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| pořadí v jakém návrhy přišly | pracoviště/přednosta | název projektu/řešitel  |
|  | [Stomatologická klinika, 1. lékařská fakulta, Univerzita Karlova a Všeobecná fakultní nemocnice v Praze](https://www.lf1.cuni.cz/kontakty?sWorkPlaceID=LF118&nInstitution=1#contacts)prof. MUDr. René Foltán, Ph.D. | **Biomimetic remineralization and hard tissue biomodulation**Dr. Antonín Tichý, PhD. |
|  | Ústav biologie a lékařské genetiky, 1. lékařská fakulta, Univerzita Karlova a Všeobecná fakultní nemocnice v Prazeprof. MUDr. Ondřej Šeda, Ph.D. | **Physiopathology of T-type calcium channels in motor neuron function**Dr. Norbert Weiss, Ph.D. |
|  | Ústav biologie a lékařské genetiky, 1. lékařská fakulta, Univerzita Karlova a Všeobecná fakultní nemocnice v Prazeprof. MUDr. Ondřej Šeda, Ph.D. | **DNA distribution in the cell nucleus - a multidisciplinary imaging approach**doc. RNDr. Dušan Cmarko, Ph.D. |
|  | Ústav biologie a lékařské genetiky, 1. lékařská fakulta, Univerzita Karlova a Všeobecná fakultní nemocnice v Prazeprof. MUDr. Ondřej Šeda, Ph.D. | **Genetics and Mechanisms of Amyotrophic Lateral Sclerosis (ALS)**Lenka Šlachtová, PhD. |

**Title of the research project:** Biomimetic remineralization and hard tissue biomodulation

**Description:** As a consequence of the age-related gingival recession and the frequent exposure of cervical root dentin, the risk of root dentin caries has increased. However, root cavities may be difficult to treat because of the complex etiology and structure.Biomimetic remineralization could be a powerful approach for the treatment of such defects. Specifically, self-assembling peptides (SAPs) are increasingly gaining interest for potential use as scaffolds in tissue engineering [1]. As previous studies reported that cross-linking agents such as proanthocyanidin (PA) reinforced the properties of dentin collagen matrix and improved the bond strength of adhesives to dentin [2], PA could also reinforce the scaffold self-assembled within the body of a subsurface lesion. The remineralization of the scaffold would be stimulated by bioactive glass particles (BAGs) or casein phosphopeptides-amorphous calcium phosphate (CPP-ACP). BAGs are highly biocompatible materials with a wide variety of use in medical and dental fields because of their ability to support the growth of bone cells and formation of hydroxyapatite (Fig. 2) [3]. CPP-ACP is a bioactive material used to initiate and promote the remineralization of enamel and dentin structures as CPP has the ability to stabilize calcium phosphate in solution by binding the ACP with phophoserine residues, leading to formation of nano CPP-ACP clusters [4].

This project is aimed at evaluating the potential of SAPs combined with BAGs or CPP-ACP to induce biomimetic remineralization of enamel, dentin and bone tissues. The properties of the remineralized tissues would be assessed using various methods including micro-computed tomography, scanning electron microscopy, transmission electron microscopy, microhardness, FTIR spectroscopy, and X-ray diffraction. It is expected that the biomechanical properties of the remineralized tissues and hence the clinical outcome of the treatment would be enhanced if biomimetic remineralization is achieved.

**References:**

[1] Alkilzy M, Santamaria RM, Schmoeckel J, Splieth CH. Treatment of carious lesions using self-assembling peptides. Advances in dental research. 2018 Feb;29(1):42-7.

[2] Vidal CM, Leme AA, Aguiar TR, Phansalkar R, Nam JW, Bisson J, McAlpine JB, Chen SN, Pauli GF, Bedran-Russo A. Mimicking the hierarchical functions of dentin collagen cross-links with plant derived phenols and phenolic acids. Langmuir. 2014 Dec 16;30(49):14887-93.

[3] Skallevold HE, Rokaya D, Khurshid Z, Zafar MS. Bioactive glass applications in dentistry. International journal of molecular sciences. 2019 Jan;20(23):5960.

[4] Oshiro M, Yamaguchi K, Takamizawa T, Inage H, Watanabe T, Irokawa A, Ando S, Miyazaki M. Effect of CPP-ACP paste on tooth mineralization: an FE-SEM study. Journal of oral science. 2007;49(2):115-20.

