UNIVERSITY OF PÉCS

MEDICAL SCHOOL

Nephrology, diabetes and hypertension, with a focus on oxidative stress and modified amino acids

Dr. Gergő A. Molnár

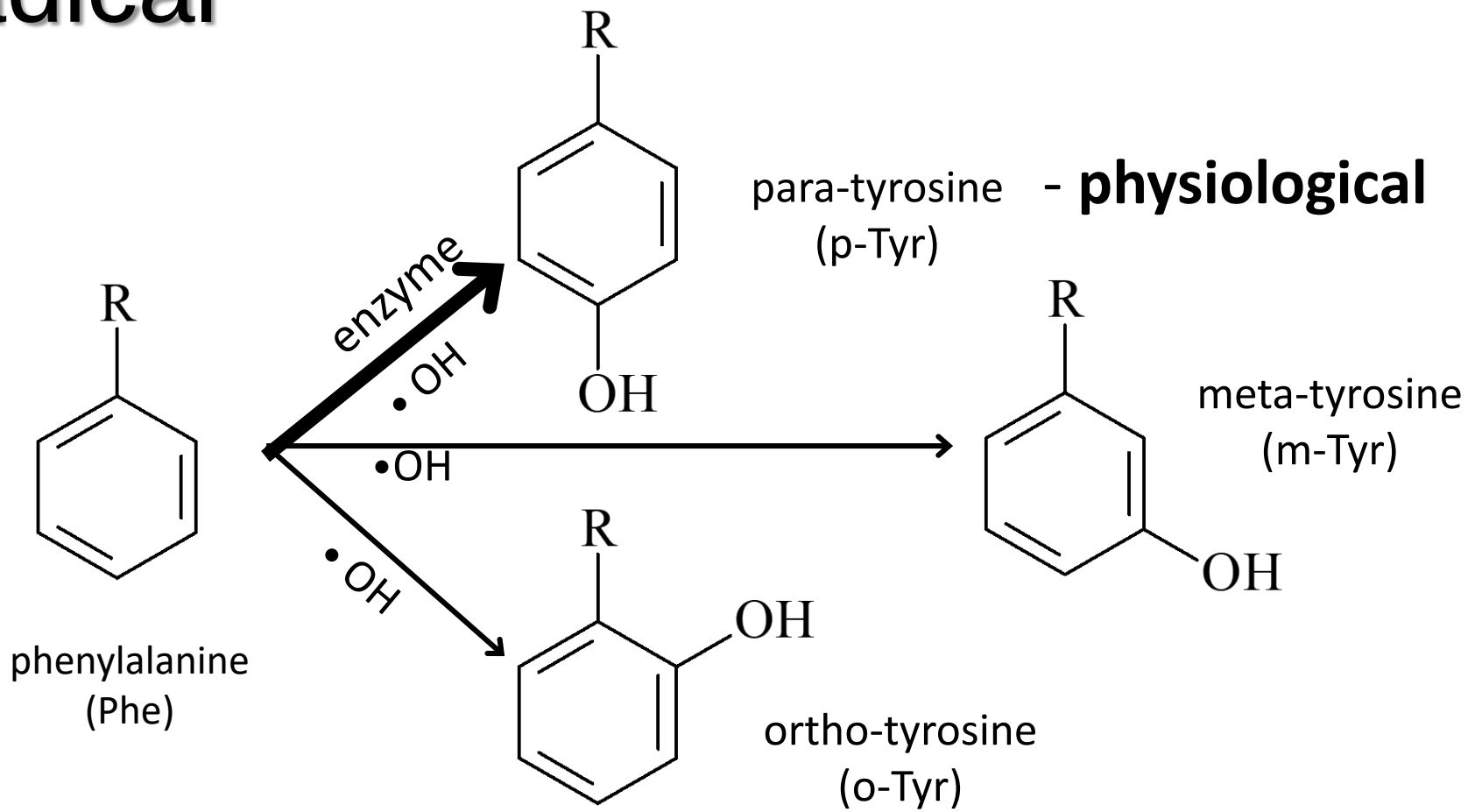
University of Pécs

Clinical Centre/Medical School

2nd Department of Medicine and

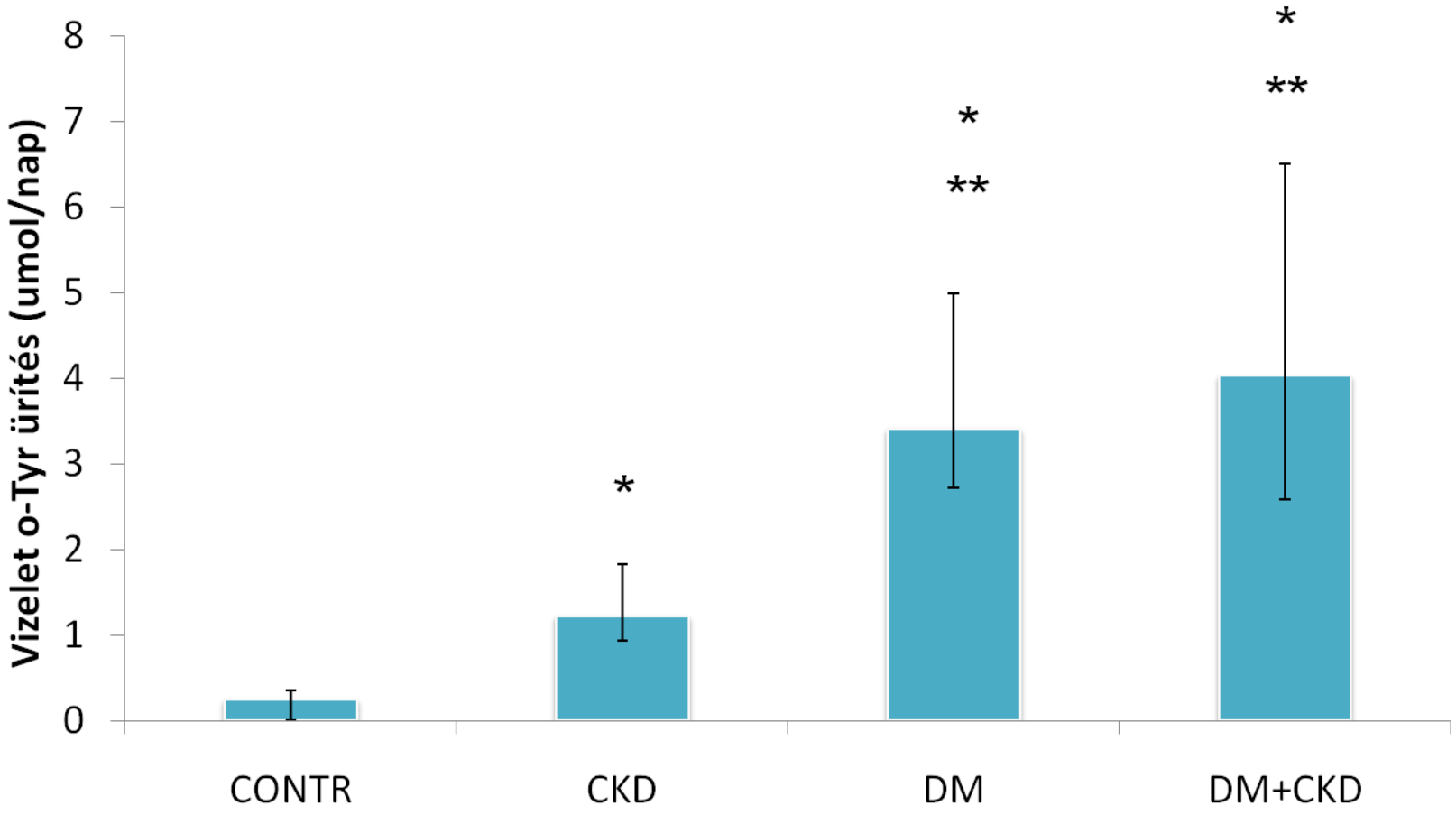
Nephrology, Diabetology Centre

Tyrosine isomers produced by hydroxyl free radical



R=$CH_2CH(NH_2)CO_2H$

The 24 h o-Tyr excretion in patients with CKD and/or T2DM

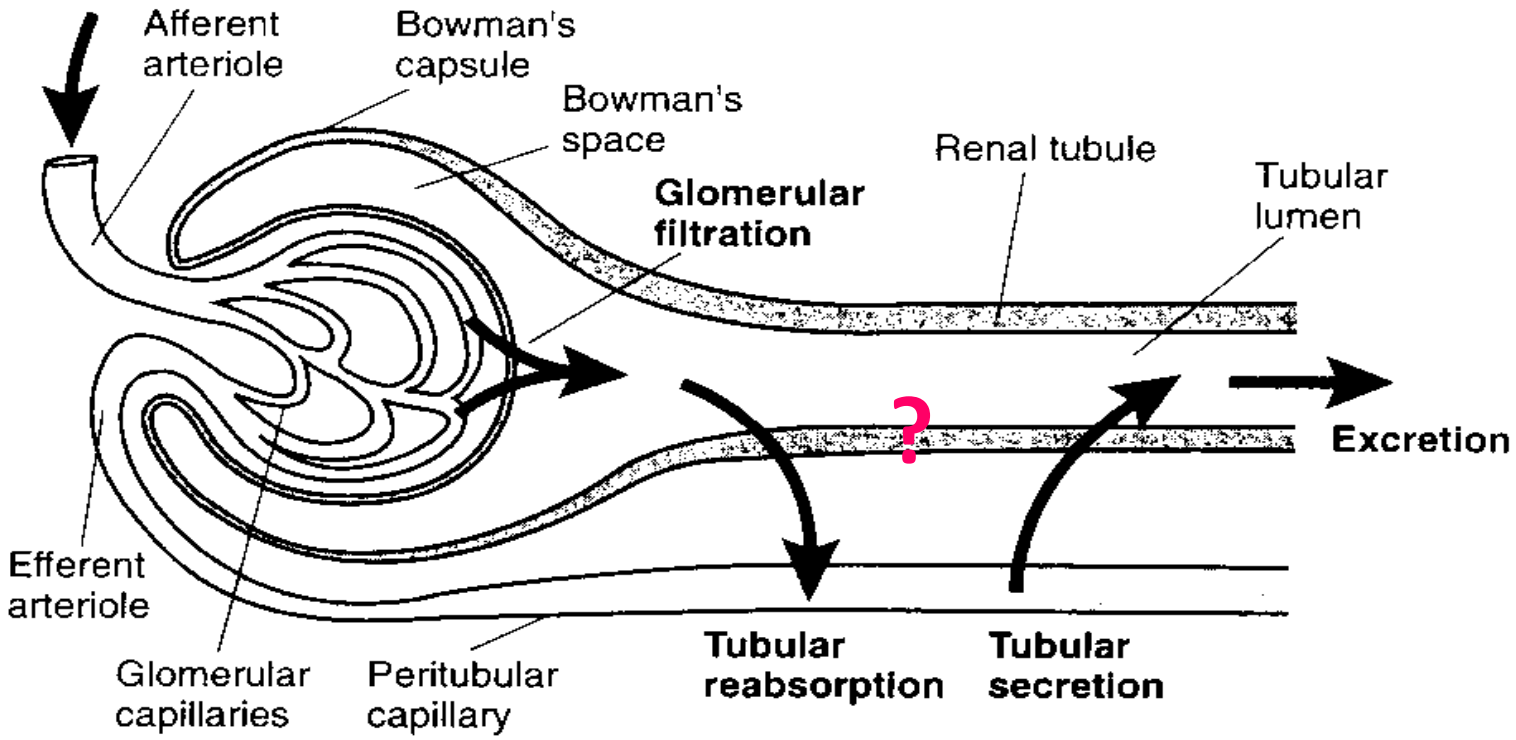


*: $p < 0.05$ vs. CONTR

**: $p<0.05$ vs. CKD

Molnár G. et al, Kidney International 68 (5):2281-2287 (2005)

