

SCHOOL OF PHARMACEUTICAL SCIENCES
GENEVA - LAUSANNE

ANNUAL REPORT 2012



UNIVERSITÉ
DE GENÈVE

Ecole de Pharmacie
EPGL
Genève – Lausanne

Unil

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ABBREVIATIONS

<i>PO</i>	<i>Professeur ordinaire</i>
<i>PAS</i>	<i>Professeur associé</i>
<i>PA</i>	<i>Professeur assistant</i>
<i>PT</i>	<i>Professeur titulaire</i>
<i>PI</i>	<i>Professeur invité</i>
<i>PD</i>	<i>Privat docent</i>
<i>MER</i>	<i>Maître d'enseignement et de recherche</i>
<i>CS</i>	<i>Collaborateur scientifique</i>
<i>CC</i>	<i>Chargé de cours</i>
<i>CE</i>	<i>Chargé d'enseignement</i>

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Dr Philippe CHRISTEN, MER

PHARMACOLOGY

Prof Urs RUEGG, PO, (until 31.7.2012)

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Mayank SINGHAL
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Henri THOOS
Simone VIGNOLA
Kyoko WATANABE
Maria Luiza ZERAIK

BUDGET

BUDGET 2012

*STAFF SALARY ¹	11'858'909.--	(TABLEAU 1)
FONCTIONNEMENT BUDGET SECTION	1'249'497.--	(TABLEAU 2)
TOTAL BUDGET SALARY AND FUNCTIONMENT	13'108'406.--	1
FACULTY INVESTMENT	303'394.--	
SECTION INVESTMENT	288'200.--	
TOTAL INVESTMENT FUND	591'594.--	(TABLEAU 3)
SWISS NATIONAL SCIENCES FOUNDATION	1'860'108.--	
OTHERS FUNDS	3'006'693.--	
TOTAL EXTERNAL FUNDS	4'866'801.--	(TABLEAU 2)
TOTAL BUDGET EPGL	18'566'801.--	2

*STAFF 2012

NUMBER OF PEOPLE³ : 318

¹ Without social security contributions

² including:
 - contribution Etat VD CHF 5'093'014.—
 - subsidies "universitaire intercantonale" AIU CHF 1'450'000.—

³ Total number of people working at EPGL during 2012

TABLEAU 1

TOTAL BUDGET STAFF (9.87 Mio)

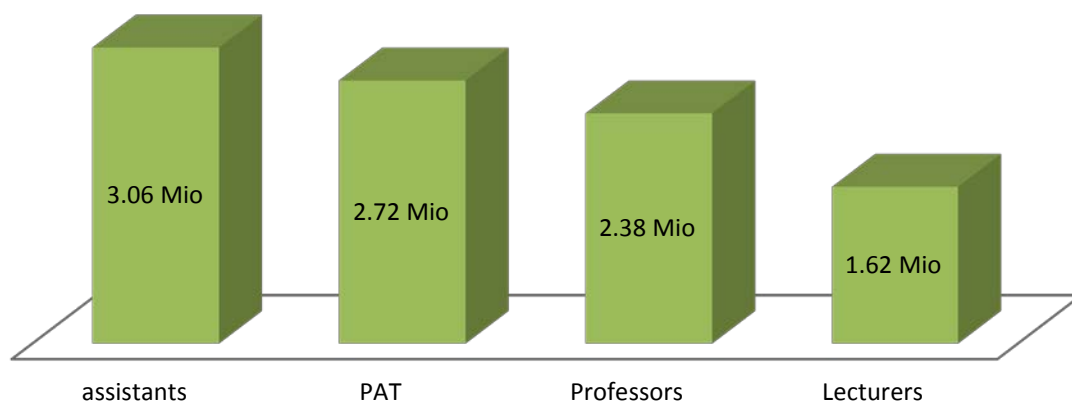


TABLEAU 2

TOTAL PUBLIC AND EXTERNAL FUNDS

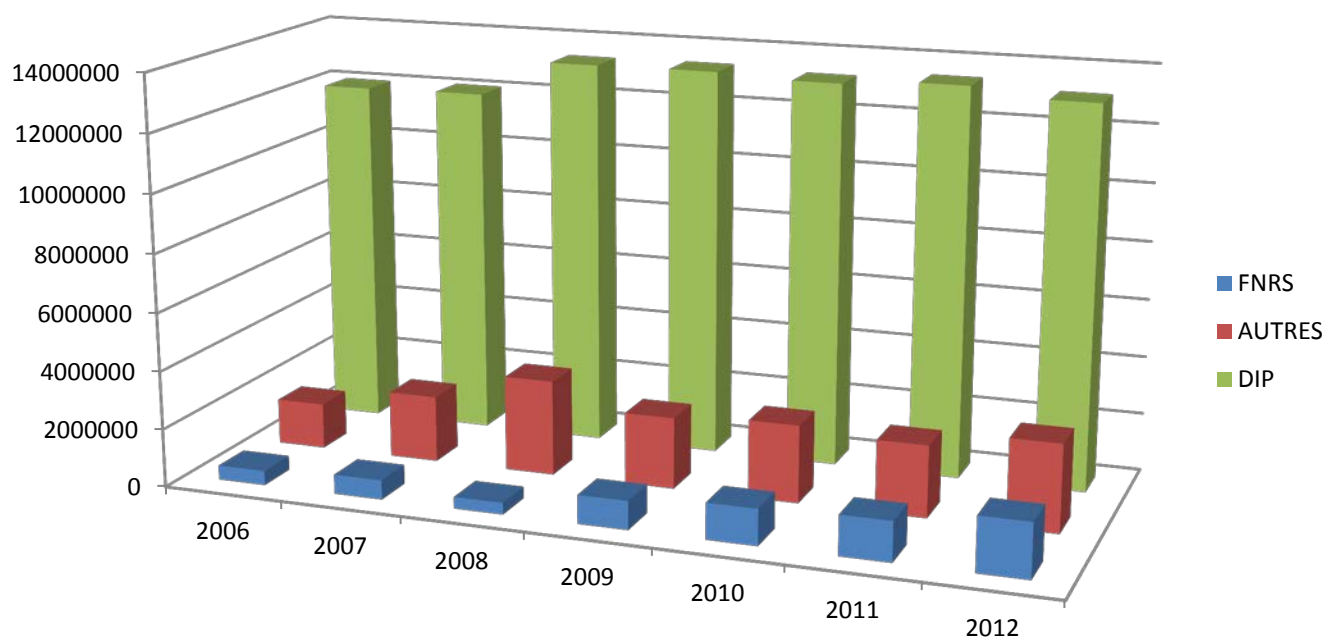
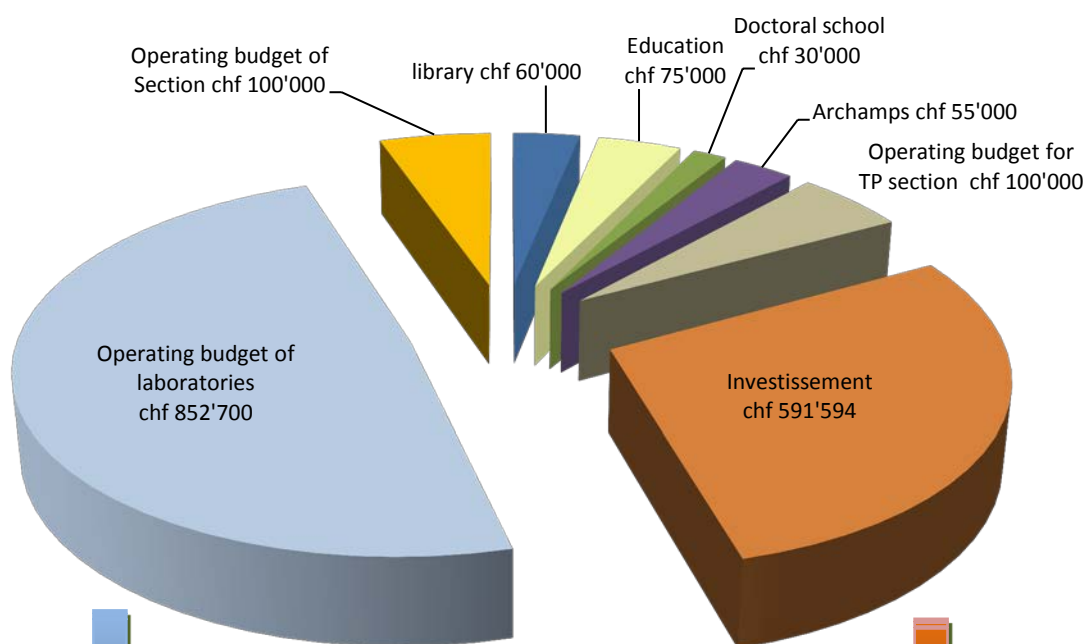
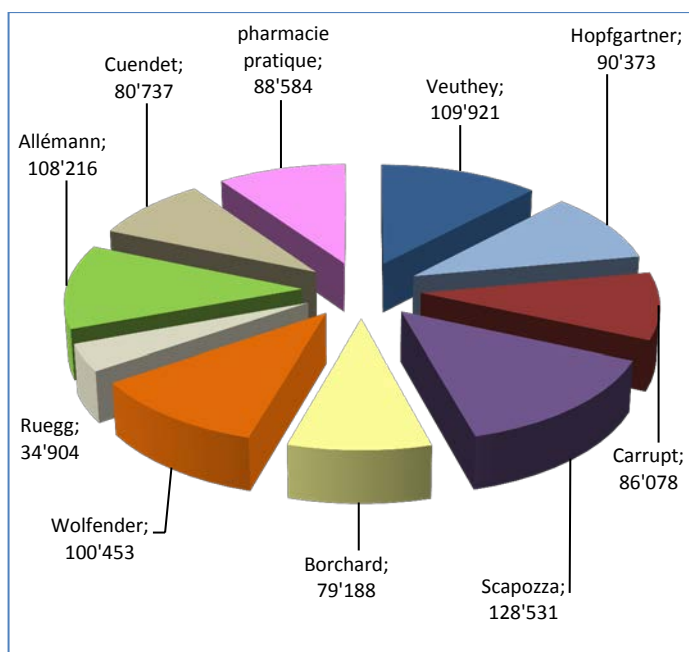
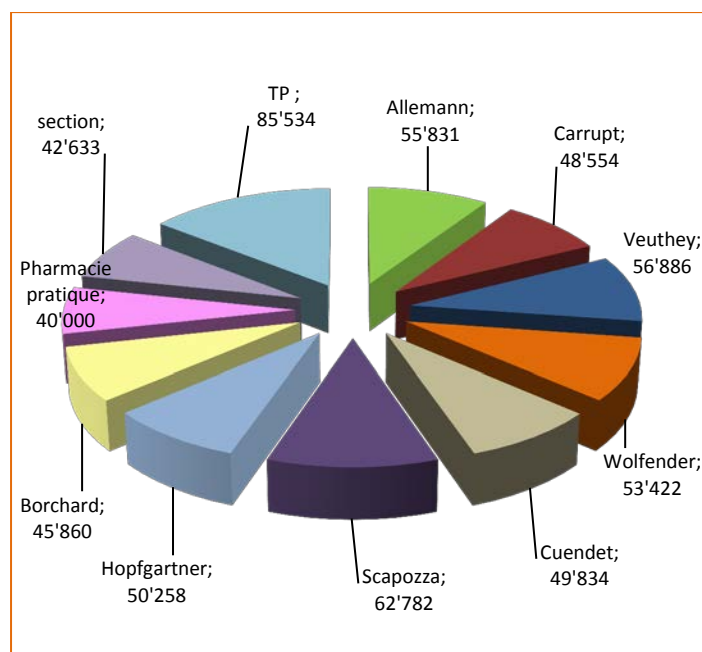


TABLEAU 3

OPERATIONAL BUDGET (1.24 Mio) AND INVESTISSEMENT (0.59 Mio)

ALLOCATION OPERATIONAL BUDGET
(CHF 852'700)ALLOCATION INVESTMENT BUDGET
(CHF 591'594)

2012 AT A GLANCE

Staff (headcount)	318
Students:	353
- Bachelor	241
- Master	108
- Master of advanced studies	4
Ph.D. students	126

Total budget CHF	18.5 Mio
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Patents	5
Publications with impact factor	145
Publications without impact factor	40
Presentations & posters	192
Books and chapters	28
Number of projects at FNRS and assimilated	44
Projects of collaboration with the industry	47
Ph.D. Thesis presented in 2012	14

BIOPHARMACEUTICALS



PROFESSOR

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SPECIFIC RESEARCH FIELDS

Biopharmaceutics describes the interaction of biological systems involved in absorption, distribution, metabolism, elimination, but also toxicity and immune recognition of drugs and their formulations and carrier systems. The adaptation of drug and drug carrier properties then is defined by observation of these biological systems. With an expertise in cell-based assay development, formulation of macromolecules, the design of polymeric drug carrier systems ("nanomedicines") and functionalized biopolymers, the group of Biopharmaceutics focuses on the fields of oncology and immunotherapy.

In the past year we have for instance established that certain ligands of the Toll-like receptor 2 (TLR2), a receptor involved in pathogen recognition and expressed in epithelial as well as immune cells, is actually involved in the regulation of tight junction permeability in bronchial epithelia. A unique mechanism, involving a specific protein kinase, was identified to be responsible for the decrease in epithelial permeability on ligation of TLR2. This observation may indeed be used in the development of new strategies for inflammatory respiratory diseases.

Another project, still in the domain of immune recognition, focuses on the combination of several ligands of different pathogen pattern recognition receptors (PRRs). These are located in the endosomal compartment (TLR) and in the cytosol (NOD2), and their simultaneous ligation, along with antigen presentation, is supposed to yield enhanced immune responses. In vitro, this strategy has already resulted in massive release of pro-inflammatory cytokines from both epithelial cell and macrophages. 2013 will see the proof-of-concept of this strategy to improve mucosal vaccination against *M. tuberculosis*.

The preparation and application of biopolymers is one of the main foci of the group. These polymers, as a technology platform, are applied to the formulation of macromolecular drugs as well as drugs of low solubility, and to interact with cells of different origin with the purpose to change their phenotype with regard to a therapeutical outcome. In 2012, the in vitro phase of a project focusing on the synthesis and testing of chitosan derivatives to improve skin cell adhesion, differentiation and proliferation in wound healing was successfully concluded. The chitosan derivative was further combined with a

compound of the extracellular matrix, chondroitin sulfate, to form self-assembling nanocarriers systems to be applied to slow-healing wounds. This project will be continued this year and will yield first in vivo results.

In the field of oncology, we investigate microspheres releasing an anti-angiogenic tyrosine kinase inhibitor, sunitinib, to treat hepatocarcinoma. The bioactivity of the released inhibitor was confirmed in cell culture models and in vivo on rabbit tumor model. Results were favourably received in clinical congresses.

In another project, nanocomposite-based injectable carriers for the treatment of spine metastases have been designed to combine thermal therapy and chemotherapy. In vitro studies on prostate cancer cells demonstrated the bioactivity of the eluted antitumoral agent. In situ gelling systems capable of bone reinforcement have been obtained, in view of osteolytic vertebra stabilization. Combined with its heat-generation ability, the carrier holds promises for bone metastases local treatment. This project, carried out in cooperation with EPFL (Prof. H. Hofmann) and Insel Hospital, Bern (Prof. G. Thalmann), is funded by the Swiss National Science Foundation.

