

***Elevated Serum Levels of Adropin in Patients with
Type 2 Diabetes Mellitus and its Association with
Insulin Resistance***

Mehrnoosh Shanaki, Ph.D.

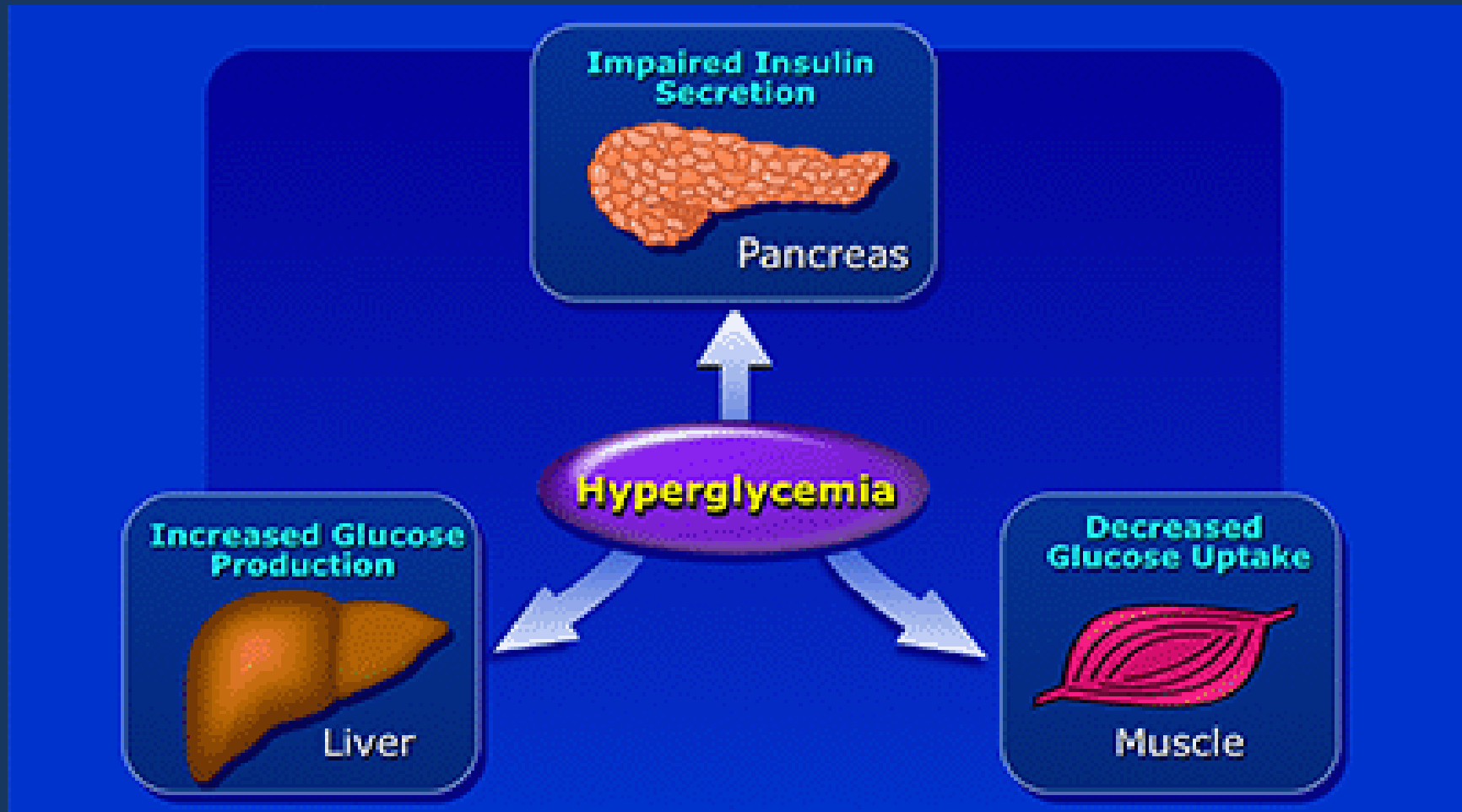
**Assistant Professor of Clinical Biochemistry
Shahid Beheshti University of Medical Sciences**