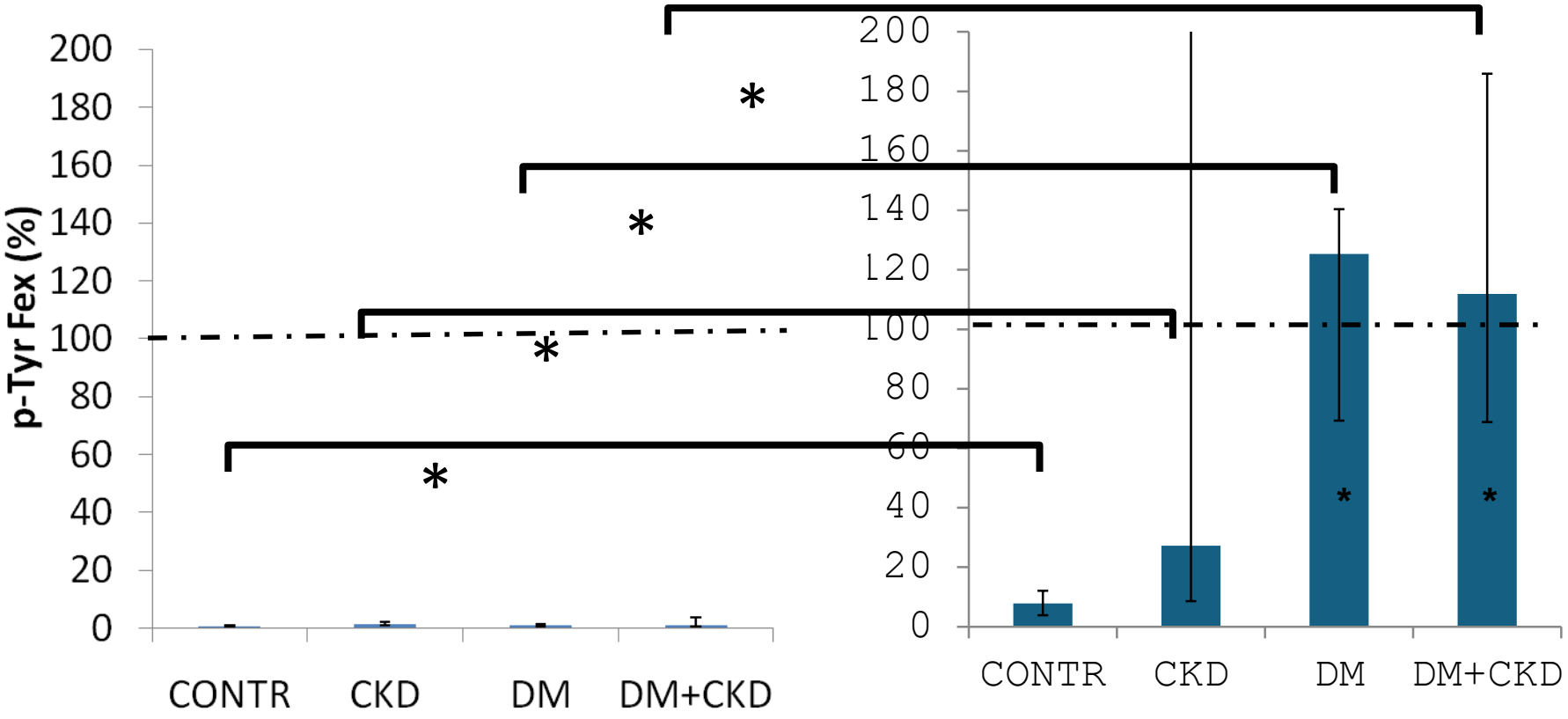
Fractional excretion (F_{ex})



$$Fex_{o-Tyr} = \frac{Clear_{o-Tyr}}{Clear_{Kreat}} = \frac{U_{o-Tyr} \times \cancel{V}}{P_{o-Tyr}} / \frac{U_{Kreat} \times \cancel{V}}{P_{Kreat}} = \frac{U_{o-Tyr} \times P_{Kreat}}{U_{Kreat} \times P_{o-Tyr}}$$

vs. 100 %

Fractional excretion of p-Tyr and o-Tyr



*: p <0.05 vs. p-Tyr

Molnár G. at al, Kidney International 68 (5):2281-2287 (2005)

Ph.D. theses (2007.)

- Pathogenesis of the chronic complications of type 2 diabetes mellitus, chronic kidney disease and ageing. The role of oxidative stress, endothelial dysfunction and the renin-angiotensin system.

