

# Systems Biomedicine in Luxembourg



# FROM AGRICULTURE TO STEEL TO FINANCE TO HEALTH

**1890**



**1990**



**2010**



**2013**



# The National Vision of Personalized Medicine

From Financial Banks...



to Biobanks...



*Personalized  
Medicine  
Luxembourg*





# Building up Systems Biomedicine in Luxembourg

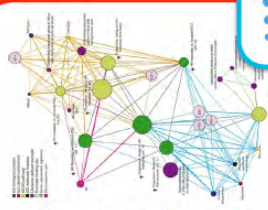
## The LCSB on the Belval Campus



### Experimental Biology



### Technology-Platforms



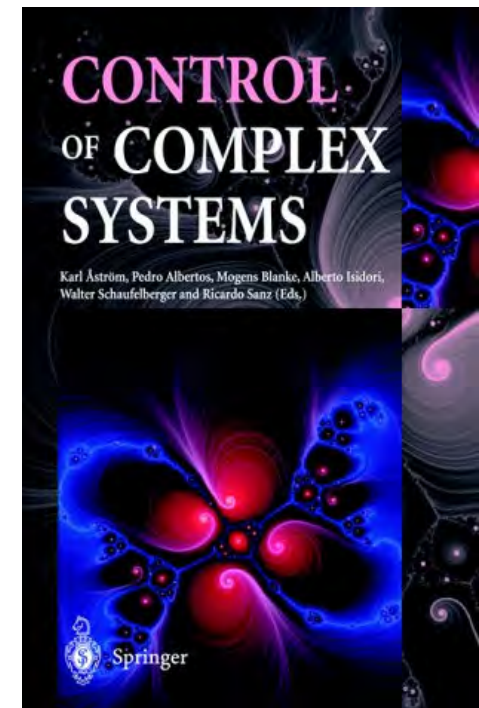
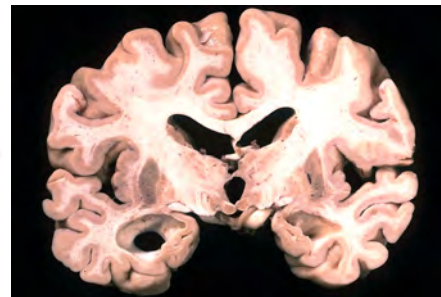
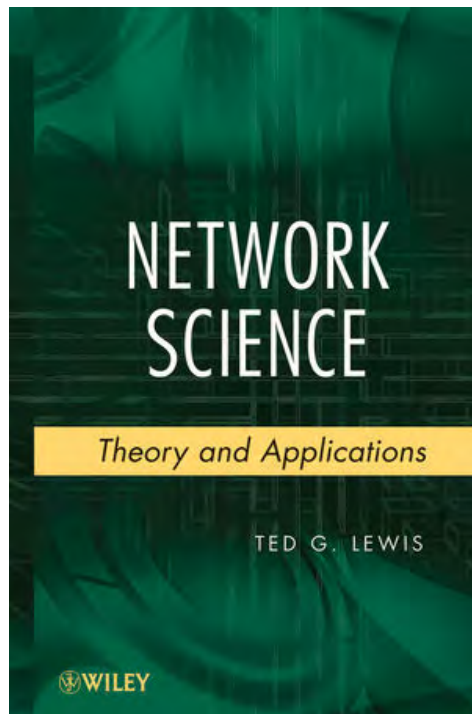
### Computational Biology