Outline

- Introduction:
 - Type 2 Diabetes Mellitus
 - Metabolic Homeostasis
 - Adropin
- Methods
- Results
- Discussion & conclusion

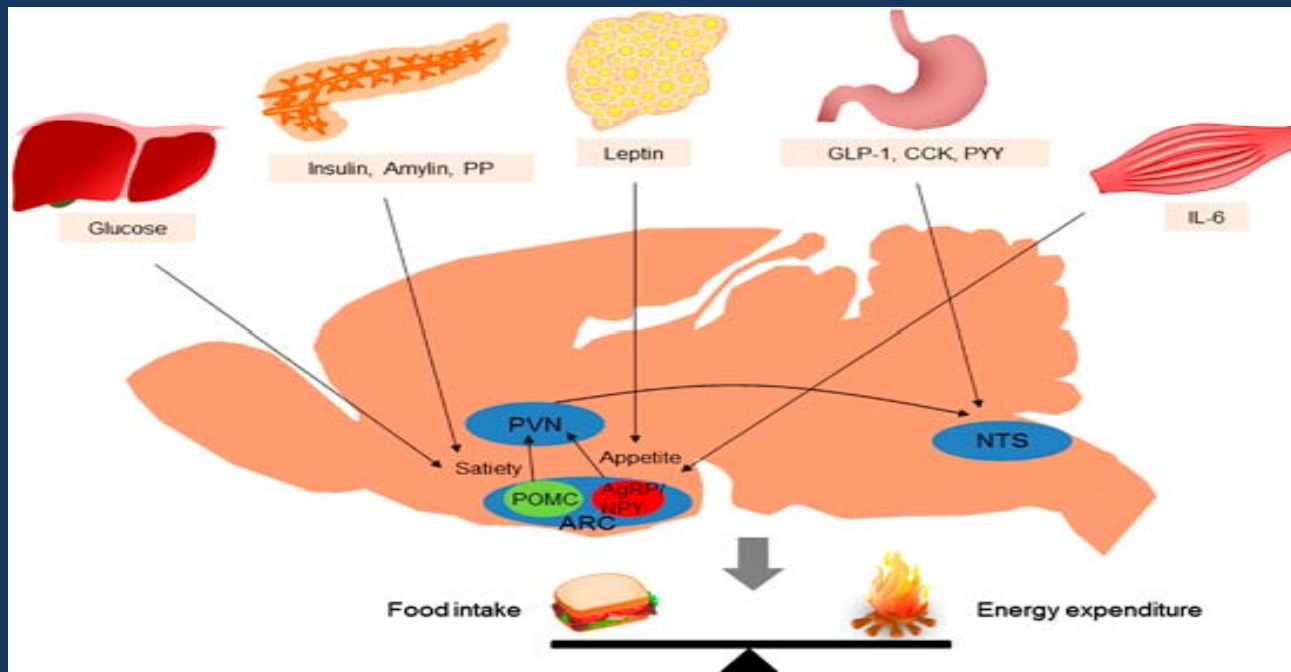
Introduction

Pathogenesis of T2DM



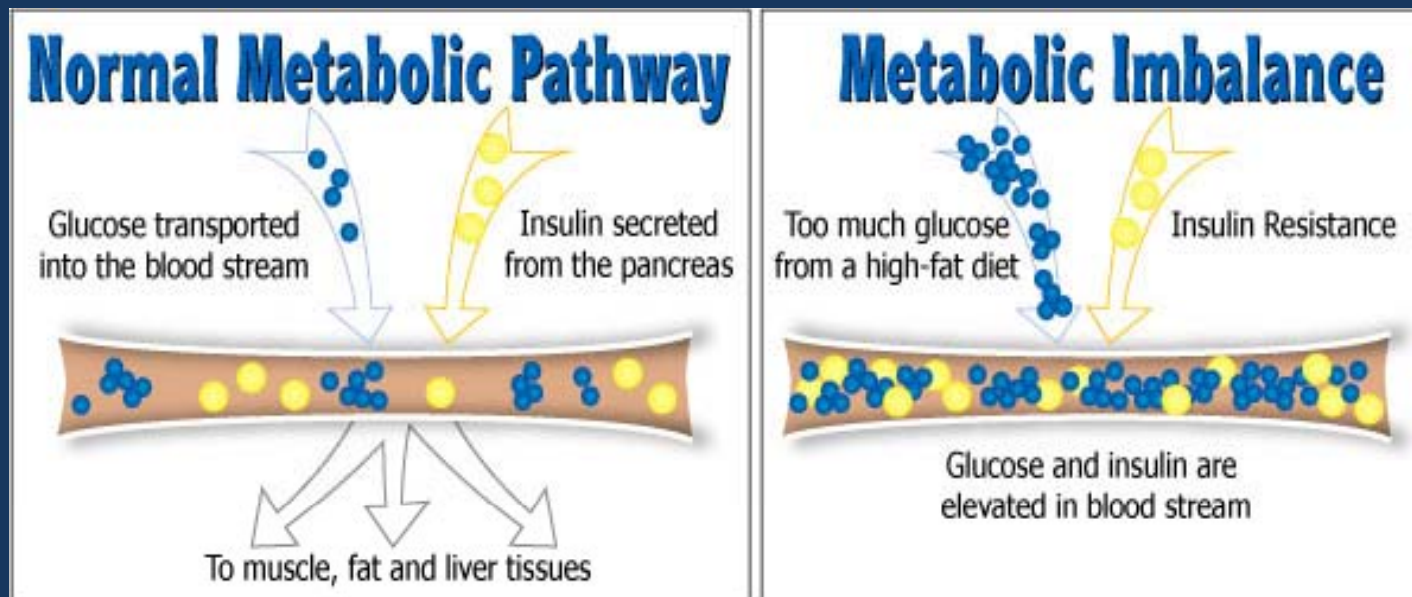
Metabolic homeostasis

- Peptides secreted from peripheral organs regulate metabolism in key insulin-target tissues and are important for energy homeostasis and maintaining insulin sensitivity



Metabolic homeostasis in pathogenesis of T2DM

- Role of molecules involved in regulation of metabolic homeostasis and complicated interactions between its components in pathogenesis of T2DM.



Adropin

**A metabolic homeostasis-related protein
(novel secreted peptide)**

**liver / brain
Peripheral tissues**

**Energy Homeostasis
Associated gene (Enho)**

Adropin



**Regulation of :
Carbohydrate and lipid metabolisms**



To prevent:

- ✓ **Insulin resistance**
- ✓ **Dyslipidemia**
- ✓ **Impaired glucose tolerance**

Methods

Study Population

Blood Sampling

Serum Separation

ELISA

Patient selection

40(men)/ 40-65 years
T2DM , based on ADA criteria

- ✓ FBG \geq 126 mg/dL or
- ✓ OGTT \geq 200 mg/dL or
- ✓ Random blood glucose \geq 200 mg/dL or
- ✓ HbA1c $>$ 6.5%

Healthy subjects

40 Men with 40-65 years

Exclusion criteria

- ✓ Chronic liver and renal disease
- ✓ History of inflammatory
- ✓ Infectious
- ✓ Malignant diseases

Laboratory & anthropometric data recorded

- Age
- Height
- Weight
- BMI
- Consumed drugs
- FBS
- Lipid profile(TG,TC,LDL-c,HDL-c)
- HbA1c
- HOMA-IR
- Adropin Elisa

