



# The 9th International Electronic Conference on Medicinal Chemistry (ECMC 2023)

01–30 November 2023 | Online

## The importance of selected adipokines in the diagnosis of neuroendocrine neoplasms of various locations

Chaired by **Dr. Alfredo Berzal-Herranz**  
and **Prof. Dr. Maria Emília Sousa**



*pharmaceuticals*



**Marlena Budek <sup>1,\*</sup>, Jarosław Nuskiewicz <sup>1</sup>, Jolanta Czuzejko <sup>2,3</sup>, Marcin Gackowski <sup>4</sup>, Magdalena Zdral <sup>5</sup>  
and Karolina Szewczyk-Golec <sup>1</sup>**

<sup>1</sup>Department of Medical Biology and Biochemistry, Faculty of Medicine, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, 24 Karłowicza St, 85-092 Bydgoszcz, Poland;

<sup>2</sup>Department of Psychiatry, Faculty of Medicine, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, 9 M. Curie Skłodowskiej St, 85-094 Bydgoszcz, Poland;

<sup>3</sup>Department of Nuclear Medicine, Oncology Centre prof. Franciszek Łukaszyk Memorial Hospital, Bydgoszcz, 2 dr I. Romanowskiej St, 85-796 Bydgoszcz, Poland.

<sup>4</sup>Department of Toxicology and Bromatology, Faculty of Pharmacy, L. Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Torun, A. Jurasza 2 Street, PL–85089 Bydgoszcz, Poland

<sup>5</sup>Independent Public Specialized Health Care Center in Lębork, Węgrzynowicza 13 St, 84-300 Lębork, Poland

\* Corresponding author: [mmarkiewicz@doktorant.umk.pl](mailto:mmarkiewicz@doktorant.umk.pl)