In terms of protein formulation, we have shown the concept of “non-covalent PEGylation” to be a valid approach for certain excipients developed by us. An ongoing project, performed with the help of the Dept. of Pharmaceutical Biotechnology at the Hochschule Biberach (Germany; Prof. Hannemann and Dr. R. Handrick), is now aiming at increasing the strength of interaction between the PEG-exciipient and the protein. In order to be able work with a therapeutically relevant protein, we established facilities and developed an advanced method for the expression and purification of granulocyte-colony stimulating factor (G-CSF). A new project, started in September 2012, now focuses on the characterization of the interaction of protein drug aggregates with the immune system after subcutaneous injection. Again intending to work with a relevant protein, we established up- and downstream protocols for interferon-alpha, a cytokine used in the therapy of hepatitis and recurrent melanoma.

In the future, we will seek to increase our knowledge in the formulation of carrier systems and their interaction with biological systems to obtain rational concepts for the design of nanomedicines.

OUTSTANDING PUBLICATIONS

A. Hansson, O. Jordan, P. Rousselle, F. Falson and G. Borchard, The use of small synthetic RGD peptides in wound healing: Promotion of cell adhesion and migration in keratinocytes and fibroblasts. *International Journal of Pharmaceutics* 439, 73-80.

G. Borchard, B. Flühmann and S. Mühlebach. Nanoparticle iron medicinal products – Requirements for approval of intended copies of non-biological complex drugs (NBCD) and the importance of clinical comparative studies. *Regulatory Pharmacology and Toxicology* 64, 324-328.

PARTICULAR PROJECTS INITIATED

A project focusing on the use of superparamagnetic iron oxide particles (SPION) for diagnosis and therapy of cerebral ischemia was initiated with the Institute of Material Sciences (ICMAB) and the Neurovascular Research Laboratory at Vall d'Hebron Hospital (both in Barcelona, Spain).

CONGRESSES

Prof. G. Borchard was co-organizer of the 5th Swiss Pharma Science Day in Bern, Switzerland, in August 2012, and the Rencontre Pharmapeptides in Archamps (France) in November 2012.

1. PUBLICATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 6)

1.1	SCIENTIFIC PUBLICATIONS (WITH IMPACT FACTOR)	10
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2. POSTERS PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 7)

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3. ORAL PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012– PAGE 9)

3.1	CONGRESSES & SYMPOSIA	15
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4. THESIS PRESENTED

4.1. INTRA-MUROS THESIS

Hansson Annasara

Polymeric controlled release systems for RGD peptides delivery in skin repair.

University of Geneva-2012

Supervisor: Prof. G. Borchard

Co-Supervisor: Dr. O. Jordan

Vacher Gaelle

Oral thin films (OTF) for virosomal vaccines.

University of Geneva-2012-thesis n° 4515

Supervisor: Prof. G. Borchard

Co-Supervisor: Prof. R. Gurny

5. PUBLIC RESEARCH FUNDS (FNSR, NIH, CTI)

SWISS NATIONAL SCIENCE FOUNDATION

Locoregional treatment of prostate cancer metastases to bone using implant-mediated hyperthermia, SNF No. 31003A-127513/1

Main applicant: O. Jordan

Co-applicants: G. Borchard, G. Thalmann, H. Hofmann, E. Doelker

Allocation **2012**: CHF 86'400

Duration: 3 years

Starting date: 2010

6. PATENTS

S. Kaderli, O. Jordan, R. Gurny

US provisional patent application US 616 938 03: Hybird hydrogels, 2012.

LIFE SCIENCES MASS SPECTROMETRY



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Dario BOTTINELLI

Tobias BRUDERER
Sandrine CUDRE
Antoine LESUR
Tiffany PORTA

Tatjana SAJIC
Jonathan SIDIBE
David TONOLI
Ying ZHANG

ADMINISTRATIVE AND TECHNICAL STAFF

Chantal GRIVET

Eliane KUEHN

Dominique STORZ

GENERAL DESCRIPTION OF THE UNIT

The Life Sciences Mass Spectrometry (LSMS) group focuses on the development of mass spectrometry (MS) in combination with separation techniques (chip-based nanoUHPLC, nanoUHPLC, UHPLC) for the quantitative and qualitative analysis of low molecular weight compounds and large molecules in biological matrices. It is well equipped with various ionisation techniques including MALDI, ESI, APCI, APPI, DESI and various types of mass spectrometers such as ion mobility, quadrupole-time-of-flight, triple quadrupole linear ion traps and Fourier transform ion cyclotron resonance mass spectrometry. In collaboration with external industrial partners the group develops new MS strategies based on high-resolution mass spectrometry, ultra-fast MS/(MS) acquisition workflows, MALDI-imaging, and differential ion mobility spectrometry for life sciences. The group is also developing software approaches for analyzing large set of MS/MS data to support structure elucidation in drug metabolism and metabolomics. Various studies are on-going in the field of toxicology to understand the binding of reactive metabolites to proteins, to image the distribution of drugs and their metabolites in tissues, and to characterize the effects of pharmaceuticals on the metabolome, lipidome and proteome of mammals or cell systems.

SPECIFIC RESEARCH FIELDS

- Metabolomic, Lipidomic and Proteomic Analyses
- Development of QUAL/QUAN MS/(MS) analytical strategies for pharmaceuticals and biopharmaceuticals in complex matrices
- High-Resolution Mass Spectrometry
- Mass Spectrometry Imaging
- Dried Blood Spots Analysis and related techniques
- Structure elucidation by LC-MSⁿ and High Resolution MS
- Miniaturized separation and infusion techniques
- Ultrafast and High-throughput Analysis
- Quality control and validation of analytical methods

SPECIFIC PROJECTS INITIATED AND RECOGNITIONS

- Prof. Hottiger, University of Zurich, SRM-Proteomics

1. PUBLICATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 11)

1.1	SCIENTIFIC PUBLICATIONS (WITH IMPACT FACTOR)	9
1.2	BOOK CHAPTERS	2

2. POSTERS PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 12)

2.1	POSTERS PRESENTATIONS	6
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3. ORAL PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 13)

3.1	CONGRESSES & SYMPOSIA	11
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4. THESIS PRESENTED

4.1. INTRA-MUROS THESIS

Antoine LESUR

Novel Analytical Strategies for the Quantitative Analysis of Proteins by Mass Spectrometry

University of Geneva, 28 September 2012

David TONOLI

Qualitative and Quantitative Determination of Drugs, Metabolites and their Adducts to Proteins in Biological Matrices by Liquid Chromatography Hyphenated to Low and High Resolution Mass Spectrometry

University of Geneva, 29 October 2012

5. RESEARCH FUNDS (INDUSTRY AND ASSIMILATED)

Code	Service Development Research	Amount end 2012 (CHF)
Div. Spectro	Service	217'929
FB_Alghanem	Recherche	18'235
Fonds National CRSI3_136282	Recherche	282'440
		518'604

6. DEVICES IN LEND

MS detectors	1x ESI-Single Quadrupole
	2x ESI-Triple Quadrupole Linear Ion Traps (QqQ _{LIT}) + peripherals
	1x MALDI-Triple Quadrupole Linear Ion Trap (QqQ _{LIT}) + peripherals
	2x Quadrupole-Time of Flight (QqTOF) + peripherals
	1x Quadrupole-Time of Flight (TripleTOF) + peripherals
	1xShimadzu LCMS 8040
Robot	1xShimadzu MS8080
	1x Automated chip-based nanospray system
	1x Automated dried blood spots (DBS) system
	1x Automated SPE device
	1x Microfraction collector
LC	1x Dual UHPLC system with column-switching valves
	1x Micro-UHPLC pump
	1x Micro-LC system with column-switching valves
	1x Narrowbore LC system with column-switching valve
	1x Dual nano-UHPLC system

CE	1x Chip-based nano-LC system
	1x Splitless nano-LC pump
	1x Nano-LC system with column-switching unit
	1x 2D nano-LC system with column-switching unit
	1xShimadzu UHPLC Nexera
	1x Capillary Electrophoresis system

PHARMACEUTICAL ANALYTICAL CHEMISTRY



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(vice-chancellor since January 2011)

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Christophe FRANCEY

Charlène MEYLAN (apprentie)
Jessica ORTELLI

Emilie REGINATO
Cédric SCHELLING

GENERAL DESCRIPTION OF THE UNIT

The group focuses its activities on separation techniques mainly liquid chromatography (LC), capillary electrophoresis (CE) and supercritical fluid chromatography (SFC) coupled with various detectors, including mass spectrometry (MS) for the analysis of pharmaceutical and biopharmaceutical compounds. New chromatographic supports are evaluated and original strategies to gain selectivity and/or sensitivity of the analytical process are developed. Reduction of the analysis time is also studied. Special focus is given to environmentally friendly analytical and sample preparation techniques (green chemistry).

The research of this group also focuses on the development and the use of methods for mathematical and statistical analysis of data produced from chemical instrumentation. The use of chemometric tools for developing analytical methods, determining optimised or robust conditions, as well as for treating data with pattern recognition techniques are applied in many projects within the School of Pharmaceutical Sciences and numerous external academic and/or industrial collaborations. Three main fields are currently developed, namely Design of experiments (DOE), method validation, and data mining (exploratory data analysis). For the latter, numerous important collaborations are under progress, particularly in the field of metabolism, metabolomics, and toxicology.

Research areas consist in:

- pharmaceutical and drugs of abuse analysis
- doping substances analysis
- chiral separation of pharmaceutical products
- study of the impact of sample preparation procedures in the analytical process
- characterization of chromatographic supports for pharmaceuticals analysis
- drug metabolism
- affinity chromatography

- UHPLC and SFC
- separation techniques
- screening method for metabolomic purpose
- data mining

SPECIFIC RESEARCH FIELDS

- Liquid chromatography (LC)
- Capillary electrophoresis (CE)
- Supercritical fluid chromatography (SFC)
- Hyphenation to mass spectrometry (MS)
- Sample preparation
- Validation
- Chemometrics
- Metabolomics
- Toxicology

COLLABORATIONS INITIATED WITH INDUSTRY

Collaboration with Sanofi (France)

1. PUBLICATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 15)

1.1	SCIENTIFIC PUBLICATIONS (WITH IMPACT FACTOR)	22
1.2	SCIENTIFIC PUBLICATIONS (WITHOUT IMPACT FACTOR)	5
1.3	BOOKS OR BOOKS CHAPTERS	5

2. POSTERS PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 17)

2.1	POSTERS PRESENTATIONS	27
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3. ORAL PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 19)

3.1	CONGRESSES & SYMPOSIA	35
3.2	CONTINUING EDUCATION & OPEN TO THE PUBLIC LECTURES	22

4. THESIS PRESENTED

4.1 INTRA-MUROS THESIS

K. VUIGNIER

Analytical strategy to characterize drug-protein interactions: from high throughput to in-depth analysis

Co-directeur de thèse: Pr. P.-A. Carrupt

Université de Genève – Thèse N° 4489 - 2012

5. PUBLIC RESEARCH FUNDS (FNSR, NIH, CTI)

MISCELLANEOUS

Swiss Center for Applied Human Toxicology (SCAHT). S. RUDAZ, M. SAUGY. A steroidomics approach for investigation of modulation of steroid metabolism and profiles. In Core project 1: Discovery of Toxico-Biomarker Panels using a "System Approach".

Total allocation chf 600'000

Duration 4 years

Starting date : 2009

Allocation 2012 : chf 150'000

2011-2013 Swiss National Science Foundation: J.-L. Wolfender, t. Farmer, s. Rudaz. "Targeted and metabolomic study of the early chemical events of the wound response in *A. thaliana*: dynamics of signalling and search for long distance biomarkers."

N° 205320/135 190 – 1: 130'620 CHF

Commission administrative de l'Université de Genève (COMAD),. Financial support for UPC2 - Waters
 Applicant : D. Guillearme
 Total Allocation : 50'000.—
 Allocation 201 : 50'000 CHF

Marie Curie Actions Intra European Fellowships (IEF), « ConFirMS ». S. RUDAZ (PI). "Contaminant analysis in Food by Liquid Chromatography Mass Spectrometry towards a generic extraction and screening for pesticides and veterinary drugs"

Project N° 299455 / Call (part) identifier FP7-PEOPLE-2011-IEF

Applicant : S. Rudaz

Allocation 2012 : chf 165'027.41

Starting date : 2012

Total allocation : euro 184'709.40

CTI funding application "Neurospectrum": "in vitro assay for neurotoxicity assessment".

Co-applicants : L. Stoppini (PI), K.K. Krause (CI), S. Rudaz (CI).

Collaboration with Neurix (Minibrain) N° 13759.1 / Risky innovations

Allocation 2012 : chf 77'674.00

Duration : 2 years

Starting date : 2012

Total allocation chf 579'000

6. RESEARCH FUNDS (INDUSTRY AND ASSIMILATED)

Code	Service Development Research	Amount for 2012 (CHF)
Teoxane SA. Genève, Suisse	Service – analytical investigations and dosages	50'848.00
Industrial funds	Confidential – Collaboration with Prof. Wolfender	200'000.00
Sanofi, France	Service – analytical investigations and dosages	69'401.00

6.1 INSTRUMENTS ON LOAN

Code (LENDER)	Total Amount 2012 (CHF)
UPC ² Waters (WATERS)	170'260.00
CE Agilent (LAD)	75'000.00
CE Agilent (LCT)	75'000.00
UPLC-DAD Waters (AGEMEL)	120'000.00
G7100 CE Agilent with CE-MS interface Kit and G1310A 1200 isocratic pump (AGILENT)	100'000.00
UPLC H-Class (Waters) (WATERS)	160'000.00
HPLC Series 1500 Waters (AGEMEL)	65'000.00

7. AWARDS & DISTINCTIONS

A.-L. GASSNER, S. RUDAZ, J. SCHAPPLER

Contribution of capillary zone electrophoresis to the analysis of monoclonal antibody drugs

Award for excellence in oral presentation, 2nd price to A.-L. Gassner

SBCN 2012, Bordeaux, France, October 23-26, 2012

I. KOHLER, J. SCHAPPLER, T. SIERRO, J.-L. VEUTHEY, S. RUDAZ

Dispersive liquid-liquid microextraction combined with capillary electrophoresis and time-of-flight mass spectrometry for urine analysis

Agilent best poster award to I. Kohler

MSB 2012, Geneva, Switzerland, February 12-13, 2012

B. DEBRUS, A. PERIAT, A. GRAND-GUILLAUME-PERRENOUD, S. FEKETE, S. RUDAZ, D. GUILLARME

Method Development Olympics at the University of Geneva

Most innovative method of development procedure, 3rd price

CoSMoS 2012, Providence, RI, USA, September 10-12, 2012

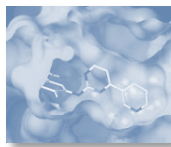
S. FEKETE, J.-L. VEUTHEY, D. GUILLARME

The effect of ultrahigh-pressure on the retention properties in RP-HPLC: from small to very large analytes (biomolecules)

Best poster award, 1st price to S. Fekete

ISC 2012, Torun, Poland, September 2012

PHARMACEUTICAL BIOCHEMISTRY



PROFESSOR

Leonardo SCAPOZZA

MER

Yogeshvar KALIA

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Dhaval KALARIA

Yong CHEN
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Alessandra MONACO
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Olivier PETERMANN

GENERAL DESCRIPTION OF THE UNIT

The Pharmaceutical Biochemistry group includes two distinct fields of research (<http://www.unige.ch/sciences/pharm/pb/>).