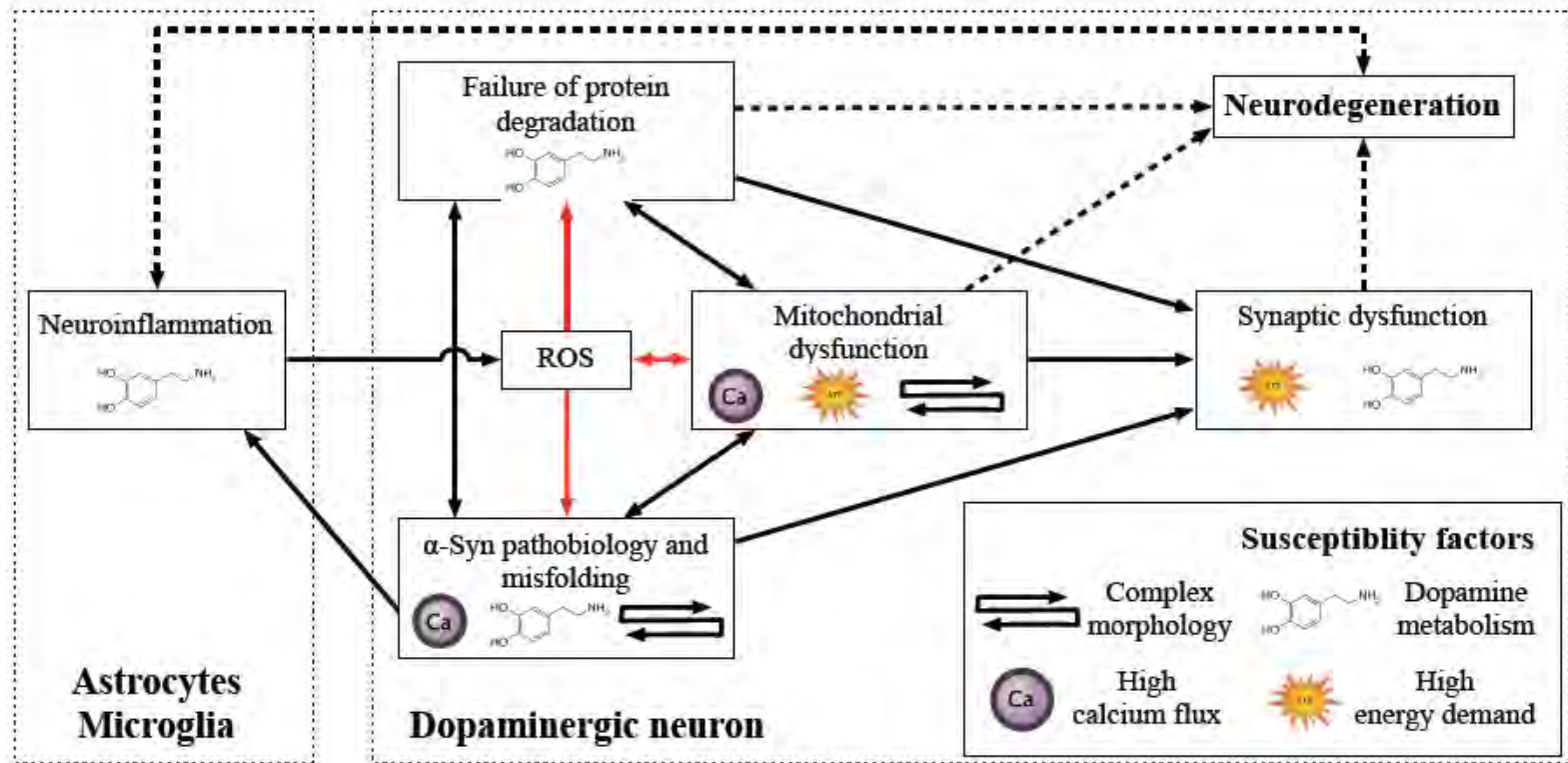
### Clinical Research

# A Focus on Neurodegenerative diseases

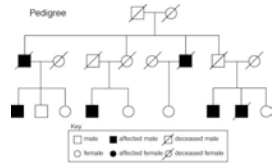
Alzheimer  
**Parkinson**  
Huntington  
ALS  
Multiple Sclerosis



# Pathways implicated in Parkinson disease



# From cohorts to animal models – and back again



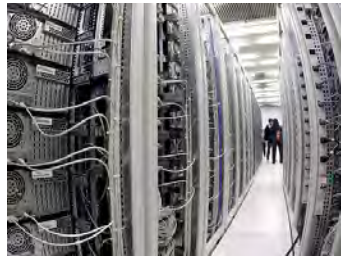
**Familial Studies**



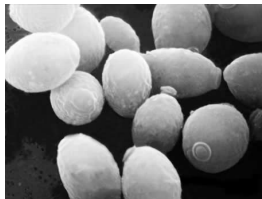
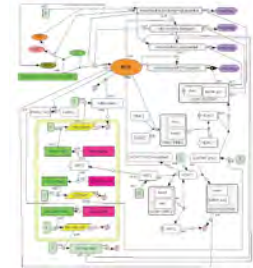
**Crosssectional Cohorts**