Supervisor and tutor: Prof. Dr. István Wittmann

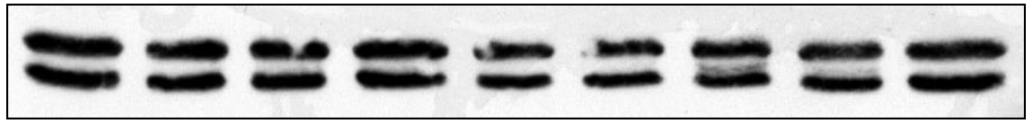
Corticosterone-induced Erk 1/2-phosphorylation in smooth muscle cells

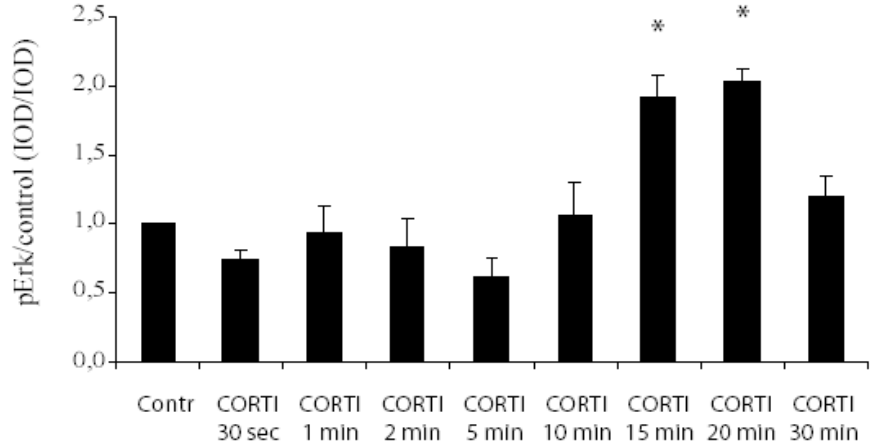
pErk 1/2

ContrCortiCortiCortiCortiCortiCortiCortiCorti

30 sec 1min 2 min 5 min 10 min 15 min 20 min 30 min

Erk 1/2

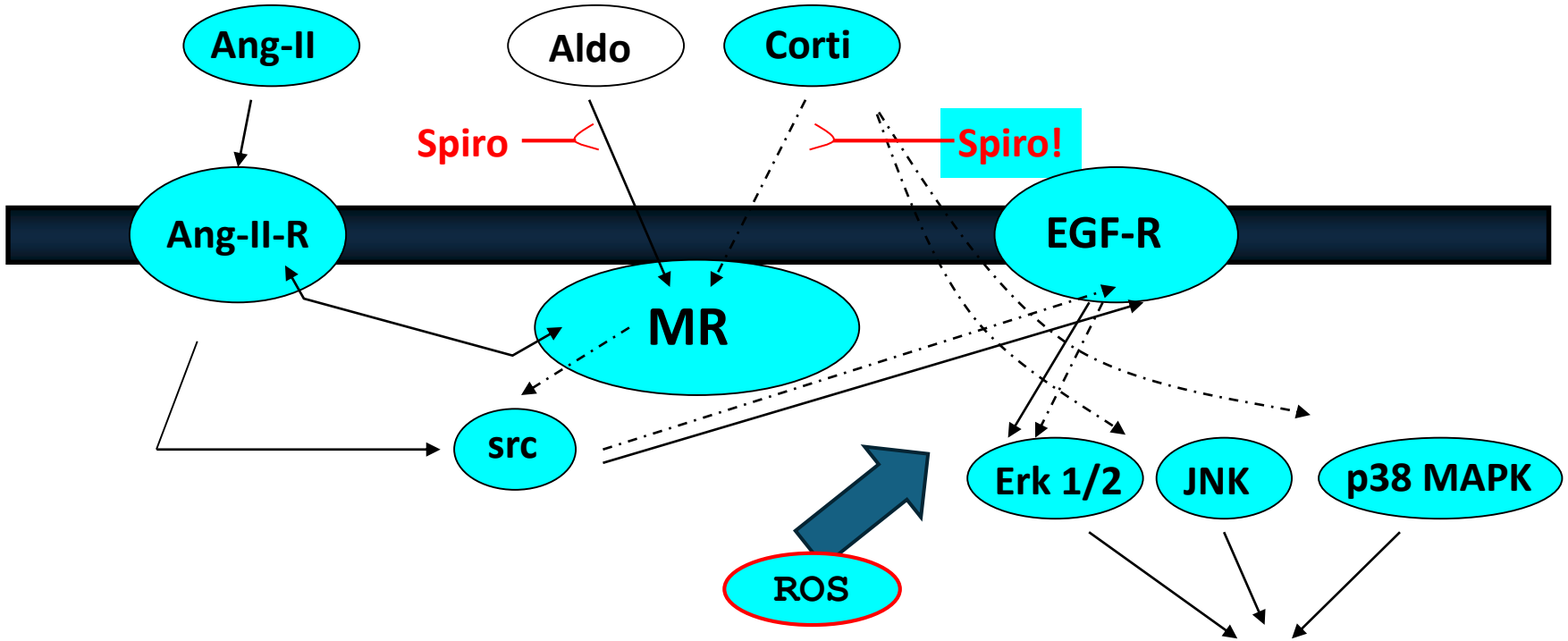




Corti: 10^{-6} M

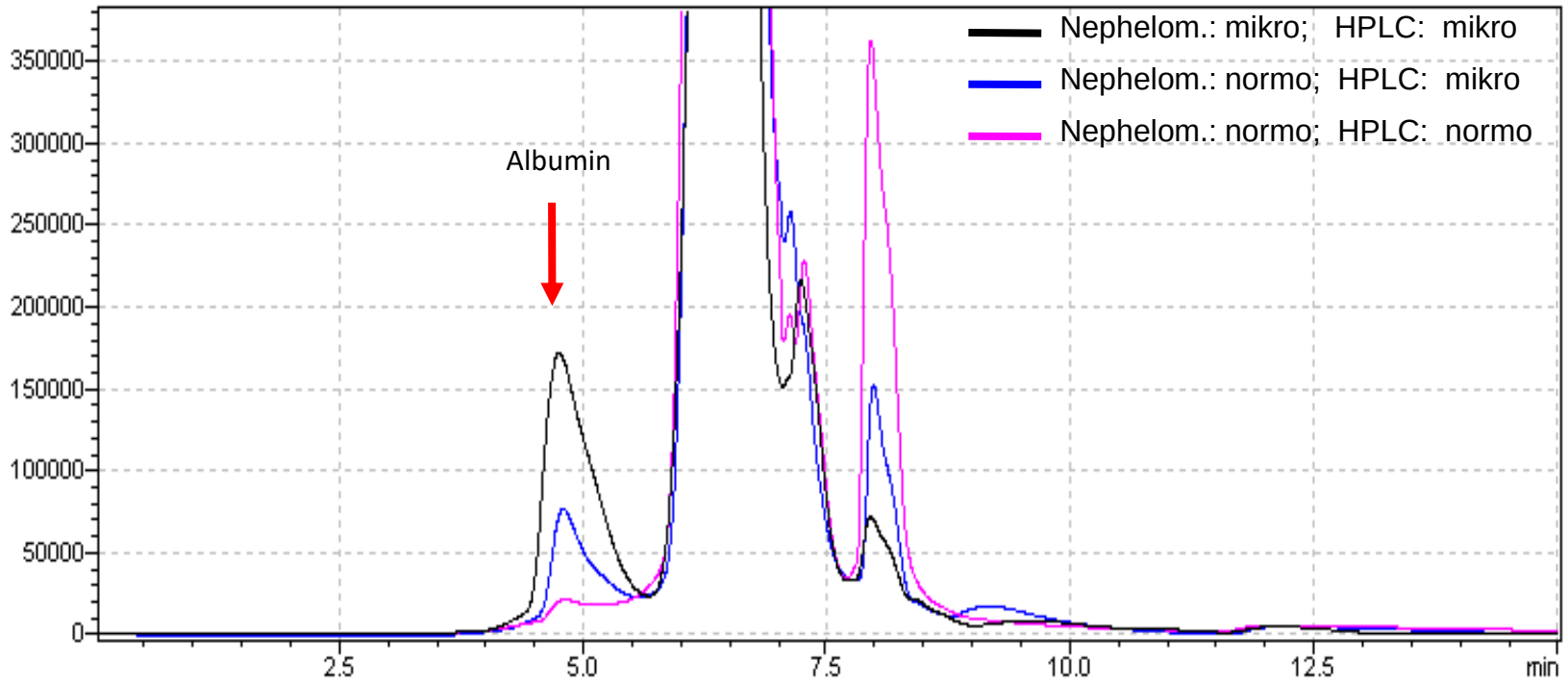
* p<0.05 vs. Contr

Molnár et al. Hypertension 51:1372-1378 (2008)