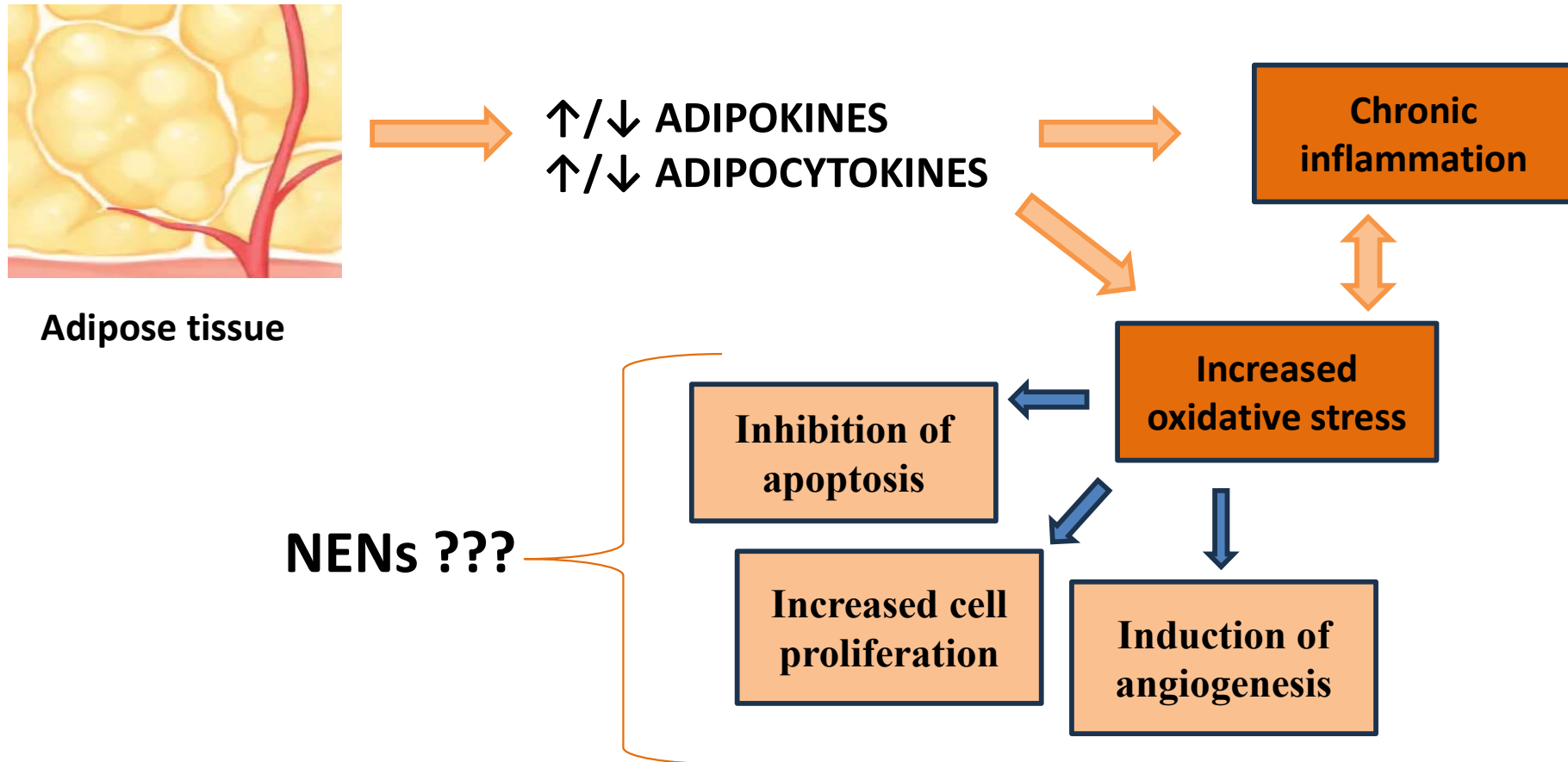


UNIWERSYTET  
MIKOŁAJA KOPERNIKA  
W TORUNIU

Wydział Lekarski  
Collegium Medicum w Bydgoszczy



## The importance of selected adipokines in the diagnosis of neuroendocrine neoplasms of various locations





## **Abstract:**

Adipose tissue performs important endocrine functions. In the case of obesity, which is associated with chronic inflammation, the balance in the release of adipokines is disturbed. Metabolic disorders of adipose tissue may contribute to the development and progression of cancer, including neuro-endocrine neoplasms (NENs).

The aim of this study was to determine the concentration of leptin, omentin-1, visfatin and resistin in healthy people and in patients with NENs of the gastrointestinal tract, pancreas and lung.

The study included 68 patients of the Prof. F. Łukaszczyk Oncology Center in Bydgoszcz with NENs of the gastrointestinal tract (GT, n=34), NENs of pancreas (PA, n=22), NENs of lungs (L, n=12) and in the control group (CTRL, n=35). The concentration of the adipokines was measured by the enzyme immunoassay method using ready-made ELISA kits and Bio-Plex Pro Human Diabetes. A statistical analysis was performed and  $P < 0.05$  was considered as statistically significant.

The results were presented as the mean value and the standard error of the mean. There were statistically significant changes in the levels of visfatin and resistin in patients with NENs compared to CTRL, but no statistically significant difference was found in the concentration of leptin, an adipokine responsible for regulating the body's energy storage. The concentrations of the measured adipokines were similar in the analyzed subgroups of NENs. However, a statistically significant increase in omentin-1 concentration was observed in patients with NENs, the only tested adipokine with anti-inflammatory activity, which may have a prognostic significance.

**Keywords:** adipokines, adipose tissue, neuroendocrine neoplasms



## Introduction

- Neuroendocrine tumors are rare tumors that can release biogenic amines and hormones (hormonally active tumors).
- Currently, the incidence rate of NENs is 3-5/100,000/year with an increasing tendency over the past years.
- The most common are gastroenteropancreatic NENs: GEP-NENs (64-70%) and lung: L-NENs (20-30%).
- General markers used for screening diagnosis of NENs without characteristic symptoms of hormone overproduction are chromogranin A (CgA), neuron-specific enolase (NSE), pancreatic polypeptide (PP) and subunits glycoprotein hormones.
- Functional NENs, which constitute a minority, are characterized by the release of hormones and biologically active substances that are responsible for a specific clinical manifestation of the tumor (for example insulin, glucagon, somatostatin or gastrin).
- White adipose tissue (WAT) is metabolically dynamic and releases many bioactive peptides that regulate metabolic homeostasis.
- Adipokines perform pleiotropic functions in the body, eg. they influence energy balance and immune response, cause insulin resistance but also participate in the process of carcinogenesis. However, their impact on the development of NENs is not fully known.



## Material and methods

- The study group consisted of 68 patients with NENs (gastrointestinal: GT, n=34; pancreatic: PA, n=22; lung: L, n=12) and control group (CTRL, n=35).
- Blood serum samples were obtained after collecting venous blood specimens.
- The concentration of the inflammatory markers was measured with the use of the ready-made Multi-Plex Immunoassay System.
- The results were presented as means and the standard error of the mean (SEM).
- $p < 0.05$  was considered as statistically significant.



## Results and discussion

	CTRL	GT-NENs	PA-NENs	L-NENs	p		
					CTRL vs GT-NENs	CTRL vs PA-NENs	CTRL vs L-NENs
N	35	34	22	12			
Age [years]	52.60±1.83	58.78±1.96	60.38±1.43	60.55±2.19	<b>0.004</b>	<b>0.002</b>	<b>0.025</b>
Body mass [kg]	61.11±1.29	74.38±2.59	82.82±2.24	86.92±2.88	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>
Height [cm]	165.63±1.23	169.62±1.41	169.50±1.48	168.83±1.63	<b>0.038</b>	0.092	0.309
BMI [kg/m <sup>2</sup> ]	22.23±0.31	25.69±0.69	28.75±0.59	30.50±0.89	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>

The results are presented as the mean value  $\pm$  SEM

BMI - body mass index; GT-NENs – gastrointestinal tract neuroendocrine neoplasms; L-NENs – lung neuroendocrine neoplasms; PA-NENs: pancreatic neuroendocrine neoplasms; p - statistical significance.





## Results and discussion

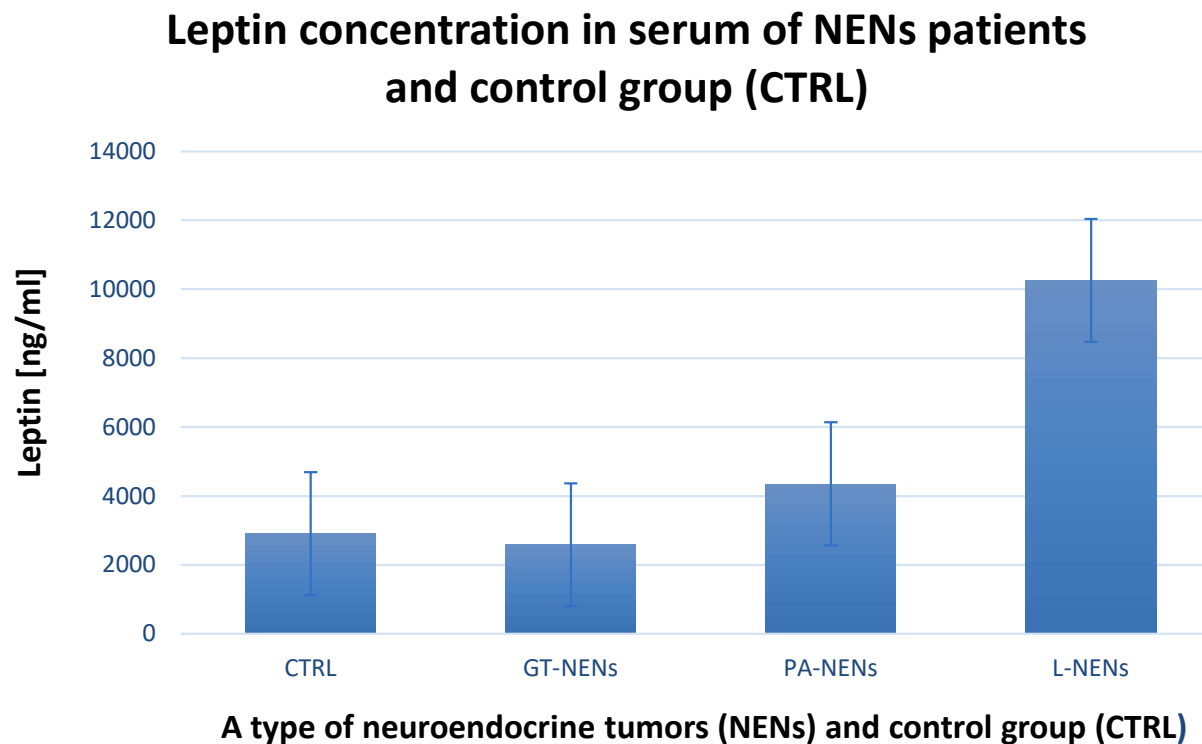
	CTRL	GT-NENs	PA-NENs	L-NENs	p		
N	35	34	22	12	CTRL vs GT-NENs	CTRL vs PA-NENs	CTRL vs L-NENs
Leptin [ng/ml]	2907± 341.64	2582.11± 429.42	4351.68± 731.51	10254.49± 2566.41	0.249	0.531	0.428
Resistin [ng/ml]	10530.31± 923.29	3486.96± 149.05	3946.51± 508.68	5277.22± 725.14	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>0.001</b>
Visfatin [ng/ml]	88.11± 44.01	280.44± 16.57	437.22± 82.13	500.07± 81.49	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>
Omentin-1 [ng/ml]	563.93± 32.75	781.28± 48.22	769.31± 48.22	755.66± 40.43	<b>0.001</b>	<b>0.008</b>	<b>0.023</b>

The results are presented as the mean value  $\pm$  SEM

GT-NENs – gastrointestinal tract neuroendocrine neoplasms; L-NENs – lung neuroendocrine neoplasms; PA-NENs: pancreatic neuroendocrine neoplasms; p - statistical significance.



## Results and discussion

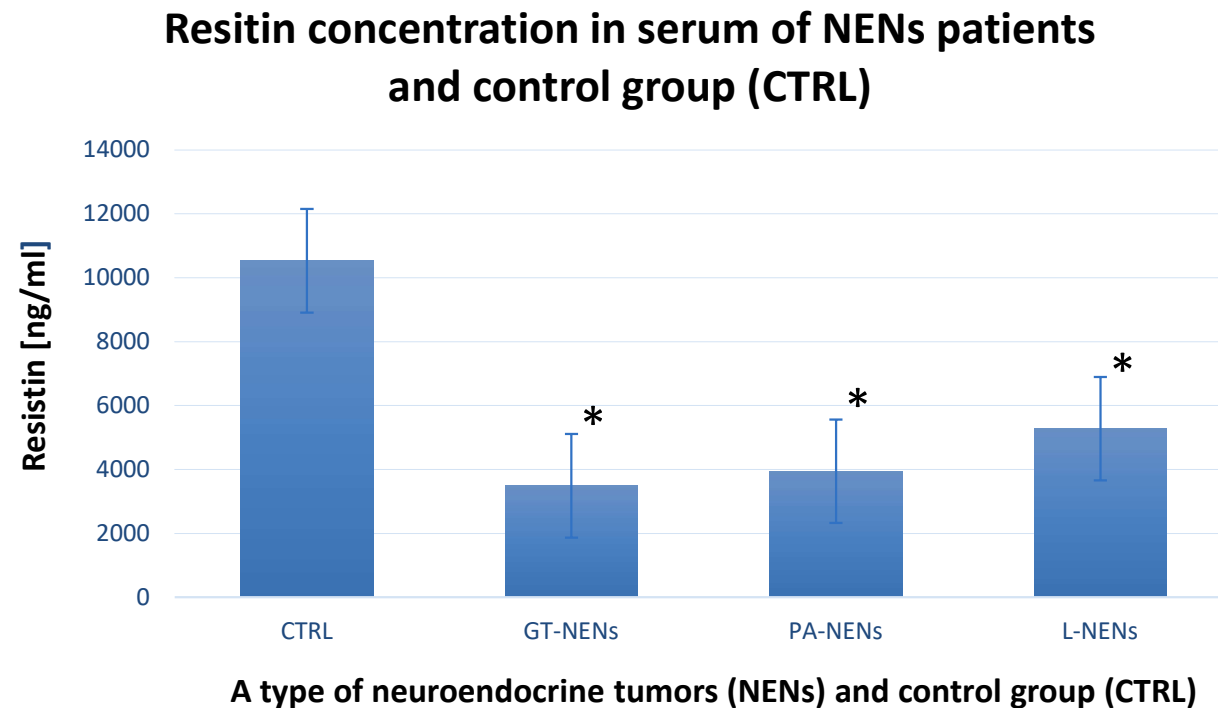


The results are presented as the mean value  $\pm$  SEM  
Not statistically significant difference





## Results and discussion



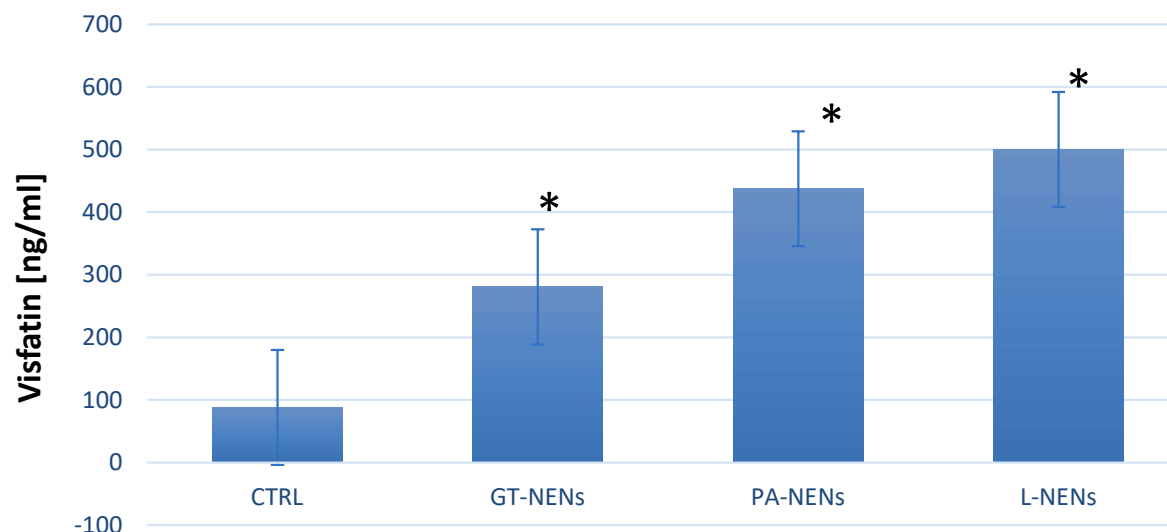
The results are presented as the mean value  $\pm$  SEM

\* Statistically significant difference  $p < 0.05$  vs. CTRL



## Results and discussion

**Visfatin concentration in serum of NENs patients  
and control group (CTRL)**



**A type of neuroendocrine tumors (NENs) and control group (CTRL)**

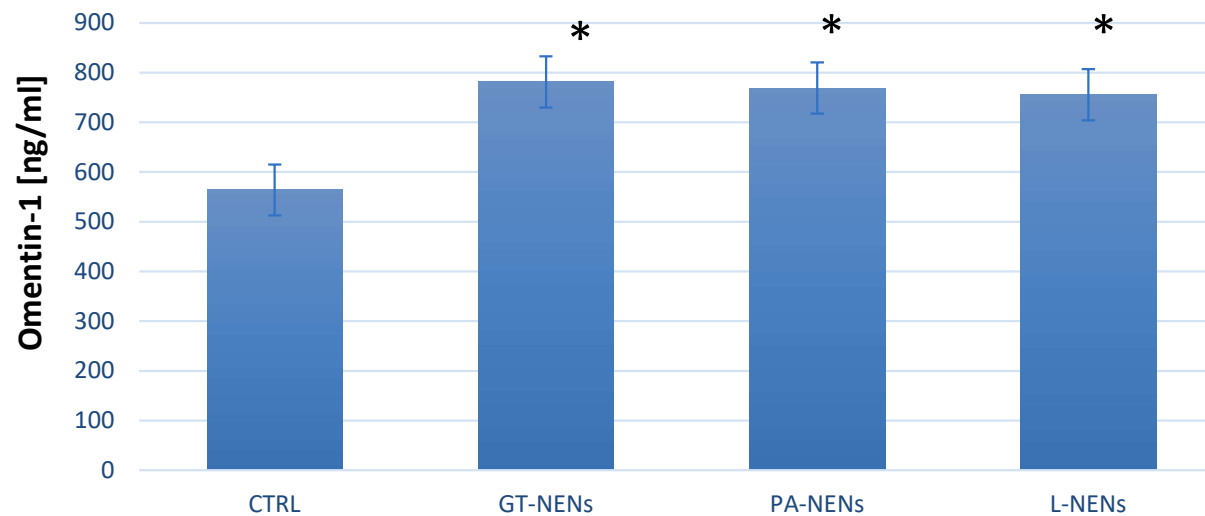
**The results are presented as the mean value  $\pm$  SEM**

**\* Statistically significant difference  $p < 0.05$  vs. CTRL**



## Results and discussion

Omentin-1 concentration in serum of NENs patients and control group (CTRL)



A type of neuroendocrine tumors (NENs) and control group (CTRL)

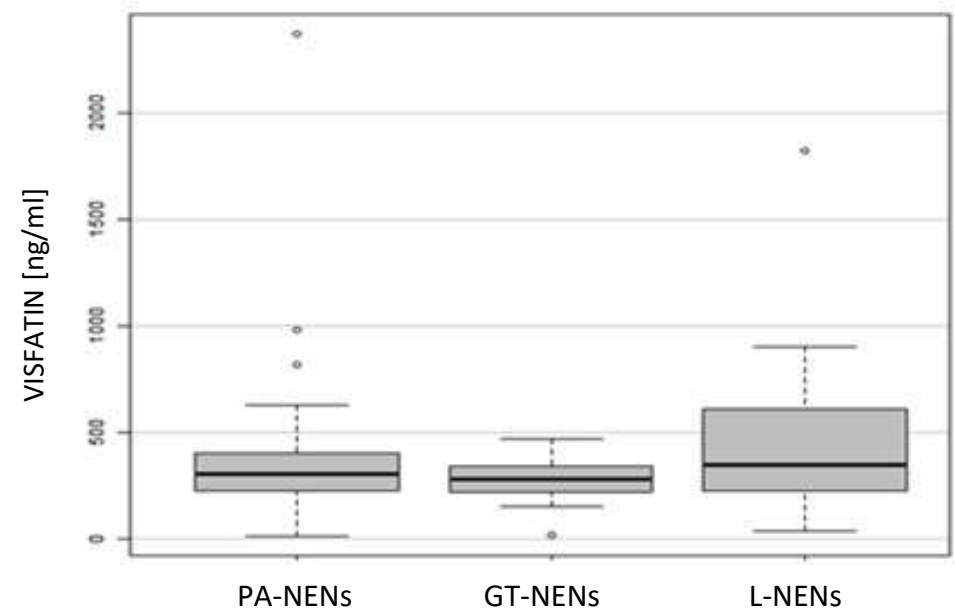
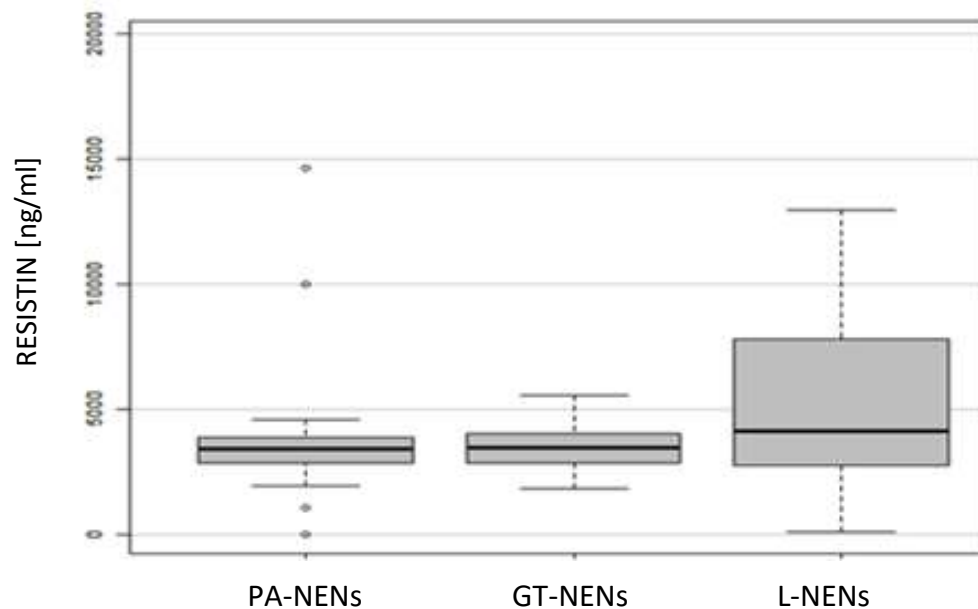
The results are presented as the mean value  $\pm$  SEM