**Longitudinal Cohorts**



## **Pathway and Network Analysis Computational Models**



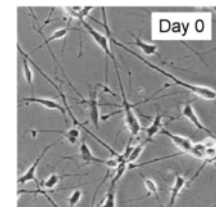
**Yeast**



**Zebrafish**



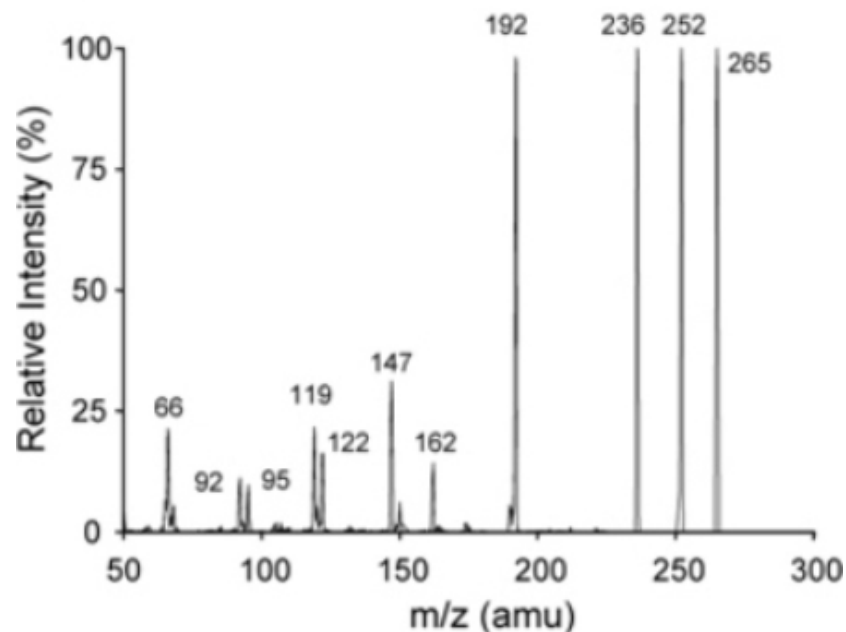
**Mouse**



**iPS**



# Metabolomics and metabolic reconstruction



88

*Current Biotechnology*, 2012, 1, 88-97

## The Application of Stable Isotope Assisted Metabolomics in Biomedicine

André Wegner<sup>#</sup>, Thekla Cordes<sup>#</sup>, Alessandro Michelucci and Karsten Hiller<sup>\*</sup>

*University of Luxembourg, Luxembourg Centre for Systems Biomedicine, 7 Avenue des Hauts-Fourneaux, L-4362 Esch-Belval, Luxembourg*



**Karsten Hiller**



**PNAS**

### Immune-responsive gene 1 protein links metabolism to immunity by catalyzing itaconic acid production

Alessandro Michelucci<sup>a,1</sup>, Thekla Cordes<sup>a,1</sup>, Jenny Ghelfi<sup>a</sup>, Arnaud Pailot<sup>a</sup>, Norbert Reiling<sup>b</sup>, Oliver Goldmann<sup>c</sup>, Tina Binz<sup>d</sup>, André Wegner<sup>e</sup>, Aravind Tallam<sup>e</sup>, Antonio Rausell<sup>e</sup>, Manuel Buttini<sup>e</sup>, Carole L. Linster<sup>e</sup>, Eva Medina<sup>e</sup>, Rudi Balling<sup>e</sup>, and Karsten Hiller<sup>a,2</sup>

<sup>a</sup>Luxembourg Centre for Systems Biomedicine, University of Luxembourg, L-4362 Esch-Belval, Luxembourg; <sup>b</sup>Division of Microbial Interface Biology, Research Center Borstel, Leibniz Center for Medicine and Biosciences, 23845 Borstel, Germany; and <sup>c</sup>Infection Immunology Research Group, Helmholtz Centre for Infection Research, 38124 Braunschweig, Germany

Edited by Philippa Marrack, Howard Hughes Medical Institute, National Jewish Health, Denver, CO, and approved March 27, 2013 (received for review October 24, 2012)





