

## CELL CULTURE MODEL FOR HUNTINGTON'S DISEASE

Professor David Rubinsztein and his team have generated two stable inducible rat PC12 cell lines for the study of Huntington's disease:

- HD-Q74 cell line with 74 glutamine repeats, which models many features of Huntington's disease
- HD-Q23 cell line with 23 glutamine repeats (control)

### Potential Uses:

- *In vitro* drug screening to evaluate compounds for the treatment of Huntington's disease (and other polyglutamine diseases) which cause selective growth inhibition or death of HD-Q74 cells
- Further study of Huntington's disease and its associated pathways

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## Background

Huntington's disease is a neurodegenerative disease associated with a reduction of neurite outgrowth, formation of aggregates containing gene products encoded by the mutated huntingtin (htt) gene and caspase-dependent cell death. Huntington's disease is caused by a polyglutamine repeat expansion, however the exact mechanism by which the CAG trinucleotide repeat causes Huntington's disease is still unclear.

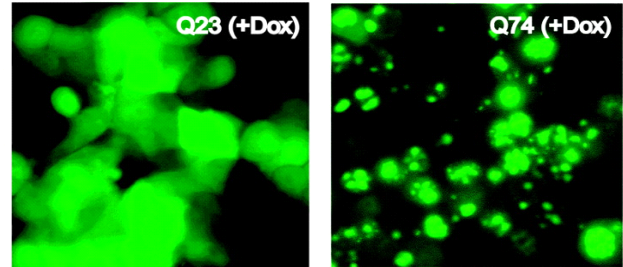
Tissue culture models of Huntington's disease are useful for evaluating compounds to treat the disease. Such models allow scientists to gain a better understanding of the disease and pathways that could have a wide impact on many neurodegenerative processes.

## Technology

Professor David Rubinsztein and his team at the Cambridge Institute for Medical Research at the University of Cambridge have generated two stable inducible rat pheochromocytoma (PC12) cell lines expressing GFP-tagged exon 1 of the huntingtin gene with either 23 or 74 glutamine repeats (PC12 HD-Q23 or PC12 HD-Q74), driven by a doxycycline-dependent Tet-On promoter.

Sufferers of Huntington's disease have 38 or more repeats and it has been shown that the PC12 HD-Q74 cell line with 74 glutamine repeats exhibits many of the features of Huntington's disease including the formation of aggregates with an EM structure similar to those observed *in vivo*, reduced neurite outgrowth and moderate caspase dependent cell death in cycling cells. The HD-Q23 cell line, which only has 23 glutamine repeats, as does not exhibit characteristics of Huntington's disease.

## Immunofluorescence of HD-Q23 and HD-Q74 cells



Insoluble aggregates produced by HD-Q74 cells appear as bright EGFP signals that are distinct from non-aggregated EGFP in HD-Q23 cells.

These cell lines can be used for *in vitro* studies to evaluate compounds to treat Huntington's disease. Assays using these two cell lines could identify compounds that cause selective growth inhibition or death of HD-Q74 cells suggesting the potential of such compounds for treating disease. The HD-Q74 cells appear to model the juvenile form of the disease (invariably found to have expansions of 70 CAG units or above) and could be used to evaluate compounds that specifically target this form.

## Publication

Wytenbach A. *et al.* Polyglutamine expansions cause decreased CRE-mediated transcription and early gene expression changes prior to cell death in an inducible cell model of Huntington's disease. *Human Molecular Genetics*. (2001). 10:1829.

## Commercialisation

We are seeking to establish non-exclusive licensing relationships for commercialisation of these cells that are a model for Huntington's disease in tissue culture.

GE Healthcare is the owner of the GFP patent portfolio and TET Systems is the owner of the patent portfolio relating to tetracycline regulated gene expression in eukaryotes. Any licensee of the cell lines will require valid licences to GFP and to the TET System.