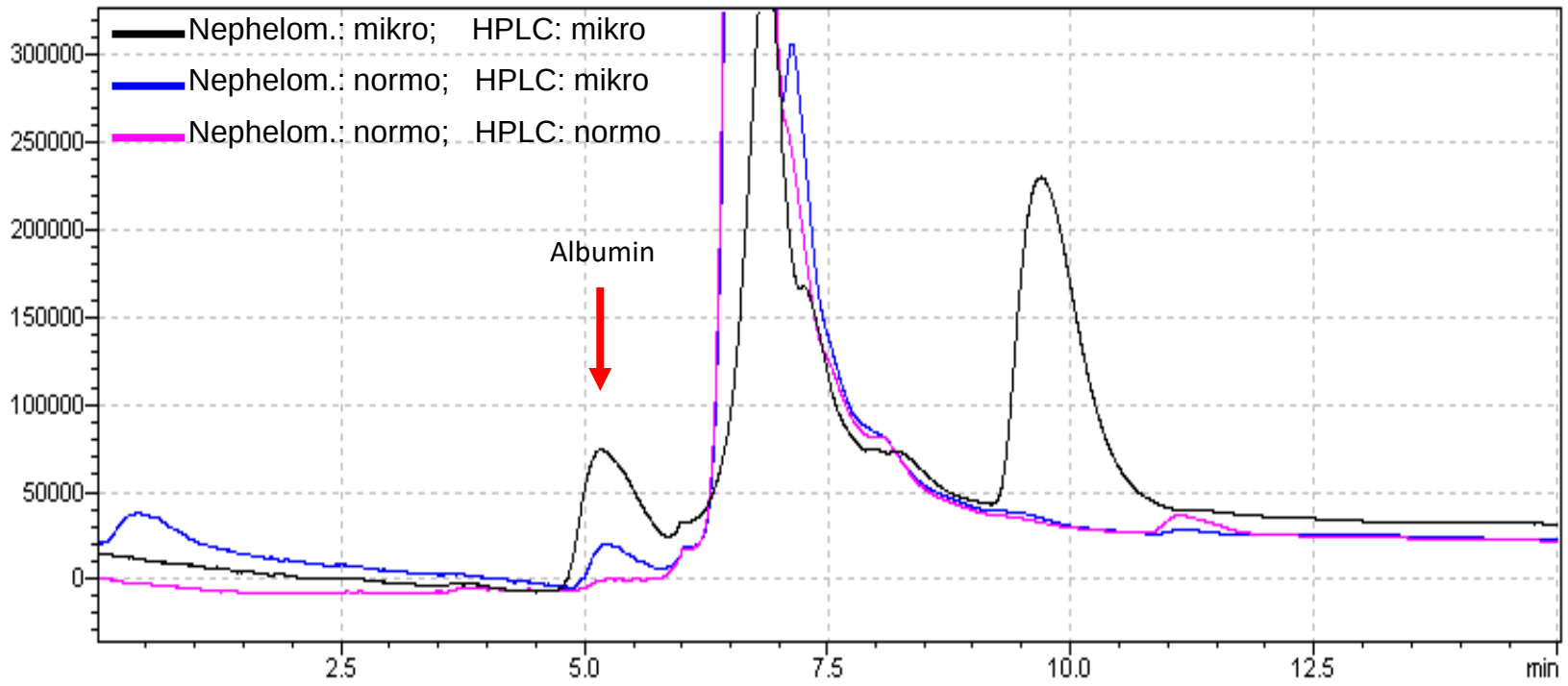
Molnár et al. Hypertension 51:1372-1378 (2008)

Detection of urinary albumin *via* UV-HPLC



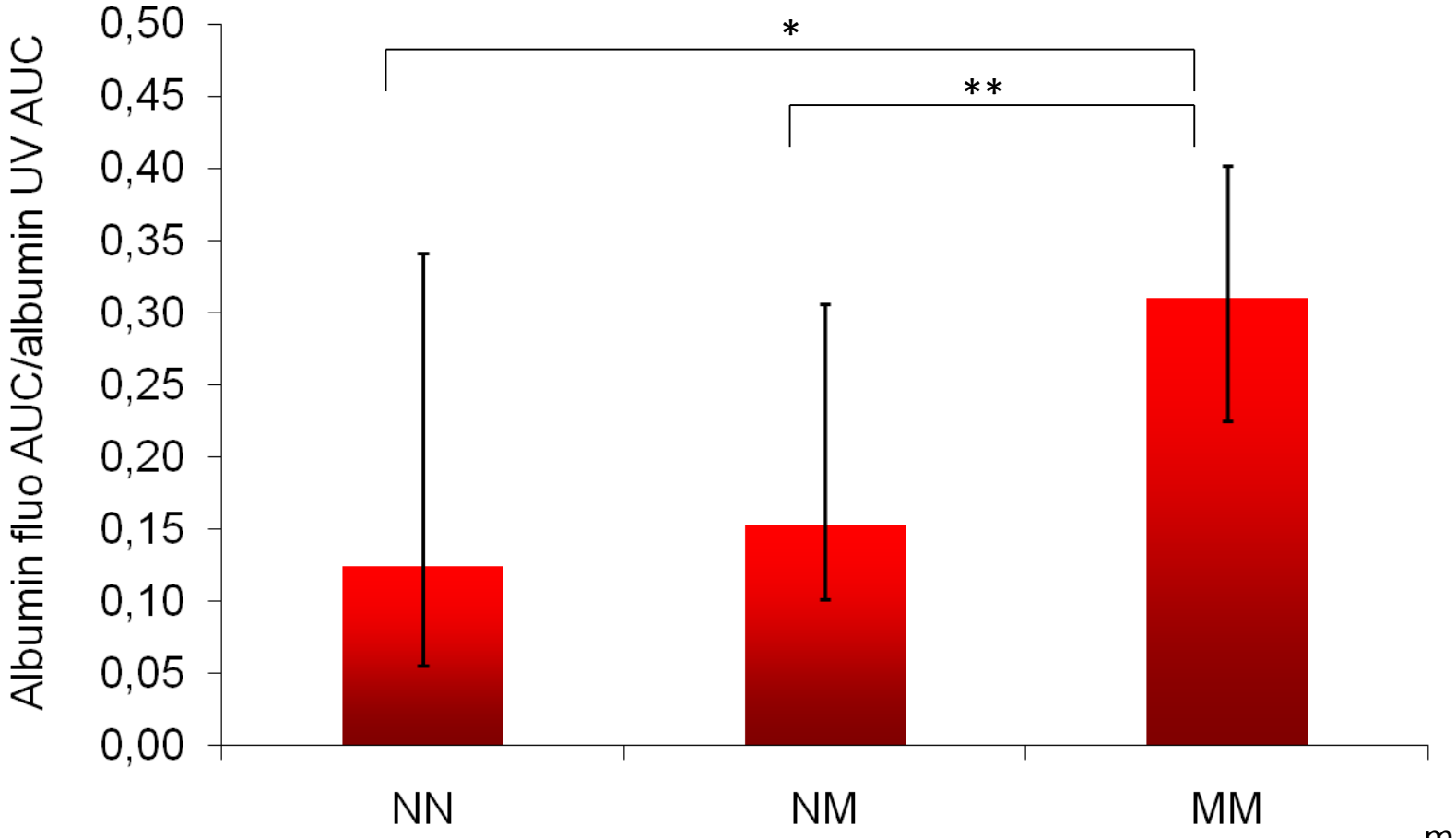
Markó et al. Physiol. Meas. 30 (2009) 1137–1150