# Functional validation and drug screening in Zebrafish



Alex Crawford



- Gain and loss of function mutants
- Live imaging

ACS Chemical  
Neuroscience

Research Article  
pubs.acs.org/chemneuro

## Tanshinone IIA Exhibits Anticonvulsant Activity in Zebrafish and Mouse Seizure Models

Olivia Erin Buenafe,<sup>1</sup> Adriana Orellana-Paucar,<sup>1,3</sup> Jan Maes,<sup>3</sup> Haq Huang,<sup>3</sup> Xuhui Ying,<sup>1,4</sup> Wim De Borggraeve,<sup>4</sup> Alexander D. Crawford,<sup>1,11</sup> Walter Luyten,<sup>5</sup> Camila V. Esguerra,<sup>6,7</sup> and Peter de Witte<sup>6,7</sup>

OPEN ACCESS Freely available online

PLOS ONE

## Optimization and Pharmacological Validation of a Leukocyte Migration Assay in Zebrafish Larvae for the Rapid *In Vivo* Bioactivity Analysis of Anti-Inflammatory Secondary Metabolites

Maria Lorena Cordero-Maldonado<sup>1,2,4\*</sup>, Dany Siverio-Mota<sup>1,3\*</sup>, Liliana Vicet-Muro<sup>1,3</sup>, Isabel Maria Wilches-Arizabala<sup>2</sup>, Camila V. Esguerra<sup>1</sup>, Peter A. M. de Witte<sup>1</sup>, Alexander D. Crawford<sup>1,4\*</sup>

<sup>1</sup>Laboratory for Molecular Biodiscovery, Department of Pharmaceutical and Pharmacological Sciences, University of Leuven, Leuven, Belgium, <sup>2</sup>Faculty of Chemical Sciences, School of Biochemistry and Pharmacy, University of Cuenca, Cuenca, Ecuador, <sup>3</sup>Department of Pharmacy, Faculty of Chemistry-Pharmacy, Central University "Marta Abreu" of Las Villas, Santa Clara, Cuba, <sup>4</sup>Luxembourg Centre for Systems Biomedicine, University of Luxembourg, Esch-sur-Alzette, Luxembourg



REPORT

## De Novo Loss-of-Function Mutations in *CHD2* Cause a Fever-Sensitive Myoclonic Epileptic Encephalopathy Sharing Features with Dravet Syndrome

Arvid Suls,<sup>1,2,38</sup> Johanna A. Jaehn,<sup>3,38</sup> Angela Kecskés,<sup>4,38</sup> Yvonne Weber,<sup>5,38</sup> Sarah Weckhuysen,<sup>1,2</sup> Dana C. Craiu,<sup>6,7</sup> Aleksandra Siekierska,<sup>4</sup> Tania Djémié,<sup>1,2</sup> Tatiana Afrikanova,<sup>4</sup> Padhraig Gormley,<sup>8</sup> Sarah von Spiczak,<sup>3</sup> Gerhard Kluger,<sup>9</sup> Catrinel M. Iliescu,<sup>6,7</sup> Tiina Talvik,<sup>10,11</sup> Inga Talvik,<sup>10,11</sup> Cihan Meral,<sup>12</sup> Hande S. Caglayan,<sup>13</sup> Beatriz G. Giraldez,<sup>14</sup> José Serratos,<sup>14</sup> Johannes R. Lemke,<sup>15</sup> Dorota Hoffman-Zacharska,<sup>16</sup> Elzbieta Szczepanik,<sup>17</sup> Nina Barišic,<sup>18</sup> Vladimir Komarek,<sup>19</sup> Helle Hjalgrim,<sup>20,21</sup> Rikke S. Møller,<sup>20</sup> Tarja Linnankivi,<sup>22</sup> Petia Dimova,<sup>23</sup> Pasquale Striano,<sup>24</sup> Federico Zara,<sup>25</sup> Carla Marini,<sup>26</sup> Renzo Guerrini,<sup>26</sup> Christel Depienne,<sup>27,28,30</sup> Stéphanie Baulac,<sup>27,28,29</sup> Gregor Kuhlenbäumer,<sup>31</sup> Alexander D. Crawford,<sup>4,32</sup> Anna-Elina Lehesjoki,<sup>33,34,35</sup> Peter A.M. de Witte,<sup>4</sup> Aarno Palotie,<sup>8,36,37</sup> Holger Lerche,<sup>5</sup> Camila V. Esguerra,<sup>4,39</sup> Peter De Jonghe,<sup>1,2,39,\*</sup> Ingo Helbig,<sup>4,39</sup> and the EuroEPINOMICS RES Consortium

