Epigenome-wide association of DNA methylation markers in peripheral blood from Indian Asians and Europeans with incident type 2 diabetes: a nested case-control study.

Indian Asians, who make up a quarter of the world's population, are at high risk of developing type 2 diabetes. We
investigated whether DNA methylation is associated with future type 2 diabetes incidence in Indian Asians and whether differences in methylation patterns between Indian Asians and Europeans are associated with, and could be used to predict, differences in the magnitude of risk of developing type 2 diabetes. We did a nested case-control study of DNA methylation in Indian Asians and Europeans with incident type 2 diabetes who were identified from the 8-year follow-up of 25,372 participants in the London Life Sciences Prospective Population (LOLIPOP) study. Patients were recruited between May 1, 2002, and Sept 12, 2008. We did epigenome-wide association analysis using samples from Indian Asians with incident type 2 diabetes and age-matched and sex-matched Indian Asian controls, followed by replication testing of top-ranking signals in Europeans. For both discovery and replication, DNA methylation was measured in the baseline blood sample, which was collected before the onset of type 2 diabetes. Epigenome-wide significance was set at p<1 × 10(-7). We compared methylation levels between Indian Asian and European controls without type 2 diabetes at baseline to estimate the potential contribution of DNA methylation to increased risk of future type 2 diabetes incidence among Indian Asians. 1608 (11·9%) of 13,535 Indian Asians and 306 (4·3%) of 7066 Europeans developed type 2 diabetes over a mean of 8·5 years (SD 1·8) of follow-up. The age-adjusted and sex-adjusted incidence of type 2 diabetes was 3·1 times (95% CI 2·8-3·6; p<0·0001) higher among Indian Asians than among Europeans, and remained 2·5 times (2·1-2·9; p<0·0001) higher after adjustment for adiposity, physical activity, family history of type 2 diabetes, and baseline glycaemic measures. The mean absolute difference in methylation level between type 2 diabetes cases and controls ranged from 0·5% (SD 0·1) to 1·1% (0·2). Methylation markers at five loci were associated with future type 2 diabetes incidence; the relative risk per 1% increase in methylation was 1·09 (95% CI 1·07-1·11; p=1·3 × 10(-17)) for ABCG1, 0·94 (0·92-0·95; p=4·2 × 10(-11)) for PHOSPHO1, 0·94 (0·92-0·96; p=1·4 × 10(-9)) for SOCS3, 1·07 (1·04-1·09; p=2·1 × 10(-10)) for SREBF1, and 0·92 (0·90-0·94; p=1·2 × 10(-17)) for TXNIP. A methylation score combining results for the five loci was associated with future type 2 diabetes incidence (relative risk quartile 4 vs quartile 1 3·51, 95% CI 2·79-4·42; p=1·3 × 10(-26)), and was independent of established risk factors. Methylation score was higher among Indian Asians than Europeans (p=1 × 10(-34)). DNA methylation might provide new insights into the pathways underlying type 2 diabetes and offer new opportunities for risk stratification and prevention of type 2 diabetes among Indian Asians. The European Union, the UK National Institute for Health Research, the Wellcome Trust, the UK Medical Research Council, Action on Hearing Loss, the UK Biotechnology and Biological Sciences Research Council, the Oak Foundation, the Economic and Social Research Council, Helmholtz Zentrum Munich, the German Research Center for Environmental Health, the German Federal Ministry of Education and Research, the German Center for Diabetes Research, the Munich Center for Health Sciences, the Ministry of Science and Research of the State of North Rhine-Westphalia, and the German Federal Ministry of Health.
Institut für Humangenetik

Occurences:
- Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > Institut für Humangenetik > 2015

entries: