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HelmholtzZentrum münchen
German Research Center for Environmental Health

LCSB

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# Collaboration Agreement

This agreement – hereinafter referred to as the "Agreement" – is concluded between

The Helmholtz Zentrum München

having its registered office at Helmholtz Zentrum München, Deutsches Forschungszentrum für Gesundheit und Umwelt GmbH, Ingolstädter Landstraße 1, D-85764 Neuherberg, Germany, represented by its board of directors Prof. Dr. Günther Wess, Dr. Nikolaus Blum and Dr. Alfons Enhsen

hereinafter referred to as "HMGU"

acting for its Institute of Developmental Genetics, represented by its director Prof. Dr. Wolfgang Wurst,

hereinafter referred to as "IDG"

and

The University of Luxembourg, a Public Establishment of Higher Education and Research,

having its registered office at 162a, avenue de la Faïencerie, L-1511 Luxembourg, represented by its President, Prof. Dr. Rolf TARRACH,

hereinafter referred to as the "UL",

acting for its Luxembourg Centre for Systems Biomedicine, represented by its director Prof. Dr. Rudi Balling,

hereinafter referred to as "LCSB",

HMGU and UL/LCSB hereinafter sometimes individually referred to as a "Party" or collectively as "Parties".

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German Research Center for Environmental Health

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Principle Contacts

| | HMGU | UL |
|---|---|---|
| Principal Investigator | Wolfgang Wurst<br>Director<br>Institute of Developmental Genetics (IDG)<br>Ingolstädter Landstraße 1<br>85764 Neuherberg<br>Germany<br><br>Phone: +49 (0) 89 3187 4110<br>Fax:+49 (0) 89 3187 3099<br>Email: wurst@helmholtz-muenchen.de | Rudi Balling<br>Director<br>Luxembourg Centre for Systems Biomedicine (LCSB)<br>Université du Luxembourg<br>7, avenue des Hauts-Fourneaux<br>L-4362 Esch-sur-Alzette |
| Legal Affairs and Licenses | Paul Göttlich<br>Legal Affairs<br>Ingolstädter Landstraße 1<br>85764 Neuherberg<br>Germany<br>Phone.: +49 89 3187 1184<br>Fax.: +49 89 3187 3695 | Khalid Larget (Legal Affairs Officer)<br>Sigmar Lampe (Licenses and Tech Transfer)<br>University of Luxembourg<br>162a, avenue de la Faïencerie,<br>L-1511 Luxembourg |
| Legal Representative | Prof. Dr. Günther Wess, Dr. Nikolaus Blum and Dr. Alfons Enhsen<br>Ingolstädter Landstraße 1<br>85764 Neuherberg<br>Germany | Rolf Tarrach<br>President<br>University of Luxembourg<br>162a, avenue de la Faïencerie,<br>L-1511 Luxembourg |

Preamble

The IDG research focus is to unravel the molecular mechanisms underlying neuropsychiatric diseases, in particular Parkinson Disease and depression. Furthermore, the HMGU focuses to determine the influence of environment-gene interaction on the disease pathomechanisms. The experiments are performed in mouse models as well as in human and mouse models in vitro to recapitulate the molecular network underlying disease pathomechanisms. Based on these models the molecular and cellular basis of disease etiology will be determined and new biological markers will be identified serving for preventive diagnosis and therapy development.

The LCSB is a research institution that carries out research projects on the pathogenesis of Parkinson's disease (PD). New candidate genes involved in the pathogenesis and biological targets for medical prevention and intervention strategies as well as new tools to improve the predictability of the efficacy and safety of new treatments are being identified. The disease pathogenesis and the role of candidate genes will be analysed in the context of complex biological network composition and behaviour and perturbations in the homeostasis of physiological networks. Various models from in-vitro to in-vivo as well as mathematical descriptions of the underlying networks will be developed and used for the modelling and simulation of how diseases develop and how diseases are influenced by genetic predisposition or by external environmental parameters.