The first is the Pharmaceutical Biochemistry/Chemistry field in which the research is focused on understanding ligand-macromolecule interactions to develop new therapeutic strategies including new chemical entities, new targets using an interdisciplinary approach based on the combination of Biochemistry/Biophysics and Chemistry with Computational Chemistry/Molecular Modelling.

The second is in the field of drug delivery and focuses on the topical and transdermal delivery of therapeutic agents by investigating the effect of molecular properties on both passive and active transport processes. In addition, innovative approaches to increase the range of therapeutic agents that can be delivered across the skin and so provide new treatment options are also investigated.

SPECIFIC RESEARCH FIELDS

The research in the field of pharmaceutical biochemistry/chemistry covers three main topics, namely Cancer, Neglected Diseases and Antibiotics Research.

- In Cancer Research we have two main objectives, namely the development of a thymidine kinase based safety and monitoring tool for stem cells therapy and the development of inhibitors of the tyrosine kinase domain of oncogenic fusion proteins involved in signalling pathways.
- Within the research area of Neglected Diseases we aim at elucidating and validating new potential drug targets against the major parasitic diseases of the Third World e.g. Malaria, Tripanosomiasis and Leishmaniosis as well as finding potential lead compounds against such diseases.
- The objective of our sinergia-based antibiotics project is to find compounds inhibiting bacterial virulence with novel mechanisms of action.

In addition, a new activity has recently been initiated to develop a molecular recognition-based approach for improving antibody formulation.

The research in the field of cutaneous drug delivery includes:

- Development of new formulations to increase local and systemic bioavailability of topical and transdermal therapeutics.
- Investigation of the influence of physicochemical properties on electrically-assisted transport across the skin.
- Synthesis and characterisation of prodrugs optimised for transdermal iontophoretic administration.
- Development of new techniques for the non-invasive delivery of biotechnology-derived therapeutics across the skin ("pharmaceutical biotechnology").
- Evaluation of dermal exposure, risk assessment and the development of predictive mathematical models.
- Investigation of new therapeutic applications.

OUTSTANDING PUBLICATIONS

S. LOVERA, L. SUTTO, R. BOUBEVA, L. SCAPOZZA, N. DOLKER, F. L. GERVASIO. The Different Flexibility of C-Src and C-Abl Kinases Regulates the Accessibility of a Druggable Inactive Conformation. *J. Am. Chem. Soc.* 134(5): 2496-9, **2012**.

R. WEISS, M. HESSENBERGER, S. KITZMÜLLER, D. BACH, E. WEINBERGER, W. D. KRAUTGARTNER, C. HAUSER-KRONBERGER, B. MALISSEN, C. BOEHLER, Y. N. KALIA, J. THALHAMER, S. SCHEIBLHOFER. Transcutaneous vaccination via laser microporation. *J Control Release*, **2012**; 162(2): 391-399.

T. GRATIERI, B. WAGNER, D. R. KALARIA, B. ERNST AND Y. N. KALIA. Transdermal delivery of CGP69669A, a sialyl Lewisx mimetic, across intact porcine and human skins. *Exp Dermatol.* **2012**, 21(3): 226-228.

SPECIFIC PROJECTS INITIATED AND RECOGNITIONS

- Substrate and inhibitor complexes of Plasmodium falciparum Ca-dependent protein kinase 2 (PfCDPK2). Proposal ID 20120055, 2 shifts of 8 hours at the PXIII Synchrotron SLS Villigen, May-August 2012, L. Scapoza, R. Perozzo, L. Pernot, L. Lancellio.
- R. Perozzo, L. Scapoza. Phoenix prize for an innovative scientific work in pharmaceutical chemistry. October 2012
- European project: Scaffolds for alternative delivery (SADEL) (FP7-HEALTH-2011), 2012-2016, Euro 643'544.-, L. Scapoza (Principal Investigator)
- SNF project: Identification and analysis of the putative AMP-activated protein kinase (AMPK) in blood-stream form of Trypanosoma brucei (SNF No 31003A-140722), 2012-2015, CHF 237'840.-, R. Perozzo (Principal Investigator)
- CRUS-SCIEX: "New strategies to improve topical iontophoretic delivery of photosensitizers for photodynamic therapy". Programme 2011-2013, CHF 70'000, Y. KALIA (Principal Investigator).
- Swiss Innovation Promotion Agency. CTI no. 14416.1 "Development of a new alcohol-free gel product for the controlled transdermal delivery of testosterone to treat sexual dysfunction" 2012-2014, CHF 206 470 (Total project CHF 436 615) Y. KALIA (Principal Investigator).
- Swiss Innovation Promotion Agency. CTI no. 14334.1 "Peptides based on animal venom constituents as new active ingredients for cosmetic products" 2012-2014, CHF 194 400 (Total project CHF 565 480) Y. KALIA (Co-Investigator).
- UNITEC: "Topical, localized iontophoretic delivery of chemotherapy agents for the treatment of head and neck cancers", Programme 2011-12, CHF 29 800 – Y. KALIA (Principal Investigator).

CONGRESSES ORGANISED

L. SCAPOZZA. Organizer of the USGEB Annual Meeting 2012 entitled "Molecular Recognition: When Biology meets Chemistry" (more than 500 participants), 6-7 February 2012, Campus University of Lausanne, Lausanne (Switzerland).

W. BISSON, L. SCAPOZZA. Organizers of the Conference entitled "Computational Chemogenomics to understand System Biology & Computational Medicinal Chemistry" (40 participants), 14-16 May, 2012, University of Geneva, Geneva (Switzerland).

L. SCAPOZZA. Co-organizer of the Symposium entitled “Fortschritte in der Pharmakologie: Cardiovascular Pharmacology” (ca 300 participants) 26. January 2012, Bern (Switzerland)

1. PUBLICATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 24)

1.1	SCIENTIFIC PUBLICATIONS (WITH IMPACT FACTOR)	20
1.2	SCIENTIFIC PUBLICATIONS (WITHOUT IMPACT FACTOR)	1
1.3	BOOKS CHAPTERS (WITH IMPACT FACTOR)	1

2. POSTERS PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 26)

2.1	POSTERS PRESENTATIONS	26
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3. ORAL PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 28)

3.1	CONGRESSES & SYMPOSIA	16
3.2	CONTINUING EDUCATION & OPEN TO THE PUBLIC LECTURES	2

4. THESIS PRESENTED

4.1. INTRA-MUROS THESIS

Dhaval KALARIA

Transdermal Iontophoresis for the Controlled Delivery of Therapeutic Agents to Treat Neurodegenerative Diseases.

University of Geneva – **2012**– thesis n° 4480

Supervisor: Prof. Leonardo SCAPOZZA

Co-supervisor: Dr. Yogeshvar KALIA

5. PUBLIC RESEARCH FUNDS (FNSR, NIH, CTI)

SWISS NATIONAL SCIENCE FOUNDATION

Development of PET Reporter Probes With Improved Sensitivity And Specificity For In Vivo Monitoring of Gene And Cell-Based Therapy Using HSV1-tk As a Reporter Gene SNF No. 31003A-126963/1)

Main applicant: S. AMETAMEY

Co-applicant: L. SCAPOZZA

Total allocation: CHF 288'000.-

Allocation **2012**: CHF 43'200.-

Duration: 3 years

Starting date: 1.9.2010

Identification and analysis of the putative AMP-activated protein kinase (AMPK) in blood-stream form of *Trypanosoma brucei* (SNF No 31003A-140722)

Main applicant: R. PEROZZO

Co-applicant: L. SCAPOZZA

Total allocation: CHF 237'840.-

Allocation **2012**: CHF 85'680.-

Duration: 3 years

Starting date: 1.9.2012

Identification and characterization of novel antibacterial compounds using protozoan hosts SNF No CRSI33_130016

Main applicant: L. SCAPOZZA

Co-applicants: T. SOLDATI, P. COSSON, H. HILBI, J. MCKINNEY

Total allocation: CHF 1'638'377.-

Allocation **2012**: CHF 554'080.-

Duration: 3 years

Starting date: 1.9.2010

Development of novel C-5 fluoroalkyl N-acyclic pyrimidine nucleoside analogs as PET tracers for in situ monitoring of gene and cell-based therapies using HSV1-TK as a reporter gene (SCOPES joint research proposal, SNF no. IZ73ZO_127978/1)

Main applicant: S. AMETAMEY

Co-applicant: L. SCAPOZZA, S. RAIC-MALIC, D. ZAVRSNIK

Total allocation: CHF 185'000.-

Allocation **2012**: CHF 60'000.- (the money has gone to the east-european countries)

Duration: 3 years

Starting date: 1.11.2009

FONDATION ERNEST ET LUCIE SCHMIDHEINY

Demande de subside pour l'achat d'un détecteur de masse triple quadripolaire

Main applicant: Y. KALIA

Total allocation: CHF 19'714.-

Allocation **2012**: CHF 19'714.-

COMMISSION ADMINISTRATIVE DU RECTORAT

Demande de subside pour l'achat d'un détecteur de masse triple quadripolaire

Main applicant: Y. KALIA

Total allocation: CHF 61'362.-

Allocation 2012: CHF 61'362.-

SECRETARIAT D'ETAT A L'EDUCATION ET A LA RECHERCHE (SER) – SWISS-INDO CO OPERATION IN SCIENCE AND TECHNOLOGIE EXECUTIVE PROGRAMME.

Therapeutic approaches using controlled transdermal delivery to neurodegenerative conditions in aging populations (ISJRP 123 143)

Main applicant: Y. KALIA

Total allocation: CHF 217'810.-

Allocation 2012: CHF 68'157.-

Duration 4 years

Starting date: 1.6.2009

EU FUNDING

Scaffolds for alternative delivery (SADEL) (FP7-HEALTH-2011)

Main applicant: L. SCAPOZZA

Total allocation: Euro 643'544.-

Allocation **2012**: CHF 254'457.05

Duration 5 years

Starting date: 1.1.2012

INNOGAP FUNDING

INNOGAP funding from UNITEC #702-A569 " Topical, localized iontophoretic delivery of chemotherapy agents for the treatment of head and neck cancers"

Main applicant: Y. KALIA

Total allocation: CHF 29'800.-

Allocation **2012**: CHF 29'800.-

Duration: 1 year and 6 months

Starting date: 1.7.2011

SCIEX (SCIENTIFIC EXCHANGE PROGRAMME BETWEEN SWITZERLAND AND THE NEW MEMBER STATES OF UE)

SCIEX 10.012 "ECGtoA – In Silico Chemical Genomics Driven Design and Synthesis of new antibacterials"

Main applicant: L. SCAPOZZA

Total allocation: CHF 103'000.-

Allocation **2012**: CHF 103'000.-

Duration: 1 year and 6 months

Starting date: 1.1.2011

SCIEX 11.054 CRUS-SCIEX: "New strategies to improve topical iontophoretic delivery of photosensitizers for photodynamic therapy"
 Main applicant: Y. KALIA
 Total allocation: CHF 70'000.-
 Allocation **2012**: CHF 70'000.-
 Duration: 1 year
 Starting date: 1.2.2012

COMMISSION INNOVATION AND TECHNOLOGY (CIT)

CTI-14416.1 PFLS-LS: "Development Development of a new alcohol-free gel product for the controlled transdermal delivery of testosterone to treat sexual dysfunction"
 Main applicant: Y. KALIA
 Total allocation: CHF 206'470.-
 Allocation **2012**: CHF 165'176.-
 Duration: 2 years
 Starting date: 1.10.2012

CTI-14416.1 FERRING : "Development Development of a new alcohol-free gel product for the controlled transdermal delivery of testosterone to treat sexual dysfunction"
 Main applicant: Y. KALIA
 Total allocation: CHF 60'105.- (Industrial partner contribution to CTI no. 14416.1)
 Allocation **2012**: CHF 60'105.-
 Duration: 2 years
 Starting date: 1.10.2012

CTI-14334.1 PFLS-LS : "Peptides based on animal venom constituents as new active ingredients for cosmetic products"
 Main applicant: M. CUENDET
 Co-applicant: Y. KALIA
 Total allocation: CHF 194'400.-
 Allocation **2012**: CHF 155'520.-
 Duration: 2 years
 Starting date: 1.10.2012

CTI-14334.1 ACTIVEN: Peptides based on animal venom constituents as new active ingredients for cosmetic products"
 Main applicant: M. CUENDET
 Co-applicant: Y. KALIA
 Total allocation: CHF 27'000.- (Industrial partner contribution to CTI no. 14334.1)
 Allocation **2012**: CHF 4'000.-
 Duration: 2 years
 Starting date: 1.10.2012

6. RESEARCH FUNDS (INDUSTRY AND ASSIMILATED)

Code	Service Development Research	Amount for 2012 (CHF)
Collaboration 1	Research	40'953.60
Collaboration 2	Research	58'388.90
Collaboration 3	Research	31'590.00
Collaboration 4	Research	39'000.00
Collaboration 5	Research	9'800.00
Collaboration 6	Research	116'217.04
Collaboration 7	Research	35'723.80
Ind-1	Research	7'502.17
Ind-2	Research	125'198.57
Ind-3	Research	25'800.00
Ind-4	Research	209'949
Ind-5	Research	16'341.59
Ind-6	Research	6'032.12
		722'496.80

7. PATENTS

S. KADERLI, O. JORDAN, R. GURNY.

IP: US Pat Appl. 61693803 (July 2012).

S. KADERLI, R. GURNY, M. MÖLLER, L. SCAPOZZA.

IPPreliminary US Pat. EFS ID 14508328, (December 2012.)

C. GAMBACORTI-PASSERINI, L. MOLOGNI, L. SCAPOZZA, W.H. BISSON, P. GOEKJIAN, S. TARDY, A. ORSATO. *Alpha-Carbolines For the Treatment of Cancer. European Patent Application EP12167755, 11 May 2012.*

PHARMACEUTICAL TECHNOLOGY



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(*supervised by prof. R. gurny)

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Florence VON OW

GENERAL PRESENTATION OF THE ACTIVITY OF UNITS

Research at the unit of Pharmaceutical Technology is focused on the delivery of therapeutic agents and contrast agents for medical imaging at the right site on the right time. Eric Allémann has activities in nanomedicine, energy-activated drug delivery systems, targeted-contrast agents for medical imaging. Florence Delie leads research in nanomedicine and vectorization. Norbert Lange leads research in photodetection, photodynamic therapy and enzymatically activated prodrugs. In 2012, various collaborations were continued with the University Hospital of Geneva and the EPFL. Collaboration projects with start-up companies and established companies were initiated.

SPECIFIC RESEARCH FIELDS

The specific fields of research are:

- Development of drug formulations for intra-articular delivery
- Development of treatment modality for stroke by sonothrombolysis
- Enzymatically-activated prodrugs and supramolecular constructs
- Development of new contrast agents for MRI
- Polymeric photosensitizers projects
- Imaging of β -cells and amyloids

OUTSTANDING PUBLICATIONS

M.F. ZULAGA, D. GABRIEL, N. LANGE. *Enhanced prostate cancer targeting by modified protease sensitive photosensitizer prodrugs*. Mol Pharm, 9, 1570-1579 (2012)

PARTICULAR PROJECTS INITIATED

In 2012, Eric Allémann and Norbert Lange started to collaborate within the BetaTrain project (www.betatrain.eu). BetaTrain is a Marie Curie Initial Training Network (ITN): “European Training Network for Excellence in Molecular Imaging in Diabetes”. It is a four-year project funded by the European Commission bringing together 7 renowned research institutes and 3 private sector partners, each specialized in different aspects of beta cell/diabetes imaging.

COLLABORATIONS INITIATED

Eric Allémann initiated a collaboration with PharmAlp on the development of different formulations for the prevention and treatment of vaginal candidosis.

1. PUBLICATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 30)

1.1	SCIENTIFIC PUBLICATIONS (WITH IMPACT FACTOR)	17
1.2	SCIENTIFIC PUBLICATIONS (WITHOUT IMPACT FACTOR)	1

2. POSTERS PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 31)

2.1	POSTERS PRESENTATIONS	2
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3. ORAL PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 32)

3.1	CONGRESSES & SYMPOSIA	4
3.2	CONTINUING EDUCATION & OPEN TO THE PUBLIC LECTURES	7

4. THESIS PRESENTED

4.1 INTRA-MUROS THESIS

Lutz ASMUS

Injectable sustained-release formulations based on polyesters from small molecule solutions to protein delivery to the eye

University of Geneva - thesis n° 4403,

Co-Directors of thesis: Prof. R. Gurny and Dr. M. Moeller

Gesine HEUCK

New strategies for the induction of endogenous porphyrins in eukaryotic and prokaryotic cells

University of Geneva - thesis n° 4415

Director of thesis: N. Lange

5. RESEARCH FUNDS (FNSR, NIH, CTI)

SWISS NATIONAL SCIENCE FOUNDATION

Peptidic scaffolds for targeted delivery of photosensitizer prodrugs in photodynamic therapy – (205320-138309/1)

Main applicant: N. Lange

Allocation 2012: CHF 0

Duration: 3 years

Starting date: 2011

Non invasive in vivo imaging of pancreatic beta cells: developing and testing innovative ligands and MRI contrast agents – (CR3213-129987/1)

Main applicant: P. Meda

Co-applicant: N. Lange

Allocation 2012: CHF 125'000

Duration: 3 years

Starting date: 2010

Protease-sensitive nanoscaled micelles for the targeted delivery of chemotherapeutics to prostate cancer – (205321-126834)

Main applicant: N. Lange

Allocation **2012**: CHF 209'700

Duration: 3 years

Starting date: 2010

Amyloid peptide grafted to Gd-nanoparticles for amyloidosis diagnosis – (31NM30_141416/1)

Main applicant: X. Montet (CMU)

Co-applicant: E. Allémann

Allocation **2012**: CHF 98'125

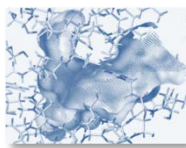
Duration: 3 years

Starting date: 2012

6. RESEARCH FUNDS (INDUSTRY AND ASSIMILATED)

Code	Service Development Research	Amount for 2012 (CHF)
OM	Service	10'200
VIROBLOCK	Service	5'000
TRB	Service	20'000
PHARMALP	Research	12'500
DEBIO	Service	1'500
BRACCO	Service	6'000
SWISSMEDIC	Service	6'000
		61'200

PHARMACOCHEMISTRY



PROFESSOR

Pierre-Alain CARRUPT

READERS

Davy GUILLARME

RESEARCH ASSOCIATES

Sophie MARTEL

SENIOR RESEARCHERS

Claudia AVELLO SIMOES PIRES

Julietta GRADINARU

Alessandra NURISSO (*since 1.8.2012*)

Antoine DAINA

POST DOCTORAL STUDENTS

Alessandra NURISSO (*until 31.7.2012*)

Alessandra ZIZZARI

PH.D STUDENTS

Alban BUJARD
Sarrah DE VALENCE
Philippe EUGSTER
Elisabeth FAVRE

Céline LE BOURDONNEC-PASSELEU
Nils OBERHAUSER
Charlotte PETIT
Stephanie ROMAND

Lucie RYCKEWAERT
Lionel SACCONNAY
Karine VUIGNIER
Vincent ZWICK

CO-TUTELLE

Cecilia FORTUGNO

ADMINISTRATIVE AND TECHNICAL

Virginie BEYELER (*apprentie laborantine*)
Christophe FRANCEY

Fabrice GILLERAT
Irena NIKOLOVA

Sylvia PASSAQUAY-RION
Emilie REGINATO

GENERAL DESCRIPTION OF THE UNIT

The team of pharmacocchemistry developed original theoretical and experimental methods able to quantify intermolecular interactions of a drug with its biological partners such as therapeutic targets or biological membranes.

This research intended to accelerate the discovery of chemical compounds of therapeutic interest and to optimize the effectiveness, the selectivity and the safety of the selected drug candidates.

They were centered on the development and validation of *in silico* and *in vitro* HTS filters to characterize physicochemical properties, passive membrane permeation and cellular efflux of new chemical entities.

Virtual and *in vitro* HTS screening approaches were optimized to study the interactions with some specific bio-targets involved in neurodegenerative diseases like Alzheimer and Parkinson's diseases were measured in order to identify multifunctional drug candidates.

SPECIFIC RESEARCH FIELDS

- Biochemical screening: enzyme inhibition; antioxidant profiling of NCEs; antiapoptotic properties of NCEs; enzymatic hydrolysis of drugs and prodrugs; inhibition of hERG channel; inhibition of HDAC and SIRT proteins.
- Molecular modelling: Intermolecular interaction fields; indirect molecular modelling; direct molecular modelling; quantum chemistry.
- Physicochemical screening: Physicochemical profiling; antioxidant properties.
- Permeation screening: passive permeation profiling using PAMPA-membranes to mimic the skin, the intestinal barrier and the blood-brain barrier. 3D-QSAR models associated with proteins responsible of cellular efflux in membrane permeation or multi-drug resistance.

OUTSTANDING PUBLICATIONS

A. NURISSO, C. SIMOES-PIRES, S. MARTEL, D. CRESSEND, A. GUILLOT, PA. CARRUPT. *How to increase safety and efficacy of compounds against neurodegeneration? A multifunctional approach*. Chimia, 66: 286-290, **2012**.

K. VUIGNIER, JL. VEUTHEY, PA. CARRUPT, J. SCHAPPLER. *Characterization of drug-protein interactions by capillary electrophoresis hyphenated to mass spectrometry*. Electrophoresis, 33: 3306-3315, **2012**.

L. SACCONNAY, MPB. SOARES, D. SMIRLIS, E.F.QUEIROZ, JL. WOLFENDER, PA. CARRUPT, A. NURISSO. *Toward a novel high-throughput screening assay based on PAMPA-GIT to detect potential interaction with P-Glycoprotein*. Chimia, 66: 346, **2012**.

SPECIFIC PROJECTS INITIATED AND RECOGNITIONS

The binding mode study of several reported TollLikeReceptor4/MD2 modulators by means of docking techniques, especially with the use of MLP Tools recently developed in our research group, with the aim of designing new ligands and elucidating the mechanism at atomic detail.

The virtual screening of natural compounds on the RNA dependent RNA polymerase of Hepatitis C virus with the aim of isolating new active compounds and proposing structural modifications for increasing affinity and efficacy.

COLLABORATIONS INITIATED

With S.M. SANTAMARIA (University San Pablo CEU Madrid)

With A. BOUMENDJEL (University of Grenoble)

With M. CUENDET (University of Geneva)

1. PUBLICATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 34)

1.1	SCIENTIFIC PUBLICATIONS (WITH IMPACT FACTOR)	15
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2. POSTERS PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 35)

2.1	POSTERS PRESENTATIONS	12
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3. ORAL PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 36)

3.1	CONGRESSES & SYMPOSIA	10
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4. THESIS PRESENTED

4.1. INTRA-MUROS THESIS

Elisabeth FAVRE

In silico studies of tyrosinases: structures and interactions.

University of Geneva – 2012

Supervisor: Prof Pierre-Alain CARRUPT

Karine VUIGNIER

Analytical strategy to characterize drug-protein interactions: from high throughput to in-depth analysis.

University of Geneva – 2012

Supervisor: Prof. Pierre-Alain CARRUPT

Cristina POMILIO (Tesi di Laurea)

Liposomal formulations of antiparkinson agents: study of passive diffusion using a PAMPA-BBB model

University of Chieti – 2012

Supervisor: Prof. Pierre-Alain CARRUPT

5. PUBLIC RESEARCH FUNDS (FNSR, NIH, CTI)



Establishment of a predictive model for chemical permeation across the human airway epithelium in vitro using MucilAir™ (No 14000.1 PFLS-LS).

Main applicant: EPITHELIX

Co-applicant: P.A. CARRUPT

Total Allocation: CHF 242'027.-

Allocation **2012**: CHF 128'849.-

Duration: 18 mois

Starting Date : 2012

6. RESEARCH FUNDS (INDUSTRY AND ASSIMILATED)

Code	Service Development Research	Amount for 2012 (CHF)
Indu-1		49'936.-
Indu-2		4'200.-
Indu-3		4'000.-
Indu-4		3'600.-
Indu-5		1'282.-
		63'018.-

PHARMACOGNOSY



PROFESSOR

Muriel CUENDET

MER

Philippe CHRISTEN

SENIOR RESEARCHERS

Claudia AVELLO SIMOES PIRES

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Andreas NIEVERGELT-MEIER

PH.D. STUDENTS

Olivier CICLET
Mélanie HOERLE

Mark ISSA
Caroline MATHON

Vincent ZWICK

ADMINISTRATIVE AND TECHNICAL STAFF

Martine CABO

Natalie SCHREGLE

GENERAL DESCRIPTION OF THE UNIT

The team of pharmacognosy is focused on the discovery of bioactive natural products. Compounds with cancer chemopreventive and antimalarial activity are of particular interest. In these areas, the development of new and better drugs remains a principal need. As established by ample precedent, nature provides broad chemical diversity. Prevention is well developed in the field of cardiovascular disease, but similar drugs that could prevent cancer on this scale are still a long way off. A panel of *in vitro* bioassays indicative of inhibiting major stages of carcinogenesis (initiation, promotion and progression) is used. Also, antimalarial drugs available on the market have a limited efficacy and strong side effects. Some plant extracts having shown good *in vitro* and *in vivo* activity are currently being investigated to uncover the compounds responsible for the activity and their mechanism of action. The absorption and the metabolism of pure compounds and phytopreparations are also being evaluated *in vitro* and *in vivo*.

Another area of interest is the appearance of botanical preparations on the market with medicinal claims which escape to registration because they are voluntarily sold as conventional food derived products. Nowadays, such herbal remedies are sold in health food stores, supermarkets or over the internet without seriously questioning their potential activity, side effects or toxicity. Furthermore, there is a misconception and general belief that these plant derived preparations are natural and therefore are perceived as "safe", regardless of potential dangers. Thus there is an urgent need to assess the safety of botanicals and establish a compendium of botanical ingredients which may be of health concerns when used in food derived products. To support food safety authorities, adequate screening approaches and analytical methods are being developed to provide chemical evidence of the presence of an undesired botanical or toxicant. The authenticity of the ingredients is also checked.

SPECIFIC RESEARCH FIELDS

- Cancer chemopreventive screening of natural products: quinone reductase induction, HDAC inhibition, and anti-inflammatory activity
- Antimalarial activity
- Activity-guided fractionation
- Absorption and metabolism studies of phytopreparations and pure natural products using Caco-2 cells and a rat *in vivo* model
- In depth studies to uncover the mechanism of action of pure natural products and phytopreparations
- Development of a LC-MS/MS method able to screen simultaneously for 62 species whose presence in food might be problematic

CONGRESSES

Prof. Muriel Cuendet and Prof. Jean-Luc Wolfender were the organizers of the 27th Seminar in Pharmaceutical Sciences in Zermatt, Switzerland, in September 2012, Drugs from Nature: from Discovery to Clinic.

Prof. Muriel Cuendet was the organizer of the WG3 COST meeting (COST TD0905, Epigenetics – Bench to Bedside), 11 September, 2012, Geneva (Switzerland).

OUTSTANDING PUBLICATIONS

S.M. AL-MASSARANI, S. BERTRAND, A. NIEVERGELT, A.M. EL-SHAFAR, T.A. AL-HOWIRINY, N.M. AL-MUSAYEIB, M. CUENDET, J.-L. WOLFENDER. *Acyalted pregnane glycosides from Caralluma sinaica*. *Phytochemistry*, 79, 129-140. 2012.

C. MATHON, M. DURET, M. KOHLER, P. EDDER, S. BIERI, P. CHRISTEN. *Multi-targeted screening of botanicals in food supplements by liquid chromatography with tandem mass spectrometry*. *Food Chemistry*, 138 (1), 709-717. 2012.

1. PUBLICATIONS

(DETAILS IN SCIENTIFIC PRODUCTIONS 2012 - PAGE 38)

1.1	SCIENTIFIC PUBLICATIONS (WITH IMPACT FACTOR)	6
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2. POSTERS PRESENTATIONS

(DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 39)

2.1	POSTERS PRESENTATIONS	4
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3. ORAL PRESENTATIONS

(DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 39)

3.1	CONGRESSES & SYMPOSIA	5
3.2	CONTINUING EDUCATION & OPEN TO THE PUBLIC LECTURES	1
3.3	RADIO/TELEVISION INTERVENTION	1

4. PUBLIC RESEARCH FUNDS (FNSR, CTI, ETC....)



Argemone Mexicana
MMV 11/0003– Medicines for Malaria Venture
Applicants: P. CHRISTEN and M. CUENDET
Total allocation: CHF 289'505.32
Allocation 2012: CHF 89'598.79
Duration: 3 years
Starting date: 2011



Functional genome analysis in a genetically intractable system: an interdisciplinary proof-of-concept study
SUBSIDE CRSII3-141837
Main applicant of P2: M. CUENDET
Total allocation: CHF 335'016.—
Allocation 2012: CHF 79'680.—
Duration: 3 years
Starting date: 2012

Evaluation of the health benefits of Brazilian fruits and vegetables for the development of safe and valuable functional foods

Brazilian Swiss Joint Research Program – BSJRP

Applicants: J.-L. WOLFENDER, M. CUENDET, E. FERREIRA-QUEIROZ.

Total allocation: CHF 173'400. —

Allocation **2012**: CHF 112'000. —

Duration: 2 years

Starting date: 2012



Peptides based on animal venom constituents as new active ingredients for cosmetic products

CTI-Projet 14334.1 PFLS-LS

Main applicant: M. CUENDET

Co-applicant: Y. KALIA

Total allocation: CHF 194'400. —

Allocation **2012**: CHF 155'520. —

Duration: 2 years

Starting date: 2012

Peptides based on animal venom constituents as new active ingredients for cosmetic products

CTI-Projet 14334.1 ACTIVEN

Main applicant: M. CUENDET

Co-applicant: Y. KALIA

Total allocation: CHF 27'000. —

Allocation **2012**: CHF 4'000. —

Duration: 2 years

Starting date: 2012



Integrated technologies for the discovery and development of cosmeceutical agents from plant biodiversity

NATPROTEC

IAPP-Marie Curie

Main applicant: M. CUENDET

Co-applicant: J.-L. WOLFENDER

Total allocation: CHF 263'225.23 (€ 222'131. —)

Allocation **2012**: CHF 59'400.51

Duration: 4 years

Starting date: **2012**

5. RESEARCH FUNDS (INDUSTRY AND ASSIMILATED)

Code	Service Development Research	Amount for 2012 (CHF)
Fonds Industrie (J.L. Wolfender, M. Cuendet, Ph. Christen)	Research & Services	90'712.--

PHARMACOLOGY



PROFESSOR

Urs T. RUEGG

SENIOR RESEARCHERS

Olivier DORCHIES

POST DOCTORAL STUDENTS

Karin JACOBSON-JOHANSSON

Miriam KOVACS-STROSOVA

Julie PATTE-REUTENAUER

PH.D. STUDENTS

Hesham MOHAMED ISMAIL

ADMINISTRATIVE AND TECHNICAL STAFF

Dominique HUNZIKER
Colette SAUTY-DEFFERARD

Ophélie PATTHEY-VUADENS

Olivier PETERMANN

GENERAL DESCRIPTION OF THE UNIT

Our projects aim to identify new therapeutic targets in the area of muscle disorders in order to find novel treatments. Focus is on treatment of muscular dystrophy, in particular Duchenne muscular dystrophy (DMD). DMD is one of the most common hereditary diseases of childhood leading to progressive weakness, loss of walking ability during the first decade of life, with death occurring usually at age 20 to 30. The molecular basis of this disease is characterized by the absence of dystrophin, a large protein in the cytosol of the cell. Mutations of the dystrophin gene, located on the X chromosome, cause muscle degeneration in humans and in mdx mice, a mouse model of DMD. Even though the gene - with its 200 or more mutations - and the resulting protein products are well known, the functional role of dystrophin has not yet been completely elucidated. In particular, it is not clear why the absence of dystrophin has dramatic consequences on the patients.