Detection of glycoxidation of urinary albumin *via* fluorescence-HPLC



Markó et al. Physiol. Meas. 30 (2009) 1137–1150

The glycoxidation of urinary albumin



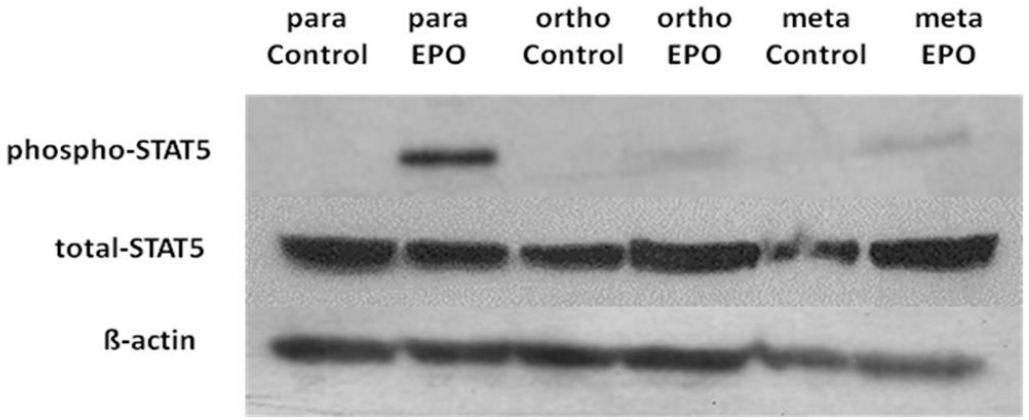
median±quartiles

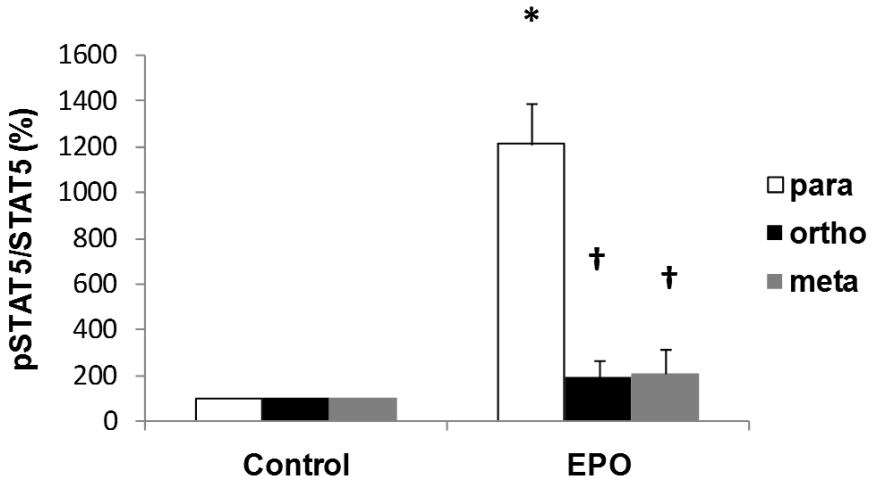
* p=0.019 NN vs. MM

** p<0.01 NM vs. MM; M-W U-test

Markó et al. Physiol. Meas. 30 (2009) 1137–1150

Ortho- and meta-tyrosine inhibit the proliferation of erythroblasts

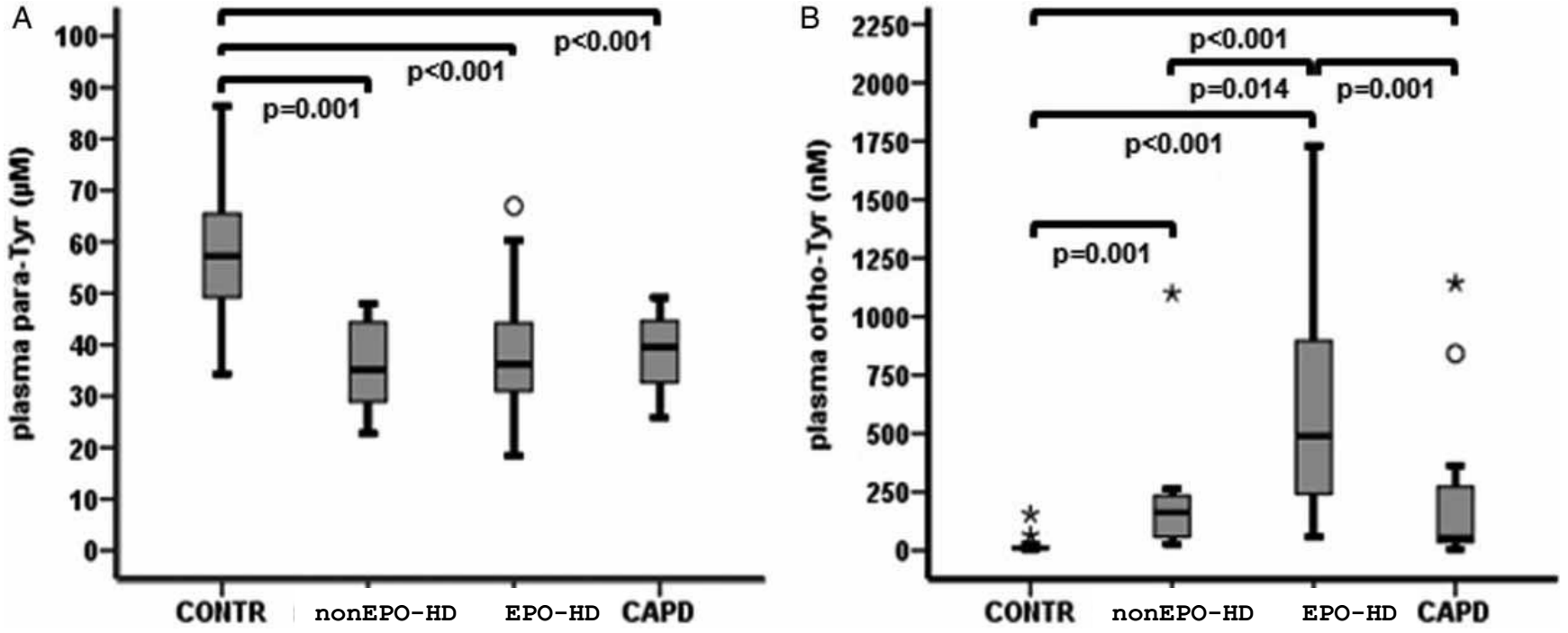




Mikolas E, Kun S, Laczy B, **Molnár GA** et al. Kidney Blood Press Res 2013; 38: 217–225, **IF: 1,820**

Molnár GA et al. World J Diabetes 2015; 6(3): 500-507, **Molnár GA** et al. Curr Med Chem 23(7):667-685 (2016), **IF: 3,455** (reviews)

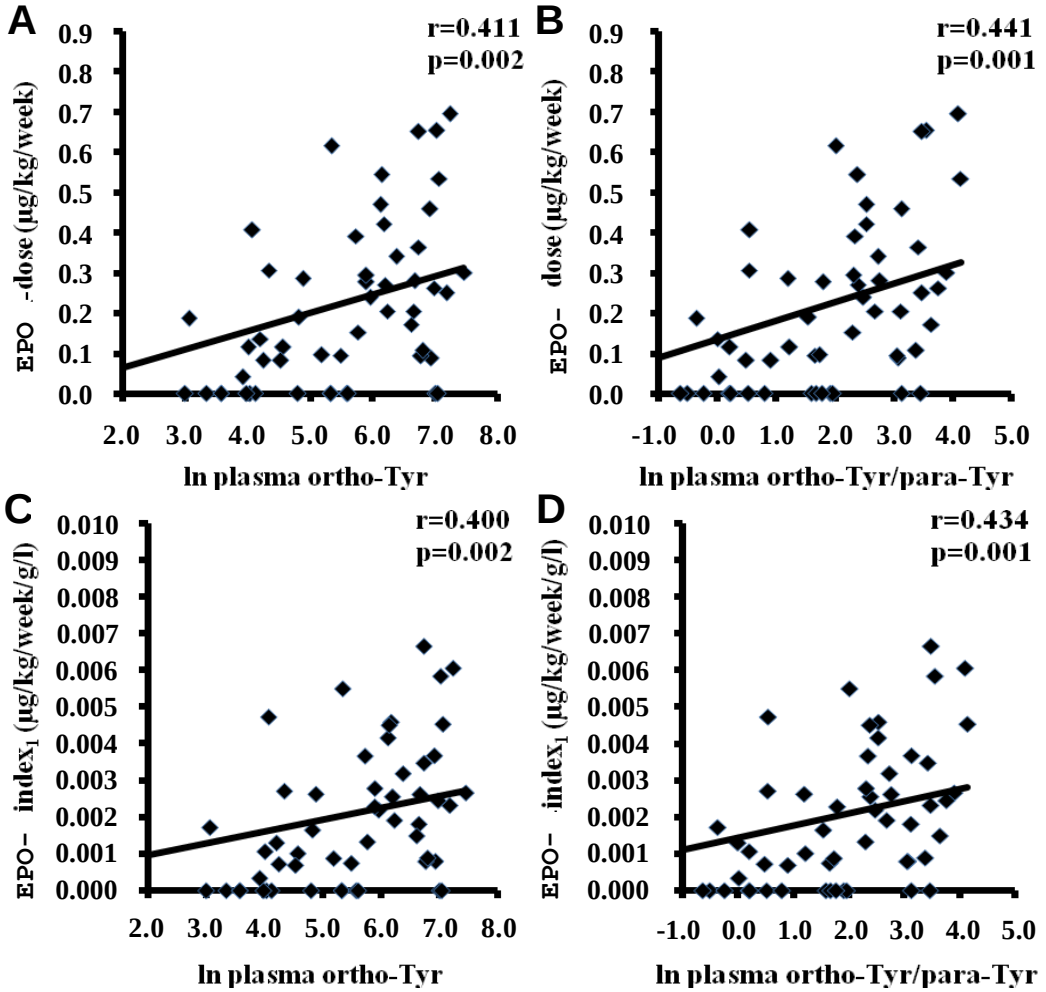
Ortho-tyrosine and Epo-resistance *in vivo*