During its first years after foundation, LCSB benefited very much from strategic knowledge collaboration partnerships that contributed to many excellent projects and a fast growing and maturation of LCSB's research. LCSB aims extend from the current knowledge transfer programme targeted strongly to data analysis and integration to a multi-lateral collaboration network that reflects the fast development and grown maturity of LCSB and supports the outreach to systems medicine. The area of activities will focus on systems medicine by focussing on in vivo model systems, imaging and the outreach to healthcare and the patients. The current Collaboration Agreement is concluded in this context.

## 1 DEFINITIONS

As used in this Agreement, the following terms, when used in capital letters, shall have the following respective meanings:

1.1 "Research Project" shall mean all work set out in the annex.

1.2 "Foreground" means the Results, including Materials and information, whether or not they can be protected, which are generated under the Research Project. Such results include rights related to copyright; design rights; patent rights; plant variety rights; or similar forms of protection.

1.3 "Background" shall mean: information and knowledge (including inventions, databases, etc.) held by a Party prior to the conclusion of this Agreement or acquired by a Party independently of the collaborative activities, as well as any existing intellectual property rights held by a Party which are needed for carrying out the Research Project or for using Foreground.

1.4 "Access Rights" means licences and user rights to Foreground or Background;

1.5 "Confidential Information" with respect to a Party or its affiliates (the "Disclosing Party") means all confidential technical, business and financial information including, where appropriate and without limitation, all information, licenses, business plans, data, patent disclosures, patent applications, structures, models, techniques, processes, compositions, and compounds relating to the same disclosed by the Disclosing Party to the other Party (the "Receiving Party") or obtained by the Receiving Party through observation or examination of information, but only to the extent such information is maintained as confidential, including, without limitation, any third party confidential information, by the Disclosing Party and is disclosed in writing and designated "Confidential," or disclosed in any manner such that a reasonable person would understand its confidential or proprietary nature.

1.6 "Invention" shall mean: any invention or discovery, made by investigator(s) of either and/or both of the Parties, whether a patent application has been filed thereon or not, that is conceived in the performance of a Research Project.

1.7 "Material" shall mean: any models, samples, materials, goods, software, chemical or biological reagents and prototypes.

1.8 "Information" shall mean any results, data, and/or information.

1.9 "Principal Investigator(s)" means the person(s) designated respectively by the Parties to this Agreement who will be responsible for the scientific and technical conduct of the research as well as the implementation of the specific plans to conduct the Research Project. The Principal Investigators should, as far as is reasonably practicable, ensure that researchers and staff in the LCSB and/or HMGU laboratories under their control abide by the legal terms and conditions contained in this Agreement.

1.10 "Results" shall mean: any and all data, tangible know-how, Material, instructions and other information, which is generated during the Research Project.

1.11 "Use" means the direct or indirect utilisation of Foreground in further research activities other than those covered by the Research Project , or for developing, creating and marketing a product or process, or for creating and providing a service.

1.12 "Needed" means:
For the implementation of the Research Project:
Access Rights are Needed if, without the grant of such Access Rights, carrying out the tasks assigned to the recipient Party would be impossible, significantly delayed, or require significant additional financial or human resources.

For Use of own Foreground:
Access Rights are Needed if, without the grant of such Access Rights, the Use of own Foreground would be technically or legally impossible.

1.13 "Fair and Reasonable Conditions" means appropriate conditions including possible financial terms taking into account the specific circumstances of the request for Access Rights, for example the actual or potential value of the Foreground or Background to which Access Rights are requested and/or the scope, duration or other characteristics of the use envisaged.

## 2 The Collaboration

2.1 The purpose of this Collaboration Agreement is to provide a framework for collaborative work and conducting common Research Project. The Collaboration Agreement defines the rights and obligations of the Parties inter alia liability, access rights and dispute resolution.

2.2 The Parties carry out the Research Project together, which is described in the Annex A to this Agreement. The Research Project will be updated when necessary by mutual agreement of the Parties in written form signed by persons authorized to sign for the respective Parties.

2.3 The Parties will make their unique infrastructure and expertise available to each other within the Research Project that will define the costs and the corresponding sharing.

2.4 The Parties may provide and support research staff for each other to establish common research groups and to work on the Research Project.

2.5 Each Party undertakes to take part in the efficient implementation of the Research Project respecting the current state of the scientific and technical knowledge and to notify the other Party promptly about any significant information, facts, problems or delays likely to affect a Research Project. Each Party will assure that the work is done according to the laws, regulations and ethics applicable in the country.