**Qualifications:**

* Ph.D. degree in dental medicine, life sciences, or related fields (max. 5 years from graduation)
* Record of publications in IF journals: at least 3 publications in IF journals (IF above 1.5), at least one as a first author
* Ability to communicate in both spoken and written English (minimum level B2 in the Common European Framework of Reference or equivalent)
* High motivation, ability to conduct collaborative research.

**Funding:** Cooperatio (Dental medicine)

**Workplace/Institution:** Institute of Dental Medicine (First Faculty of Medicine of the Charles University and General University Hospital in Prague)

**Supervisor:** Dr. Antonin Tichy, PhD

**E-mail of the supervisor:** antonin.tichy@lf1.cuni.cz

**Phone of the supervisor**: +420 224 96 68 05

**Position available from:** January 1, 2022

**Title of the research project:**

**Physiopathology of T-type calcium channels in motor neuron function**

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder characterized by the progressive loss of cortical, brain stem, and spinal motor neurons that leads to muscle weakness and death. ALS is regarded as a complex genetic disorder with a Mendelian pattern of inheritance in 5-10% of cases (familial ALS), but most patients have no discernable family history of the disease (sporadic ALS). However, several genes in apparent sporadic ALS are believed to increase the risk and/or modify the onset/progression of the disease. Recent studies from our laboratory suggest that CACNA1H encoding for Cav3.2 T-type Ca2+ channels may represent a risk factor for the disease. The goal of this research proposal is to address clinically relevant, fundamental questions regarding the role of T-type Ca2+ channels in motor neuron function, with a key translational aim of elucidating their pathogenic role in the development of motor neuron disorders such as (ALS).

*Relevant literature from our group:*

* Stringer RN, Jurkovicova-Tarabova B, Huang S, Haji-Ghassemi O, Idoux R, Liashenko A, Souza IA, Rzhepetskyy Y, Lacinova L, Van Petegem F, Zamponi GW, Pamphlett R, **Weiss N** (2020) A rare *CACNA1H* variant associated with amyotrophic lateral sclerosis causes complete loss of Cav3.2 T-type channel activity. ***Mol Brain*** 13:33.
* **Weiss N**, Zamponi GW (2020) Genetic T-type channelopathies. ***J Med Genet*** 57:1-10.
* Rzhepetskyy Y, Lazniewska J, Blesneac I, Pamphlett R, **Weiss N** (2016) *CACNA1H* missense mutations associated with amyotrophic lateral sclerosis alter Cav3.2 T-type calcium channel activity and reticular thalamic neuron firing. **Channels** 10:466-77.

**Work environment:**

The candidate will benefit from modern instrumentation including a patch clamp electrophysiology, confocal microscopy, efficient animal and cell culture facilities, as well as all the necessary equipment for regular molecular biology and biochemistry. More information can be found on our lab webpage <http://theweisslab.com>

**Candidate profile:**

The candidate must have a Ph.D or equivalent degree in neuroscience, cell biology or equivalent. Prior experience with patch clamp electrophysiology will be appreciated. Experience with primary neuronal cell culture, basic molecular (PCR, mutagenesis) and biochemistry (western blot) techniques, or confocal imaging microscopy will be an added advantage.

**Salary:** co-funding 1000 EUR/month is ensured

**Project supervisor:** Dr. Norbert Weiss, Ph.D (nalweiss@gmail.com)

**Department:** Institute of Biology and Medical Genetics, First Faculty of Medicine, Charles University

**Position available from:** January 1, 2022

**How to apply:** If you are interested in this position, please send a short cover letter describing your scientific interests along with a CV directly to Dr. Norbert Weiss nalweiss@gmail.com no later than **June 30, 2021** to discuss and prepare your application (university deadline July 18, 2021).

**Title of the research project:**

**DNA distribution in the cell nucleus - a multidisciplinary imaging approach**

The cell nucleus is probably the most complex compartment of the cell. It contains the genome and is the site of all related activities such as DNA replication and repair, RNA synthesis, as well as RNA maturation and transport. These activities take place within dynamic three-dimensional non-membrane domains. A comprehensive structural-functional study of these domains requires an approach integrating state-of-the-art *in situ* imaging methods at various levels of resolution, and a combination of *in vivo* analysis with a subsequent ultrastructural investigation performed on the same cells.