Kun S, Mikolás E, **Molnár GA** et al. Redox Report 19(5):190-198 (2014), **IF: 1,522**

Molnár GA et al. Current Medicinal Chemistry 23(7):667-685 (2016), **IF: 3,455** (review)

Ortho-tyrosine and Epo-resistance *in vivo*



Kun S, Mikolás E, **Molnár GA** et al. Redox Report 19(5):190-198 (2014), **IF: 1.522**

Molnár GA et al. Current Medicinal Chemistry 23(7):667-685 (2016), **IF: 3.455** (review)

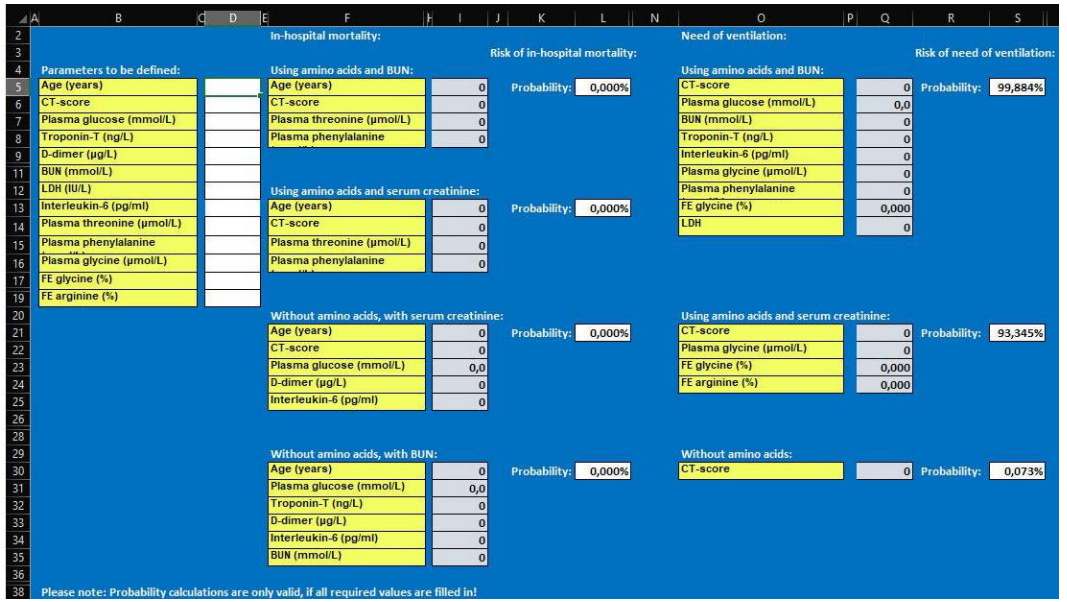
metabolites

MDPI

Article

Plasma Levels and Renal Handling of Amino Acids Contribute to Determination of Risk of Mortality or Feed of Ventilation in Patients with COVID-19

Gábor Bánfai [1], Péter Kanizsai [1], Csaba Csontos [2], Szilárd Kun [3], Ágnes Lakatos [4], Anikó Lajtai [4], Vanessza Lelovics [4], Sándor Szukits [5], Péter Bogner [5], Attila Miseta [4], István Wittmann [3,*] and Gergő A. Molnár [3]