Affected patients are treated in a symptomatic way, most often with glucocorticoids; these increase life expectancy but do not improve the long-term outcome. Recent therapeutic efforts have focused on replacement of the primary genetic defect by gene-transfer or stem cell therapy, or on its correction via the exon-skipping approach. Results suggest cautious optimism. We are of the opinion that an effective curative treatment will be available at best in 10-30 years and will be very costly. Thus, pharmacological approaches are justified for the benefit of both, patients and their parents.

Cellular and molecular assays, in particular those linked to calcium channels (electrophysiology, calcium imaging via fluorescence), muscle force assay and histology. We proceed from cell lines (of murine and human origin) to purified myotubes, primary myotube cultures, to freshly isolated fibers and finally to mice in order to verify important in vitro findings. The techniques applied at the in vitro level include gene deletion and overexpression, Ca^{2+} influx and imaging as well as electrophysiological studies combined with exposure to pharmacological agents to determine pathways and endpoints such as cell/fiber survival or apoptosis. In vivo experiments on control and dystrophic mice are designed in a way allowing investigations of tissue quality, muscle force and recovery from tetanus, assessment of biomarkers and of the skeleton by whole body X-ray tomography.

SPECIFIC RESEARCH FIELDS

We, and others, have found that muscle cells from DMD patients, or from mdx mice, display abnormally elevated calcium influx leading to an increase in cytosolic calcium concentrations when these cells are exposed to mechanical or oxidative stress. It is likely that this triggers the death of muscle cells. In most cases, our results show that normalizing this calcium deregulation in mdx muscle cells or fibers with the use of drugs also improves the muscle function of these mice. Investigations by others show that NADPH oxidases are the major producers of oxidative stress, that these produce an

excessive amount of stress, namely superoxide anion radical, a major component of oxidative stress, and that the downstream targets are store-operated calcium channels.

RECENT RESULTS:

- Glucocorticoids improve the quality of dystrophic muscle but cause atrophy in normal muscle; however, the mechanisms are not well understood. We found that glucocorticoids inhibit stress-induced calcium entry into mdx muscle cells.
- It is known that lysophospholipids produced by a particular isoform of phospholipase A₂ (iPLA_{2δ}) lead to the activation of store-operated calcium channels. Using patch-clamp and calcium imaging technology, we found that inhibition, or down-regulation, of iPLA_{2δ} prevents the activation of store-operated channels.
- We found that iPLA_{2δ} is overexpressed 2-3-fold in mdx muscle at the age of 4-8 weeks when the rate of necrosis is highest. Similar findings were made in DMD boys whose iPLA_{2δ} levels were 10-20-fold higher at age 3 to 5 years. Such elevated levels of iPLA_{2δ} will produce higher amounts of lysophospholipids (cf. point 2), which would activate store-operated channels. This cascade of events could be the underlying reason for the increased calcium entry into dystrophic muscle.
- In addition, we found that mdx muscles contain 6-times less of the PLA₂-inhibitor annexin-1, thus facilitating lysophospholipid production. Consistent with the fact that expression levels of annexin-1 are known to be upregulated by glucocorticoids, we found that the glucocorticoid receptor agonist prednisolone increased expression of this inhibitor two-fold in dystrophic myotubes.
- Store-operated calcium channels are formed by Orai1 and TRPV2 proteins but not by TRPC1, as shown by our investigations on TRPC1 k/o mdx hybrid mice.
- We found that polyphenols from green tea, in particular the major constituent, epigallocatechin gallate, have a beneficial effect on the muscle of mdx mice. These compounds also reduce the elevated calcium influx into dystrophic muscle and consequently normalize the cytosolic calcium levels. A clinical trial using epigallocatechin gallate in DMD boys has been initiated at Charité Hospital in Berlin.
- Recently, we found that tamoxifen, a partial agonist at the estrogen receptor, given orally at 10 mg/kg/day for 15 months to mdx mice, led to enhanced muscle force and resistance to fatigue, decreased fibrosis of the diaphragm, and reduced plasma creatine kinase levels. A grid test revealed that the same dose of tamoxifen given for 10 weeks to 6 month-old mdx mice led to an amelioration of their performance, such that after about four weeks, scores identical to those of wild-type mice were attained. Furthermore, tamoxifen increased the spontaneous locomotor activity of these mdx mice to near-normal values, fully normalized the phasic tension, and corrected by ~ 65% the tetanic tension deficit that was found between normal and dystrophic triceps surae muscle. In addition, the proportion of Evans blue-permeable fibers decreased ~ 2.5-fold in the diaphragm of treated dystrophic mice compared to untreated ones. Importantly, most effects of tamoxifen were evident even at the lowest dose tested (0.1 mg/kg/day). This dose is similar to, or below, the one prescribed for patients suffering from breast cancer, and corresponds to about 10 times less than the dose of prednisolone required to elicit some improvement of the dystrophic phenotype in humans. Although more investigations are required, tamoxifen is a promising candidate for clinical trials since it has already been approved for other indications, has been widely used in patients for many years, is readily available, and has an acceptable safety profile with generally few side-effects at low doses.

OUTSTANDING PUBLICATIONS

J. REUTENAU-PATTE, F.X. BOITTIN, O. PATTHEY-VUADENS, U.T. RUEGG, O.M. DORCHIES, Urocortins improve dystrophic skeletal muscle structure and function through both PKA- and Epac-dependent pathways. *Am J Pathol.* (Epub **2012**), 180:

Y. NAKAE, O.M. DORCHIES, P.J. STOWARD, B.F. ZIMMERMANN, U.T. RUEGG, Quantitative evaluation of the beneficial effects in the mdx mouse of epigallocatechin gallate, an antioxidant polyphenol from green tea. *Histochem Cell Biol.* 137, 811-27 (**2012**).

N. ITO, U.T. RUEGG, A. KUDO, Y. MIYAGOE-SUZIKI, S. TAKEDA, Activation of calcium signaling through Trpv1 by nNOS and peroxynitrite as a key trigger of skeletal muscle hypertrophy. *Nat Med.* 19:101-6. Epub(**2012**) Dec 2. doi: 10.1038/nm.3019.

COLLABORATIONS INITIATED

Charité Medical University Berlin and Max Delbrueck Center for Molecular Medicine, Berlin, D-13125, Germany
Department of Basic Medical Sciences, University of Arizona College of Medicine, Phoenix, Arizona 85004 - USA

1 PUBLICATIONS

(DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 40)

1.1	SCIENTIFIC PUBLICATIONS (WITH IMPACT FACTOR)	4
1.2	SCIENTIFIC PUBLICATIONS (WITHOUT IMPACT FACTOR)	1
1.3	BOOK CHAPTER	1

2. POSTERS PRESENTATIONS

(DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 41)

2.1	POSTERS PRESENTATIONS	3
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3. ORAL PRESENTATIONS

(DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 41)

3.1	CONGRESSES & SYMPOSIA	5
3.2	CONTINUING EDUCATION & OPEN TO THE PUBLIC LECTURES	1

4. PUBLIC RESEARCH FUNDS (FNSR, NIH, CTI)

ASSOCIATION FRANÇAISE CONTRE LES MYOPATHIES

Essai pré-clinique sur le traitement de la myopathie de Duchenne par le tamoxifène

Applicant : U.T. Ruegg

Allocation **2012** : CHF 68'000

Duration : 2 years

Starting date: 01.03.2011

DUCHENNE PARENT PROJECT, NL

Investigation of the beneficial effects of tamoxifen in dystrophic muscle

Applicant : U. T. Ruegg

Allocation **2012** : CHF 57'500

Duration : 3 years

Starting date: 1.01.2010

SWISS NATIONAL SCIENCE FOUNDATION

A pharmacological strategy to treat Duchenne Muscular Dystrophy – No. 3100-122548/2

Main applicant: U. T. Ruegg

Allocation **2012**: CHF 53'545

Duration: 4 years

Starting date: 1.01.2009

PHYTOCHEMISTRY AND BIOACTIVE NATURAL PRODUCTS



PROFESSOR

Jean-Luc WOLFENDER

MER

Emerson FERREIRA-QUEIROZ

SENIOR RESEARCHERS

Elisabeth RIVARA-MINTEN

Guillaume MARTI

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Samuel BERTRAND

Lise BREANT

Florence MEHL

PH.D. STUDENTS

Nadine BOHNI
Véra OLDRATI
Daniel MAAG

Soura CHALLAL
Philippe EUGSTER

Adeline CHAUVIN
Quentin FAVRE-GODAL

ADMINISTRATIVE AND TECHNICAL STAFF

Laurence MARCOURT

Karine NDJOKO IOSET

Natalie SCHREGLE

GENERAL DESCRIPTION OF THE UNIT

The main research activities of the unit are related to the development of methodologies for the rapid isolation identification and bioactivity characterisation of natural products (NPs) at the microgram scale. State-of-the-art LC-MS and LC-MS/MS as well as microNMR techniques are used for dereplication purposes or *de novo* identification of NPs in crude extracts from different origins (plants, fungi, and microorganisms). Microfractionation methods in 96 well plates allow bioassays to be performed on LC peak in crude extracts, quantitative estimation of the well content and further structural determination by CapNMR. Rational large scale isolation strategies are developed for the rapid obtention of pure NPs in the mg scale for further testing bioactivities and mode of action. The range of biological activities studied in house or in collaboration covers mainly antifungal, antiprotozoal, antiinflammatory and antiepileptic activities. The interest of the group is also focused on plant metabolomics, in this respect the focus is on the investigation of bioactive NPs dynamically induced in various stress situations (fungi confrontation, biotic and abiotic stresses, metabolite elicitation...). With the idea to generate original sources of bioactive NPs other strategies including biotransformation or chemical derivatisation of crude extracts from common sources are also investigated. Finally the analytical and metabolomic methods are also used for studying the metabolism of crude extracts in view of a better understanding of the mode of action (synergy, prodrugs) and the potential toxicity of phytopharmaceuticals or nutraceuticals.

SPECIFIC RESEARCH FIELDS

- Search for new lead compounds from natural sources
- On-line identification of natural products by LC-UV-NMR-MS (dereplication)
- Rapid microfractionation of crude extracts for chemical and bioactivity profiling
- Plant metabolomics
- Search for original bioactive stress-induced natural products of various origin
- Study of antifungal compounds from pathogen fungi in co-culture
- Qualitative quantitative analysis of phytotherapeutics

- Study of the metabolism of phytopreparation by metabolomics in relation with their mode of action
- Investigation of natural products involved in diseases associated with problems of ageing
- Search for new lead compounds for use against tropical parasitic diseases

CONGRESSES

Prof. Jean-Luc Wolfender and Prof. Muriel Cuendet were the organizers of the 27th Seminar in Pharmaceutical Sciences in Zermatt, Switzerland, in September 2012, Drugs from Nature: from Discovery to Clinic.

As President of the ccCTA (Centre of Competence in Toxicological and Analytical Chemistry, Prof. Jean-Luc Wolfender was responsible for organisation of the “Grand Public” Conference from the ccCTA, at the “Institut National Genevois” in Geneva, Switzerland, in March 2012: Art et Chimie Analytique.

As member of the local program advisory board from MSB, Prof. Jean-Luc Wolfender was one of the organizers of the 27th International Symposium on MicroScale Bioseparations and Analysis (MSB2012) in Geneva, Switzerland.

OUTSTANDING PUBLICATIONS

S. M. AL-MASSARANI, S. BERTRAND, A. NIEVERGELT, A. M. EL-SHAFEE, T. A. AL-HOWIRINY, N. M. AL-MUSAYEIB, M. CUENDET, J.-L. WOLFENDER. Acylated pregnane glycosides from *Carallum sinaica*. *Phytochemistry*, 79: 129-140, 2012

P. J. EUGSTER, D. BIASS, D. GUILLARME, P. FAVREAU, R. STÖCKLIN, J.-L. WOLFENDER. Peak capacity optimisation for high resolution peptide profiling in complex mixtures by Liquid Chromatography coupled to Time-of-Flight Mass Spectrometry: Application to the *Conus consors* cone snail venom. *J. Chromatogr. A*, 1259: 187-199, 2012.

C. S. FUNARI, P. J. EUGSTER, S. MARTEL, P.-A. CARRUPT, J.-L. WOLFENDER, D. H. S. SILVA. High resolution ultra-high pressure liquid chromatography-time-of-flight mass spectrometry dereplication strategy for the metabolite profiling of Brazilian *Lippia* species. *J. Chromatogr. A*, 1259: 167-178, 2012.

J.-L. WOLFENDER, S. RUDAZ, Y. H. CHOI, H. K. KIM. Plant Metabolomics: From Holistic Data to Relevant Biomarkers. *Curr. Med. Chem.*, 20: 1056-1090, 2012.

