Editorial

Themed issue: Neurodegenerative diseases

Neurodegenerative diseases are important. Certainly, this is the case if one uses the criterion that one prime minister of the UK is said to have used to decide the nation’s medical research priorities. A list of topics submitted was said to have been drawn up and reviewed with the following question: “How much do we spend because of this disease in a year?” If the amount was substantial, then applications in this area were favoured, and if the answer was very little, then the opposite applied.

The quality of the proposed science in an application was thought of less importance. The story is probably untrue, but it makes the point about the growing economic impact such diseases pose as we progress to an increasingly elderly society. If we survive everything else, we have one of two things to look forward to, either Alzheimer’s disease or Parkinson’s disease.

Although neurodegenerative diseases are important, they pose formidable intellectual problems. They are complex. Consequently, despite all the lip service of government and the real efforts of wonderful charities to fund research in this area, the technical developments that are revolutionising biomedical science, and the prompting of self preservation motivating still further the intellectual curiosity of researchers, the immediate prospects for patients are somewhat gloomy. The treatments available for such diseases are less than perfect, and the causes are often unknown.

This seems a depressing picture but, to an extent, it is false. Great progress is being made in some areas. The reviews included in this issue concentrate on the biochemical processes and pathways underlying neurodegeneration. Slowly, common themes are beginning to emerge. Of particular importance is the catabolism of proteins such as α-synuclein in Parkinson’s disease and τ in progressive supranuclear palsy and other tauopathies. Many of the ideas about neurodegeneration have been around for a decade or more, such as excitotoxicity and mitochondrial dysfunction, without their roles being understood, leading to the state where it is uncertain whether they are causal processes or epiphenomena. A major part of the difficulty in elucidating what is happening in vivo has been the lack of good model systems. However, over the past 20 years, molecular biological techniques have gone from the arcane, to the obscure, to the merely difficult, until today, where they are “off the shelf”. Nowhere is this more apparent than with genetically modified animals, which are commercially available as knockout and knockin for whatever gene one chooses to nominate. Consequently, one can study the effects of gene expression in these, and in the offspring that result from crossbreeding knockouts with knockins and transgene carriers. A second area that is likely to make advance possible is that of stem cells. Growing neurones in primary culture has been a difficult and haphazard business. The possibility of being able to develop neural progenitor cells into relatively uniform cultures of dopaminergic neurones offers real prospects of being able to explore both the physiology and pathophysiology of these cells in a way that was hitherto impossible.

Several colleagues and at least one charity have expressed to me the notion that we can and should concentrate on cures, via gene therapy, and not worry about causes. My profound belief is that only when we understand fully the normal physiology of cells will we truly understand what goes wrong in disease. Hopefully, this series of articles reflects the importance of basic sciences. Whether this translates into cures is another matter. Only time will tell. As someone once said: “Prediction is a difficult art, particularly when it concerns the future”.

Finally, I would like to thank the people who have very generously given of their time to contribute to this issue. For me, putting this together has been hugely informative, both intellectually and emotionally. In this last aspect moods swung from the elated to desperation, as contributors have either delivered their copy or not. One learns whom one can rely on. The publication of this issue was delayed because of an editorial decision, owing to the backlog of original articles, so apologies to all those contributors whose articles have been delayed. I would also like to thank three undergraduates—Sarah Clusky, Sarah Davies, and Kiran Tawana—whose superlative endeavours enabled three extra articles to be written at short notice. To them I owe tremendous thanks.

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Guest Editor