

co-ordinated with the Director of the Institute / Research Unit

**Institute of Epidemiology II / AME**

**PSP-Element:**

G-504091-003

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**Title of the highlight:**

Metformin lowers LDL cholesterol levels

**Keywords:**

Metabolomics, LDL cholesterol, AMPK pathway, Type 2 diabetes, Cardiovascular diseases

**Central statement of the highlight in one sentence:**

Metformin significantly reduces the levels of three metabolites, reflecting a suppressed activity of FADS which also leads to reduced levels of LDL cholesterol.

**Text of the highlight:**

Despite metformin's use as an anti-hyperglycemic agent for more than 50 years its primary mode of action is not yet completely understood.

We observed that metformin treatment reduced levels of the three acyl-alkyl PC metabolites in type 2 diabetes patients. This change in the metabolic profiles may mediate lowered blood levels of LDL-C. The underlying mechanism is most likely the metformin-induced activation of AMPK, and the consequent suppression of SREBP1c and FADS, which leads to reduced levels of PUFA and LDL-C. Our study suggests that Metformin might have an additional beneficial effect with regards to cardiovascular diseases among diabetes patients.

The results of our study were cited in more than 20 national and international online health portals, as well as renowned newspapers (i.e. 'Der Standard'). Furthermore, a well-meaning comment in the same journal and our response are currently in press. With this our efforts to elucidate the physiological effect of metformin are not yet finished. Other studies, focussing on the effect of metformin are in progress.

**Publication:**

Xu T, Brandmaier S, Messias AC, Herder C, Draisma HH, Demirkan A, Yu Z, Ried JS, Haller T, Heier M, Campillos M, Fobo G, Stark R, Holzapfel C, Adam J, Chi S, Rotter M, Panni T, Quante AS, He Y, Prehn C, Roemisch-Margl W, Kastenmüller G, Willemsen G, Pool R, Kasa K, van Dijk KW, Hankemeier T, Meisinger C, Thorand B, Ruepp A, Hrabé de Angelis M, Li Y, Wichmann HE, Stratmann B, Strauch K, Metspalu A, Gieger C, Suhre K, Adamski J, Illig T, Rathmann W, Roden M, Peters A, van Duijn CM, Boomsma DI, Meitinger T, **Wang-Sattler R\***. Effects of Metformin on Metabolite Profiles and LDL Cholesterol in Patients With Type 2 Diabetes. **Diabetes Care**. 2015 Aug 5. pii: dc150658. [Epub ahead of print]

**Taking account of the HMGU mission:**

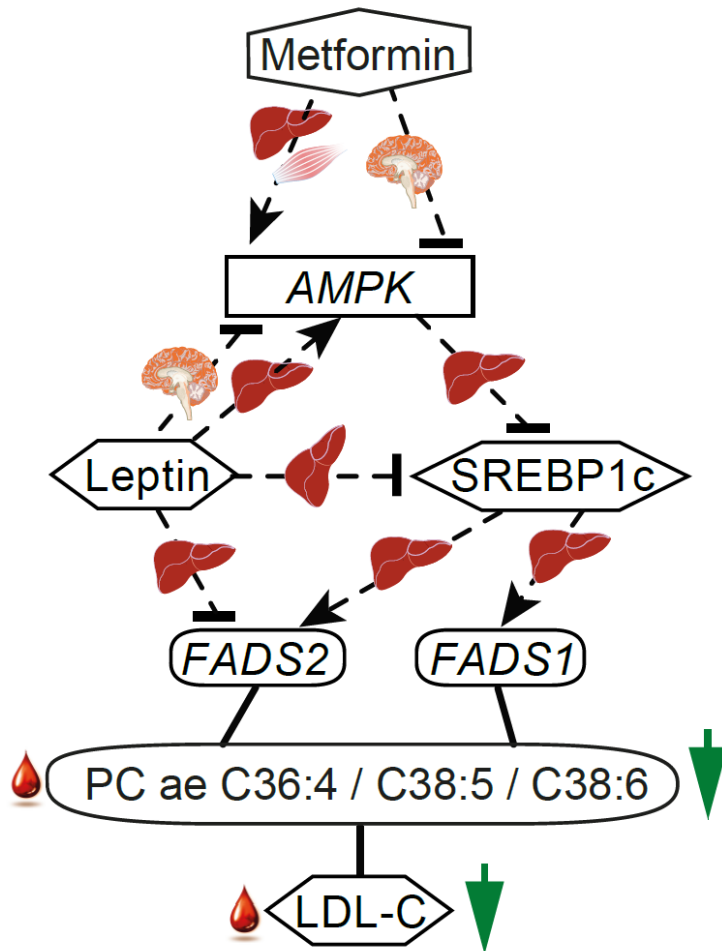
Metformin, the subject to our study, is the most frequently prescribed drug for the oral treatment of type 2 diabetes, one of the diseases the HMGU research focusses on. Metformin has an additional beneficial effect with regards to cardiovascular diseases among the Diabetes patients

**The internal HMGU co-operation partners with whom the highlight was compiled, if appropriate:**

Institute of Epidemiology II [EPI II] (AG 'Cardiovascular and Metabolic Diseases', AG 'Diabetes Epidemiology', AG 'Environmental Risks', AG 'National Cohort')  
Institute of Structural Biology [STB] (AG 'Sattler')  
Institute of Human Genetics [IHG]  
Institute of Bioinformatics and Systems Biology [IBIS] (AG 'Metabolomics', AG 'Curation of Human Disease Networks', AG 'Systems Biology of Small Molecules')  
Institute of Genetic Epidemiology [IGE]  
Institute of Experimental Genetics [IEG]  
Institute of Experimental Genetics, Genome Analysis Center [IEG/GAC]  
Institute of Health Economics and Health Care Management [IGM] (AG 'Ökonomische Evaluation')  
German Center for Diabetes Research, Neuherberg, Germany [DZD]

# Metformin Effects on Metabolite Profiles and LDL Cholesterol

EPI II/AME



- Metformin is used for more than 50 years, but the mode of action is **not fully understood**
- **Activation of AMPK** in the liver leads to an anti-hyperglycemic effect
- We analyzed 1800 KORA participants and found **decreased levels of three phosphatidycholines**
- **Suppressed FADS activity** appears to be the underlying reason
- This also leads to **decreased levels of LDL cholesterol** and beneficial cardiovascular effects
- Our findings are cited or reported in **more than 20** online health portals or newsletters
- **Further studies** on metformin's physiological effects are in progress