# iPS-derived neural stem cells & dopaminergic neurons



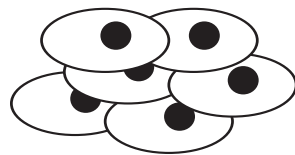
**Jens Schwamborn**

STEM CELLS AND DEVELOPMENT  
Volume 22, Number 18, 2013  
© Mary Ann Liebert, Inc.  
DOI: 10.1089/scd.2013.0163

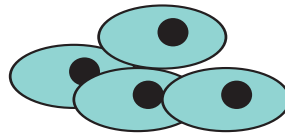
ORIGINAL RESEARCH REPORT

## The Parkinson's Disease-Associated LRRK2 Mutation R1441G Inhibits Neuronal Differentiation of Neural Stem Cells

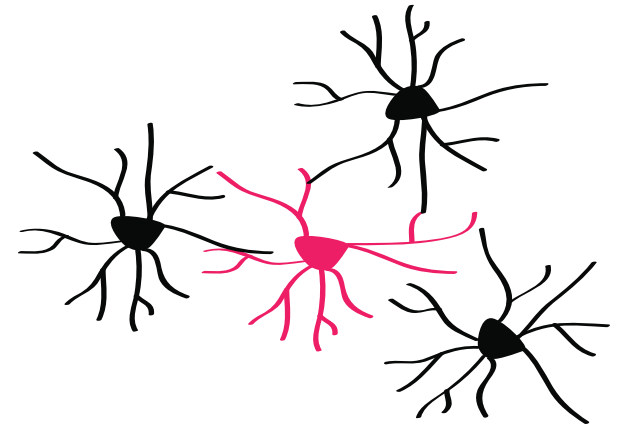
Lamia'a Bahnassawy,<sup>1-3</sup> Sarah Nicklas,<sup>1-3</sup> Thomas Palm,<sup>1,2</sup> Ingeborg Menzl,<sup>1,2</sup> Fabian Birzele,<sup>4</sup> Frank Gillardon,<sup>4</sup> and Jens C. Schwamborn<sup>1-3</sup>



**Pluripotent stem cells**

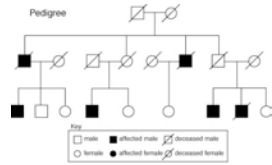


**Neural stem cells**



**Dopaminergic neurons**

# From cohorts to animal models – and back again



**Familial Studies**



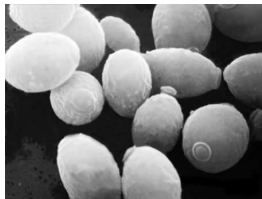
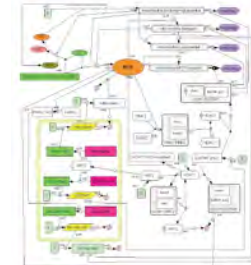
**Crosssectional Cohorts**



**Longitudinal Cohorts**



## **Pathway and Network Analysis Computational Models**



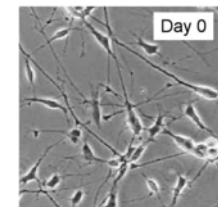
**Yeast**



**Zebrafish**



**Mouse**



**iPS**



Systems biology

Advance Access publication November 28, 2011

## PathVar: analysis of gene and protein expression variance in cellular pathways using microarray data

Enrico Glaab<sup>1,2,\*</sup> and Reinhard Schneider<sup>1,2</sup>

<sup>1</sup>Structural and Computational Biology Unit, EMBL, Meyerhofstrasse 1, 69117, Heidelberg and <sup>2</sup>Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg, Luxembourg, Germany