1.	PUBLICATIONS	(DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 42)
1.1	SCIENTIFIC PUBLICATIONS (WITH IMPACT FACTOR)	13
2.	POSTERS PRESENTATIONS	(DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 43)
2.1	POSTERS PRESENTATIONS	24
3.	ORAL PRESENTATIONS	(DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 45)
3.1	CONGRESSES & SYMPOSIA	31
3.2	CONTINUING EDUCATION & OPEN TO THE PUBLIC LECTURES	5
3.3	RADIO/TELEVISION INTERVENTION	1
4.	PUBLIC RESEARCH FUNDS (FNSR, NIH, CTI)	

NCCR

NCCR Plant Survival WP2, plants antagonists and mutualists (N° 110-108)

Main applicant: T. TURLINGS, UNINE

Co-applicants: J.L. WOLFENDER

Total allocation: CHF 169'000.--

Allocation 2012: CHF 36'670.--

Duration: 4 years

Starting date: 2009

SWISS NATIONAL SCIENCE FOUNDATION

Fusarium in human and plant pathology: Investigation of phytoalexins and mycoalexins with fungitoxic activity for the search of new antifungal agents and characterisation of common traits (CRSII3_127187/1)

Main applicant: J.L. WOLFENDER

Co-applicant: M. MONOD, CHUV, K. GINDRO and S. SCHÜRCH, ACW

Allocation **2012**: CHF 251'369.--

Duration: 3 years

Starting date: **2009**

Targeted and metabolomic study of the early chemical events of the wound response in *A. thaliana*: dynamics of signaling and search for long distance biomarkers (No 205320/135 190 – 1)

Applicant: J.L. WOLFENDER

Co-applicant: S. RUDAZ

Co-applicant : T. FARMER, UNIL

Total allocation: CHF 130'620.--

Allocation **2012**: CHF 66'660.--

Duration: 2 years

Starting date: **2011**

SINO SWISS SCIENCE AND TECHNOLOGY COOPERATION – SSSTC

Collaboration between the School of Pharmaceutical Sciences of the University of Shandong and Geneva

Sino Swiss Science and Technology Cooperation Program (SSSTC) IP18-092011

Main applicant: J.L. WOLFENDER

Total allocation: CHF 31'100.--

Allocation **2012**: CHF 7'800.--

Duration: 3 years

Starting date: **2012**

SECRETARIAT D'ETAT A L'EDUCATION ET A LA RECHERCHE (SER)

Evaluation of the Health Benefits of Brazilian Fruits and Vegetables for the Development of Safe and Valuable Functional Food

Brazilian Swiss Joint Research Program - BSJRP

Applicants: J.L. WOLFENDER, M. CUENDET, E. FERREIRA-QUEIROZ

Total funding: CHF 173'400.--

Total allocation: CHF 112'000.--

Allocation **2012**: CHF 53'000.--

Duration: 2 years

Starting date: **2012**

FP7-PEOPLE-IRSES /IAPP- EUROPEAN GRANT

Exploring Chemical Biodiversity with Innovative Approaches for Fighting Chagas and Leishmaniasis

Proposal N°269301 – acronym: ChemBioFight :

Applicant: L. SKALTSOUNIS (EU Coord)

Co-Applicant: J.L. WOLFENDER (CH Coord.)

Other countries: GRC, FRA, NLD, BRA, ARG, CHI

Total allocation: Euros 434'700.—

Allocation **2012**: 0.--

Duration: 4 years

Starting date: 2011

Integrated Technologies for the Discovery and Development of Cosmeceutical Agents from Plant Biodiversity

Proposal No 286287 – acronym: NATPROTEC

Applicant: L. SKALTSOUNIS (EU Coord.)

Co-Applicant: M. CUENDET (CH Coord.), UNIGE

Co-applicant: J.L. WOLFENDER

Other countries: GRC, FRA, AUS

Total funding: Euros 1'813'624.—

Allocation **2012**: Euros 50'118. — (CHF 59'400.--)

Duration: 4 years

Starting date: **2012**

5. RESEARCH FUNDS (INDUSTRY AND ASSIMILATED)

Code	Service Development Research	Amount for 2012 (CHF)
Fonds Industrie (J.L. Wolfender, S. Rudaz)	Research & Services	216'000
Fonds Industrie (J.L. Wolfender, M. Cuendet, Ph. Christen)	Research & Services	66'183
Fonds Industrie (J.L. Wolfender, M. Cuendet, Ph. Christen)	Research & Services	90'712

6. PATENTS

No 12 54209 : Extraits de sarments de vigne, compositions les contenant et leur utilisation comme agent antipathogène pour les plantes (2012), Gindro, K., Maxant, F.-X., Schnee, S., Dubuis, P. H., Wolfender, J.-L., Ferreira Queiroz, E. F. and Godefroy, P.

CLINICAL PHARMACEUTICAL



ASSOCIATE PROFESSOR

Chantal CSAJKA

SCIENTIFIC COLLABORATORS

Monia GUIDI

Alice PANCHAUD

PH.D STUDENTS

Etienne WEISSKOPF

Elyes DAHMANE

Verena GOTTA

GENERAL DESCRIPTION OF THE LABORATORY OR GROUP

Clinical Pharmacy is an emerging discipline whose main aims are to develop drug research and education oriented towards patient care.

The activities of the group is divided into two main aspects that comprises (i) drug individualization through population pharmacokinetic, pharmacodynamic and pharmacogenetic modelling that allows characterisation of the dose-concentration-response relationships of drugs and (ii) drug optimization in vulnerable populations, such as paediatrics, geriatrics or critically ill patients. The population approach is a very suitable method to capture the combined effects of multiple demographic, environmental, or genetic factors that can influence drug levels and potentially modulate drug response or toxicity. The group's interests are also focused on dose adjustment strategies for drugs followed by therapeutic drug monitoring.

Our group is working in close collaboration with several research groups and clinical units for specific research projects and is participating to local national and international clinical studies. Several important projects in the area of anti-infective, oncologic and psychotropic treatments are on-going. The group is also mandated by industrial companies to conduct population pharmacokinetic studies for drugs during their clinical development phases. Our expertise allows for drug analyses and simulations, which can provide a more global understanding of the drug kinetics along with intersubject variability and covariate effect, which is of major interest for the clinical development of new compounds.

The group is also involved into the pregraduate teaching of clinical pharmacy at the Master level and is supervising master theses and doctoral theses in the field of clinical pharmacy. Since 2012, it is also teaching and supervising bachelor thesis at the "Haute Ecole Santé Vaud" for mid-wives.

SPECIFIC RESEARCH FIELDS

Anti-HIV/HCV drugs. The group has been involved in the field on HIV therapy for several years. This research area has been extended to the study of HCV drugs frequently used in combination with antiretroviral drugs. This year has been focused on the elaboration of protocols and research plans aiming at studying the pharmacokinetics of recent HCV anti-proteases drugs in the target population of co-infected patients and for HIV/HCV interaction studies. Support from the FNS has been granted for this project in 2012. Optimisation of the therapeutic drug monitoring (TDM) by providing better interpretation tools is another important focus of the group in collaboration with the CHUV and the EPFL (IsyPem Project part of the nano-tera project). This includes the development of new methods for the description of the kinetic profile of HIV and other drugs based on meta-analysis approaches and the elaboration of a TDM software that will be made accessible to clinicians.

Oncologic treatments. Several studies are continuing in the field of oral oncologic treatments. The pharmacokinetics and metabolite profiling of tamoxifen in patients treated for breast-cancer, in relation to genetic polymorphism and other sources of variability is currently under investigation. Research support by a private foundation has been granted for this study (Tamoxifen metabolism and the impact of tamoxifen dose on the level of the active metabolites in endocrine sensitive breast cancer patients. (K. Zaman, main applicant, LA. Décosterd, C.Csajka, CB. Eap, T. Buclin, co-applicants).

The study of imatinib in patients with chronic myeloid leukaemia or gastro-intestinal stromal tumour has provided confirmatory results regarding the concentration-effect relationships of this drug. The first randomized study evaluating the utility of the TDM of imatinib has been fulfilled. Although insufficient patients could be enrolled to provide conclusive results, this study could demonstrate some utility of the TDM approach in case of toxicity or treatment failure. A first prototype tool for dosage individualisation based on population pharmacokinetic analyses is available through collaboration with the EPFL (IsyPem, nano-tera project).

Psychotropic drugs. A multicentre study involving two Swiss and two French maternities has started in 2012, whose objectives are to assess the exposure of breastfed infants to antidepressant drugs and to evaluate the impact of this treatment on their neuro-behavioral development. In addition, several collaborative projects on the pharmacokinetics of pro-cognitive and psychotropic drugs have been performed in collaboration with the CHUV.

Anti-infectious agents: The pharmacokinetic, pharmacodynamic and pharmacogenetics analyses of some antibiotics, anti-malaria and antifungal drugs have allowed a better comprehension of their pharmacokinetics and sources of variability and have contributed to optimisation of their therapeutic management.

SPECIFIC PROJECTS INITIATED AND RECOGNITIONS

A new research project on newly marketed anti-hepatitis C drugs that are frequently associated to antiretroviral drugs and susceptible to many drug-drug interactions has been initiated. A grant has been granted to the SNF (Clinical pharmacology and pharmacogenetics in the complex care of HIV and HIV/HCV co-infected individuals. LA. Décosterd, main applicant, A. Rauch, C. Csajka, T. Buclin, A. Telenti, co-applicants).

The group is in charge of updating the book "Médicaments, Grossesse et Allaitement. J-F. Delaloye et al. Editors Médecine & Hygiène. The setting up of a new certificate of advanced studies in clinical pharmacy (CAS) within the continuous education program at the UNIGE is in progress.

1. PUBLICATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 49)

1.1	SCIENTIFIC PUBLICATIONS (WITH IMPACT FACTOR)	8
1.2	SCIENTIFIC PUBLICATIONS (WITHOUT IMPACT FACTOR)	2
1.3	BOOK CHAPTER	2

2. POSTERS PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 PAGE 50)

2.1	POSTERS PRESENTATIONS	8
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3. ORAL PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 PAGE 51)

3.1	CONTINUING EDUCATION & OPEN TO THE PUBLIC LECTURES	8
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4. PUBLIC RESEARCH FUNDS (FNSR, NIH, CTI)

FNSR

FN 324730 141234_1. Clinical Pharmacology and Pharmacogenetics In the Complex Care of HIV and HIV/HCV co-infected Individuals. Dr. L. Decosterd, Dr A. Rauch, Dr. C. Csajka, Prof. T. Buclin, Prof. A. Telenti (co-applicant : 472'000.- ; (1 post-doctoral position 50% for 3 years)

FOUNDATION ROBERTO ET GIANNA GONNELLA

Tamoxifen metabolism and the impact of tamoxifen dose on the level of the active metabolites in endocrine sensitive breast cancer patients. Dr K. Zaman, Dr. C. Csajka, Dr LA Decosterd, Dr T. Buclin, Prof S. Leyvraz (co-applicant; CHF 116'490.-).

5. RESEARCH FUNDS (INDUSTRY AND ASSIMILATED)

Code	Service Development Research	Amount for 2012 (CHF)
Industry	Mandate for a pharmacokinetic study	16'000.- CHF

COMMUNITY PHARMACY



PROFESSOR ASSOCIATE

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Nadia MARTEL

Raphaël NAOUX
Matthias REYMERMIER
Mirjam RUFENACHT
Ljiljana SCHLAEFLI,

GENERAL DESCRIPTION OF THE UNIT

The fact of prescribing, recommending or swallowing a drug seems banal and yet there are many traps: side effects, insufficient efficacy, too high costs, non-adherence, waste, lack of motivation, altered quality of life, etc. These topics, as well as the evolution of pharmaceutical practices are considered as priorities of action for academic and clinic activities of the Pharmacy of the PMU (Polyclinique Médicale Universitaire), a unique place in Switzerland, which combines community pharmacy practice with collaborative community pharmacy research and university teaching.

Olivier Bugnon, chief pharmacist, is on the other hand an associated professor to the School of pharmaceutical sciences (University of Geneva, University of Lausanne); like this, he participates in the development of community pharmacy practice, a pharmaceutical science which respects the healthcare priorities and the central role of the patient. His main teaching responsibility is the organization of the second year of the Master in Pharmacy (year of assistantship). He supervises the examinations of the Master and represents the School of pharmaceutical sciences in the Federal Committee for the organization and evaluation of the federal examination for pharmacists. His research activities (5 PhD students in pharmaceutical sciences in 2012) explore ways of collaboration between physicians, pharmacists and other professionals to improve the responsible use of medicines (effectiveness, safety, efficiency).

Internationally, the group of community pharmacy is represented especially within the International Pharmaceutical Federation (FIP), the European Society of Clinical Pharmacy (ESCP), the Pharmaceutical Care Networks in Europe (PCNE) and the European Society for Patient Adherence, Compliance and Persistence (ESPACOMP).

SPECIFIC RESEARCH FIELDS

The research of the Group of Community Pharmacy Practice covers the three following areas:

1. INTEGRATED CARE

The global trend for health systems is coordination, networking and continuity of care. Pharmacists are at the interface of the treatments prescribed by the physicians and the OTC treatments. The evolution of their role turns towards collaborative pharmacy practice, aiming at the quality of the care and control of the costs. In 2012, the area « integrated care » of the pharmacy of the PMU worked on the following topics and projects:

- Quality circles physicians-pharmacists-nurses in nursing homes (cantonal projects in Fribourg and Vaud)
- *Risk evaluation and mitigation strategies – REMS* and patient programs (e.g. Patient with cardiovascular risk; patients with oral anticancer medications)
- Animation of the network of the pharmacists specialized in Addiction Medicine in the French-speaking part of Switzerland - COROPHA (project supported by the FOPH)

The research on integrated care is closely linked to the two other areas « therapeutic adherence » (e.g. oncology) and « safety and cost effectiveness of drugs » (e.g. in geriatrics). This research involves transverse scientific collaborations between pharmaceutical, medical, human and economic sciences.

2. MEDICATION ADHERENCE

The daily and prolonged taking of medicine is difficult for chronic patients, especially in case of side effects, complex treatments, lack of motivation, incomprehension or refusal of the treatment. To sometimes forget to take one's medicine is nevertheless a normal human behavior. The medication adherence defines itself as an active process in which the patient works to maintain his health in collaboration with the medical team.

The researchers of the Pharmacy of the PMU, in collaboration with various physicians and nurses, are interested in the scientific development and evaluation of a routine adherence consultation in domains like for example high blood pressure, VIH infections, oral anticancer medications, transplantations. The adherence consultation is concretized by:

- Motivational, semi-structured interviews, lead by a pharmacist;
- The measure of medication adherence through an electronic medication box and its relation with the effects of the therapy;
- The sharing of data collected in pharmacies (persistence, quality of execution, side effects, perceptions of patients and their relatives) with the medical and caretaking team

The research on the adherence also contributes to the goals of the area « integrated care » (e.g. in oncology).

3. SAFETY AND COST EFFECTIVENESS OF DRUGS

Drugs represent the option most frequently used by the physicians. The prescription formalizes the therapeutic plan with the concordance of the patient; it represents an essential communication tool for the collaboration with the pharmacist. Drug related problems experienced by the patients and medication errors are too frequent. They are usually a sign of system failure, a cost factor and breaks of the seamless care: many good reasons to study scientifically the provided services likely to control drug risk management as well as to improve safety, effectiveness and efficiency of the medicines.

A **medication review** is a global and structured analyze of the whole pharmaceutical record of chronic patients. This provided service can, in addition to the medication record, base itself on interviews with patients as well as on some clinical data (laboratory values, therapeutic goals, past histories,...) supplied by the physicians. Those can now act by taking into account propositions formulated by the pharmacists.

This research area is naturally closely linked with the two other areas « therapeutic adherence » and « integrated care ».

OUTSTANDING PUBLICATIONS

G. GRAS, M.-P. SCHNEIDER, M. CAVASSINI, F. LUCHT, M. LOILIER, R. VERDON, L. BERNARD, J.-J. PARIENTI *Patterns of Adherence to Raltegravir-Based Regimens and the Risk of Virological Failure Among HIV-Infected Patients : The RALTECAPS Cohort Study*.JAIDS 2012, 61 : 265 -269

O. BUGNON, D. HUGENTOBLE-HAMPAÏ, J. BERGER, M.-P. SCHNEIDER
New Roles for Community Pharmacists in Modern Health Care Systems : A Challenge for Pharmacy Education and Research. CHIMIA (2012 February); 66: No. 5, 304-307

I. KRUMMENACHER, M. CAVASSINI, O. BUGNON, M.-P. SCHNEIDER
Characteristics of HIV patients referred to a medication adherence program in Switzerland. Int J Clin Pharm 2012, 34: 426-431

SPECIFIC PROJECTS INITIATED AND RECOGNITIONS

Since 1st August 2012, consolidation of academic supervision of the Community Pharmacy Group of the School of pharmaceutical sciences (University of Geneva, University of Lausanne) by the appointment of Dr Marie Paule Schneider as "collaboratrice scientifique 2".

