PhD project in the Computational Biology of Neurodegenerative Diseases

Title: Method development and integration of data from high-throughput experiments towards identifying prion susceptibility genes and their pathways

Funding: MRC PhD studentship

Start date & duration: 1st October 2011, 3 years

Location: Prion Unit and Department of Neurodegenerative Diseases (Institute for Neurology) UCL, in collaboration with School of Information Systems, Computing and Mathematics, Brunel University

Supervisors:
- Dr Holger Hummerich (MRC Prion Unit, UCL)
- Professor Xiaohui Liu (Director: Centre for data Analysis) and Professor David Gilbert (Director: Centre for Systems and Synthetic Biology) at Brunel University.

Topic

A PhD studentship is available in the Bioinformatics section of the Prion Unit with the aim of building a comprehensive data mining infrastructure to detect relationships and patterns in data-sets in neurodegenerative disease (which exhibit protein aggregation and a variety of common threads) with an emphasis on prion susceptibility disease genes. Publicly available data, heterogeneous in nature, will be collated and stored in a customised database system.

It has long been established that the remarkably consistent pathogenesis and incubation periods seen in transmission in inbred mice, which die within 2 -3 days after a year-long incubation time depending on the genotype) is under genetic control. To understand this genetic control of prion disease susceptibility in human and mouse large scale experiments have been undertaken to identify key molecular co-factors and their pathways.

It has become feasible over the last few years to generate large datasets (QTL, microarray, GWAS, Exome sequencing). The challenge is to analyse these mouse/human genomic, annotated data in detail identifying candidate genes and integrate them using a wide variety of evidence available in the public domain.
It is also established that other neurological diseases such as Alzheimer's disease have certain pathologies and molecular mechanisms in common.

We plan to follow a disease/gene-centric approach and apply methods derived from the fields of Systems Biology and Statistics. Due to the disparate nature of these data sources and the problem of uncertainty associated with different states of knowledge we intend to deploy mathematical modelling techniques and statistical methods such as Bayesian reasoning, clustering methods and machine learning techniques.

Keywords/phrases:
Degenerative neurological disease, prion, large scale data integration and analysis, data mining, bioinformatics, systems biology, high throughput data, microarray, next generation sequencing

Required qualifications: First/upper second class honours degree in Computer Science, Statistics, Computational Biology, or other relevant disciplines.

Contact: For more information about this PhD studentship please contact Holger Hummerich (email: h.hummerich@prion.ucl.ac.uk).

Website: http://www.prion.ucl.ac.uk/

Stipend: £15,740 per annum

Applications are handled by the RCUK Shared Services Centre; to apply please visit the job board at https://ext.ssc.rcuk.ac.uk and complete an online application form.

References

1. Collinge J. Molecular neurology of prion disease.J Neurol Neurosurg Psychiatry.2005 ; 76(7): 906-19.

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3. Prion disease genetics. Mead S. Eur J Hum Genet. 2006 Mar;14(3):273-81.

4. HECTD2 is associated with susceptibility to mouse and human prion disease. Lloyd SE, Maytham EG, Pota H, Grizenkova J, Molou E, Uphill J, Hummerich H, Whitfield J, Alpers MP, Mead S, Collinge J. PLoS Genet. 2009;5(2): e1000383. Epub 2009 Feb 13.

5. Genetic risk factors for variant Creutzfeldt-Jakob disease: a genome-wide association study. Mead S, Poulter M, Uphill J, Beck J, Whitfield J, Webb TE, Campbell T, Adamson G, Deriziotis P, Tabrizi SJ, Hummerich H, Verzilli C, Alpers MP, Whittaker JC, Collinge J. Lancet Neurol. 2009; 8(1): 57-66