Figure 1. Hypothetical model for the relationship between baseline natriuretic peptide levels and the development of type 2 diabetes.

The mechanisms that may explain the inverse association between natriuretic peptides (NP) and a decreased risk of incident diabetes are shown in supplemental figure 1. A decrease in NP synthesis, resistance to NP, the release of biologically inactive NP, or an increase in the clearance of NP can lead to a substantial and prolonged decrease in the physiological effects of NP [1, 2]. Less NP can lead at a molecular level, to a decrease activation of the gene the codes for the peroxisome proliferator-activated receptor γ coactivator-1 α (PGC1A). This gene is essential in regulating energy metabolism and mitochondrial biogenesis [3]. This can lead to a decrease in fat and glucose oxidation, lower mitochondrial density [4], accumulation of visceral and liver fat [5] and insulin resistance [6]. Furthermore, NP are involved in vessel growth, thus low levels of NP may be associated with a decreased formation of capillaries [7]. Collectively, mitochondrial and microvascular dysfunction are all implicated in the development of insulin resistance [8, 9], which is a primary risk factor in the development of type 2 DM. In agreement that an increase in NP, within the normal range, is associated with improved glucose control, the Look AHEAD clinical trial showed that those individuals assigned to the lifestyle intervention group had a 22% increase in NT-proBNP and that this was inversely associated with change in BMI and HbA_{1c} [10]. Similar results were reported by Chainani-Wu N. et al [11] who describes that changes in BNP were inversely associated with change in insulin and BMI. These findings further support the notion that within a physiological range (50 to 100 pg/mL), higher levels of NT-proBNP may lower BMI, improve glucose metabolism and prevent the development of diabetes.

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