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Huntington's disease. However, since their identification in the mice, polyglutamine aggregates have been widely reported in HD post mortem patient brains. Max Perutz in Cambridge, UK and Erich Wanker, working with Hans Lehrach at the Max Planck Institute for Molecular Genetics in Berlin showed that these fibres have a cross-β-sheet structure more commonly known as amyloid.

For the past three and a half years, the R6/2 mice have been distributed to the research community either by my own lab or by the Jackson Laboratory in the USA. There are already around forty publications describing research that has been conducted on these mice by many groups. Insights into the early molecular stages of HD are arising. Polyglutamine aggregates form very early in some brain regions, before the onset of symptoms. Work initiated with Jang Ho Cha and Anne Young and MGH, Boston, showed that selective genes, many known to be important for nerve cell function, are turned down early in the transgenic mouse brains. Finally, the mice have been used for testing pharmaceutical compounds and two drugs are already entering the early stages of clinical trials in the UK and USA. The mouse model has revolutionised our knowledge of this disease and in the space of only four years is already beginning to have an impact on the treatment of HD.

STEPHEN WHITWORTH DAVIES

Research Interests

My laboratory has a long standing interest in molecular mechanisms of transcriptional regulation in the striatum following neuronal injury

I am currently focussing on the mechanism of neurodegeneration in Huntington's disease and other diseases caused by trinucleotide repeat expansions. These studies are in collaboration with Dr. Gillian Bates (UMDS). Current research projects are: immunocytochemical characterisation of neuropathological changes in Huntington's disease, post-mortem brain and transgenic mouse models of HD (Barbara Cozens and Elizabeth Slavik-Smith), ultrastructural and biochemical characterisation of *in vitro* and *in vivo* fibrous aggregates of Huntington's disease (Aysha Raza), transcriptional regulation in transgenic mouse models of Huntington's disease, and ultrastructural and molecular characterisation of sub-domains within the neuronal nucleus (Dr. Michael Gilder), ultra-

structural and molecular characterisation of cell death in HD transgenic mouse models (Mark Turmaine and Lee-Jay Bannister), and a detailed analysis of the ultrastructure and molecular properties of the Cajal Body, Gemmini body, PML bodies and the nucleolus (Dr. Michael Gilder, Elizabeth Slavik-Smith and Cheryl Jones).

I am expanding these investigations to encompass neurodegeneration within the CNS of transgenic mouse models of Parkinson's disease and MSA (Rushee Jolly in collaboration with Dr Michel Goedert, LMB Cambridge), investigating the role of a-synuclein in the formation of neuropathological inclusions and in a transgenic mouse model of spinal muscular atrophy (SMA) in collaboration with Dr Arthur Burghes (Columbus, Ohio).