Research/art/teacher profile of a person

Name and surname	doc. PharmDr. Tomáš Rajtík, PhD.
Document type:	Research/art/teacher profile of a person
The name of the university	Comenius University Bratislava
The seat of the university	Šafárikovo námestie 6, 818 06 Bratislava

I. - Basic information

I.1 - Surname	Rajtík
I.2 - Name	Tomáš
I.3 - Degrees	doc. PharmDr., PhD.
I.4 - Year of birth	1988
I.5 - Name of the workplace	Department of Pharmacology and Toxicology
I.6 - Address of the workplace	Odbojárov 10, 83232 Bratislava
I.7 - Position	Associate professor
I.8 - E-mail address	rajtik@fpharm.uniba.sk
I.9 - Hyperlink to the entry of a person in the Register of university staff	https://www.portalvs.sk/regzam/detail/24993
I.10 - Name of the study field in which a person works at the university	Pharmacy
I.11 - ORCID iD	0000-0002-8320-5276

II. - Higher education and further qualification growth

II.1 - First degree of higher education

II.2 - Second degree of higher education

II.a - Name of the university or institution	Faculty of Pharmacy, Comenius University Bratislava, Slovakia
II.b - Year	2006-2011
II.c - Study field and programme	Pharmacy

II.3 - Third degree of higher education

II.a - Name of the university or institution	Faculty of Pharmacy, Comenius University Bratislava
II.b - Year	2011-2015
II.c - Study field and programme	Pharmacology

II.4 - Associate professor

II.a - Name of the university or institution	Faculty of Pharmacy, Comenius University Bratislava
II.b - Year	2024
II.c - Study field and programme	pharmacology

II.5 - Professor

II.6 - Doctor of Science (DrSc.)

III. - Current and previous employment

III.a - Occupation-position	III.b - Institution	III.c - Duration
Associate professor	Faculty of Pharmacy, Comenius University Bratislava	2024-
Assistant professor	Faculty of Pharmacy, Comenius University Bratislava	2015-2023
Scientific assistant	Institute for Heart Research, Slovak Academy of Sciences, Bratislava, Slovakia	2022-

IV. - Development of pedagogical, professional, language, digital and other skills

IV.a - Activity description, course name, other	IV.b - Name of the institution	IV.c - Year
Basic life support	Operačné stredisko záchrannej zdravotnej služby Slovenskej Republiky	2022
First Aid Instructor Course	Operačné stredisko záchrannej zdravotnej služby Slovenskej Republiky	2023
Scientific qualification level IIa	Slovak Academy of Sciences	2022

V. - Overview of activities within the teaching career at the university

V.1 - Overview of the profile courses taught in the current academic year according to study programmes

V.1.a - Name of the profile course	V.1.b - Study programme	V.1.c - Degree	V.1.d - Field of study
Pharmacology 1/2	Pharmacy	Master	Pharmacy
Anatomy and Physiology	Pharmacy	Master	Pharmacy
Human Anatomy and Physiology	Medical devices	Bachelor	Pharmacy
Pathology	Pharmacy	Master	Pharmacy
Pathology	Medical devices	Bachelor	Pharmacy

V.3 - Overview of the responsibility for the development and quality of the field of habilitation procedure and inaugural procedure in the current academic year

V.3.a - Name of the field of habilitation procedure and inaugural procedure	V.3.b - Study field to which it is assigned
Pharmacology	Pharmacology

V.4 - Overview of supervised final theses

V.4.1 - Number of currently supervised theses	
V.4.b - Diploma (second degree)	2
V.4.c - Dissertation (third degree)	1
V.4.2 - Number of defended theses	
V.4.a - Bachelor's (first degree)	1
V.4.b - Diploma (second degree)	16
V.4.c - Dissertation (third degree)	1

V.5 - Overview of other courses taught in the current academic year according to study programmes

V.5.a - Name of the course	V.5.b - Study programme	V.5.c - Degree	V.5.d - Field of study
Medical Propaedeutics	Pharmacy	Master	Pharmacy
First Aid	Pharmacy	Master	Pharmacy
First Aid	Medical Devices	Bachelor	Pharmacy
Human Anatomy and Physiology	Medical Devices	Bachelor	Pharmacy