2.6 Each Party shall appoint a Principal Investigator responsible for the performance of the Research Project and as contact person for this Agreement.

2.6.1 The Principle Investigators responsible for the Research Project are:

a. at HMGU:
Wolfgang Wurst

Director
Institute of Developmental Genetics
Ingolstädter Landstraße 1

85764 Neuherberg
Germany

Phone: +49 (0) 89 3187 4110
Fax:+49 (0) 89 3187 3099
Email: wurst@helmholtz-muenchen.de

b. at UL:

Prof. Dr. Rudi Balling, Director of the LCSB
Luxembourg Centre for Systems Biomedicine (LCSB)
Université du Luxembourg
Campus Belval
7, avenue des Hauts-Fourneaux
L-4362 Esch-sur-Alzette
Luxembourg

2.7 The Principal Investigators oversee the Research Project, and report to each other on its status and its Foreground. The PIs should, as far as is reasonably practicable, ensure that researchers and staff in the LCSB and/or HMGU under their control abide by the legal terms and conditions contained in this Agreement.

## 3 Financial Contributions

3.1 All financial contributions are stipulated in the Budget Section of the Research Project.

3.2 All payments to HMGU will be invoiced by HMGU. All amounts are net values and will be invoiced plus VAT if applicable. The payment shall be due within thirty (60) days after receipt of an invoice from HMGU.

3.3 All payments due shall be without deduction of taxes or other fees that may be imposed by state or federal government.

## 4 Knowledge Transfer and Assignment of Personnel

4.1 The Parties agree to engage in activities to provide knowledge transfer and to facilitate joint teaching and training of students and others, which include but are not limited to:

- staff and student exchanges;
- exchanging information and materials;
- teaching systems biology and / or technical training courses
- exploring educational initiatives that bring together science, societal and policy issues.

4.2 It is contemplated that each Party may assign personnel to the other Party's facility to participate in or observe the research to be performed under this Agreement. Such personnel shall not during the period of such assignments be considered employees of the host Party for any purposes, including but not limited to any requirements to

provide workers' compensation, liability insurance coverage, payment of salary or other benefits, or withholding of taxes, unless through a separate mutual written agreement of the Parties.

4.3 Notwithstanding the foregoing, the host Party shall have the right to exercise routine administrative and technical oversight of the occupational activities of such personnel during the assignment period and shall have the right to approve the assignment of personnel or request their removal. The assigning Party's employees and agents shall observe the working hours, security and safety rules, and holiday schedule of the host Party while working on the host Party's premises.

4.4 Unless otherwise agreed to in writing by the Parties, the assigning Party shall bear any and all costs, expenses, and liabilities (including salary and fringe benefits) with regard to its personnel assigned to the host Party's facilities under this Agreement. The host Party's policies and procedures relating to employment-related matters, such as (among others) minimum and maximum salaries, financial rights, and employment benefits for which there is a monetary outlay (such as health insurance and retirement contributions), shall not apply to the assigned employee.

4.5 Unless otherwise agreed in writing, the host Party shall bear facility costs of such assignments.

4.6 For visiting personnel, the host Party may require confidentiality agreements to protect confidential or proprietary information not related to the Research Project under this Agreement.

## 5 Confidentiality

5.1 Each Party shall treat the services, data, Material and Results obtained from or provided by the other Party, and which shall be Confidential Information of the Disclosing Party, as confidential and shall use them exclusively for the collaboration. Subject to the furnishing Party's approval, the receiving Party shall not release any information to any person or entity other than the researcher/s involved in the collaboration and staff under the involved researchers' direct supervision and who are bound by confidentiality obligations not less strict than those set out herein.

5.2 The obligations according to Section 5.1 shall not apply to any piece of information which:

a) at the time of disclosure is generally known or publicly available, or after disclosure becomes generally known or publicly available through no fault of the Parties; or

b) written evidence proves that the Party was already in lawful possession of the information prior to disclosure; or

c) a Party properly obtained the information from a third party who is entitled to disclose the information and not under a confidentiality obligation to the other Party in respect of the information.

d) is required by law, regulation, administrative or court order to be disclosed; provided, however, that in such case, the Receiving Party shall notify the

Disclosing Party to allow the Disclosing Party to assert whatever limitations, exclusions, or exemptions may be available to protect the Disclosing Party's interests.