In 2012, the Community Pharmacy of PMU goes successfully through the following certification/accreditation steps:

1. Renewal of the certification ISO 9001:2008 / Healthmark – 2. First intermediate QMS-Pharmacy Audit (pseudo-patient with a Rx prescription) in accordance with the professional standard ISAS QMS-Pharma 2010.

O. BUGNON, representative of the School of pharmaceutical sciences (University of Geneva, University of Lausanne) in the Federal Committee in charge of the organization of the annual federal exam in Pharmacy, as requested by the federal law on the medical professions (LPMed).

O. BUGNON, president of the national working group PAP ("Plattform Ausbildung Pharmazie") of pharmaSuisse (Swiss society of pharmacists) aiming at the coordination in pre-graduate education between the universities (Basel, Bern, Fribourg, Geneva, Neuchâtel, Zürich), the Swiss association of pharmacy students (asep), the Federal Office of Public Health (FOPH) and the professional associations and other interest groups (pharmaSuisse, Swiss society of hospital pharmacists, Swiss society of industry pharmacists); meetings in Bern (27.06.2012 and 07.11.2012).

M.P. SCHNEIDER, mandated for Switzerland by the ABC project (Ascertaining Barriers to Compliance: policies for safe, effective and cost-effective use of medicines in Europe), funded by the European Commission Seventh Framework programme (FP7 Theme Health); principal investigator: Dr W. Clyne, School of Pharmacy, Keele University. Project: *Management of patient medication adherence: a survey of doctors, pharmacists and nurses in 16 European countries*. Survey conducted from June 2011 to May 2012.

O. BUGNON, mandated for the development, teaching and evaluation of the module "Risk Management" for the new Executive MBA in Healthcare Specialisation launched by the « Institut d'économie et management de la santé (IEMS) » (University of Lausanne): « Risk management strategies for optimizing the performance of health care system, providers and industries. », Lausanne, 12-13.10.2012.

A. Niquille, MP Schneider, D. Nanchen and J. Cornuz, in charge of the development and implementation of the clinical research quality project of the Policlinique Médicale Universitaire (PMU) and the University Department of Community Medicine and Health (DUMSC), University of Lausanne.

O. BUGNON, N. MARTEL, S. DESSELBERGER, responded positively to the request to visit the "Pharmacie de la PMU" 3 days by a delegation of the Japanese Association of Pharmacy interested by the following topics: quality circles physicians, pharmacists, nurses in primary care and in nursing homes; collaborative programs promoting the medication adherence, innovative trends in community pharmacy practice.

Establishment of an agreement of collaboration between PMU, O. Bugnon and the start-up SISPha SA (www.sispha.com), created to facilitate the implementation in community pharmacies of collaborative pharmaceutical services currently remunerated by the insurers (RBP) and more particularly the coaching of chronic patients, medication adherence and postmarketing risk evaluation and mitigation programs (Phase IV).

CONGRESSES ORGANISED

O. BUGNON, scientific expert for the Symposia Pharmacy on Top, organized by MEPHA Pharma SA with the support of SISPha SA, on the topic of leadership and change strategies:

- «Retrouver un nouveau souffle: l'exemple de ceux qui ont réussi» in Montreux (26.4.2012) and in Lausanne-Bussigny (27.4.2012)
- «Premiers pas en Entretiens motivationnels», in Lugano (3.5.2012).

M.J. ZEUKENG, member of the symposium committee and chairman of the PhD Day 2012 of the School of pharmaceutical sciences (University of Geneva and University of Lausanne), Fondation Brocher, Hermance (Geneva), 15.06.2012.

M.P. SCHNEIDER, member of the scientific committee, of the best poster committee and workshop leader of the 15th Annual meeting of ESPACOMP (European Society for Patient Adherence, COMPLIance and Persistence, Ghent (Belgium), 26-27.10.2012.

O. BUGNON, member of the symposium committee and chairman for the scientific symposium organized at the occasion of the Policlinique Médicale Universitaire's (PMU) 125th anniversary: « Littérature et Web 2.0 : chances et défis pour la santé », Lausanne, 14.11.2012.

O. BUGNON, member of the conference committee and workshop leader of the 8th Pharmaceutical Care Network in Europe (PCNE) Working Conference [Collaborative pharmaceutical care in research and practice] planned for 6-8 February 2013 in Berlin [www.pcne.org].

1. PUBLICATIONS

(DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 52)

1.1	SCIENTIFIC PUBLICATIONS (WITH IMPACT FACTOR)	3
1.2	SCIENTIFIC PUBLICATIONS (WITHOUT IMPACT FACTOR)	15
1.3	PUBLICATIONS EXTRAMUROS	2
1.4	BOOKS OR BOOKS CHAPTERS	8

2. POSTERS PRESENTATIONS

(DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 55)

2.1	POSTERS PRESENTATIONS	6
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3. ORAL PRESENTATIONS

(DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 55)

3.1	CONGRESS & SYMPOSIA	25
3.2	CONTINUING EDUCATION & OPEN TO THE PUBLIC LECTURES	34

4. THESIS PRESENTED

M. SCHÜTZ

Violences conjugales envers les femmes: que peut faire le pharmacien d'officine?

Pharmacie communautaire, Section des sciences pharmaceutiques, Université de Genève et Université de Lausanne.

Unité de Médecine des violences, DUMSC, CHUV, Université de Lausanne

Supervisor : Dr Marie-Claude Hofner

5. PUBLIC RESEARCH FUNDS (FNSR, NIH, CTI)

FEDERAL OFFICE OF PUBLIC HEALTH (FOPH)

Réseau médecins-pharmaciens dans le domaine de l'addiction – Formation et intégration du pharmacien dans le réseau interdisciplinaire de prévention et de prise en charge de l'addiction.

"Consolidation des acquis d'études précédentes et développement des standards de qualité pour la pratique officinale s'appliquant à la prise en charge des problématiques d'addiction (drogue, alcool et tabac)" - (Contrat No. 09.004964 / 204.0001 / - 650) [Integration of pharmacists in the interdisciplinary network for the management of addictions]

Main applicant: O. Bugnon

Co-applicant: S. du Pasquier

Total allocation : CHF 79'000.-

Allocation **2012**: CHF 7'000

Duration: 4 years

Starting date: 2009

Elaboration de l'Examen fédéral en Pharmacie : participation des experts de la Section des sciences pharmaceutiques (Université de Genève, Université de Lausanne) - (Contrat No. 12.002085 / 704.0001 / - 527) - [Elaboration of the Federal Exam for Pharmacy 2012]

Main applicant: O. Bugnon

Allocation **2012**: CHF 187'348

Duration: 1 year

CANTONAL OFFICE OF PUBLIC HEALTH – VAUD

Encadrement scientifique d'un programme d'assistance pharmaceutique des établissements médico-sociaux pour personnes âgées (EMS) vaudois

[Development, implementation and evaluation of a new cantonal collaborative care management programme in nursing homes (physicians-nurses-pharmacists quality circles)]

Main applicant: O. Bugnon

Total allocation : CHF 180'000.-

Allocation **2012**: CHF 30'000

Duration: 6 years

Starting date: 2007

5. RESEARCH FUNDS (INDUSTRY AND ASSIMILATED)

Code	Mandats de prestations et de recherche	Montants pour 2012 (CHF)
ABEC3	Recherche et développement	6'500
CP3	Formation	7'900
SAN6	Recherche et développement	20'000
SM10	Recherche et développement	10'000
SOVAPH	Recherche et développement	10'000
NOV8	Recherche et développement	48'160
PFI6	Recherche et développement	17'000
PHA11	Formation	7'000
PFI6	Recherche et développement	17'000
TAS11	Recherche et développement	30'000
		173'560

* Les fonds de recherche du Prof. O. Bugnon sont officiellement contrôlés par le département des Finances, PMU, Lausanne.

HOSPITAL PHARMACY



PROFESSORS ASSOCIATES

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HUG Pharmacy

Prof André PANNATIER

CHUV Pharmacy

PH.D STUDENTS HUG

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Laurent CARREZ

Delphine CARLI
Mapi FLEURY

Olivia FRANCOIS
Laure-Zoé KAESTLI

PH.D STUDENTS CHUV

Jean-Christophe DEVAUD
Anne HENRY

David PALMERO
Catherine PLUESS-SUARD

Hanitra RAVELOJAONA

GENERAL DESCRIPTION OF THE UNIT

The two professors of the group are head of the hospital pharmacies at *CHUV* (Lausanne) and *HUG* (Geneva) and, in this context, develop research and education activities in hospital and clinical pharmacy.

The undergraduate education is especially focusing on the following topics:

- Drug selection, drug flow, and pharmacoeconomics
- Production and quality control of drugs at the hospital
- Medical devices and materiovigilance
- Risk management
- Information on drugs, infovigilance
- Clinical pharmacy, especially:
 - o Pharmacy in clinical nutrition
 - o Pharmacy in intensive care units
 - o Pharmacy in paediatrics
 - o Pharmacy in surgical units

A post-graduate education (MAS) in hospital pharmacy is also proposed on the two sites since 1999. This three year programme is a complete specialisation in hospital pharmacy, associating theoretical and practical teachings, as well as a one year research project.

Both hospitals also propose positions of PhD students in pharmaceutical sciences, either for pharmacists having finished their MAS, or in direct access.

For more information:

- *CHUV* pharmacy: www.chuv.ch/pha
- *HUG* pharmacy: <http://pharmacie.hug-ge.ch>

SPECIFIC RESEARCH FIELDS

- 1) Safety of drug use process in hospitals
 - Proactive risk analysis in hospital processes, application of the FMECA method.
 - Impact of information technologies on patient safety at prescription, dispensing and administration levels.
 - Impact of human factors on error rates at different steps of the medication use process.

- 2) Optimisation of drug administration
 - Development of ready-to-use formulations adapted to hospital specificities, and validation of aseptic production processes.
 - Evaluation of the quality of medical devices involved in drugs administration.
 - Evaluation and improvement of specific administration techniques (i.e. enteral feeding tubes, nebulisation, intrathecal).
- 3) Pharmacoeconomic analyses of drug use in the hospital
 - Evaluation of cost-benefit ratios of treatments.
 - Evaluation of spill-over effect between the hospital and the ambulatory care settings.

OUTSTANDING PUBLICATIONS HUG

S. NUSSBAUMER, L. GEISER, F. SADEGHIPOUR, D. HOCHSTRASSER, P. BONNABRY, J.-L. VEUTHEY, S. FLEURY-SOUVERAIN. Wipe sampling procedure coupled to LC-MS/MS analysis for the simultaneous determination of 10 cytotoxic drugs on different surfaces. *Analytical Bioanalytical Chemistry*, 402, 2499-509, 2012.

OUTSTANDING PUBLICATIONS CHUV

J.-C. DEVAUD, M.M. BERGER, A. PANNATIER, P. MARQUES-VIDAL, L. TAPPY, N. RODONDI, R. CHIOLERO, P. VOIROL. Hypertriglyceridemia: a potential side effect of propofol sedation in critical illness. *Intensive Care Med*, DOI 10.1007/s00134-012-2688-8; 38:1990–1998, 2012.

C. PLÜSS-SUARD, A. PANNATIER, C. RUFFIEUX, G. KRONENBERG, K. MÜHLEMANN, G. ZANETTI. Changes in the use of broad-spectrum antibiotics after cefepime shortage: a time series analysis. *Antimicrob. Agents Chemother.*, 56(2), 989-994, 2012.

1. PUBLICATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 61)

1.1A	SCIENTIFIC PUBLICATIONS (WITH IMPACT FACTOR) HUG	5
1.1B	SCIENTIFIC PUBLICATIONS (WITH IMPACT FACTOR) CHUV	9
1.2A	SCIENTIFIC PUBLICATIONS (WITH OUTIMPACT FACTOR) HUG	9
1.2B	SCIENTIFIC PUBLICATIONS (WITHOUT IMPACT FACTOR) CHUV	4
1.3A	BOOKS OR BOOKS CHAPTERS HUG	1
1.3B	BOOKS OR BOOKS CHAPTERS CHUV	1

2. POSTERS PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 64)

2.1 A	POSTERS PRESENTATIONS HUG	29
2.1 B	POSTERS PRESENTATIONS CHUV	16

3. ORAL PRESENTATIONS (DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 66)

3.1A	CONGRESSES & SYMPOSIA HUG	11
3.1B	CONGRESSES & SYMPOSIA CHUV	8
3.2A	CONTINUING EDUCATION & OPEN TO THE PUBLIC LECTURES HUG	19
3.2B	CONTINUING EDUCATION & OPEN TO THE PUBLIC LECTURES CHUV	30

4. THESIS PRESENTED

4.1. INTRA-MUROS THESIS (HUG)

Liliane GSCHWIND

Anticoagulation par antivitamines K : analyse des interactions médicamenteuses et des polymorphismes génétiques à l'origine de la variabilité de la réponse et des risques liés à l'acénocoumarol

University of Geneva – 2012 –

Supervisor: Prof. J. DESMEULES

Co-Supervisor: Prof. P. BONNABRY

4.2. INTRA-MUROS THESIS (CHUV)

Catherine PLÜSS-SUARD

Suivi de la consommation des antibiotiques pour la promotion de leur bon usage et la maîtrise de la résistance bactérienne en milieu hospitalier : mise en place et exemples d'utilisation.

University of Geneva – 2012 –

Supervisor: Prof. A. PANNATIER

Co-supervisor: Prof G. Zanetti

DOCTORAL PROGRAM

COURSES AND SYMPOSIA

Table 1

List of courses organized within the PhD Program in Pharmaceutical Sciences 2012 and number of participants

Name of course 2012	# course	Responsible Professor	# of hours	credits	# Students
Spectrométrie en masse	1506BCR	G. Hopfgartner E. Varesio	0		6 + masters
Spectrométrie de masse (exercices)	1506BEX	G. Hofgartner S. Michalet E. Varesio	28	4 inclus 1506BCR	6 + masters
Analytical tools characterizing protein-ligand interactions	19H002	R. Perozzo	6	1	10
Assistance pharmaceutique et pharmacie clinique	19H003	P. Bonnabry	18	3	13, total 23
Assurance Qualité (AQ): Rôle, activités et exigences au sein d'une industrie pharmaceutique	19H004	E. Allémann S. Campione Ph.Meuwly	16	2.5	15
Caractérisation structurale de produits naturels	19H006	J.-L. Wolfender E. Ferreira-Queiros	12	2	8
Dispositifs médicaux et matériovigilance	19H008	A. Pannatier	18	3	7, total 33
Formulation of protein biopharmaceutical and drug delivery	19H013	T. Arvinte	20	3.5	6, total 36
Initiation à l'électrophorèse capillaire	19H016	S. Rudaz	18	3	6
Les brevets dans la recherche - source d'information et moteur de l'innovation	19H018	L. Scapozza J. De Werra P. Ducor D. Kraus L. Miéville R. Tschudin P. Weibel	22	3.5	10, total 11
Essentials in molecular and applied pharmacology	19H019	U. Rüegg	14	2.5	9
Physiopathologie oculaire et moyens thérapeutiques: diabète et œdème maculaire	19H021	C. Tabatabay	12	2	3
Structural bioinformatics and molecular modeling	19H028	L. Scapozza W. Bisson H. Scheib	30	5	23
Techniques de préparation d'échantillons, cas de matrices solides	19H029	Ph. Christen	6	1	ANNULE manque inscriptions
Toxicologie Analytique Forensique	19H031	Ch. Staub	8	1.5	11

Name of course 2012	# course	Responsible Professor	# of hours	credits	# Students
Use of fluorescence spectroscopy in the study of drugs, protein and membrane	19H032	T. Arvinte	12	2	5, total 20
Validation de méthodes analytiques	19H034	S. Rudaz	18	3	12
Production stérile: Méthodes et Environnement	19H044	F. Sadeghipour	19	3	7
Therapeutic Drug Monitoring and its Application in Diagnostics and Clinical Research	19H045	L. Decosterd	6	1	8
Initiation aux méthodes d'analyse multivariées en sciences pharmaceutiques	19H046	S. Rudaz J. Bocard	12	2	15
Introduction to plant metabolomics	19H047	J.-L. Wolfender	16	2.5	11 PhD GE 21 PhD NE
Innovation collaborative ou Open innovation au secours de la recherche et du développement pharmaceutique	19H049	L. Scapozza E. Le Pouls	18	3	ANNULE à la demande de E. Le Pouls 24.9.12
Biochips for health research	GRENCR02	J. Breton	24	4	2, total 32 visitransmiss
Biotechnologie Moléculaire	GRENCR03	M. Seve	24	4	ANNULE
TOTAL	24				178 Ph 133 others

*) The course description can be found under the web page of the School of Pharmaceutical Sciences, EPGL
<http://epgl.unige.ch/pharm/fr/>

Table 2

List of symposia organized within the PhD Program in Pharmaceutical Sciences 2012 and number of participants*.