VI. - Overview of the research/artistic/other outputs

VI.1 - Overview of the research/artistic/other outputs and the corresponding citations

VI.1.1 - Number of the research/artistic/other outputs	
VI.1.a - Overall	91
VI.1.b - Over the last six years	42
VI.1.2 - Number of the research/artistic/other outputs registered in the Web of Science or Scopus databases	
VI.1.a - Overall	20
VI.1.b - Over the last six years	9
VI.1.3 - Number of citations corresponding to the research/artistic/other outputs	
VI.1.a - Overall	175
VI.1.b - Over the last six years	151
VI.1.4 - Number of citations registered in the Web of Science or Scopus databases	
VI.1.a - Overall	175
VI.1.b - Over the last six years	151
VI.1.5 - Number of invited lectures at the international, national level	
VI.1.a - Overall	1
VI.1.b - Over the last six years	1

VI.2 - The most significant research/artistic/other outputs

1	Koncsos G, Varga ZV, Baranyai T, Boengler K, Rohrbach S, Li L, Schlüter KD, Schreckenberg R, Radovits T, Oláh A, Mátyás C, Lux Á, Al-Khrasani M, Komlódi T, Bukosza N, Máthé D, Deres L, Barteková M, Rajtík T, Adameová A, Szigeti K, Hamar P, Helyes Z, Tretter L, Pacher P, Merkely B, Giricz Z, Schulz R, Ferdinandy P. **Diastolic dysfunction in prediabetic male rats: Role of mitochondrial oxidative stress.** Am J Physiol Heart Circ Physiol. 2016 Oct 1;311(4):H927-H943. doi: 10.1152/ajpheart.00049.2016. Epub 2016 Aug 12. PMID: 27521417; PMCID: PMC5114470. In this publication, we investigated the effect of prediabetes in rats on the development of diastolic dysfunction and pathological remodeling. Despite the fact that the link between contractile dysfunction and CaMKII activity was not demonstrated, at the level of calcium management, we showed that there was a decrease in phospholamban phosphorylation and thus a potential decrease in the function of the SERCA2a pump. In addition, it was shown that diastolic dysfunction and remodeling was associated with reduced markers of mitophagy (removal of damaged mitochondria) and increased oxidative stress, along with the aforementioned reduction in PKA kinase-regulated phospholamban phosphorylation.