5.3 Each Party acknowledges and agrees that its representatives involved in the collaboration will adhere to the confidentiality obligations set forth herein, as they apply to such party.

5.4 Upon completion of the collaboration, or upon the Disclosing Party's written request, which may be made up to six month after the termination of this Agreement, the Receiving Party shall return to the Disclosing Party or destroy (as directed by the Disclosing Party) all copies of the Disclosing Party's Confidential Information.

## 6 Ownership/Intellectual Property

6.1 All Results generated by Parties together should be jointly owned. When, in the course of carrying out work on the Research Project, joint Foreground is generated by the Parties, and when the contributions of the Parties to such Foreground are such that under applicable law it is not possible to separate them for the purpose of applying for, obtaining and/or maintaining and/or owning the relevant patent protection or any other intellectual property right (IPR) protecting or available to protect such Foreground, the Parties agree that all patents and other registered IPRs issued thereon, and any other IPRs protecting such Foreground, shall be jointly owned by the Parties in proportion to their intellectual contribution. The Party contributing the most important part shall be in charge of the filling of intellectual property rights applications (the Responsible Party).

6.2 Irrevocable access rights to Results for internal research activities, excluding any commercial use, are granted to the other Party on a royalty-free basis.

6.3 HMGU and UL/LCSB shall bear the reasonable patenting costs including attorney fees incurred for filing, prosecution, issuance, and maintenance of the IPR according to the share in the revenues as defined in Section 6.8. The Responsible Party shall keep the other party fully informed as of the status (including without limitation providing the other party with the information relevant to such prosecution and maintenance, and copies of all filings, submissions and correspondence with patent offices) and shall give reasonable consideration to suggestions made by the other Party in respect of the prosecution strategy.

6.4 If either Party does not want to participate in filing a patent application under the joint IPR, this Party will notify the other Party ("Filing Party") thereof in writing. If no written notice has been received by the Filing Party sixty (60) days after request by the Filing Party, the Filing Party may decide to file the patent application at its own discretion. The non-filing Party shall provide the filing Party with the reasonable support for a possible application for a patent (signatures, documents, etc.).

6.5 Either Party may decide to abandon ("Abandoning Party") the joint IPR within any national jurisdiction upon sixty (60) days written notice to the other Party ("Continuing Party") and in no event, no less than sixty (60) days prior to any potential loss of rights in any joint IPR. The Continuing Party shall be solely entitled to file a patent application on the Invention in its own name and at its own expense. The Abandoning Party shall

provide the Filing Party with the reasonable support for a possible application for a patent (signatures, documents, etc.).

6.6 The Continuing Party may elect to request an assignment of the joint IPR by the Abandoning Party and any licenses issued for the joint IPR. The Continuing Party shall on its own decision advice the Abandoning Party in writing within thirty (30) days after receipt of a notice of abandonment. The Abandoning Party shall do all things necessary to transfer all files related to such rights to the Continuing Party and shall convey the joint IPR to Continuing Party at the Continuing Party's expense. Upon perfection of assignments, the Continuing Party may thereafter separately license the Inventions, without accounting to the Abandoning Party.

6.7 The non-filing or Abandoning Party shall undertake all steps necessary to effectuate an assignment/transfer of the inventions to the Filing or Continuing Party. If this is necessary for an assignment/transfer to Filing or Continuing Party according to the respective national laws the non-filing or Abandoning Party shall claim all rights to any inventions arising in connection with this Agreement in time and unlimited. The Filing Party shall compensate these employees in accordance to the German Employee Invention Act or otherwise for the non-filing or Abandoning Party applicable national law and hold the non-filing or Abandoning Party harmless against such claims. Accordingly, the non-filing or Abandoning Party shall ensure the support of the inventors participating in the Research Project, if necessary.

6.8 The share of each party in the revenue generated by the Invention shall be split in accordance to the ration of 50% UL/LCSB and 50% HMGU. Irrespective of ownership in an Invention, the Parties grant each other an irrevocable, non-exclusive and royalty-free license to use any Invention for research purposes only, excluding all commercial uses.

