Afamin an emerging marker for type 2 diabetes mellitus

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Provenance: This is a Guest Editorial commissioned by the Section Editor Xu-Hua Mao (Department of Clinical Laboratory, Yixing People’s Hospital, Wuxi, China).


Received: 08 January 2018. Accepted: 10 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 trimester 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.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References