Results

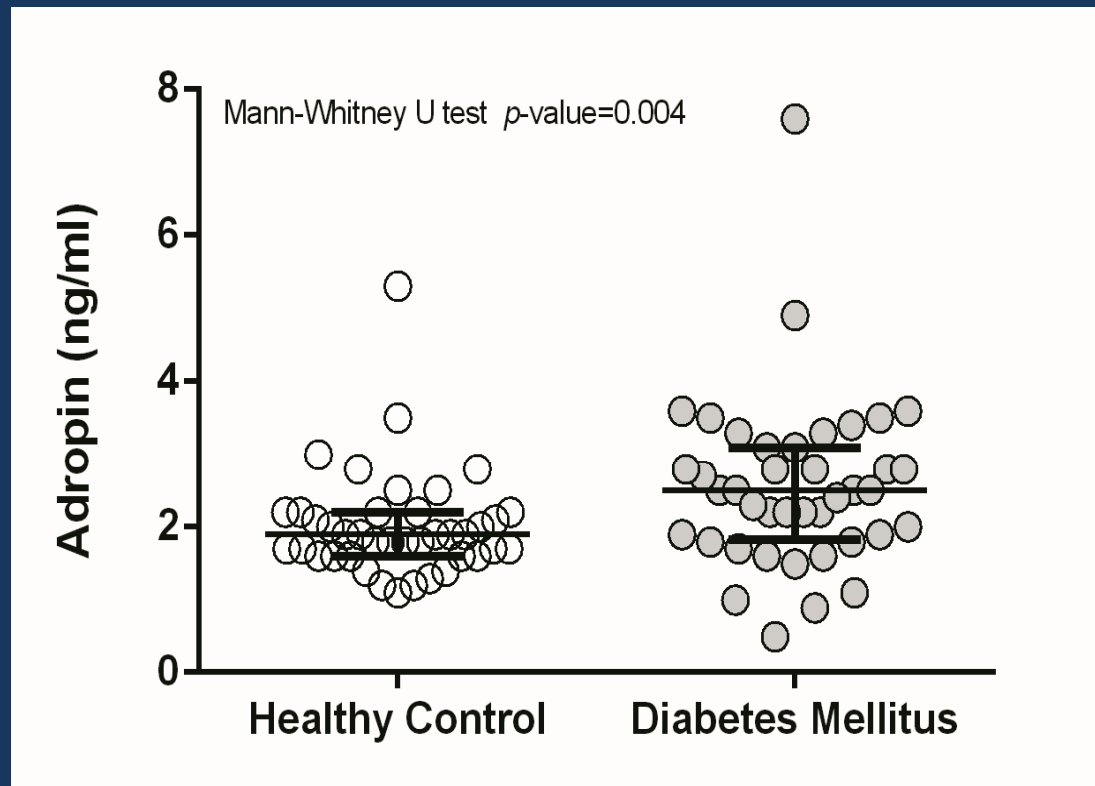
Demographic and Clinical Characteristics of T2DM patients and controls

Characteristics	Healthy Controls	T2DM	p-value
Age (yr)	58.88 ± 7.31	61.25 ± 6.94	0.140
BMI (kg/m ²)	23.21 ± 0.58	25.62 ± 3.68	<0.001
BMI ≥ 25 kg/m ²	0 (0%)	16 (40%)	<0.001
WC (cm)	85.12 ± 2.43	89.23 ± 3.31	<0.001
HC (cm)	93.41 ± 1.05	92.69 ± 0.94	0.002
WHR	0.91 ± 0.03	0.96 ± 0.04	<0.001
CFA (%)	27 (67.5%)	38 (95%)	0.002
FBG (mg/dl)	80 (72-87)	108 (87-132)	<0.001
Insulin (mU/l)	9.35 (7.7-14)	14.75 (12-22)	<0.001
HOMA-IR	1.81 (1.41-2.63)	4.57 (3.53-7.28)	<0.001
HbA1c (%)	4.88 ± 0.85	8.17 ± 1.79	<0.001
HDL-c (mg/dl)	44 (38-49)	31 (25-36)	<0.001
LDL-c (mg/dl)	102 (88-112)	70 (49- 98)	<0.001
TG (mg/dl)	144 (101-175)	150 (105- 188)	0.567
TC (mg/dl)	135 (114-151)	136 (105-160)	0.725

