Variants, Genes, and Targets: An investigative pipeline utilising Open PHACTS linked data to establish meaningful connections

Despite the abundance of GWAS data available to us, it has proven difficult to extract useful information from it in the investigation of complex non-Mendelian genetic disorders. We are therefore in need of new ways to use the information to its full potential. Open PHACTS is one project making it possible to link many different data types together easily, including expression data, pathways, and disease gene information, which has the potential to allow scientists to extrapolate novel drug targets from GWAS data more easily. Using a Lilly-developed developed variant scoring methodology as the basis for determining which variants and genes to pursue for further analysis, I propose a series of investigative questions which could be answered through the Open PHACTS platform.

1. In which pathways are the affected genes involved?
2. Which other genes are present in these pathways?
3. Are there any common or ubiquitous genes amongst the pathways?
4. What is the differential expression of these genes when the previously described variant(s) is/are present compared to absent?
5. In which tissues does the differential expression occur?
6. Is the gene a valid and druggable target?
7. Are any existing drugs or small molecules known to affect the gene in the opposite direction to its differential expression?

This investigative pipeline uses data which is or may become available on the Open PHACTS linked data platform to acquire potential targets for the disease of interest and to understand better the mechanistic effect of some variants. Although it may the case that some desired data may not yet be available, it is my hope that as we move towards an open and collaborative pharmacological space we will see the necessary data become more widely available to the scientific community. This poster will demonstrate the benefits of such an environment and provide potential uses of Open PHACTS linked data in acquiring drug targets from GWAS variant data.