Associate Editor: Martin Bishop



Enrico Glaab

## EnrichNet: network-based gene set enrichment analysis

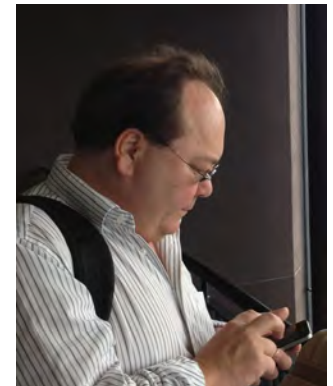
Enrico Glaab<sup>1,\*</sup>, Anaïs Baudot<sup>2,\*</sup>, Natalio Krasnogor<sup>3,†</sup>, Reinhard Schneider<sup>1,†</sup> and Alfonso Valencia<sup>4,†</sup>

<sup>1</sup>Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg, L-4362 Esch-sur-Alzette, Luxembourg

<sup>2</sup>Luminy Institute of Mathematics (IML), Université d'Aix-Marseille, 13288 Marseilles, France

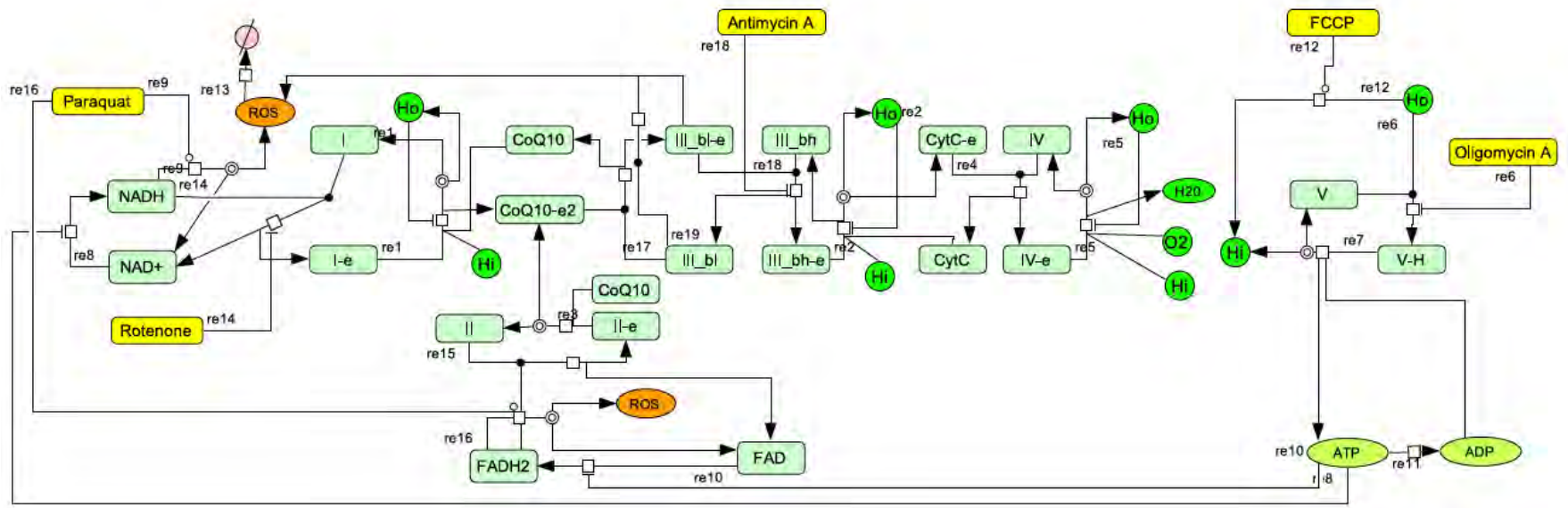
<sup>3</sup>Interdisciplinary Computing and Complex Systems (ICOS) Research Group, University of Nottingham, NG8 1BB Nottingham, UK

<sup>4</sup>Structural Biology and Biocomputing Program, CNIO, E-28029 Madrid, Spain