6.9 The Parties shall promptly report to each other in writing each Invention and/or IPR resulting from the Research Project conducted under this Agreement that is reported to them by their respective employees. Each Party shall report all Inventions and IPR to the other Party in sufficient detail to determine inventorship and/or authorship. Such reports shall be treated as Confidential Information.

## 7 Publications

7.1 The Parties will publish jointly the Results related to the Research Projects. The publication shall be prepared together and authorship should be organized according to the contribution of work and be solved in a good faith.

7.2 The Parties agree that any publication relating to the analysis shall not interfere with IP protection. Therefore, any publication shall not contain non-public information which may itself be patentable or proprietary information of a Party. When, after release of the joined publication mentioned in Section 6.1, a Party intends to make its own publication, such Party shall forward the manuscript to the other Party. The other party may object when it can reasonably demonstrate that the manuscript contains (i) proprietary information of that Party or (ii) patentable Results of the analysis. Any right to object based on (ii) shall be valid for the time necessary to file a patent application

but shall in no event exceed a period three months after submission of the respective manuscript.

## 8 Transfer of Materials

8.1 In the framework of this Agreement, Parties may transfer Material to one another, which transfer shall be subject to the conditions of this Agreement. Parties shall list such Material in Annex B to this Agreement and shall keep it up to date after each transfer of Material.

8.2 The supplying Party shall remain the sole owner of the Material.

8.3 The receiving Party shall use the Material solely in the framework of the Research Project and shall in no case seek or have any person, institution or corporate body seeking any commercial use of the Material or any other material that could not have been made but for the Material, unless explicitly agreed upon in this Research Project, the related Agreements or any amendment thereto.

8.4 The receiving Party shall not transmit by any means whatsoever all or part of the Material to any third party without the prior and written consent of the supplying Party.

## 9 Access Rights

9.1 Access to Background and Foreground

9.1.1 All requests for Access Rights shall be made in writing.

9.1.2 The granting of Access Rights shall be made conditional on the acceptance of specific conditions aimed at ensuring that these rights will be used only for the intended purpose and that appropriate confidentiality obligations are in place.

9.1.3 Without prejudice to their obligations regarding the granting of Access Rights, the Parties shall inform each other as soon as possible of any limitation to the granting of access rights to Background, or of any other restriction which might substantially affect the granting of Access Rights.

9.1.4 The termination of the participation of a Party shall in no way affect the obligation of that Party to grant Access Rights to the remaining Party.

9.1.5 Unless otherwise agreed by the owner of the Foreground or Background, Access Rights shall confer no entitlement to grant sub-licences.

9.1.6 Without prejudice to paragraph 9.1.7, any agreement providing Access Rights to Foreground or Background to third parties must ensure that potential Access Rights for the other Party are maintained.

9.1.7 Exclusive licences for specific Foreground or Background may be granted subject to written confirmation by the other Party that they waive their access rights thereto.

9.2 Access rights for implementation

9.2.1 The right to use Foreground to carry out the first Research Project as described in the Work plan is granted upon signature to the extend it is Needed to carry out the

Research Project. All other Access Rights hereunder for further research projects shall be granted with an update of the Work Plan.

9.2.2 The right to use Background to carry out the first Research Project as described in the Work plan is granted upon signature to the extend it is Needed to carry out the Research Project. All other Access Rights hereunder for further research projects shall be granted with an update of the Work Plan.

9.3 Access rights for Use

9.3.1 The Parties shall enjoy Access Rights to Foreground, if it is Needed to Use their own Foreground. Such Access Rights shall be granted under fair and reasonable conditions for commercial Use, or shall be royalty-free for non-commercial, i.e. academic and scientific research.

9.3.2 The Parties shall enjoy Access Rights to Background, if it is Needed to Use their own Foreground provided that the Party concerned is entitled to grant them. Such Access Rights shall be granted under fair and reasonable conditions for commercial Use, or shall be royalty-free for non-commercial, i.e. academic and scientific research.

9.3.3 A request for Access Rights under paragraphs 9.1.1 or 9.1.2 may be made up to one year and six month after either of the following events:

a) the end of the Research Project; or

b) termination of participation by the owner of the Background or Foreground concerned.