2	Szobi A, Rajtik T, Carnicka S, Ravingerova T, Adameova A. **Mitigation of postischemic cardiac contractile dysfunction by CaMKII inhibition: effects on programmed necrotic and apoptotic cell death.** Mol Cell Biochem. 2014 Mar;388(1-2):269-76. doi: 10.1007/s11010-013-1918-x. Epub 2013 Dec 18. PMID: 24347176. In this work, we investigated the effectiveness of the CaMKII inhibitor, substance KN-93, on the occurrence of contractile dysfunction and cell death in ischemia-reperfusion injury in rats. We presented the improvement of postischemic recovery of LVDP. Another original finding was that the inhibition of CaMKII reduced the expression of selected proteins involved in cascades and apoptotic and necroptotic cell death, thus we also indicated a link between CaMKII activity and cell death cascades, which until then, in the case of necroptosis, was not a known phenomenon and thus we indicated, that the normalization of calcium turnover also affects the necroptotic death of cardiomyocytes.
3	Lichý M, Szobi A, Hrdlička J, Horváth C, Kormanová V, Rajtík T, Neckář J, Kolář F, Adameová A. **Different signalling in infarcted and non-infarcted areas of rat failing hearts: A role of necroptosis and inflammation.** J Cell Mol Med. 2019 Sep;23(9):6429-6441. doi: 10.1111/jcmm.14536. Epub 2019 Jul 21. PMID: 31328381; PMCID: PMC6714220. In the aforementioned publication, we evaluated the role of inflammation in the induction of necroptosis in a model of chronic heart failure, also taking into account the differentiation of damage zones after myocardial infarction in the left ventricles of rats. The results of the work indicate that in myocardial infarction, apoptotic cell death is not the main characteristic of damaged and at-risk tissue, but that the activation of inflammatory cascades in these zones leads to pathological remodeling associated with the activation of the signaling complex for necroptotic cell death.
4	Rajtik T, Goncalvesova E, Varga ZV, Leszek P, Kusmierczyk M, Hulman M, Kyselovic J, Ferdinandy P, Adameova A**. Posttranslational modifications of calcium/calmodulin-dependent protein kinase IIδ and its downstream signaling in human failing hearts**. Am J Transl Res. 2017 Aug 15;9(8):3573-3585. PMID: 28861149; PMCID: PMC5575172. This publication characterizes multiple types of chronic heart failure in humans based on different etiologies (ischemic vs. non-ischemic; dilated vs. hypertrophic cardiomyopathy) with regard to calcium turnover cascades associated with CaMKII activity and the potential role of oxidative stress on its activity. We have shown that the post-translational activation of CaMKIIδ in HF varies depending on the etiology. Lower levels of downstream molecular targets of CaMKIIδ do not correlate with either CaMKIIδ activation or the expression of major protein phosphatases in HF, nor does its oxidative activation differ depending on the type of HF.
5	Rajtik T, Carnicka S, Szobi A, Giricz Z, O-Uchi J, Hassova V, Svec P, Ferdinandy P, Ravingerova T, Adameova A. **Oxidative activation of CaMKIIδ in acute myocardial ischemia/reperfusion injury: A role of angiotensin AT1 receptor-NOX2 signaling axis.** Eur J Pharmacol. 2016 Jan 15;771:114-22. doi: 10.1016/j.ejphar.2015.12.024. Epub 2015 Dec 13. PMID: 26694801. In the aforementioned publication, we investigated whether the AT1 receptor blocker losartan can affect the oxidative activation of CaMKII, and thus whether such an action can underlie its pleiotropic action in the ischemia-reperfusion injury model. We differentiated its action by using a selective CaMKII inhibitor and also evaluated their concomitant use. Losartan was shown to be able to improve post-ischemic recovery of left ventricular function, but such recovery did not correlate with the expression of any of the active forms of CaMKII (oxidized/phosphorylated). Nevertheless, simultaneous blockade of AT1 receptors and the CaMKII inhibitor KN-93 abolished this cardioprotective effect, so we pointed out a possible clinical interaction between these two drugs.

VI.3 - The most significant research/artistic/other outputs over the last six years