Reinhard Schneider

# Kinetic models of mitochondrial dysfunction



# Constraint based Modeling

\_computational  
BIOLOGY

RESOURCE

NATURE BIOTECHNOLOGY VOLUME 31 NUMBER 5 MAY 2013

## A community-driven global reconstruction of human metabolism



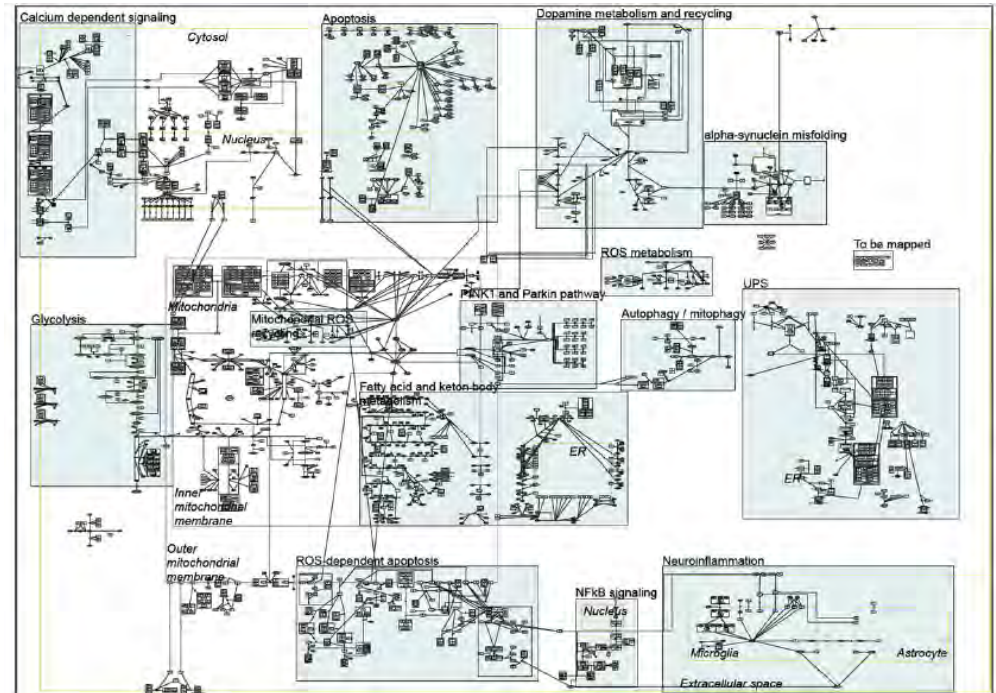
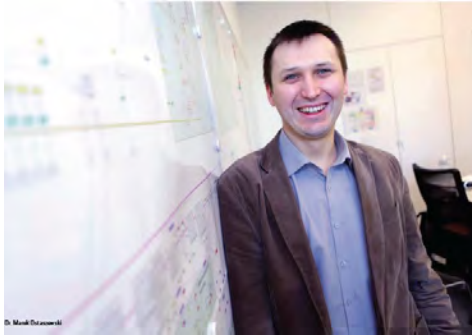
Ines Thiele

Ines Thiele<sup>1,4,37</sup>, Neil Swainston<sup>3,4,37</sup>, Ronan M T Fleming<sup>1,5</sup>, Andreas Hoppe<sup>6</sup>, Swagatika Sahoo<sup>1</sup>, Maïke K Aurich<sup>1</sup>, Hulda Haraldsdottir<sup>1</sup>, Monica L Mo<sup>7</sup>, Ottar Rolfsson<sup>1</sup>, Miranda D Stobbe<sup>8,9</sup>, Stefan G Thorleifsson<sup>1</sup>, Rasmus Agren<sup>10</sup>, Christian Bölling<sup>6</sup>, Sergio Bordel<sup>10</sup>, Arvind K Chavali<sup>11</sup>, Paul Dobson<sup>12</sup>, Warwick B Dunn<sup>3,13</sup>, Lukas Endler<sup>14</sup>, David Hala<sup>15</sup>, Michael Hucka<sup>16</sup>, Duncan Hull<sup>4</sup>, Daniel Jameson<sup>3,4</sup>, Neema Jamshidi<sup>7</sup>, Jon J Jonsson<sup>5</sup>, Nick Judy<sup>17</sup>, Sarah Keating<sup>17</sup>, Intawat Nookaew<sup>10</sup>, Nicolas Le Novère<sup>17,18</sup>, Naglis Malys<sup>3,19,20</sup>, Alexander Mazein<sup>21</sup>, Jason A Papin<sup>11</sup>, Nathan D Price<sup>22</sup>, Evgeni Selkov, Sr<sup>23</sup>, Martin I Sigurdsson<sup>1</sup>, Evangelos Simeonidis<sup>22,24</sup>, Nikolaus Sonnenschein<sup>25</sup>, Kieran Smallbone<sup>3,26</sup>, Anatoly Sorokin<sup>21,27</sup>, Johannes H G M van Beek<sup>28-30</sup>, Dieter Weichart<sup>3,31</sup>, Igor Goryanin<sup>21,32</sup>, Jens Nielsen<sup>10</sup>, Hans V Westerhoff<sup>3,28,33,34</sup>, Douglas B Kell<sup>3,35</sup>, Pedro Mendes<sup>3,4,36</sup> & Bernhard Ø Palsson<sup>1,7</sup>



