PRESS RELEASE

**Genetic Variant Associated with Improved Glycemic Response to Metformin**

**Many individuals with type 2 diabetes take the diabetes drug metformin to improve their blood glucose levels. A team of scientists at the DZD partner German Diabetes Center (DDZ) has discovered that metformin is associated with a greater decrease in blood glucose levels in individuals recently diagnosed with type 2 diabetes who carry a specific variant of the glucose transporter (GLUT2) gene than in individuals without this variant.**

**Düsseldorf (DDZ)** – A study conducted by the Metformin Genetics (MetGen) Consortium with more than 13,000 diabetes patients has shown that a specific variant in the glucose transporter gene GLUT2 has an effect on the long-term blood glucose level (HbA1c) in response to metformin therapy. Glucose transporters are proteins that are responsible for transporting glucose through the cell membrane. The glucose transporter GLUT2 is produced in humans in the kidneys, liver and small intestine and is encoded by the gene SLC2A2, among others.

Under the direction of Professor Wolfgang Rathmann, scientists at the German Diabetes Center (DDZ) have investigated the extent to which the treatment effect of metformin differs in patients with recently diagnosed type 2 diabetes with and without this genetic variant. In the prospective German Diabetes Study, they conducted a genetic analysis of 508 participants with recently diagnosed type 2 diabetes (mean age: 53 years, 65 percent male). "We specifically looked at variants in the SLC2A2 gene and investigated possible effects on fasting blood glucose levels," said Professor Michael Roden, chairman of the German Diabetes Center and the German Center for Diabetes Research (DZD). The results were published in the journal *Diabetologia*.

**Patients with a C allele showed greater blood glucose reduction**

Study participants with a specific variant of this gene (C allele) reported more diabetes symptoms than non-carriers of this gene at the time of their diabetes diagnosis. Among the 45 percent of participants who were treated with metformin alone, there was a greater reduction in blood glucose levels in carriers of the C allele (24 percent) than in non-carriers within the first year after diagnosis. Carriers of the variant recorded a reduction of 6.3 mmol/l (114 mg/dl) between the diagnosis of diabetes and the time of measurement in the first year thereafter, compared with 3.9 mmol/l (70 mg/dl) for non-carriers. The difference persisted after a statistical adjustment of the values in terms of age, gender, body mass index (BMI) and diabetes duration of the participants. However, such blood glucose differences were only seen in patients who controlled their blood glucose with metformin monotherapy. There were no differences in patients who additionally took another antidiabetic drug.

**Conclusion: Genetic variant modifies glycemic response**

There could be various reasons why people with diabetes with the relevant variant in the glucose transporter gene respond better to a blood glucose reduction by metformin. The researchers suspect that the blood glucose lowering agent metformin inhibits glucose formation in the liver and promotes the absorption of glucose into the muscle. Gene analyses of tissue samples of the liver have revealed that the SL2A2 gene is less active in humans with the C allele and the protein encoded by the gene, the glucose transporter GLUT-2, also shows lower activity. Scientists suspect that metformin positively influences this genetic deviation and helps the glucose transporter become more active.

**Source:** Rathmann W et al. A variant of the glucose transporter gene SLC2A2 modifies the glycaemic response to metformin therapy in recently diagnosed type 2 diabetes. *Diabetologi*a February 2019 <https://doi.org/10.1007/s00125-018-4759-z>

**Photo:** German Diabetes Study

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**German Diabetes Study (DDS)**

The German Diabetes Study (DDS) observes patients with newly diagnosed type 1 or type 2 diabetes in the first year after diagnosis for a period of 10 years. The objective of the German Diabetes Study is to identify early markers for various courses of diabetes in order to develop new treatment concepts and use them in a targeted manner. In this way, early warning signs for later complications can be detected, and approved therapy methods can be compared in parallel. In this study, the influence of genes on the course of the disease is also being investigated.

Within the framework of the German Center for Diabetes Research (DZD), the study is being conducted at eight locations in Germany: Berlin/Potsdam, Dresden, Düsseldorf, Heidelberg, Leipzig, Lübeck, Munich, and Tübingen.

Within the framework of the German Center for Diabetes Research (DZD), the study is being conducted at eight locations in Germany: Berlin/Potsdam, Dresden, Düsseldorf, Heidelberg, Leipzig, Lübeck, Munich, and Tübingen. Participants of the German Diabetes Study receive, free of charge, the opportunity of early detection of diabetic secondary diseases such as nerve, vascular and retinal damage. If you are interested in participating in the study, you will find further information at <https://deutsche-diabetes-studie.de>

The German Diabetes Center (DDZ) serves as the German reference center for diabetes. Its objective is to contribute to the improvement of prevention, early detection, diagnosis and treatment of diabetes mellitus. At the same time, the research center aims at improving the epidemiological data situation in Germany. The DDZ coordinates the multicenter German Diabetes Study and is a point of contact for all players in the health sector. In addition, it prepares scientific information on diabetes mellitus and makes it available to the public. The DDZ is part of the Leibniz Association (Wissenschaftsgemeinschaft Gottfried Wilhelm Leibniz, WGL) and is a partner of the German Center for Diabetes Research (DZD e.V.).

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