1	Bartosova L, Horvath C, Galis P, Ferenczyova K, Kalocayova B, Szobi A, Duris-Adameova A, Bartekova M, Rajtik T. **Quercetin alleviates diastolic dysfunction and suppresses adverse pro-hypertrophic signaling in diabetic rats.** Front Endocrinol (Lausanne). 2022 Dec 8;13:1029750. doi: 10.3389/fendo.2022.1029750. PMID: 36568083; PMCID: PMC9772025. In this publication, we dealt with the potential therapeutic effects of quercetin (Qct) on the heart of obese diabetic rats, we observed the anti-hypertrophic action of Qct, both at the molecular level and at the level of structural changes of the left ventricle. Qct inhibited the pro-hypertrophic cascade HDAC4/MEF2, calcineurin/NFAT as well as the upstream modulator Erk5 in diabetic animals. At the structural level, it reduced the thickness of the walls of the left ventricle and, on the contrary, potentiated the increase in the internal diameter. Qct further selectively reduced collagen content in the left ventricles of diabetic animals. Chronic Qct therapy also effectively reversed a marker of diastolic dysfunction (increased E/A ratio) in ZDF rats, while this effect was selective in diabetic animals. With these results, we showed cardioprotective potential of Qct and suggested its new potential role in reducing the pro-hypertrophic signalling.
2	Rajtik T, Galis P, Bartosova L, Paulis L, Goncalvesova E, Klimas J. **Alternative RAS in Various Hypoxic Conditions: From Myocardial Infarction to COVID-19.** Int J Mol Sci. 2021 Nov 26;22(23):12800. doi: 10.3390/ijms222312800. PMID: 34884604; PMCID: PMC8657827. The aim of this review is to bring a comprehensive view of the mechanisms of different forms of hypoxic insults on the activity of alternative branches of the RAAS system, based on different duration of stimuli and causes (acute vs. intermittent vs. chronic), localization and tissue (heart vs. vessels vs. lungs) and clinical significance of the studied phenomenon (experimental vs. clinical condition). In addition, in this publication we provide new insights into future strategies using the alternative RAAS as a diagnostic tool as well as a promising pharmacological target in severe cardiovascular and cardiopulmonary diseases related to hypoxia and ischemia.
3	Lichý M, Szobi A, Hrdlička J, Horváth C, Kormanová V, Rajtík T, Neckář J, Kolář F, Adameová A. **Different signalling in infarcted and non-infarcted areas of rat failing hearts: A role of necroptosis and inflammation.** J Cell Mol Med. 2019 Sep;23(9):6429-6441. doi: 10.1111/jcmm.14536. Epub 2019 Jul 21. PMID: 31328381; PMCID: PMC6714220. In the aforementioned publication, we monitored the role of inflammation in the induction of necroptosis in a model of chronic heart failure, also taking into account the differentiation of damage zones after myocardial infarction in the left ventricles of rats. The results of the work indicate that in myocardial infarction, apoptotic cell death is not the main characteristic of damaged and at-risk tissue, but that the activation of inflammatory cascades in these zones leads to pathological remodeling associated with the activation of the signaling complex for necroptotic cell death.
4	Rajtik T, Goncalvesova E, Varga ZV, Leszek P, Kusmierczyk M, Hulman M, Kyselovic J, Ferdinandy P, Adameova A**. Posttranslational modifications of calcium/calmodulin-dependent protein kinase IIδ and its downstream signaling in human failing hearts**. Am J Transl Res. 2017 Aug 15;9(8):3573-3585. PMID: 28861149; PMCID: PMC5575172. This publication characterizes multiple types of chronic heart failure in humans based on different etiologies (ischemic vs. non-ischemic; dilated vs. hypertrophic cardiomyopathy) with regard to calcium turnover cascades associated with CaMKII activity and the potential role of oxidative stress on its activity. We have shown that the post-translational activation of CaMKIIδ in HF varies depending on the etiology. Lower levels of downstream molecular targets of CaMKIIδ do not correlate with either CaMKIIδ activation or the expression of major protein phosphatases in HF, nor does its oxidative activation differ depending on the type of HF.

5	Giricz Z, Koncsos G, Rajtík T, Varga ZV, Baranyai T, Csonka C, Szobi A, Adameová A, Gottlieb RA, Ferdinandy P. **Hypercholesterolemia downregulates autophagy in the rat heart.** Lipids Health Dis. 2017 Mar 23;16(1):60. doi: 10.1186/s12944-017-0455-0. Erratum in: Lipids Health Dis. 2017 Jul 5;16(1):133. PMID: 28330474; PMCID: PMC5363032. This is the first comprehensive analysis of autophagy and programmed cell death pathways of apoptosis and necroptosis in hypercholesterolemic rat hearts. This study showed that isolated hypercholesterolemia suppresses basal cardiac autophagy and that the decrease in autophagy may result from an activated mTOR pathway. Decreased autophagy was accompanied by increased apoptosis, whereas cardiac necroptosis was not modulated by isolated hypercholesterolemia. Decreased basal autophagy and increased apoptosis may be responsible for the loss of cardioprotection in hypercholesterolemic animals.

