Researchers investigating ways to improve type 2 diabetes treatments

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A better understanding of how the transcription factor Peroxisome Proliferator-Activated Receptor Gamma (PPARgamma) works is critical to find new ways to improve medications to treat type 2 diabetes. Drugs that activate PPARgamma, called thiazolidinediones (TZDs), have long been regarded as a treatment for type 2 diabetes based on their anti-inflammatory and potent insulin-sensitizing activity. When taken orally, TZDs help decrease insulin resistance. However, most medications in that class have now been withdrawn from the market, or severely limited in their usage, given their dangerous side effects, which include weight gain, water retention and heart failure.

One promising approach to target PPARgamma to treat the issues related to type 2 diabetes is to dissect the regulatory strategies that control different subsets of PPARgamma target genes in cells. The ultimate goal would be to target the "negative" side of PPARgamma activity without impacting on the "good" ones.

A recent study led by BUSM researchers, published in *Cell Reports*, identifies one such strategy regulating fat tissue activity and PPARgamma in adipose cells. It is based on a group of cellular factors that bind to DNA and help PPARgamma in the regulation of a specific subset of target genes, including enzymes important for the mobilization of lipids.

"There is a great need to develop new treatments for people with type 2 diabetes," said Valentina Perissi, PhD, assistant professor of biochemistry at BUSM and the study's corresponding author. "Targeting PPARgamma still represents a powerful approach, however we need to further improve our understanding of PPARgamma function and how its activity is regulated in normal cells in orderdevelop more effective treatments."

More information: "GPS2/KDM4A Pioneering Activity Regulates Promoter-Specific Recruitment of PPAR?." M. Dafne Cardamone, Bogdan Tanasa, Michelle Chan, Carly T. Cederquist, Jaclyn Andricovich4, Michael G. Rosenfeld, Valentina Perissi. *Cell Reports* Published Online: June 19, 2014. DOI: dx.doi.org/10.1016/j.celrep.2014.05.041

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