

Pharmacogenetics for Type 2 Diabetes: Practical Considerations for Study Design

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Abstract

There is a relative dearth of studies designed to elucidate genetic variation that can explain differences in the response to diabetes pharmacotherapy. When designing such studies, appropriate consideration of the various nongenetic variables that can affect the treatment response is necessary. In addition, disease stage and prior pharmacotherapy also influence drug efficacy. Selecting the appropriate genetic variant to test in such studies is also important, and common variants (known to be functional or otherwise) in a given candidate locus should be tested for the effect on the treatment response. Finally, an appropriate measure of treatment response is necessary to enable detection of pharmacogenetic effects. Perhaps prior to undertaking such studies, smaller studies utilizing well-characterized, homogenous populations with normal glucose tolerance or prediabetes (to avoid the problem of disease effects on treatment response) and surrogate measures of response such as insulin secretion should be completed.

J Diabetes Sci Technol 2009;3(4):705-709

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Abbreviations: (DPP) Diabetes Prevention Program, (GLP-1) glucagon-like peptide-1, (HbA1c) hemoglobin A1c, (*KCNJ11*) potassium inwardly rectifying channel, subfamily J, member 11, (OCT1) organic cation transporter 1, (*PPARG*) peroxisome proliferator-activated receptor γ , (SNP) single nucleotide polymorphism, (*TCF7L2*) transcription factor 7-like 2

Keywords: common genetic variation, drug response, tag SNPs

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