**10 Warranties and Liability**

10.1 EACH PARTY MAKES NO WARRANTIES, EXPRESS OR IMPLIED, AS TO ANY MATTER WHATSOEVER, INCLUDING, WITHOUT LIMITATION, THE RESULTS OF THE RESEARCH PROJECT, ITS MATERIALS, OR ANY INVENTION, PROCESS OR PRODUCT, WHETHER TANGIBLE OR INTANGIBLE, CONCEIVED, DISCOVERED, OR DEVELOPED UNDER THIS AGREEMENT; OR THE OWNERSHIP, MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE OF ANY INVENTION OR PRODUCT MADE UNDER A RESEARCH PROJECT. NO PARTY SHALL BE LIABLE FOR ANY DIRECT, CONSEQUENTIAL, OR OTHER DAMAGES SUFFERED BY ANY OTHER PARTY, ANY LICENSEE, OR ANY OTHERS INCLUDING, BUT NOT LIMITED TO, DAMAGES ARISING FROM LOSS OF DATA OR TERMINATION OF THE RESEARCH PROJECT, OR FROM THE USE OF THE RESULTS OF THE RESEARCH PROJECT, OR ANY INVENTION OR PRODUCT MADE UNDER A RESEARCH PROJECT.

10.2 The Material and Results provided by either Party is understood to be experimental in nature and may have hazardous properties. Both Parties make no representations and extend no warranties of any kind, expressed or implied, as to merchantability of the services, Material and Results or fitness for a particular purpose, or that the use of the services, Material and Results will not infringe any patent, copyright, trademark, or other

proprietary rights of a third party. Any claims, statutory or contractual, based on legal or other defects of the data shall be excluded.

10.3 Both Parties shall use the Material and Results at their own risk. They hereby assume all and any liability for damages which may arise from its use of the services, Material and Results. Both Parties hereby hold each other, its officers and its researcher/s harmless for any loss, claim or demand which could be raised against them by any other Party, due to or arising from the use of the services, Material and Results, except to the extent harm or damage has been caused by the gross negligence or willful misconduct.

## 11 Compliance with law

11.1 Each Party shall use the data, Material and Results obtained from or provide by the other Party in compliance with all laws and regulations applicable to such information in their respective country.

11.2 Any clinical data that is transmitted between the Parties shall be anonymised. Each Party shall be responsible for complying with any data protection requirements it may be subject to.

## 12 Term and Termination

12.1 This Agreement shall enter into force on the date of the last signature. It will run for a period of five years and may be extended upon written agreement for any period to be determined between the Parties.

12.2 Each Party shall have the right to terminate this Agreement with 6 months' notice following an initial period of 3 years.

12.3 Each Party shall have the right to terminate this Agreement without notice following any breach by the other Party if not remedied in 30 days.

12.4 All provisions, which are designed to have effect after expiry or termination of this agreement, shall survive expiry or termination. Sections 4,5, and 6 shall extend for a period of five (5) years after expiry or termination of this Agreement.

## 13 Miscellaneous

13.1 If any provision of this Agreement should be or become invalid, the validity of the remaining provisions shall not be affected. The invalid provision shall be replaced by one which comes closest to the underlying scientific intent of the parties.

13.2 This document contains the entire Agreement of the Parties. There are no oral side agreements. The provisions of this Agreement cannot be changed, modified, amended or waived except by a written instrument signed by the Parties. This also applies to this form provision.

13.3 This Agreement shall be construed according to the laws of Luxembourg.. Any dispute arising from the interpretation and/or implementation of this Agreement, which cannot be settled amicably, shall be brought before a competent court of first instance in the city of Luxembourg.