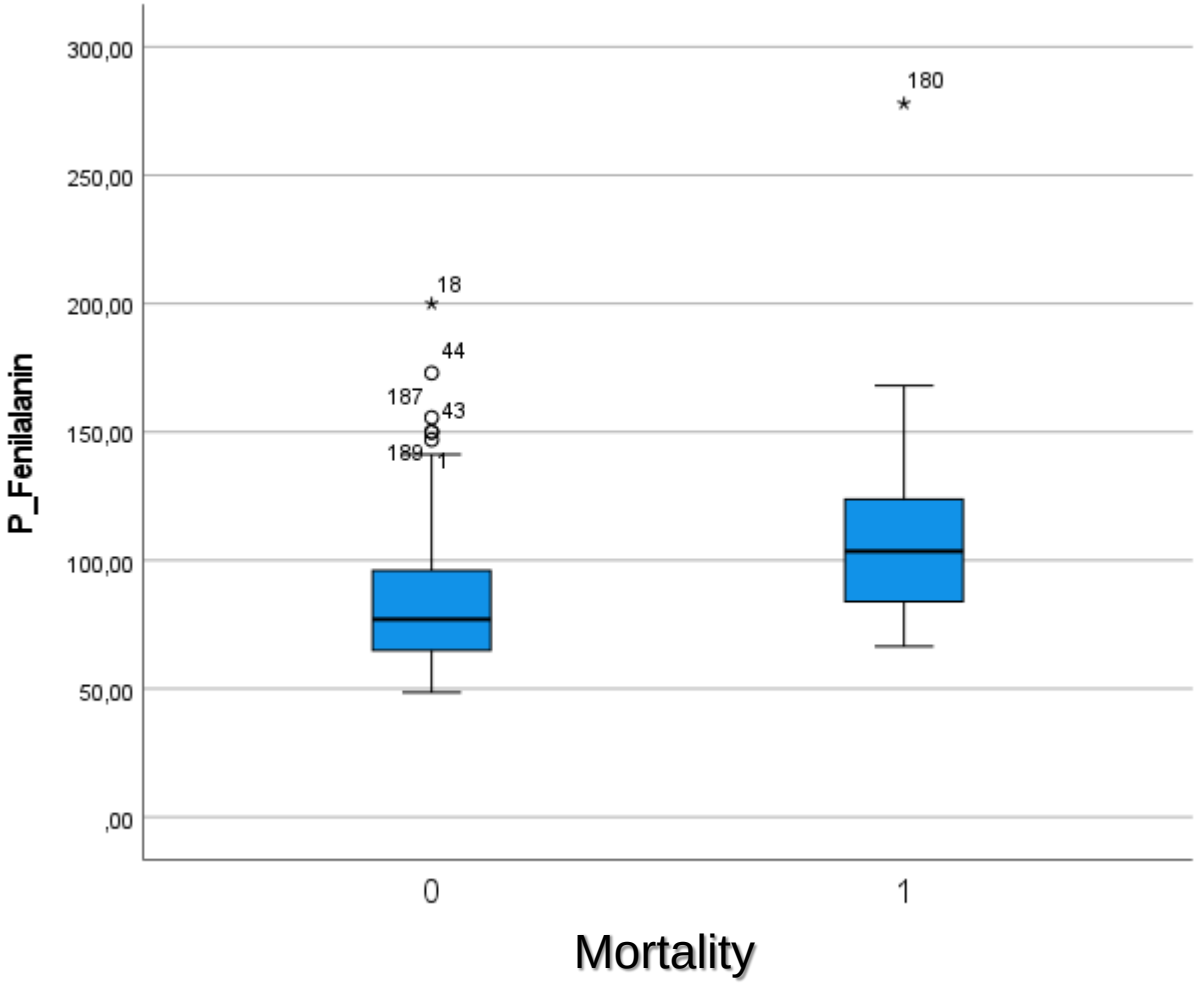
| | | |

Survived vs. deceased – amino acid parameters

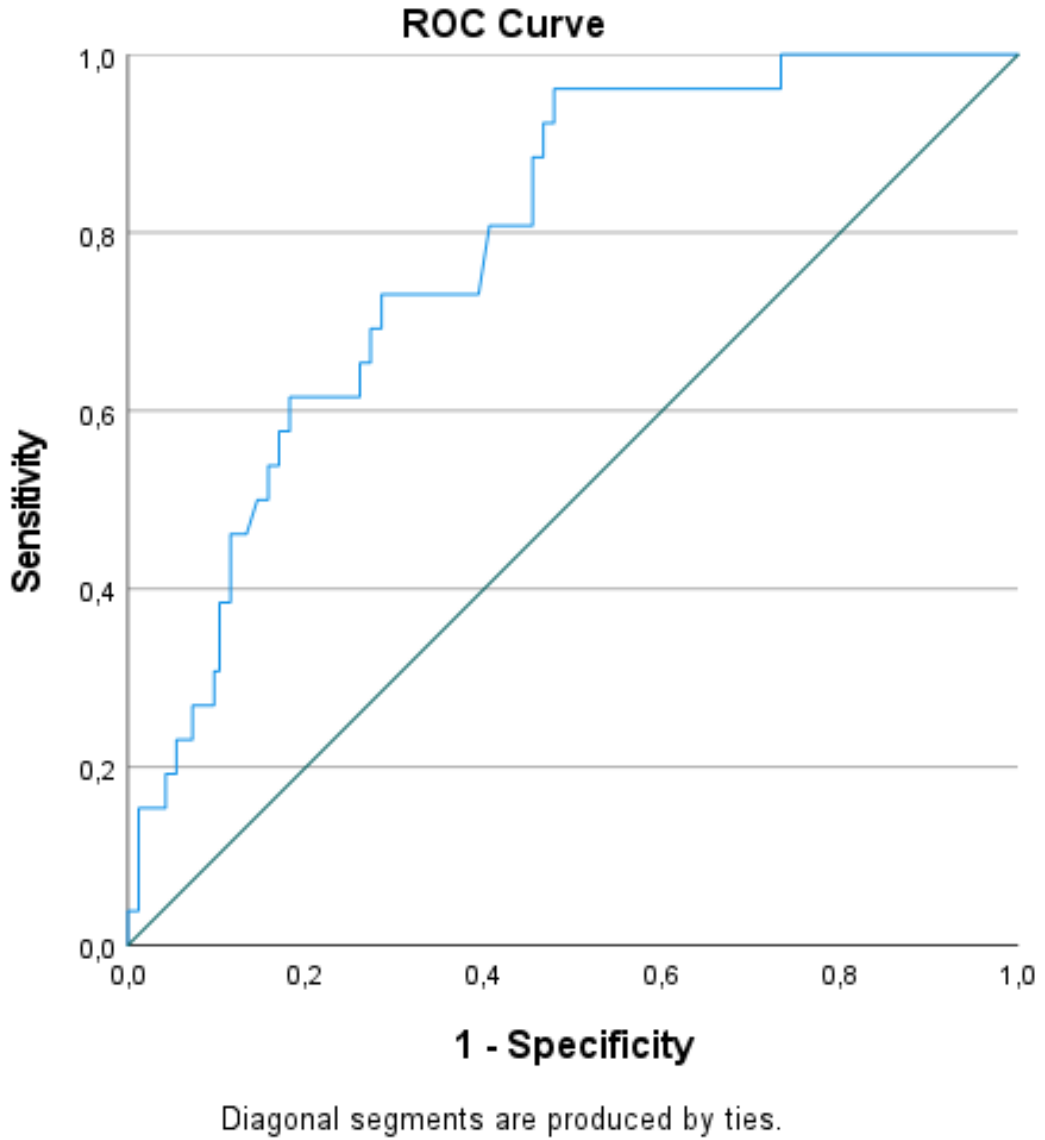
Test Statistics[a]				
	Serin_P	Threonin_P	Triptophan_P	Phenylalanine_P
Mann-Whitney U	296,500	288,500	216,000	214,500
Wilcoxon W	387,500	379,500	307,000	2699,500
Z	-1,987	-2,087	-2,996	-3,014
Asymp. Sig. (2-tailed)	0.047	0.037	0.003	0.003

Test Statistics[a]						
	Arginine_FE	Methionin_FE	Isoleucin_FE	Leucin_FE	Lysine_FE	Proline_FE
Mann-Whitney U	219,000	292,000	276,500	281,500	263,000	291,000
Wilcoxon W	2634,000	2707,000	2691,500	2696,500	2678,000	2706,000
Z	-2,914	-1,987	-2,184	-2,120	-2,355	-2,000
Asymp. Sig. (2-tailed)	***0.004***	***0.047***	***0.029***	***0.034***	***0.019***	***0.046***
a. Grouping Variable: Mortality						