The major aim of the proposed project is an analysis of the DNA distribution within the nuclear volume including a reconstruction of the large scale three-dimensional (3D) chromatin arrangement in mammalian cell nuclei. This will shed light on the longstanding controversies about chromatin architecture in the interphase nucleus.

This project will be pursued with synchronised cell lines. To visualise transcriptionally active chromatin, the cells will be labelled by *in vivo* incorporation of uridine marked with halogens and/or stable isotope 15N or 13C. Heavy-metal stains that selectively enhance the contrast of chromatin will be used. For structure and function analysis, transmission and scanning electron microscopy (TEM and SEM) approaches (SEM array tomography and combination of SEM with focused ion-beam milling) together with the nanoscale secondary ion mass spectrometry (NanoSIMS) will be applied.

**Funding:** Position will be co-financed from projects funded by the Czech Science Foundation (GACR), Ministry of Health of the Czech Republic and by Charles University.

**Workplace:** Institute of Biology and Medical Genetics, First Faculty of Medicine, Charles University and General University Hospital in Prague

**Supervisor:** Dusan Cmarko, Ph.D.

**E-mail:** dusan.cmarko@lf1.cuni.cz

**Deadline date for applications:** July 26, 2020

**Position available from:** January 1, 2021

**Title of the research project:**

**Genetics and Mechanisms of Amyotrophic Lateral Sclerosis (ALS)**

**Supervisor: Lenka Šlachtová, PhD.**

**Institute of Biology and Medical Genetics, First Faculty of Medicine, Charles University in Prague**

Amyotrophic lateral sclerosis  is the third most common neurodegenerative disorder after Parkinson`s and Alzheimer`s. ALS is a devastating disorder affecting people in their 40–60 years of age, with an average survival of 2–3 years. There is no cure. Genetic defects have been found in both, familial and sporadic ALS, and twin studies estimate the heritability to about 60 %. Mutations causing ALS leads to various biological consequences disturbing pathways of cellular energy metabolism, protein homeostasis, RNA metabolism, neuroinflammation, cytoskeletal pathways and many others. The diversity of genetic architecture and clinical phenotypes challenges the ultimate goal to find a cure. Up today, defects in more than 30 genes have been identified to cause ALS, including  c9orf72, TARDBP, SOD1, FUS, ATXN2, TBK1, and other. Also about 20 genes contribute to disease development as risk factors. Therefore, current drug development focuses on numerous targets, but for clinical trials we must also cluster patients according to their phenotypes.  Therefore, we want to characterize the genotype and phenotype in our cohort of patients with sporadic and familial ALS. We have selected Slavic population from central Europe, characterized by common lifestyle and similar epidemiology. For phenotyping, we will collaborate with Neuromuscular centers to obtain clinical data and questionnaires.

This project aims to

1. design and to build a database for data describing ALS phenotypes
2. analyze genetic and genomic data of Slavic population (NGS, GWAS) and to compare the results with the current studies
3. identify the risk factors affecting the disease or its course

To collect and to analyze the data describing ALS phenotype, we will build secured database, which will be used for further analyses. As inclusion criteria, only patients with certain ALS diagnosis confirmed by a neurologist will be included. General epidemiologic data will be collected as age, sex, occupation, as well as data specific to ALS: the age of onset, site of onset of the disease, contact sports, attendance in military service, ALSFRS-R (a scale describing disease progression).

Results from genetic/genomic analyses from Next Generation Sequencing or Genotyping Arrays (Illumina) will be analyzed with R software.

This is a collaborative work with neuromuscular centers from university hospitals, state-of the-art facilities (Charles University, BIOCEV), and bioinformatic structures. This work is supported by PRIMUS 21/MED/012 and other funding.

**References:**

*Al Chalabi et al., J Neurol Neurosurg Psyc 2010. (12) 1324-6 Abramzon et al.,Front Neurosci 2020; 5:14 McLaughlin R. et al, Nature Comm 2017; 8: 14774 Chio A et al, Neurology 2021; 96 (15) Manjaly et al, Amyotroph Lateral Scler 2020 11(5):439-442 Brown R et al, N Engl J Med 2017; 377: 162-72 Mc Kay et al, Acta Neurol Scand 2020, 143:39-50*