**Contract on cooperation**

closed under provisions.., Civil Code, as amended, on the day, month and year between the following parties:
(Hereinafter the "Contract")

**Národní ústav duševního zdraví,** contributory organization

se sídlem Topolová 748, 250 67 Klecany

IČ: 00023752

represented prof. MUDr. Cyrilem Höschlem, DrSc. FRCPsych, director

represented , VYMAZÁNO Experimental neurobiology

Hereinafter

RECIPIENT

**Technische Universität Dresden**

Represented by the chancellor 01062 Dresden, Germany

Acting site:

Carl Gustav Carus Faculty of Medicine

Department of Child and Adolescent

Psychiatry and Psychotherapy

Cognitive Developmental Neurobiology

Director: VYMAZÁNO

Hereinafter

PROVIDER

**I.**

**Recitals**

RECIPIENT and PROVIDER for the PURPOSE of the conduction of certain PROJECTS agree in a long-term scientific collaboration that includes the transfer of money to the RECIPIENT in accordance with sec. **IV of this contract.**

**II.**

**Definitions**

PLANNED PROJECTS:

1) (ONE) Effect of Tsc2+/- plus developmental status epilepticus (DSE), “extended project” in relation to the pilot study and as described there in the discussion (Schneider et al. (2016) mTOR inhibitor reverses autistic-like social deficit behaviors in adult rats with both Tsc2 haploinsufficiency and developmental status epilepticus. EAPCN in press). The project includes differential analysis of the factors Tsc2+/-, DSE (or a similar seizure mechanism), analysis of social and global cognition including attention (if appropriate), reversal of behavioral deficits by mTOR inhibitors, analysis of mTOR pathway signaling and EEG during these conditions.

2) (TWO) Effect of different doses of DSE (or a similar seizure mechanism) in Tsc2+/- or wild-type rats on social and global cognition including attention (if appropriate), mTOR pathway signaling, MAPK path-way signaling and EEG during these conditions. The project definition includes experi-mental therapies with mechanisms affecting the mTOR signaling pathway or MAPK signaling pathway.

3) (THREE) Effects of Tsc2+/-, the mTOR pathway, the MAPK pathway and DSE (or a similar seizure mechanism) on the spatial and temporal dynamics of mRNA and protein regulation of neuroplasticity genes, for ex-ample arc/arg3.1 (Plath et al. (2006) Arc/Arg3.1 is essential for the consolidation of synaptic plasticity and memories. Neuron 52:437-44). The project definition includes experimental therapies with mechanisms affecting the mTOR sig-naling pathway or MAPK signaling pathway.

OTHER PROJECTS: These are PROJECTS not under the definition of PLANNED PROJECTS, however performed by PROVIDER or RECIPIENT using the MATERIAL.

RESSOURCES are RESSOURCES OF THE PROVIDER and RESSOURCES OF THE RECIPIENT.

RESSOURCES OF THE RECIPIENT: The representative of the RECIPIENT operates over scientific personnel, instruments and space that enables the realization of the PROJECTS. The representative of the RECIPIENT has years of experience in the fields of systems neuroscience with an emphasis on a multidisciplinary systems level approach, recording the activity of single neurons in awake behaving macaque monkeys, probing cell type specific functions in transgenic rodents via optogenetics and measuring perceptual / cognitive abilities with psychophysical methods as well as electroencephalography, electrocorticography and brain imaging in healthy “normal” human subjects and patients suffering from psychiatric illness.

RESSOURCES OF THE RECIPIENT do not include funding for materials, additional personnel, additional instruments or other costs that are not part of the regular facilities of the RECIPIENT.

RESSOURCES OF THE PROVIDER: The PROVIDER works since many years in the fields of molecular and cellular biology of the nervous system and the behavior of rodents, the genes arc/arg3.1, Srgap3 and Tsc2, tuberous sclerosis (TSC), mTOR and MAPK signaling pathways, autism, epilepsy and schizophrenia, in the clinical fields of neurology, adult psychiatry, child and adolescent psychiatry and as scientific advisor in TSC to pharmaceutical companies and patient associations. The PROVIDER has in these fields an MD and a habilitation degree, has supervised students and is part of professional networks.

**III.**

**Therefore the parties conclude the following agreement**

The PROVIDER agrees to fully provide required RESSOURCES OF THE PROVIDER for the realization of PLANNED PROJECTS, as far as possible.

The PROVIDER agrees to fully provide external funds, received by third parties to realize PROJECTS between RECIPIENT and PROVIDER, as far as these as realized at the RECIPIENT.

The RECIPIENT agrees to fully realize PLANNED PROJECT 1 (ONE) and to provide the required RESSOURCES OF THE RECIPIENT, as far as technically possible.

THE RECIPIENT declares to intend to realize PLANNED PROJECTS 2 (TWO) and 3 (THREE). RECIPIENT and PROVIDER can also agree to investigate other fields of interest, especially if the RECIPIENT has not sufficient scientific interest in PLANNED PROJECTS 2 (TWO) and 3 (THREE). However, RECIPIENT and PROVIDER agree that, any additional research (OTHER PROJECTs) carried out by the RECIPIENT that is not related to Autism Spectrum Disorder or a direct extension of the above described projects 1 (ONE), 2 (TWO)and 3 (THREE) is at the RECIPIENTs full discretion. The PROVIDER has based upon the PROVIDERs scientific and material contribution the possibility to join any such project as equal partner.

Between RECIPIENT and PROVIDER there shall be regular meetings, preferably at least every 2 months, preferably at the RECIPIENT in Klecany.