Plasma Phe vs. mortality

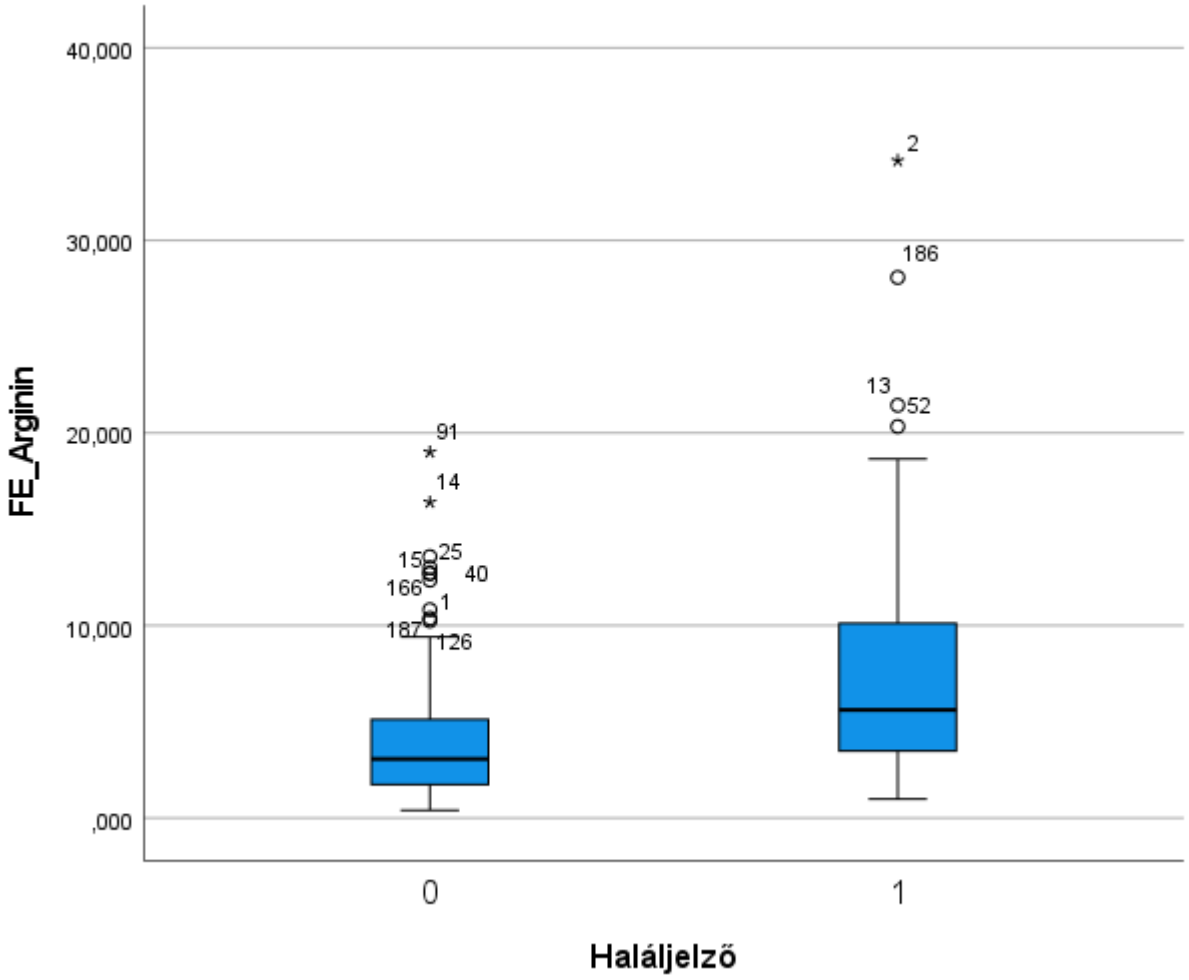


Mann-Whitney u test: P<0.001

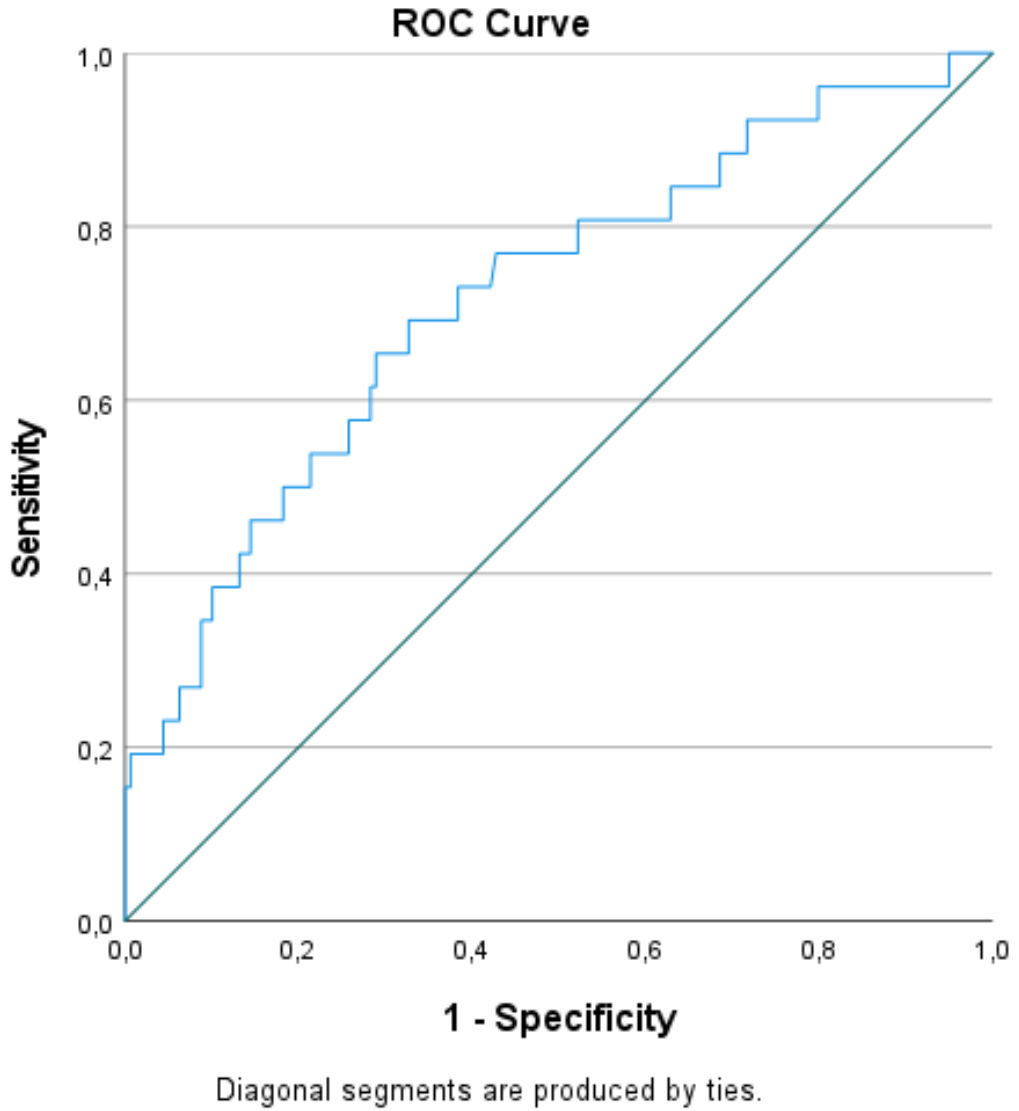


AUC: 0.633, cut-off: 78.7, Sens: 96.2%, Spec: 52.1%

Arg FE(%) vs. mortality

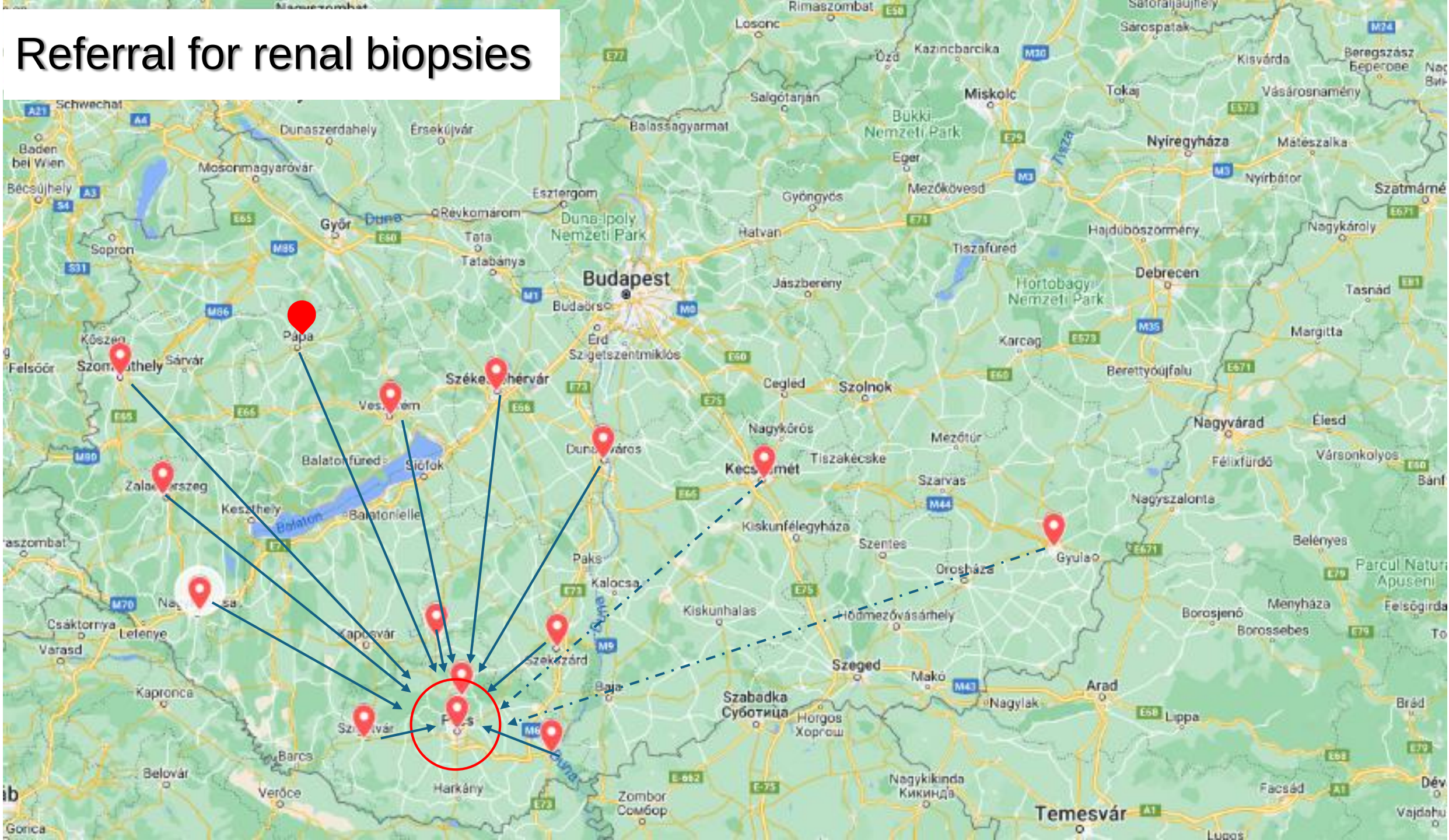


Mann-Whitney u test: P<0.001



AUC: 0.718, cut-off: 4.27, Sens: 69.2%, Spec: 67.3%

Referral for renal biopsies



Kidney & Blood Pressure Research

Kidney Blood Press Res 2012;35:26–34
DOI: 10.1159/000329939

Received: February 17, 2011
Accepted: June 1, 2011
Published online: August 18, 2011

Histological Diagnosis Determines Complications of Percutaneous Renal Biopsy: A Single-Center Experience in 353 Patients

Viktória Fisi[a] István Mazák[a] Péter Degrell[a] Richárd Halmai[a] Gergő A. Molnár[a] Eszter Fehér[b] Kinga Németh[b] István Pintér[c] Tibor Kovács[a] István Wittmann[a]

[a]Second Department of Medicine and Nephrological Center, and [b]Department of Radiology, University of Pécs, Pécs, and [c]Outpatient Department, Hospital of Siklós, Siklós, Hungary

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2006-2009.

2017-2024?

BRIEF COMMUNICATION

MEDICINA (Buenos Aires) 2015; 75: 1-5

META

Tumor and Stem Cell Biology

Cancer Research

Tyrosine Isomers Mediate the Classical Phenomenon of Concomitant Tumor Resistance

Raúl A. Ruggiero[1], Juan Bruzzo[1], Paula
Norma Speziale[2], Roberto P. Meiss[3], C

Montagna *et al. BMC Cancer* (2022) 22:845
https://doi.org/10.1186/s12885-022-09941-2

BMC Cancer

RESEARCH Open Access

Inhibition of hyperprogressive cancer disease induced by immune-checkpoint blockade upon co-treatment with meta-tyrosine and p38 pathway inhibitor

Daniela R. Montagna[1*], Alejandra Duarte[2], Paula Chiarella[1], Bárbara Rearte[3], Oscar D. Bustuoabad[1], Mónica Vermeulen[4] and Raúl A. Ruggiero[1]