cold storage and for centrifugation, at the expense of anticipating expenditure in view for future years. What I feel the situation that has now arisen requires is some expansion in personnel beyond that for which the present grant was planned. In the initial programme provision was made for the appointment of a second assistant from October 1937, and I should like to anticipate this appointment by one year, at a total final cost of about £300. At the same time it is clear that further routine assistance is needed in the laboratory, which could be achieved by appointing a new junior boy to take over the duties of the present boy in the animal house, and to transfer the latter's time wholly to laboratory work. This would require, with reasonable pay for a laboratory assistant, for which he seems to be qualified, an additional 30/- a week, or £80 a year. Finally, I should be glad if you could give favourable consideration to the possibility of appointing a young medical assistant to Dr Taylor, with qualifications for research sufficient to enable him to take responsibility

for some definite branch of the work now opening out, which might be assigned to him personally.

Until recently, although I felt confident that in the course of five years Dr Taylor's work would prove its importance, I had not anticipated that there would be any call for more rapid expansion than had been provided for. In view of what has been found, however, I think there is evidence to satisfy you, or other persons whom you may appoint to look into the matter, that the most sanguine expectations that could at first have been formed are likely to be realised, provided that the technical conditions for a sufficiently extensive pursuit of the problem can be provided.

I am sending a parallel letter to Dr Mellanby and Dr Landsborough Thomson.

Yours sincerely,