Factor present in gestational and type 2 diabetes could provide new treatment options

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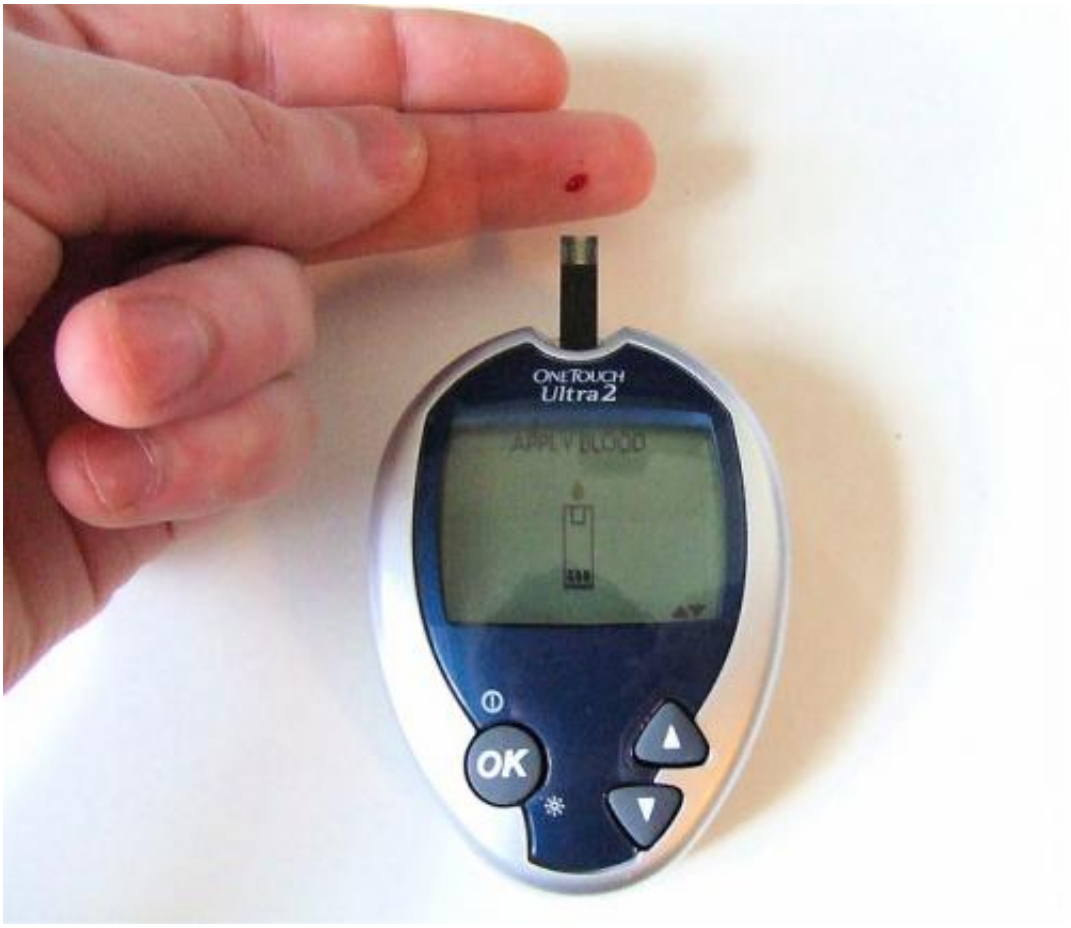

Blood glucose monitoring. Credit: Wikipedia

New research reveals that both pregnant women with diabetes and with type 2 diabetics have high levels of a fat metabolite that impairs

pancreatic cells from secreting insulin. The findings, which are published in the April 1 issue of the Cell Press journal *Cell Metabolism*, suggest that blocking the effects of this fat metabolite may help prevent and treat diabetes.

In nearly one-fifth of pregnancies, diabetes can arise (called gestational diabetes), and when this happens, it puts the woman at an increased risk for developing type 2 diabetes later in life. To gain better insights into the shared mechanisms behind these two types of diabetes, researchers in Dr. Michael Wheeler's lab at the University of Toronto examined more than 340 molecules in blood samples from individuals with gestational diabetes, individuals with type 2 diabetes, and individuals without diabetes. The researchers used a metabolomics approach, which involves the study of chemical processes involving metabolites.

The team found that the blood of both gestational and type 2 diabetic patients contained a remarkable number of changed metabolites, including sugars, amino acids, and fats, compared with samples from nondiabetic controls. One particular fat metabolite, called CMPF, was dramatically increased in both gestational and type 2 diabetic individuals compared to those without diabetes. Experiments in mice showed that this increased concentration of CMPF caused a decrease in insulin secretion from beta cells in the pancreas, which led to the development of diabetes.

More detailed mechanistic experiments revealed that CMPF enters a beta cell through what's called organic anion transporter 3 (OAT3), and once inside the cell it causes oxidative stress and other negative effects. Next, the researchers found that the effects of CMPF could be prevented through either blocking the transport of CMPF into insulin-producing beta cells or treatment with antioxidants.

"Based on our findings we believe that CMPF and its transporter OAT3

represent novel targets for prevention and treatment of diabetes," says first author Kacey Prentice. "If we can reduce levels of CMPF in the blood, or prevent CMPF from entering the beta cell through blockage of OAT3, we believe that we can preserve beta cell function and prevent the beta cell failure that ultimately causes diabetes."

According to Prentice, it is important to note that the treatment of gestational diabetes is a very sensitive topic due to potential risks to both the mother and the developing fetus. "Due to this, we believe the prevention and treatment of type 2 diabetes is a more realistic and widely acceptable goal; however, CMPF has great potential for use as a biomarker of both conditions."

More information: Prentice et al.: "CMPF is Elevated in Diabetes and Induces Beta Cell Dysfunction." *Cell Metabolism*, dx.doi.org/10.1016/j.cmet.2014.03.008

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