Functional Gene Annotation Initiative

Using the Gene Ontology to describe proteins and microRNAs

Newsletter September 2020

Annotation projects

The blood-brain barrier annotation project has been completed with the role of 81 human proteins in this process now captured. This project led to the review of over 170 articles and the creation of more than 1,600 GO annotations. Our current annotation focus is on Alzheimer's disease (AD) susceptibility loci. Genome Wide Association Studies (GWAS) have identified several loci to be associated with an increased or reduced risk to AD. A number of these variants are located within or near protein-coding genes, many of which are described in a review by Carmona *et al.*, 2018. The goal of this project is, therefore, to annotate proteins contributing to AD susceptibility, starting with the proteins that have the least number of associated annotations. For example, the only GO annotations associated with ZCWPW1, zinc finger CW-type and PWWP domain containing 1, described ZCWPW1 binding L3MBTL3 (L3MBTL histone methyl-lysine binding protein 3), MEOX2 (mesenchyme homeobox 2) and zinc. This protein now has 5 GO annotations that describe its role in positively regulating double-strand break repair during meiotic recombination in spermatocytes. As DNA damage and DNA repair are now being associated with neurodegeneration the association of ZCWPW1 with DNA repair may help towards the identification of further dementia-associated risk alleles through the application of pathway-based GWAS.

ARUK-UCL Annotation Statistics

In total, all ARUK-UCL projects have resulted in 13,489 annotations for 2,532 distinct gene products, of which over 10,000 annotations are associated with 1,777 human gene products (data from QuickGO, 1 September 2020).

MSc annotation projects

All four MSc students have now completed the annotation aspect of their dissertations and are now writing up. In total the students have created over 600 annotations. The majority of these annotations have captured the role of microRNAs at the blood-brain barrier, regulating amyloid-beta biosynthesis and regulating the expression of peroxisome proliferator-activated receptors. These captured over GO annotations to over 120 different microRNAs with over 60 different mRNA targets. Consequently, 19 microRNAs are now annotated as regulating the expression of APP (amyloid beta precursor protein).

In addition, one student has used GO to describe the role of PI3Kinase subunits in regulating cell adhesion and migration. This project led to the association of the GO term 'angiogenesis' with both PIK3CB and PIK3CD and also the role of PIK3CA in cell projection assembly and actin cytoskeleton organization, information not previously associated with these proteins. Due to the coronavirus all of the MSc project deadlines have been extended into September.

Recent Publications

Breuza L, et al. **A Coordinated Approach by Public Domain Bioinformatics Resources to Aid the Fight Against Alzheimer's Disease Through Expert Curation of Key Protein Targets**. J Alzheimers Dis. 2020 Jul 20. PMID: 32716361.

Touré V, et al. **The Minimum Information about a Molecular Interaction Causal Statement (MI2CAST)**. Bioinformatics. 2020 Jul 8:btaa622. PMID: 32637990.

Tomkins JE, Ferrari R, Vavouraki N, Hardy J, Lovering RC, Lewis PA, McGuffin LJ, Manzoni C. **PINOT: an intuitive resource for integrating protein-protein interactions**. Cell Commun Signal. 2020. 18(1):92. PMID: 32527260.

George MJ, et al. **Novel Insights Into the Effects of Interleukin 6 Antagonism in Non-ST-Segment-Elevation Myocardial Infarction Employing the SOMAscan Proteomics Platform**. J Am Heart Assoc. 2020. Jun 9:e015628. PMID: 32515246.

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