VI.4 - The most significant citations corresponding to the research/artistic/other outputs

1	[o1] 2019 ~ Hall, J.E. - do Carmo, J.M. - da Silva, A.A. - Wang, Z. - Hall, M.E.: **Nature Reviews Nephrology**, Vol. 15, No. 6,2019, s. 385 -- SCOPUS
2	[o1] 2018 ~ Zhang, Y.M. - Whaley-Connell, A.T. - Sowers, J.R. - Ren, J.: **Pharmacology & Therapeutics**, Vol. 191, 2018, s. 22 -- SCI
3	[o1] 2019 ~ Depaoli, M.R. - Bischof, H. - Eroglu, E. - Burgstaller, S. - Ramadani-Muja, J. - Rauter, T. - Schinagl, M. - Waldeck-Weiermair, M. - Hay, J.C. - Graier, W.F. - Malli, R.: **Pharmacology and Therapeutics**, vol. 202, 2019, s. 98-119 --SCI ; SCOPUS
4	[o1] 2016 ~ Moreno-Gonzalez, G. - Vandenabeele, P. - Krysko, D.V.: **American Journal of Respiratory and Critical Care Medicine**, Vol. 194, No. 4, 2016, s. 428 -- SCOPUS
5	[o1] 2018 ~ Lahm, T. - Douglas, I.S. - Archer, S.L. - Bogaard, H.J. - Chesler, N.C. - Haddad, F. - Hemnes, A.R. - Kawut, S.M. - Kline, J.A. - Kolb, T.M. - Mathai, S.C. - Mercier, O. - Michelakis, E.D. - Naeije, R. - Tuder, R.M. - Ventetuolo,C.E. - Vieillard-Baron, A. - Voelkel, N.F. - Vonk-Noordegraaf, A. - Hassoun, P.M.: **American Journal of Respiratory and Critical Care Medicine**, Vol. 198, No. 4, 2018, s. e43 -- SCOPUS

VI.5 - Participation in conducting (leading) the most important research projects or art projects over the last six years

1	VEGA 1/0775/21 - **Cardioprotective potential of TRP channels: role in remodeling, inflammation and calcium dysregulation.** Principal Investigator The role of TRP channels (TRP) has been confirmed in several cardiac pathologies such as ischemia-reperfusion injury (IR), remodeling and heart failure (HF). Similarly, the role of calmodulin-dependent kinase II (CaMKII) in the heart is considered an important part of the development of IR and HF, but there are still discrepancies in its action, manifested in clinical studies, limiting the possibilities of its modulation in a real scenario. It is not investigated whether there is a direct connection between TRP function and CaMKII-associated cascades in the development of severe phenotypes such as IR or SZ. The development of new TRP modulators, some of which are already in clinical trials as potential therapies for improving HF symptoms, represents a pharmacological tool to elucidate the link between these channels and CaMKII-associated pathways. Together with the use of modulators of TRP channels relevant for HF and IR, we want to establish the role of such a connection in the development of IR and HF in in vitro/in vivo models of heart damage and clarify their cardioprotective potential.

2	VEGA 2/0151/17 - **Hypoxia as prevention of rat heart failure and its influence in different phases of failure: Characterization of functional, structural and molecular changes.** Co-investigator for the Faculty of Pharmacy. The application of a spectrum of cardioprotective interventions can slow down the progression from cardiac hypertrophy to heart failure, but the effectiveness of these interventions is negatively affected by the presence of cardiovascular comorbidities as well as older age. The project is aimed at studying the possibilities of reactivation of the adaptation potential in the pathologically changed (remodeled) myocardium also in the case of older individuals through modulation of the intensity and timing of the adaptation stimulus. So far, markers of oxidative stress have been determined in different cellular compartments, which we correlated with CaMKII activity in a model of ischemic heart failure in rats. Current results indicate that increased CaMKII activity in the membrane fraction of cardiomyocytes correlates with the modification of membrane proteins through S-glutathionylation. This mechanism, together with the "up-regulation" of the antioxidant catalase, may indicate an endogenous protection of membrane proteins by preventing protein carbonylation.
3	VEGA 1/0016/20 - **Linking some forms of cell death to the necrotic phenotype: signaling and a multi-target tool to mitigate cardiac damage due to ischemia?** Deputy investigator. Regulated cell death (RBD) with a necrotic phenotype (necroptosis, pyroptosis) and autophagy appear to play a more important role in heart damage than apoptosis alone. Their signaling is complex and includes some common proteins whose activation, depending on the conditions, leads to the respective form of BS. In the ischemic heart, we will examine the relationship between these forms of BS and find out whether the necroptotically damaged part of the heart causes the propagation of damage to the surrounding tissue as a result of released molecules capable of activating pyroptosis. The analysis of molecules, including TNF, will be the subject of the study of BS induction, which we will differentiate into individual heart cells and evaluate paracrine pro-necroptotic signaling. We will study whether cardiac ischemia-induced autophagy coexists with or mediates necroptosis. We will test whether simultaneous inhibition of the respective forms of BS, compared to individual inhibition, is more effective in limiting the death of functional tissue and in alleviating cardiac dysfunction and remodeling.