The RECIPIENT agrees that the MATERIAL is to be used solely for the PURPOSE of the transfer. For five years the RECIPIENT shall not distribute or release the MATERIAL to any other person and shall ensure that no one will be allowed to take or send the MATERIAL to any other location unless written permission is obtained from the PROVIDER. After this five years limitation period (which started running on 29.08.2016 has passed, the RECIPIENT shall be entitled to use the MATERIAL for any purpose allowed by the legislation.

**IV.**

**Finance**

**The PROVIDER will forward 17.500,00 € to the RECIPIENT. In case the PROVIDER has to pay value-added tax (VAT), it will be subtracted from the total sum. This money amount will solely be used for the continuation of the PLANNED PROJECTS (sec. II). The transferred money amount will be used for material and services, which are associated with PLANNED PROJECT 1 (ONE) or other common PROJECTS. The money amount will be transferred to the RECIPIENT. The RECIPIENT has to request and invoice the remuneration until the end of year 2017.**

**V.**

**Licence, Publications**

Both PROVIDER and RECIPIENT agree to send all scientific abstracts and manuscripts related to the MATERIAL before first submission as a confidential information to the contrary party. This agreement is valid for all PROJECTS started within the first 5 years.

## The term "RESULTS" means (regardless if protected or protectable by intellectual property rights) any and all methods, processes, know-how, proprietary information, trade secrets, technology, anonymized clinical data, inventions, innovations and improvements made by either contractual party during the performance of tasks under this contract.

## RESULTS which are solely developed by one contracting party shall upon their generation become the sole and unlimited property of that party (“INDIVIDUAL RESULTS”).

## RESULTS which are developed jointly by PROVIDER and RECIPIENT and which are not separable, shall become the joint property of PROVIDER and RECIPIENT (“JOINT RESULTS”). The contracting parties are the authors of the JOINT RESULTS to the extent that they actually participated in the JOINT RESULTS.

## Both PROVIDER and RECIPIENT have the right use the JOINT RESULTS and the INDIVIDUAL RESULTS (regardless if their own INDIVIDUAL RESULTS or if INVIDUAL RESULTS of the other party) for its own scientific or any other purposes. For this purpose each contracting party retains from under this contract a non-exclusive, transferable, sublicensable, royalty-free and perpetual right to use the JOINT RESULTS and INDIVIDUAL RESULTS.

For PLANNED PROJECT 1 (ONE) there is agreement, that the author of the main publication in a scientific journal is the party who generated the majority of results of this PLANNED PROJECT 1 (ONE).

For PLANNED PROJECTS 2 (TWO) and 3 (THREE) are PROVIDER and RECIPIENT in continuous alternation senior author and co-senior author (second-last author) on publications in scientific journals. With consent from both parties this order can be changed. The status as senior author or co-senior author of a publication in a scientific journal requires for the PROVIDER that required RESSOURCES OF THE PROVIDER were provides for the PROJECT, and for the RECIPIENT that required RESSOURCES OF THE RECIPIENT were provided, as far as technically possible, respectively.

**VI.**

**Limitation of liability**

Unless agreed otherwise, the parties shall be liable in accordance with the statutory provisions.

The parties shall be liable for willful misconduct and negligence. Upon slight negligence, the liability of the parties for damages, which does not result from injury to life, limb or health, is limited (a) to the foreseeable damage typical for this Agreement, if the damage results from a breach of material contractual obligations, and (b) to the three-fold contract value, if the damage results from a breach of other contractual obligations. Material contractual obligations are those obligations whose fulfillment enables proper implementation of the Agreement and/or on whose fulfillment the other party regularly relies and may relay. The aforementioned liability regime also applies to representatives and vicarious agents of the parties.

**VII.**

**Severability Clause**

Should any provision of this agreement be invalid or unenforceable or should the contract contain an omission, the remaining provisions shall be valid. In the place of an invalid provision, a valid provision is presumed to be agreed upon by the parties, which comes economically closest to the invalid provision. The same shall apply in the case of an omission. This wording and the wording of the contract *,,Scientific Cooperation and Material Transfer Agreement”* contains the entire agreement between the parties; any changes of the agreement have to be made in writing. The same applies to any change in the requirement for the written form.

 **VIII .**

**Applicable law and Jurisdiction**

This Agreement is governed by the laws of Germany, excluding the Private International Law. In case of inconsistency German law shall prevail. In the event of any dispute arising between the parties in relation to the terms of this Agreement, the parties shall use their best endeavours to resolve the matter on an amicable basis. In the event the parties are unable to re-solve any dispute in accordance with the provisions of this Agreement, any action brought by either party to this Agreement shall be heard by the appropriate court of competent jurisdiction sitting in Dresden.

**IX.**

**Final provision**

RECIPIENT and PROVIDER concluded a contract *,,Scientific Cooperation and Material Transfer Agreement”* on 29.08.2016. The provisions of this *Contract of cooperation* which are incompatible with the provisions of ,,*Scientific Cooperation and Material Transfer* take precedence over the provisions of ,,*Scientific Cooperation and Material Transfer.*

V Klecanech dne \_\_\_\_\_\_\_\_ 2017

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za Národní ústav duševního zdraví

prof. MUDr. Cyril Höschl, DrSc. FRCPsych, ředitel

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VYMAZÁNO

Dresden:

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

VYMAZÁNO Chancellor

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

VYMAZÁNO Director KJP

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VYMAZÁNO PI