Editorial

Afamin an emerging marker for type 2 diabetes mellitus

Benjamin Dieplinger, Thomas Mueller

Department of Laboratory Medicine, Konventhospital Barmherzige Brueder Linz, Linz, Austria

Correspondence to: Benjamin Dieplinger. Department of Laboratory Medicine, Konventhospital Barmherzige Brueder Linz, Seilerstaette 2-4, A-4020 Linz, Austria. Email: benjamin.dieplinger@bs-lab.at.

Comment on: Kollerits B, Lamina C, Huth C, *et al.* Plasma Concentrations of Afamin Are Associated With Prevalent and Incident Type 2 Diabetes: A Pooled Analysis in More Than 20,000 Individuals. Diabetes Care 2017;40:1386-93.

Received: 08 January 2018. Accepted: 21 January 2018; Published: 22 January 2018.

doi: 10.21037/jlpm.2018.01.08

View this article at: http://dx.doi.org/10.21037/jlpm.2018.01.08

The number of people worldwide with diabetes mellitus has quadrupled in the past 30 years. Diabetes mellitus is present in 1 of 11 adults, of whom 90% have type 2 diabetes mellitus (1). Moreover, one third to one half of patients with diabetes mellitus remain undiagnosed (2). Further, diabetes mellitus is among the top ten causes of death (1). Therefore, an in-depth understanding of the pathogenesis is of major importance. Since diabetes mellitus represents an essentially curable disease (via life style changes and pharmacological intervention), the identification of early risk predictors is a major research goal.

The protein Afamin might have the potential to become such a predictor for diabetes mellitus. Afamin was first described by Lichtenstein *et al.* as the fourth member of the human albumin gene family (3,4). Afamin is a human glycoprotein and has a molecular mass of 87 kD with 15% carbohydrate content (5) and 55% amino acid sequence similarity to human albumin (3). The main source of afamin is the liver (3) but it is also expressed in other tissues such as the brain, the testes, the ovaries and the kidneys (www.proteinatlas.org). In vitro studies revealed a vitamin E -binding and -transporting function of afamin (6) which might play a role in vitamin E the transport via the blood-brain barrier (7) but, most likely, not for vitamin E transport in the blood. The (patho-)physiological functions of afamin is still largely unknown; for a comprehensive review see (8). Findings from a preliminary study on a hyperglycemic phenotype in transgenic mice overexpressing the human afamin gene support a possible causal role of afamin for the development of type 2 diabetes mellitus (9). These classical animal model experiments in search of (patho-)physiological functions for afamin were followed by a pooled analysis in three human epidemiological studies including more than 5,000 individuals and impressively demonstrated that afamin plasma concentrations was not only a predictor for the prevalence but also for the incidence of metabolic syndrome (9).

In this context, Kollerits *et al.* reported recently in a pooled meta-analysis in more than 20,000 individuals from eight prospective cohort studies a highly significant and independent association of afamin plasma concentrations with the prevalence and incidence of type 2 diabetes mellitus (10). Increasing afamin plasma concentrations (by 10 mg/L) were associated with a 20 % increased prevalence of type 2 diabetes mellitus (n=1,398 prevalent cases). Moreover, afamin plasma concentrations measured at baseline were an independent predictor for the development of type 2 diabetes mellitus (n=585 incident cases) during follow-up. Increasing afamin plasma concentrations (by 10 mg/dL) were associated with 30% increased incidence type 2 diabetes mellitus. The authors further described in their study a strong association of afamin with prediabetes and type 2 diabetes mellitus related phenotypes such as insulin resistance (10). However, the causality of afamin's association with diabetes mellitus as well as possible underlying mechanisms remain to be elucidated.

Very recently, 2 further studies reported new insights into additional diagnostic and possibly also functional properties of afamin related to the work of Kollerits *et al.* First, Tramontana *et al.* showed in a large nested case-control study significantly higher afamin concentrations in the first trimenon of pregnant women developing gestational

diabetes mellitus later in pregnancy demonstrating another promising early marker property of afamin with possibly substantial impacts for therapies of pregnancy complications such as gestational diabetes mellitus (11). Another work with potentially high impact on our understanding of afamin's function was recently published by Naschberger *et al*. The authors reported for the first time the 3-dimensional structure of afamin using state-of-the-art X-ray crystallography technology (12). The evaluation of afamin's precise molecular structure will enable the search for physiological ligands and lead to insights into its (patho-) physiological function, particularly regarding its role in the development of diabetes mellitus and related diseases.

Even though increased afamin plasma concentrations seem to be a promising marker for the prediction of diabetes mellitus, clear afamin thresholds and the optimal time point during life to measure afamin still need to be established, and further tested in prospectively planned clinical studies, before measurement of afamin could possibly be implemented in clinical routine.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned and reviewed by the Section Editor Xu-Hua Mao (Department of Clinical Laboratory, Yixing People's Hospital, Wuxi, China).

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jlpm.2018.01.08). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol 2018;14:88-98.
2. Rathmann W, Haastert B, Icks A, et al. High prevalence of undiagnosed diabetes mellitus in Southern Germany: target populations for efficient screening. The KORA survey 2000. Diabetologia 2003;46:182-9.
3 Lichenstein HS, Lyons DE, Wurfel MM, et al. Afamin is a new member of the albumin, alpha-fetoprotein, and vitamin D-binding protein gene family. J Biol Chem 1994;269:18149-54.
4. Nishio H, Dugaiczyk A. Complete structure of the human alpha-albumin gene, a new member of the serum albumin multigene family. Proc Natl Acad Sci U S A 1996;93:7557-61.
5. Jerkovic L, Voegele AF, Chwatal S, et al. Afamin is a novel human vitamin E-binding glycoprotein characterization and in vitro expression. J Proteome Res 2005;4:889-99.
6. Voegele AF, Jerković L, Wellenzohn B, et al. Characterization of the vitamin E-binding properties of human plasma afamin. Biochemistry 2002;41:14532-8.
7. Kratzer I, Bernhart E, Wintersperger A, et al. Afamin is synthesized by cerebrovascular endothelial cells and mediates alpha-tocopherol transport across an in vitro model of the blood-brain barrier. J Neurochem 2009;108:707-18.
8. Dieplinger H, Dieplinger B. Afamin--A pleiotropic glycoprotein involved in various disease states. Clin Chim Acta 2015;446:105-10.
9. Kronenberg F, Kollerits B, Kiechl S, et al. Plasma concentrations of afamin are associated with the prevalence and development of metabolic syndrome. Circ Cardiovasc Genet 2014;7:822-9.
10. Kollerits B, Lamina C, Huth C, et al. Plasma Concentrations of Afamin Are Associated With Prevalent and Incident Type 2 Diabetes: A Pooled Analysis in More Than 20,000 Individuals. Diabetes Care 2017;40:1386-93.
11. Tramontana A, Dieplinger B, Stangl G, et al. First trimester serum afamin concentrations are associated with the development of pre-eclampsia and gestational

diabetes mellitus in pregnant women. Clin Chim Acta 2018;476:160-6.
12. Naschberger A, Orry A, Lechner S, et al. Structural Evidence for a Role of the Multi-functional Human Glycoprotein Afamin in Wnt Transport. Structure 2017;25:1907-15.e5.

doi: 10.21037/jlpm.2018.01.08
Cite this article as: Dieplinger B, Mueller T. Afamin an emerging marker for type 2 diabetes mellitus. J Lab Precis Med 2018;3:5.