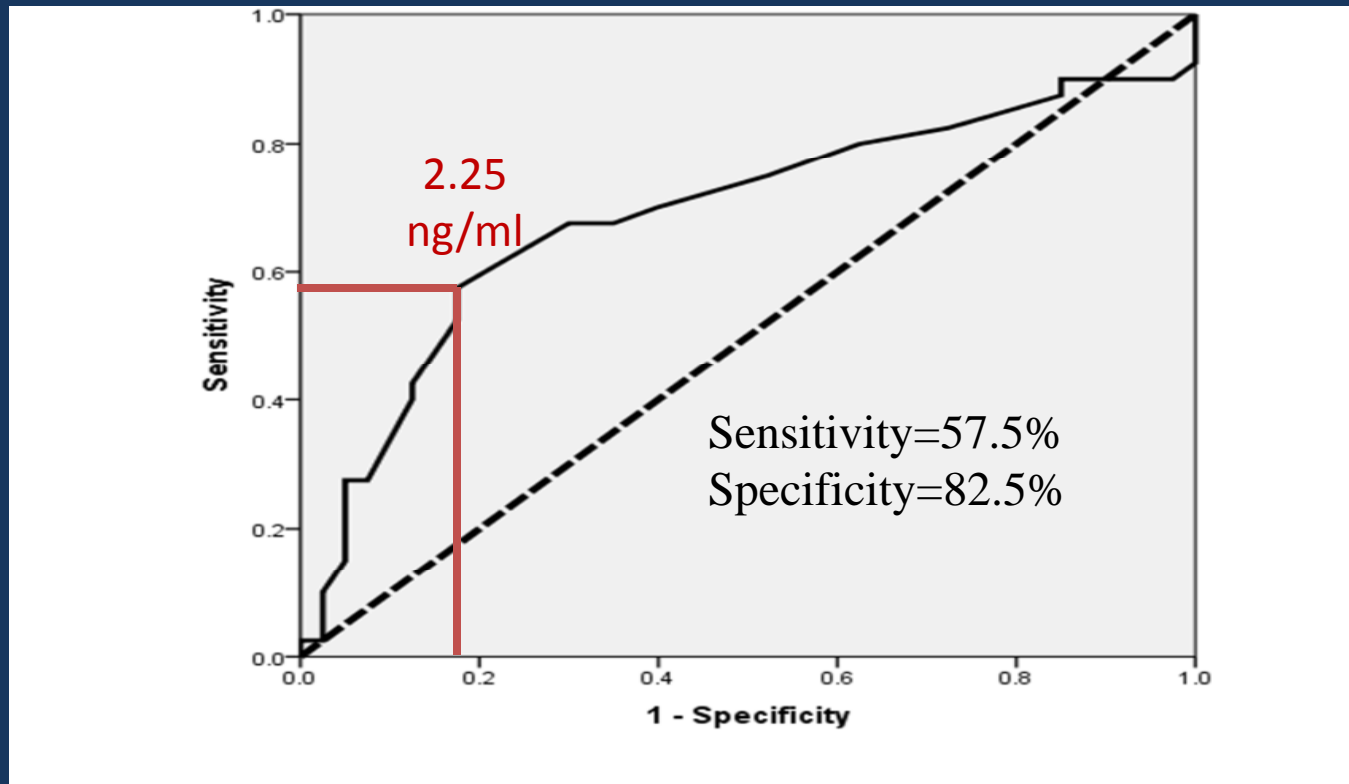
Continuous variables are described as mean ± SD for normally distributed data, but non-parametric variables are presented as median (interquartile range: P25-P75). Categorical variables are described as frequencies. Differences between cases and controls are obtained based on Student's t-test or Mann-Whitney U test, where indicated for continuous variables. Chi-square test was performed for categorical variables.

