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PRION DISEASE GROUP
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IN CONFIDENCE

Dr Bob Will
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26th October 1992

Dear Bob,

Thank you for your letter of 19th October, and for discussing some of these issues on the phone with me. I feel that we must try to put past difficulties and differences behind us and try and resolve this now as a matter of urgency, in everyone's interest. This is a highly competitive field and it really will be a pity if we allow many of the key findings to be published by overseas groups while we are unable to pursue our research findings because of this disagreement, which I hope we can make every effort to solve.

Can we try to develop and encourage an open collaboration between our groups with regular meetings about every six weeks (alternating between London and Edinburgh) at which new findings are discussed (in confidence) to ensure that things are not being missed and at which agreements of how particular findings would be pursued could be agreed? There is no shortage of work to do. From the St Mary's end, we would propose the following:

(1) 129 heterozygosity data on all currently available cases should be collated at a joint meeting and written up and submitted as a matter of urgency (before the end of next month). This would be based on our previous draft, with yourself, your research fellow(s) and if necessary other clinicians/ neuropathologists as co-authors.

(2) Details of the codon 178 case needs to be forwarded to us as quickly as possible, and we will discuss any possible publication with you immediately. We will not contact the family to extend studies until the ethical review is complete.

(3) Aliquots of DNA or blood (and brain tissue on selected cases) will be forwarded to St. Mary's on cases from the current series which have not already been sent, and routinely on new cases.

(4) Clinical case summaries which have been sent with data from

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the referring centre will be sent with samples; the PM histology report will follow when available. Minimum clinical information should enable assessment of age at onset, duration of illness and presence or absence of relevant clinical signs and EEG findings. Other case information should be discussed at the joint meetings. For our part, we will send back the genotype data on the PrP polymorphisms and mutations to you as soon as these are generated.

(5) A joint publication policy should be agreed; we suggest that this follows the usual form, with one or two authors from each group assured (as a mark of the collaboration) on most papers, and other authorships to be given corresponding to the work carried out.

We have an immediate and major concern about our unpublished finding on the codon 129 heterozygotes. This is a potentially very important finding, which we made well over a year ago. The finding should be extended to a larger sample, as we have discussed many times. We thought that you did not want us to genotype further cases with respect to this polymorphism, pending ethical review, but we find that you have gone ahead locally to replicate our work, and we don't understand where things stand. Numerous other groups are pursuing this line and I think writing this up as a matter of urgency (with authorship as before, but with the proviso that if further key clinical or pathological data is now included then appropriate acknowledgement or authorship of appropriate clinicians or pathologists should be offered) would go a long way to restore confidence in a collaboration at this end. In addition, I would very much, as you know, like to have full clinical and histology notes on the case with the 178 mutation we identified last year, which is very important to record properly as soon as possible in a refereed publication.

A rapid sign of good will on these two issues would be very welcome but clearly we need to reach an overall agreement on future work which will be both productive and lasting. My principal concern relates to access to clinicopathological data. We need to find an arrangement such that your group is adequately involved and receives appropriate acknowledgement of the work involved in collecting such data. I have always backed the idea of a single centre which collects the data, but that is different from holding it without allowing access to others, which I feel is inefficient. We will miss important observations if we continue with a "keyhole" approach where only snippets of clinical data are made available in response to individual requests. We don't need access to your detailed epidemiological data or to experimental immunocytochemistry, but rather the basic case reports and histology which are, after all, being made available to you on behalf of us all by the clinicians and pathologists concerned. Surely it makes no sense to force us into a position where we must circulate clinicians and collect these cases independently, which would represent a waste of resources (which should be nationally co-ordinated), might interfere with your ascertainment, and however delicately done would risk irritating our hard pressed clinical colleagues and of course the families concerned. It would seem likely that, while

our groups were duplicating each other's work, most of the important findings would be reported in the meantime by the US groups.

We are quite happy, and always have been, to formally agree an authorship policy with respect to the use of such data and to agree that, even if you felt your authorship was not appropriate that you would be fully informed of such results (of course in confidence) and have the opportunity to follow them up with your more detailed data. We are not epidemiologists but pathobiologists, as you know.

I hope that you will view these proposals as constructive and workable. I remain happy to meet at short notice in either London or Edinburgh to discuss these issues further, and one way or another, we need to resolve this as a matter of urgency. It is clearly in the national interest that the epidemiological centre and the major genetic group in the UK collaborate with each other, and I am sure that members of all the key coordinating committees in this difficult field would strongly support such an agreement. Can we look to the future and try to make sure that our groups capitalise on the very real resources that, between us, we have been given?

With best wishes,

Yours sincerely,

Dr John Collinge
Wellcome Senior Clinical Fellow

cc Prof Ingrid Allen
Prof Jeff Almond
Mr Peter Dukes
Dr David Gordon
Dr Hilary Pickles
Dr David Tyrrell