Name of course 2012-2013	# course	Responsible Professor	# of hours	credits	# Students
Symposium Pharmapeptides	19H001	G. Borchard	6	1	10 PhD 35 others-
PhD Day	19H020	L. Scapozza	6	1 or 2	64 PhD 7 post-doc + prof. + 1 speaker
Conférences sur sujets spécialisés		G. Hopfgartner		1,5 pour 5 conf.	

Table 3

Name of course 2012-2013	# course	Responsible Professor	# of hours	credits	# Students
Séminaire extra-muros Zermatt	19H024	M. Cuendet JLWolfender		1 or 2	35 PhD total 48

Table 4

List of networking activities organized within the PhD Program in Pharmaceutical Sciences 2012 and number of participants.

Name of course 2012-2013	# course	Responsible Professor	# of hours	credits	# Students
Rencontre avec l'Industrie	19H050	L. Scapozza	6	1	ANNULE à la demande de Novartis
Career day	19H007	L. Scapozza	6	1	46 PhD, 1 stagiaire, 1 post-doc + 1 prof.

***)) scheduled beginning of 2012

COMMENTS

The program in 2012 consisted of 23 courses. The total of hours given within the 2012 PhD program was 451 (without counting the “conferences sur sujets spécialisés”). Two types of courses were proposed, namely weekly (Hebdo) and bloc (Table 1). Within the framework of the PhD program, the PhD day, Career days, visit to Industry and the extra-muros seminar have also been organized with success (Table 2, 3 and 4). The “Symposium Pharmapeptides” was not held in 2011. The program 2012 offered for the fifth year 2 courses via a partnership with the UFR de Pharmacie de Grenoble (Table 1) which foresees an exchange of courses between the two Universities. One of the courses was cancelled and the other one was transmitted by visio-conference.

The PhD program in pharmaceutical sciences has been selected by the CUSO based on the results achieved during the 3 years project as one of the project to be supported further in the next years. The program as well as the budget were submitted to the CUSO who accepted them. The budget in 2012 for the five activities (Seminar Extra-Muros, Conférence spécialisées, Cours, Symposia as well as Networking activities) was of 79'400.- CHF covered by the fund allocated by the CUSO. The costs for 2012 for all the activities were 73'160.01 CHF, the revenues were 16'881.13.- CHF. This makes a cost of 56'278.88 CHF for the CUSO budget. Thus, we spent less than budgeted. The difference between the budget and the costs is due to the fact that: the course 19H049 (Innovation collaborative..), with a budget of CHF 4'500.00, was cancelled by the organizer as the number of participants registered did not fulfill his expectations. The costs for the seminar extra-muros were less than the 36'670. CHF budgeted and amounted to 29481.20.- because of higher revenues. Furthermore, the successful English courses have been integrated into the CUSO soft skill offer as of 2011. I take the opportunity in this report to thank the CUSO for the past and future financial support allowing offering an outstanding program to the PhD students in Pharmaceutical Sciences. For the renewal of the CUSO support, an exhaustive evaluation of the PhD program has been conducted at the end of 2011. Based on the positive evaluation, CUSO has decided in 2012 to continue to support our PhD program.

The schedule, the content of the courses, hours and credits as well as all indications concerning the PhD program in Pharmaceutical Sciences are stored in a MySQL database and posted dynamically on the web page of the PhD program ([http://epgl.unige.ch/pharm/fr/\[Etudes/programme doctoral\]](http://epgl.unige.ch/pharm/fr/[Etudes/programme doctoral])). Furthermore, the information relative to the program 2012 was sent by E-mail to all PhD students and supervisors well ahead of the beginning of the courses.

The annual information meeting for the PhD students who started the program in 2012 was held on the 9th of October 2012 in the lecture room 4-457.

Based on the results from students' demands and registration to the different courses, some of the courses have been established as annual courses, other courses are scheduled biannually or every 18 months. The number of PhD students enrolled at the EPGL increased over the last years, reaching 126 at the end of 2012. All of them are submitted to the bylaw that foresees the participation to the PhD program and the acquisition of at least 30 credits before the defense of the thesis. An interesting note is that most of the PhD students have more than 30 credits at the end of their PhD indicating their active participation to the PhD program (Table 1, Table 2, Table 3). The participation was good with a mean value of 7.5 PhD students per course. If we consider all the participants including postdocs and pre-grad this mean-value increases to more than 10 participants, which is the aim per course in respect to the number of participant.

In order to increase the exchange among PhD students and between PhD students and other scientists, the seventh PhD day was organized on the 15th of June 2012 by the PhD students of the group of Hospital Pharmacy. The PhD day was organized in Hermance at the Brocher Foundation with a program including 1 external and 16 PhD students speakers. 64 PhD students, 1 speaker, 7 post-doc and professors for a total of 72 participants participated at this event. The quality of the talks and discussion as well as the organization was very good fulfilling the objectives of this day. The next PhD day is scheduled at the 31st of May 2013 and will be organized by the PhD students of the group of pharmaceutical analytical chemistry.

Considering the success of the Career Day introduced in 2009, it was repeated on 21st of May, 2012. 46 PhD students, 1 stagiaire, 1 post-doc and 1 professor participated at the day organized by the PhD students of the Pharmaceutical Biochemistry. 8 scientists from Industry presented their company, work and career possibilities. A visit to the industry was planned for summer or autumn 2012 but finally cancelled by Novartis due to internal reorganization. Prof. Leonardo Scapozza is still discussing further possibilities for visits to Novartis, an event very appreciated by the PhD students.

The PhD students attended regularly the conferences (conferences spécialisées) proposed within the PhD program. 12 seminars have been given by international researchers from academia and industry. A total of 289 participants attended these lecture series including 75 PhD students, 12 pre-graduates, 37 post-docs and 79 senior scientists.

The yearly « extra-muros » meeting for Ph.D. students in pharmaceutical sciences was held as usual at the Parkhotel Beausite (Zermatt, VS). It took place from September 3 to 7, 2012 and was organized by Prof. Muriel Cuendet and Prof. Jean-Luc Wolfender. This year meeting was entitled “Drugs from Nature: from Discovery to Clinic” and reviewed some of the recent development in the field of Natural products research relevant to pharmaceutical sciences. Fifteen national and international speakers active in academia and industry presented recent trends in various topics ranging from access to biodiversity, lead finding from natural sources up to clinical development.

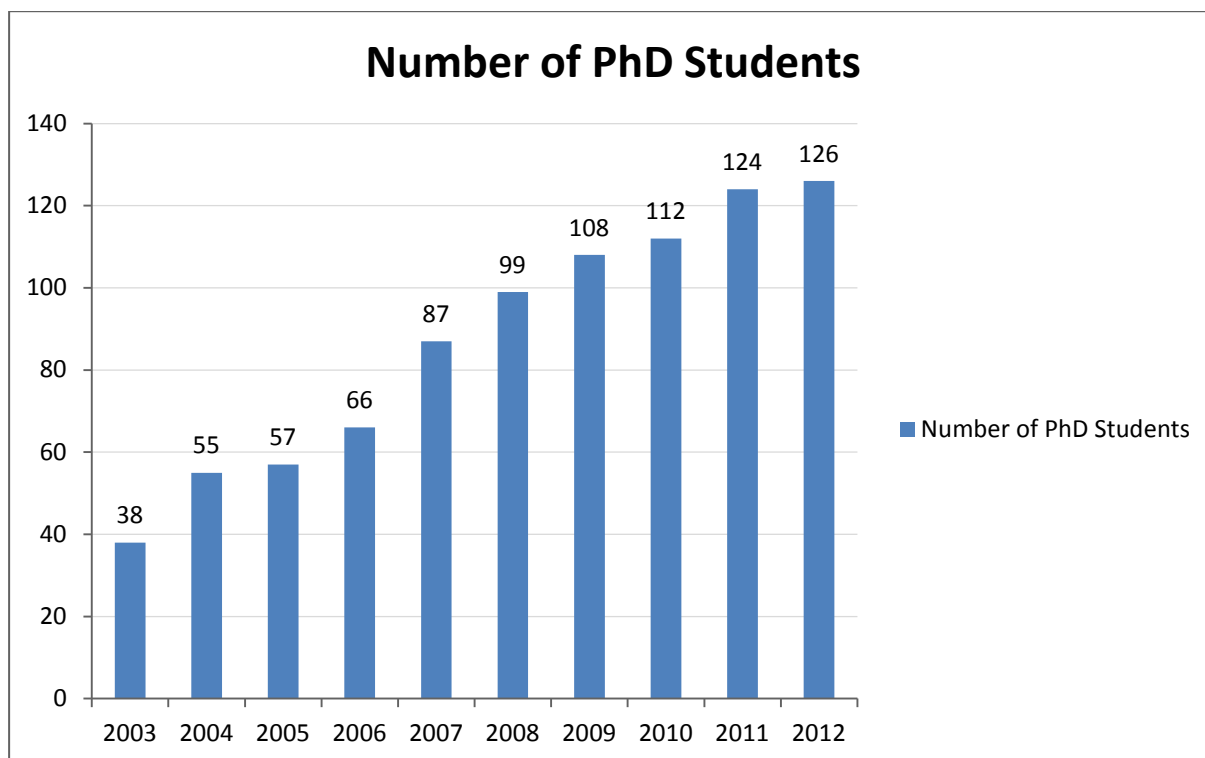
Lectures on the first day were mainly focused on sources of natural products of different origin which include traditional Chinese medicine, venoms and microorganism. The two following days were focused on strategy for lead finding, including the work on plants, animals or microorganisms. Various approaches on biological screening and their application were illustrated either by speakers from the industry or the academy. Local people involved in Wallis for the promotion of medicinal plants also presented their newly opened platform PhytoArk. Thursday was mainly reserved for clinical aspects with the example of the development of natural products based drug from the Swiss company Debiopharm and on Friday,

some provocative lectures on the paradigm of drug discovery were given for an interesting brainstorming session. Several approaches for cancer chemoprevention strategies were also brought throughout the program.

Beside the presentations from the invited speakers, two evening sessions were dedicated to ten short Ph.D. student lectures and during one evening the participant had a preview of a new documentary for ARTE on the potential of cone's venom as a drug source, presented by its author, Dr Reto Stöcklin from Atheris in Geneva.

The meeting was attended by 65 persons (speakers included). Fifty-two participants came from the EPGL and the University hospitals of Geneva and Lausanne. As usual the meeting was evaluated by the participants. Most of the participants were very satisfied by the scientific content of the program and appreciated the presentations of the speakers, as well as the setup of the meeting. This international "extra-muros" meeting offers PhD students with various opportunities for networking.

Summarizing, the key points of the activity of the PhD program in Pharmaceutical Sciences are a program covering the broad range of fields of Pharmaceutical Sciences with 23 courses for a total of 451 hours, the very good participation of the PhD students to all five activities of the PhD program in Pharmaceutical Sciences.



PROFESSOR HONORARY



PROFESSOR HONORARY

Robert GURNY

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GENERAL PRESENTATION OF THE ACTIVITY OF UNITS

The projects belong to the fields of (i) drug delivery to the eye, (ii) protein and peptide formulation and stabilization and (iii) development of novel polymeric carriers of synthetic and natural origin progressed very well with the filing of 3 patents. Novel hybrid gels based on natural polymers have been tested in horses for the treatment of articular pathologies of the joint.

SPECIFIC RESEARCH FIELDS

In the field of vascular blood flow of the retina, a novel peptide (BQ123) has been tested successfully. Locally applied into the vitreous, the bioactive substance improves the supply of oxygen by dilation of the retinal arteries. Clinical indications are acute occlusion of vessels, ischemic conditions, diabetic retinopathy, branched retinal vein occlusion, severe stenosis and embolic diseases. The research results were presented at international meetings.

OUTSTANDING PUBLICATIONS

S.de Valence, J.-C. Tille, D. Mugnai, W. Mrowczynski, R. Gurny, M. Möller, B. H. Walpoth Long term performance of polycaprolactone vascular grafts in a rat abdominal aorta replacement model *Biomaterials* 33, 38-47 (2012)
Doi:10.1016/j.biomaterials.2011.09.024

PARTICULAR PROJECTS INITIATED

A project focusing on the use of superparamagnetic iron oxide particles (SPION) for diagnosis and therapy of cerebral ischemia was initiated with the Institute of Material Sciences (ICMAB) and the Neurovascular Research Laboratory at Vall d'Hebron Hospital (both in Barcelona, Spain).

1. PUBLICATIONS

(DETAILS IN SCIENTIFIC PRODUCTIONS 2012 – PAGE 71)

1.1 SCIENTIFIC PUBLICATIONS (WITH IMPACT FACTOR)

9

2. THESIS PRESENTED

2.1. INTRA-MUROS THESIS

Lutz ASMUS (03.02.2012)

«Injectable Sustained-Release Formulations Based on Polyesters
From Small Molecule Solutions to Protein Delivery to the Eye»

University of Geneva – 2012 – thesis No. 4403

Sarra de VALENCE (30.11.2012)

«*Synthetic biodegradable vascular grafts for the regeneration of arteries*»

University of Geneva – 2012 - thesis N° 4496

3. PATENTS

M. MÖLLER, B. KAUFMANN, R. GURNY, *Process for the esterification of hyaluronic acid with hydrophobic organic compounds* PCT Int. Appl. (2012), WO 2012013670 A1 20120202.

M. MÖLLER, L. ASMUS, R. GURNY, *Compositions comprising 2-hydroxyalkanoic acid polymers and their use in drug delivery systems* PCT Int. Appl. (2012), WO 2012014011 A1 20120202.

R. GURNY, O. JORDAN, S. KADERLI *Hybrid hydrogels*, US Pat. Appl. US61693803

S. KADERLI, O. JORDAN AND R. GURNY. *Hybrid hydrogels* US PAT APPL. 61693803 (JULY 2012)

S. KADERLI, R. GURNY, M. MÖLLER AND L. SCAPOZZA. *Hyaluronic acid-antioxydants conjugates and their uses* US Pat. EFS ID 14508328, (DECEMBER 2012)