BMI, Body Mass Index; WC, Waist Circumference; HC, Hip Circumference; WHR, waist to hip ratio; CFA (central fat accumulation) was defined as WHR ratio ≥ 0.9
 FBG, Fasting Blood Glucose; HbA1c, Glycated Hemoglobin;
 LDL-c, Low Density Lipoprotein Cholesterol; HDL-c, High Density Lipoprotein Cholesterol;
 TG, Triglyceride; TC, Total Cholesterol; T2DM, Type 2 Diabetes Mellitus
 HOMA-IR, Homeostatic Model Assessment of Insulin Resistance

Adropin Levels



Receiver operating characteristic (ROC) curve

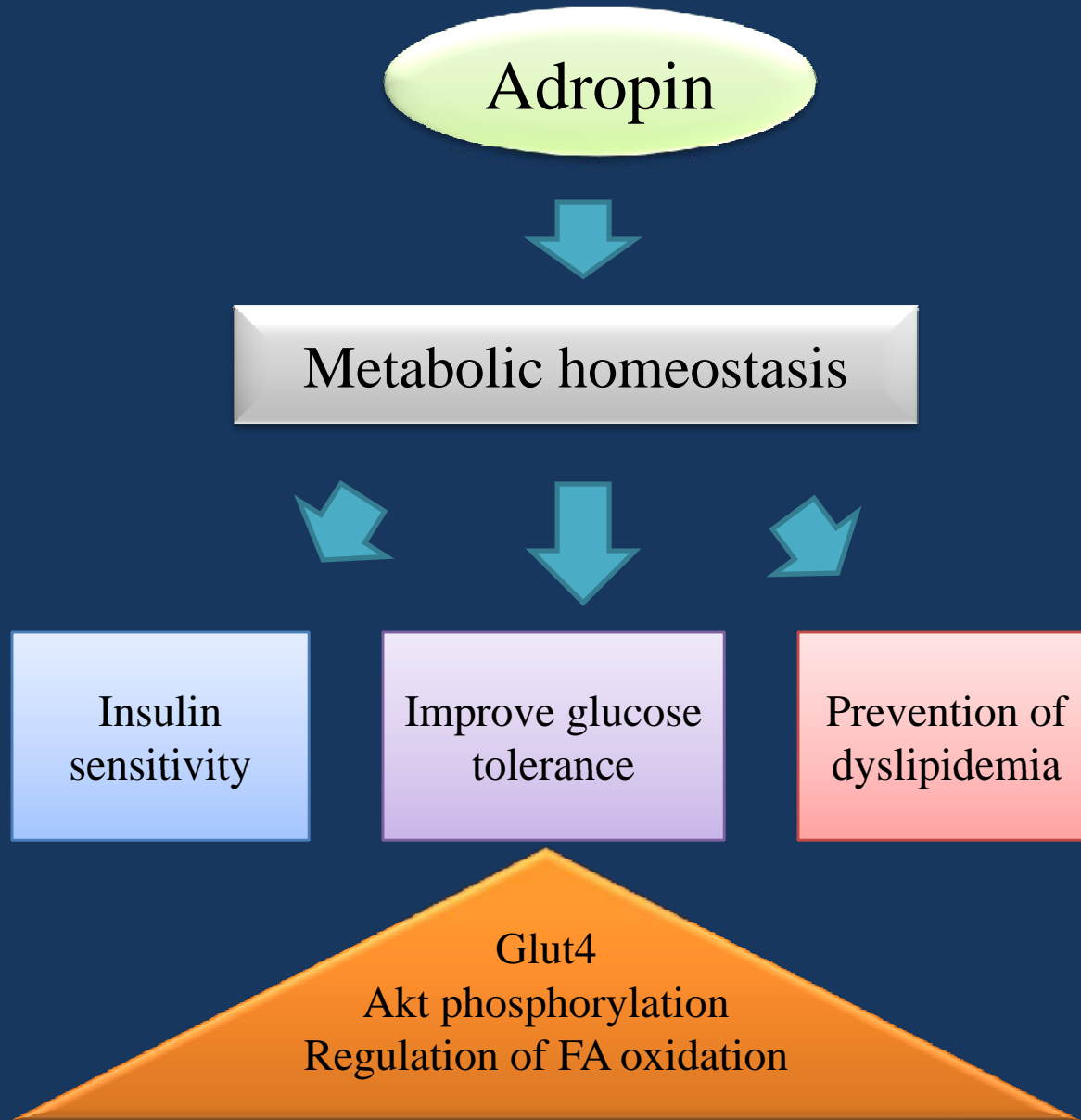


Correlations

- Adropin levels were inversely correlated with FBG (Spearman's rho= -0.335; p=0.017).
- Adropin levels were inversely correlated with HOMA-IR (Spearman's rho= -0.391, p=0.024).

