New international research defends genome-wide association studies

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(Medical Xpress) -- Since 2005, genome-wide association studies (GWAS) have successfully identified thousands of genes responsible for common human diseases.

GWAS were conceived to examine common genetic variants in different individuals to ascertain whether any particular variant is associated with a certain trait in major diseases.

Despite these impressive genetic discoveries, criticism has been aimed at GWAS for a lack of immediate therapeutic results, uncertain biological significance of findings, and because the majority of genetic variants associated with common diseases remain unidentified.

In an international study published today in the prestigious American Journal of Human Genetics, Professor Peter Visscher and Professor Matthew Brown of The University of Queensland and international colleagues Professor Mark McCarthy and Dr Jian Yang address these criticisms and defend the contribution of GWAS.

Professor Visscher is at UQ's Diamantina Institute and Queensland Brain Institute; Professor Brown is the Director of the UQ Diamantina Institute; Professor McCarthy is at the Wellcome Trust Centre for Human Genetics, University of Oxford, and the Oxford Centre for Diabetes, Endocrinology and Metabolism; and Dr Yang is with the Queensland Institute of Medical Research.

In a five-year review of the scientific and biological discoveries through the experimental design of GWAS, they argue that GWAS have brought about an unprecedented flood of biological discoveries across a broad range of common human diseases.

They said the rate of discovery and relevancy of genetic compilations using GWAS was “extremely high and unprecedented”.

The researchers provide examples of biological insights from GWAS that have already stimulated the development of therapeutics to treat chronic illnesses such as osteoporosis, arthritis, obesity and Type 2 diabetes, afflictions which affect a considerable number of people in Australia and in other countries.

They said such pathways and treatments for these particular diseases would likely have not been considered, if not for the genetic discoveries reported using GWAS.

Sceptics of GWAS complained of lack of therapeutic results and patient outcomes before Professors Visscher and Brown had even published their findings – something they felt was considerably premature.

Professor Brown dismisses criticism the GWAS received, saying there were undeniably huge benefits by using the study in human biology.

“In just a few years since GWAS was developed, these studies have identified thousands of genes which are definitely involved in most major common human diseases,” Professor Brown said.

“This provides researchers such as those working at UQ Diamantina Institute with a solid platform for research as to how the diseases are caused, and for the development of new therapies.

“This research takes time, but there are already plenty of examples of successes which indicate that the GWAS approach is bearing the fruit genetics has promised for so long.”

GWAS have also been criticised for only identifying a small proportion of the total number of genetic variants involved in common diseases.

In their paper, the researchers point out that the main contribution of GWAS was always going to be the biological insights from what it did discover, a contribution that remains relevant even if many genes remain unidentified.

They also show that the approach has actually captured a substantially greater proportion of the genetic risk than has previously been recognised.

The researchers also point out that the overall cost of the GWAS which have produced these findings is actually quite small – in the region of M.

They put this into context by pointing out that the huge advances that this investment has brought about costs the equivalent of one-two stealth fighter jets and much less than the cost of a single navy submarine.

“It is surprising how right from the start critics have taken such a dogmatic view and have not put subsequent research findings into perspective,” Professor Visscher said.

“In a period of only five years, a fantastic treasure trove of new, biologically relevant discoveries has been generated and we can be confident that this will continue for the foreseeable future, in particular when combined with the opportunities arising from the new genomics technologies that we have in-house at The University of Queensland Diamantina Institute and the Queensland Brain Institute.”

“It's interesting to observe that in historical and ongoing criticism of GWAS the goalposts keep moving.

“First it was ‘it won't work' then ‘only a few genes are identified for any particular disease', then ‘there is no biological relevance', followed by ‘there is no clinical relevance' and finally ‘the results are not yet translated into clinical practice'.

“Clearly, an objective view of this particular experimental design is that it has been very successful in a very short period of time.”

For the future, the technological advance to sequence entire genomes in large samples at affordable prices is likely to generate additional genes, pathways and biological insights, as well as the identification of causal mutations.

Provided by University of Queensland