4

APVV-20-0242 - **Necroptotic and pleiotropic effects of RIP3 kinase acting as a convergent point in cardiac cell loss: understanding the underlying mechanisms in the ischemic heart with or without metabolic stress as a tool for designing therapeutic approaches.**

Member of the investigative team

Necroptosis, which was found in the ischemic heart, seems to be a significant factor in the fate of the organism. The mechanisms responsible for executing this cell death are not fully understood, and the canonical RIP1-RIP3-MLKL pathway appears not to be the only one responsible for such cell loss. In our previous studies, we suggested a dual pronecroptotic and proinflammatory role of RIP3 kinase in the pathogenesis of post-infarction heart failure. In addition, we have clues that indicate a further pleiotropic action of RIP3 associated with oxidative stress as well as affecting the activity and dynamics of mitochondria. Thus, it appears that RIP3, rather than RIP1, may be an important node in intracellular signaling. The proposed processes in the heart damaged by ischemia and reperfusion need to be investigated in detail, and it is also necessary to find out whether RIP3 inhibition is able to limit these processes and thus alleviate cardiac dysfunction and remodeling. The considerable originality of the project is represented by the study of necroptosis in a metabolically stressed heart due to diabetes and its precursor prediabetes and its contribution to the damage of such a heart. We will review canonical as well as newly proposed RIP3-mediated signaling and review their activation in response to glucose levels and other biochemical characteristics of these disorders in glucose metabolism. We hypothesize that antidiabetic therapy is able to mitigate cardiac damage due to the limitation of necroptosis, which is intensified by an anti-necroptotic approach. An important concept of the project is the re-evaluation of released markers of necroptotic signaling into the circulation, which could be a prognostic and diagnostic approach. The proposed experiments using different methodological approaches chosen according to the latest methodological sheet for the evaluation of necroptosis in the heart will bring innovative knowledge about the pathogenesis of prediabetic and diabetic heart damage and as a result of ischemia, which, in turn, may indicate an important

VIII. - Overview of international mobilities and visits oriented on education and research/artistic/other activities in the given field of study

VIII.a - Name of the institution	VIII.b - Address of the institution	VIII.c - Duration (indicate the duration of stay)	VIII.d - Mobility scheme, employment contract, other (describe)
Semmelweis University, Medical Faculty	Budapest, Hungary	1.2.2014 – 31.5.2014	National scholarship program of the Slovak Republic to support the mobility of students, doctoral students, university teachers, research and artistic workers
European Molecular Biology Laboratory	Heidelberg, Germany	18. - 23.06.2017	Corporate Partnership Programme Fellowships

IX. - Other relevant facts

IX.a - If relevant, other activities related to higher education or research/artistic/other activities are mentioned	Slovak Academy of Sciences - Scientific qualification level IIa (2022) Ministry of the Environment of the Slovak Republic - Certificate on the use of genetic technologies and genetically modified organisms, project manager (76/10/19) Veterinary Training Institute - Certificate - Protection of animals used for scientific or educational purposes, implementation of procedures and projects (2765/2019) Operation Center of the Rescue Health Service of the Slovak Republic – Basic Life support (NFŽP/01/08-2022/2022) Operation Center of the Slovak Emergency Medical Service - First Aid Instructor Course (IPP-007/2023)
Date of last update	25.03.2024