# A community driven Parkinson disease map

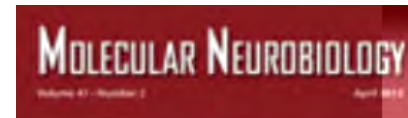
[http://minerva.uni.lu/pd\\_map/](http://minerva.uni.lu/pd_map/)



- Literature and expertise-based curation
- Map annotation
- Network analysis
- Text mining-based map enrichment
- Integration of sequencing data with map

## Integrating Pathways of Parkinson's Disease in a Molecular Interaction Map

Kazuhiro A. Fujita • Marek Ostaszewski • Yukiko Matsuoka • Samik Ghosh • Enrico Glaab • Christophe Trefois • Isaac Crespo • Thanneer M. Perumal • Wiktor Jurkowski • Paul M. A. Antony • Nico Diederich • Manuel Buttini • Akihiko Kodama • Venkata P. Satagopam • Serge Eifes • Antonio del Sol • Reinhard Schneider • Hiroaki Kitano • Rudi Balling



# LCSB European Grants



**Total Grants by LCSB  
2009-2013: > 20 Mio. €**

- eTRIKS (IMI)** - European Translational and Knowledge Services
- Aetionomy (IMI)** - Mechanisms based Aetiology of Neurodegenerative Diseases
- BIOMARK-AD (JPND)** - Alzheimer and Parkinson Biomarkers
- Courage-PD (JPND)** - Comprehensive unbiased risk factor assessment for genetics and environment in PD
- CoGIE (ESF)** - Consortium on the Genetics of Idiopathic Epilepsy
- EpiPGX (EU-7.FW)** - Epilepsy Pharmacogenomics
- CaSym (EU-7. FW)** - Concerted Action in Systems Medicine
- BioCog (EU-7. FW)** - Biomarker Development for Postoperative Cognitive Impairment in the Elderly

# In preparation: A National Centre of Excellence in Research



**Duration: 8 + 4 years**  
**Funding: 16 + 8 Mio \$**



## National Centre of Excellence in Research

*on the topic of*

### Early Diagnosis and Stratification of Parkinson's Disease

*coordinated by*

Professor Rudi Balling,  
Luxembourg Centre for Systems Biomedicine.

*Submitted on behalf of the institutions*

University of Luxembourg,  
Centre Hospitalier de Luxembourg,  
Centre de Recherche Public de la Santé,  
Integrated BioBank of Luxembourg,

*with the partner institutions*

Paracelsus-Elena-Klinik, Kassel,  
Philipps-Universität Marburg,  
Ruhr-Universität Bochum,  
Universitätsklinikum Tübingen.





# LCSB Research Groups

**Experimental Biology**  
*Rudí Balling*



**Molecular Systems  
Physiology**  
*Ines Thiele*



**Developmental and  
Cellular Biology**  
*Jens Schwamborn*



**Eco-Systems Biology**  
*Paul Wilmes*



**Systems  
Biochemistry**  
*Ronan Fleming*



**Chemical Biology**  
*Alex Crawford*



**Machine Learning**  
*Nikos Vlassis*



**Enzymology and  
Metabolism**  
*Carol Linster*



**Bioinformatics  
Core**  
*Reinhard Schneider*



**Metabolomics**  
*Karsten Hiller*



**Computational  
Biology**  
*Antonio del Sol*



**Medical Translation**  
*Jochen Schneider*