Discussion

Animal & human studies....



Animal & human studies....

- Adropin deficient mice have increased body weight due exclusively to increased fat mass (Kumar et al,2012).
- Reversal of obesity and metabolic syndrome after Roux-en-Y gastric bypass leads to increased adropin levels (Butler et al,2012)

T2DM patients with normal weights produce more adropin

Conclusion

- These data show that T2DM patients have higher adropin levels, which seem to be a feedback response to high glucose levels.
- To assess adropin therapeutic roles in T2DM patients

Thank you for your attention

Logistic Regression

Characteristics	B	SE	Wald	p-value	OR	95% CI for OR	
						Lower	Upper
Univariate Model							
Adropin \geq 2.25 ng/ml	1.853	0.525	12.463	< 0.001	6.378	2.280	17.842
Adjustment for FBG							
Adropin \geq 2.25 ng/ml	1.867	0.628	8.824	0.003	6.467	1.887	22.164
FBG	0.073	0.021	11.805	0.001	1.076	1.032	1.122
Adjustment for LDL-c							
Adropin \geq 2.25 ng/ml	1.658	0.615	7.265	0.007	5.248	1.572	17.519
LDL-c	-0.056	0.014	15.091	< 0.001	0.946	0.919	0.973
Adjustment for HbA1c							
Adropin \geq 2.25 ng/ml	2.247	0.986	5.192	0.023	9.462	1.369	65.382
HbA1c	2.493	0.734	11.537	0.001	12.097	2.870	50.980
Adjustment for HOMA-IR							
Adropin \geq 2.25 ng/ml	2.961	1.231	5.787	0.016	19.311	1.731	215.494
HOMA-IR	1.940	0.646	9.019	0.003	6.961	1.962	24.698

FBG, Fasting Blood Glucose; LDL-c, Low Density Lipoprotein Cholesterol;
HbA1c, Glycated Hemoglobin;
HOMA-IR, Homeostatic Model Assessment of Insulin Resistance

Discussion

- Serum and urine adropin levels are significantly higher in diabetic patients compared to healthy controls (Ugur *et al*).
- Administration of recombinant adropin has been demonstrated to reverse insulin resistance and dyslipidemia in mice (Kumar *et al*).
- Adropin treatment of diet-induced diabetic mice enhances glucose tolerance, improves insulin resistance (Gao *et al*).

System Integration and Homeostasis

- Metabolic homeostasis are the integration of metabolism at the cellular and the organ tissue levels
- These processes of integration are essential for the survival of the entire organism which receives its direction from body system

- The term “adropin” was coined by merging the first three letters of two Latin words: adura, which means “to set fire to”, and pinquis, which means “fats or oils”. Adropin is coded by the Energy Homeostasis Associated genes, and is symbolized as “encho” [74]. This abbreviation will be used throughout this review to refer to the Energy Homeostasis Associated gene. Adropin contains 76 amino acids and has a molecular weight of 4499.9 Da. Human, mouse, and rat adropin amino acid sequences are 100% identical. Fig. 1 presents the amino acid sequencing of adropin. The half-life of adropin has not been identified yet. However, it is assumed that the half-life of this peptide hormone is as short as several minutes, because the half-lives of peptide hormones range between 3 and 30 min. The normal adropin concentration in the blood varies between 3.1 ± 1.3 ng/mL [32], 3.4–4.5 ng/mL [28] and around 10 ng/mL [11]. The normal adropin concentration in human milk varies from approximately 9–14.5 ng/mL [11]. Urine adropin levels were found to be approximately 4 times higher than that of corresponding serum adropin concentrations