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To: ESC Council for Basic Cardiovascular Science

Re: First Contact Initiative Grant Report

Recipient

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Host

Dr Inga Prokopenko

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Imperial College London

Grant period 15th October 2017 - 25th December 2017

Dear Sir/Madame,

First of all, I would like to express my sincere gratitude to the European Society of Cardiology and the Council for Basic Cardiovascular Science for awarding me with the First Contact Initiative Grant, which gave me the opportunity to visit Dr Inga Prokopenko's research group at Imperial College London. With generous support from the ESC and CBCS, I was able to start the work on my research project targeting the shared biological pathways between cardiovascular disease and type 2 diabetes.

Scientific background of the project

An overlap between the risk factors for cardiovascular disease and diabetes and their overwhelming comorbidity suggest that these conditions share pathogenic mechanisms. Chronic low-grade systemic inflammation associated with adiposity is the key underlying process in the development of cardiovascular disease, metabolic syndrome, and diabetes. The results of large-scale genome-wide association studies have identified multiple genetic loci associated with cardiovascular disease and type 2 diabetes, many of which are part of inflammatory pathways. However, the large number of established cardiovascular disease and type 2 diabetes loci account for only a small proportion of the heritability of these traits. This dictates the necessity of employing more sophisticated and robust approaches of the analysis of GWAS data, and taking into account other type of gene regulation, including epigenetic mechanisms influencing susceptibility.

Aim

The main goal of my study was to dissect the shared biological pathways between cardiovascular disease and type 2 diabetes using high-dimensional multi-omics data.

Results

During my visit, I learned the state-of-the-art analytical methods for high-dimensional multi-omics data analysis. Longitudinal analysis methods developed in Dr Inga Prokopenko's group, including novel approaches for multi-phenotype analyses of high-dimensional omics data (implemented in the SCOPA/MARV/META-SCOPA/META-MARV tools, 2017) and their extensions, are the most suitable for the study of polygenic traits such as cardiovascular disease or diabetes.

Using data and results from published large-scale genome-wide association studies available in public domain and via collaboration with Dr Prokopenko whose team has a strong competence in genome-wide association data analysis and made a great progress in understanding the genetic architecture of type 2 diabetes, I studied the overlap among genomic factors on the molecular network level that are predictive of these traits, including loci affecting atherosclerotic markers, inflammatory markers, blood pressure phenotypes, lipid levels, glycaemic markers, obesity and related metabolic disorders, etc. by combining them in a high-dimensional framework. I was able to identify the overlapping loci for cardiovascular and metabolic traits and map them to 12 genomic regions. The study also combined the genetic, methylation, expression and phenotypic longitudinal data from large-scale studies, including >8,000/~15,000/~5,000 individuals from Northern Finland Birth Cohorts 1966/86 to identify novel omics biomarkers for both cardiovascular disease and diabetes. The manuscript has been submitted based on the results of the collaboration.

Conclusion

I would like to thank my host, Dr Inga Prokopenko, for supporting my application for the ESC First Contact Initiative Grant, for the scientific advice and guidance during my visit, and the willingness to continue our collaboration. I would also like to thank the members of the team for teaching me new techniques, for insightful discussions, and all the activities that we did together. My visit to Imperial College London not only served as a foundation and set the direction for my future work, but also provided an invaluable experience and helped me grow as a scientist.

Yours Faithfully,
Yanina Timasheva