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German Research Center for Environmental Health

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**Helmholtz Zentrum München**
**Deutsches Forschungszentrum für Gesundheit und Umwelt (GmbH)**

Neuherberg, _____

*ppa.*

PD Dr. Christian Langebartels
*Head of Program Planning and Management*

Neuherberg, 31.1.2014

*ppa.*

Gerolf Schmidl
*Head of Financial Department*

(*Read and acknowledged*)

Prof. Dr. Wolfgang Wurst

Director IDG

**University of Luxembourg**

| | | |
|---|---|---|
| Name | **Prof. Dr. Rolf Tarrach** | **Prof. Dr. Rudi Balling** |
| Title | **President University of Luxembourg** | **Director LCSB** |
| Date | 12 DEC. 2013 | 18 DEC. 2013 |
| Signature | | |

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## ANNEX A (RESEARCH PROJECT)

## PROJECT: FUNCTIONAL ANALYSIS OF NEW PD CANDIDATE GENES

ANNEX to the collaboration agreement
betweenLCSB and HMGU Munich

Project on development and analysis of mouse models for Parkinson's disease

LCSB and HMGU Munich will collaborate according to the associated collaboration framework agreement. LCSB will cooperate with the team of Wolfgang Wurst at the HMGU to validate the impact of new PD candidate genes on neurodegenerative processes and associated comorbidities in mouse models.

LCSB will benefit from the expertise and infrastructure of HMGU concerning development, introduction of genetic and environmental perturbations, and extensive phenotyping capabilities of mouse models. HMGU will benefit from the expertise and infrastructure of LCSB in bioinformatics, computational biology and neuropathology. The duration of the collaboration will be 5 years, with the option of terminating the collaboration after 3 years. The details of the scientific cooperation are the following:

Scope

- Based on experimental, computation or prior knowledge, LCSB and HMGU will aim to develop new mouse models of Parkinson's disease to identify and validate new strategies for the early diagnosis, stratification or therapies of PD. The collaboration will focus on the analysis of specific PD-related candidate genes, their genetic or environmental perturbation in mice (i.e. TALEN technology) and a detailed neurological and behavioural phenotyping of the corresponding mouse models at different time points and if appropriate comprehensive phenotyping via the German Mouse Clinic (GMC); the candidate genes and the analysis plan will be jointly agreed upon by LCSB and HMGU
- The collaboration aims to bridge and complement current LCSB and HMGU experimental research activities; LCSB will contribute and complement to the findings generated in Munich with in vitro characterization of mouse primary & and iPS cells high-content cellular imaging and non-targeted metabolomics for a detailed analysis of early onset pathological hallmarks of PD-associated neurodegeneration, i.e. mitochondrial and synaptic dysfunction or the failure of protein degradation systems. HMGU will contribute and complement to the findings generated at LCSB with additional experimental activities on primary mouse cells and tissue like targeted metabolomics or detailed molecular, neurological and behavioural phenotyping including the GMC.
- Bioinformatics and computational biology expertise of LCSB and HMGU will support the processes of experimental design, data analysis and integration of the obtained

experimental results with other PD models developed at LCSB: yeast, zebrafish and iPS cell lines.

Activities

- LCSB will employ a senior postdoctoral researcher (senior fellow) to coordinate and drive the joint research project and support LCSB in the establishment of it´s own mouse facility. The senior fellow will spend time at LCSB and at HMGU according to the need of the project.
- LCSB will employ a technician to support the senior fellow. Similar to the senior fellow, the technician will spend time at LCSB and at HMGU according to the need of the project.
- LCSB will provide to HMGU a collaboration-dedicated budget (see detals later) to support the research of PD candidate genes in mouse models at HMGU
- HMGU will provide mouse and lab space for the collaboration-dedicated research - molecular genetic laboratory, cell cultre, histopahology, metabolic analysis, animal housing
- HMGU will aim at performing at least 2 mouse models with PD candidate genes knockout/mutations
- HMGU will provide detailed phenotyping of mouse models and perform primary behavioural motor control phenotyping (rotarod, grip strength, open field vertical pole, ladder and potentially olfaction) if necessary also GMC analysis
- HMGU will provide office and lab space for visiting LCSB staff (senior fellow and technician)

**Budget**

- The salary of the senior fellow and the technician is covered by the LCSB
- In addition a collaboration-dedicated budget of 100.000 € of yearly support is provided to HMGU by the LCSB. This will cover mouse costs as well as the research activities of the project.
- The accommodation of the senior fellow and the technician in Munich will be covered by LCSB

## ANNEX B

## Transferred Material

- Mice
- Mouse tissues
- Cell lines (BV-2, ESCs, NSCs, etc.)