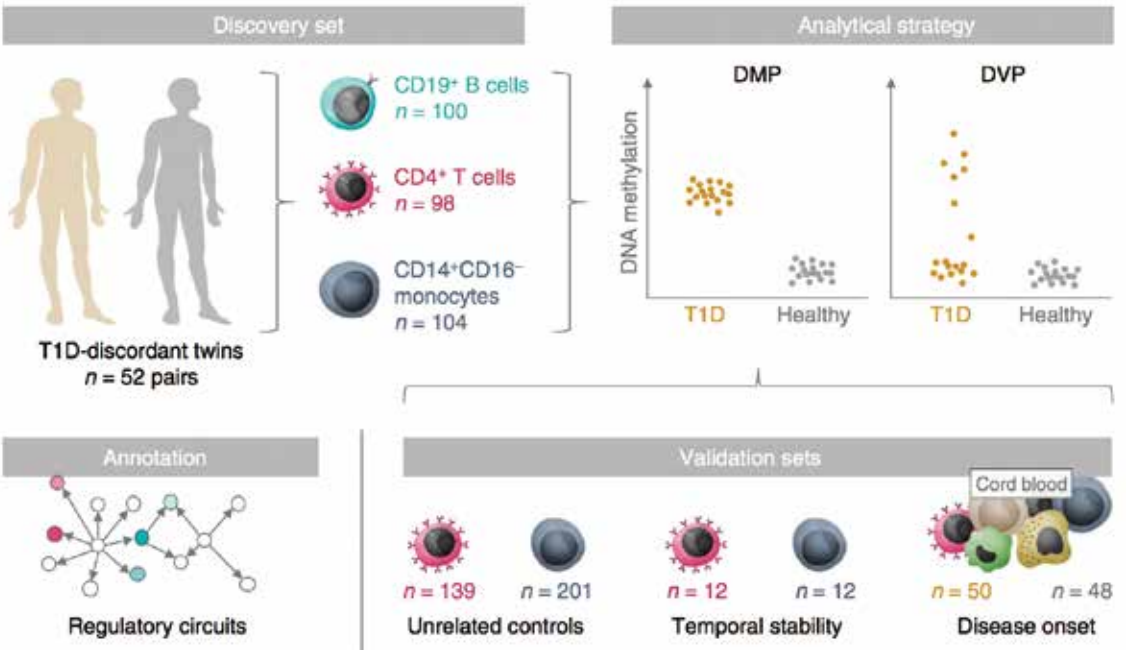
Life Sciences

New Research into Potential Epigenetic Origins of Type-1 Diabetes

Research led by scientists from University College London (UCL), Queen Mary University of London (QMUL) and Dr. Andrew E. Teschendorff from the CAS-MPG Partner Institute for Computational Biology (PICB), Shanghai Institutes for Biological Sciences (SIBS), Chinese Academy of Sciences (CAS) has identified epigenetic changes in three types of immune cells that could contribute to the development of type 1 diabetes. These changes were only found in patients with diabetes, opening the door to future biomarker development. The study, entitled "Increased DNA methylation variability in type 1 diabetes across three immune effector cell types" and published on November 29th, 2016 in *Nature Communications*, employed a unique experimental design and statistical approach.

Type 1 diabetes is an autoimmune disease that results from the loss of insulin-producing cells in the pancreas. The dramatic increase in the incidence of the disease over recent years, particularly in children younger than five years of age, suggests that non-genetic factors have a major role to play. In this study, the researchers focused on epigenetic modifications – molecular changes induced by environmental cues that have no effect on the DNA sequence itself but affect how the DNA functions. For example, DNA



Overview of the study design and analytical approach.

methylation, the type of epigenetic modification studied here, can contribute to disease development and progression through its influence on gene expression.

The team performed an Epigenome-Wide Association Study (EWAS), designed to measure DNA methylation levels in large numbers of people to look at variations between those with and without a particular disease. They set out to investigate whether methylation patterns associated with type 1 diabetes in different cell types, with the aim of gaining a greater insight into the mechanisms driving the disease. However, meaningful interpretation of EWAS findings can be hampered by confounding factors, such as genetic differences between unrelated individuals and differences in blood samples (consisting of many different types of cells). Both of these factors can then render results inaccurate and so the team designed their study specifically to address these barriers.

In the study DNA methylation was measured in over 50 pairs of identical twins discordant for type 1 diabetes, meaning one twin has the disease and the other does not. Using identical twins is a clever way of eliminating genetic differences in order to gain a clearer picture of the specific role of epigenetic factors in the disease. For each twin pair, DNA methylation was measured in three types of immune cells thought to act as key drivers in the disease process. A unique statistical approach developed by PICB member Andrew Teschendorff allowed identification of thousands of epigenetic marks in each of the three immune cell types that were only found in the twins with diabetes. Excitingly, these marks cluster near genes that play a role in immune cell metabolism.

The team hopes their experimental design and statistical approach, which was based on 772 genome-wide DNA methylation profiles, will now serve as a guide for future epigenetic studies.

The work is the result of an international collaboration as part of the International Human Epigenome Consortium (IHEC) of which the EU-FP7 Project BLUEPRINT is a member. Andrew Teschendorff is funded by SIBS, and an international fellowship sponsored by CAS and the Royal Society Newton International Fellowship.

Contact:

Andrew E. TESCHENDORFF, Ph.D., Principal Investigator
E-mail: andrew@picb.ac.cn
CAS-MPG Partner Institute for Computational Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences