

C. Aim of the project.

To gain insight into the normal function of ataxin-3 protein and to understand more about the neuropathology of the polyglutamine sequence, I wanted to perform studies by immunofluorescence microscopy to determine the subcellular localisation of the ataxin-3 protein in cell lines.

There is evidence that in all neurodegenerative disorders (HD, SCA1, SCA2, SCA3/MJD, SCA6, SCA7, SBMA, DRPLA) an elongated CAG repeat is responsible for the pathology. Recently, our group could show that in huntingtin, proteins with the polyglutamine expansions in the pathological range form insoluble protein aggregates and that the assembly of protein aggregates *in vivo* could be important for the induction of cell death (Scherzinger, *et al.* 1997).

To determine whether protein aggregation is also important for the pathomechanism in MJD, I wanted to perform expression studies with the ataxin-3 protein containing glutamine repeats of different length in cell culture systems. Furthermore, I wanted to analyse the formation of polyglutamine aggregates *in vitro* by electron microscopy (EM) and by cellulose acetate filter assay (CAFA).