\* Statistically significant difference  $p < 0.05$  vs. CTRL



## Results and discussion

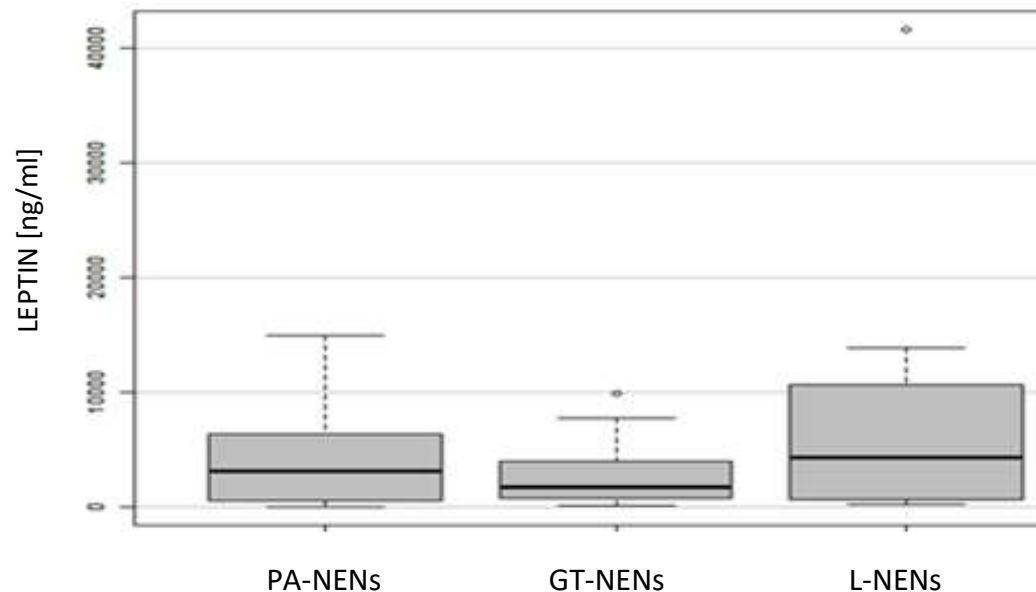
- The ANOVA analysis did not show statistically significant differences between the concentrations of resistin and visfatin in the patients with NENs of different locations.





## Results and discussion

- The ANOVA analysis did not show statistically significant differences between the concentrations of leptin in the patients with NENs of different locations.



- The ANOVA analysis did not show statistically significant differences between the concentrations of omentin-1 in the patients with NENs of different locations.



## Conclusions

- In the course of neuroendocrine tumors, there is a significant disruption of carbohydrate metabolism, as evidenced by a change in the profile of released adipokines, which was confirmed for patients with NENs in all tested locations.
- There was a statistically significant increase in visfatin, which has pro-inflammatory and procancerogenic effects (increased proliferation, angiogenesis, metastases, drug resistance). Due to the increase in the concentration of this adipokine in NENs compared to the control group, it may be a potential marker for predicting the risk of NENs.
- In this study, patients with NENs showed a statistically significant decrease in the concentration of resistin (a pro-inflammatory adipokine) in all patient groups compared to the control group, which does not coincide with its procarcinogenic function.
- A statistically significant increase in omentin-1 concentration was observed in patients with NENs compared to the control group, which may have prognostic significance.





## Bibliography

- Arrivi G, Fazio N. Gastroenteropancreatic Neuroendocrine Neoplasms (GEP NENs): The Role of Checkpoint Inhibitors. *Curr Cancer Drug Targets*. 2022 Aug 15;22(8):629-638. doi: 10.2174/1568009622666220114124335.
- Das S, Dasari A. Epidemiology, Incidence, and Prevalence of Neuroendocrine Neoplasms: Are There Global Differences? *Curr Oncol Rep*. 2021 Mar 14;23(4):43. doi: 10.1007/s11912-021-01029-7.
- Herman Mahečić D, Cigrovski Berković M, Zjačić-Rotkvić V, Čačev T, Kapitanović S, Ulamec M. Inflammation-related cytokines and their roles in gastroenteropancreatic neuroendocrine neoplasms. *Bosn J Basic Med Sci*. 2020 Nov 2;20(4):445-450. doi: 10.17305/bjbms.2020.4471.
- Booth A, Magnuson A, Fouts J, Foster M. Adipose tissue, obesity and adipokines: role in cancer promotion. *Horm Mol Biol Clin Investig*. 2015 Jan;21(1):57-74. doi: 10.1515/hmbci-2014-0037.



# The 9th International Electronic Conference on Medicinal Chemistry

01–30 November 2023 | Online



## Acknowledgments



**UNIWERSYTET  
MIKOŁAJA KOPERNIKA  
W TORUNIU**

Wydział Lekarski  
Collegium Medicum w Bydgoszczy