EDITORIAL

Chemistry and biology: a promising convergence in the "small drug discovery lab".

Drug discovery depends on the careful management of information produced by biologists and chemists. The interface between chemistry and biology is usually seen as a narrow communication band between scientists accustomed to sharing only a small proportion of their vocabulary. However, this interface is becoming with time a significant workspace as chemistry and biology tend to overlap and become indiscernible from each other. This growing overlap is a result of a very accurate molecular definition of many biological agents that control life, as well as a better and concrete structural definition of interactions between macromolecules themselves and between small compounds and macromolecules in the field of pharmacology.

Increasingly complex and diverse structures from cells and organisms are characterized at the molecular and atomic levels.

When looking at Nobel Prizes in medicine or physiology, it appears that the rewarded accomplishments are more and more the results of combined molecular (chemical) and biological approaches to the study of biological pathways. Many of them enable drug discovery: RNAi, GPCRs, proteasome, discovery of the biological role of nitric oxide, structure of membrane-bound ion channels. The characterization at the atomic level of protein-protein interfaces, catalytic sites of enzymes, protein membrane interfaces has become common, thanks to an industrialization of protein crystallography X-ray diffraction, high field NMR, atomic force microscopy, two photon spectroscopy. We can obtain the same level of detail on biomolecules as is now available for small organic compounds. The number of publicly available 3-dimensional structures of macromolecules has grown exponentially from less than 800 in 1992 to 80,000 in 2012. More importantly, almost half of these have been obtained at a resolution between 1 to 2Å (in the range of a CC bond length) giving the medicinal chemist a basis for reliable molecular docking and drug design.

In the meantime, as extremely large and complex structures have become available, highly diverse media can now be reliably and rapidly analyzed thanks to the last generation of MS and associated databases. The diversity of small organic molecules produced by living organisms has already provided many important drugs (antibiotics, alkaloids and autacoids). These chemical ensembles can be re-explored much more systematically to understand human physiology (metabolome) and find active substances (parvome) which give new models and ideas to the medicinal chemist, opening new avenues in drug discovery and development.

Fast progress in organic synthesis blurs the boundaries between small organic compounds and biologics.

During the last 15 years, many improvements in chemical synthesis such as new catalysts, microwave heating, generalization of solid phase synthesis, have significantly expanded the space of accessible compounds, both in complexity and molecular size. They also have dramatically accelerated the synthesis of biopolymers and their artificial derivatives (modified proteins, peptides and oligonucleotides, dendrimers).

Ultimately, the complete chemical synthesis of genes and genomes in small amounts is now possible without any nucleotide template, making gene synthesis a cheap commodity. Associated to high speed genome sequencing -another convergence of chemistry, physics and biology- chemical synthesis of genes has revolutionized protein production.

At the same time, drugs of increasing size and complexity such as fondaparinux, aptamers, and dsRNA can be obtained by chemical synthesis. Highly selective modifications (such as pegylation or lipidation) of peptides and proteins, synthesis of protein-albumin chimeras or dendrimers are also possible.

The border between biologics, traditionally characterized by their preparation process and chemical compounds, characterized by a complete analysis of their structure, is not so relevant anymore. Indeed, many biomolecules can now be characterized by their structure using the most accurate analytical means currently available. In contrast, synthetic statistical copolymers, defined by the synthesis process, such as glatiramer for multiple sclerosis and sevelamer, have been approved by the FDA, making the distinction between bioproducts and chemicals less clear. To account for this, new guidelines regarding the definition of biologics and NMEs have been issued by the FDA.

Chemistry in living systems.

Chemistry and biology can be even more intimately mixed. Biological objects are used by chemists as reac-

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tors (cells) or templates (proteins) to perform chemical synthesis. Bio-orthogonal chemical reactions referred to as "click chemistry" enable specific compound coupling in living cells, molecular tracking, cell imaging, and target identification. There is a growing number of examples wherein medicinal chemists have used the protein target itself as a molecular template to catalyze the synthesis of high affinity ligands or inhibitors.

Small molecule Superheroes

The rapidly increasing disk capacity of computers and the availability of cheap laser diodes have brought confocal microscopy and image-based assays into the "high throughput labs". As a result, high content screening (HCS), whereby subtle morphological and biochemical changes on cells can be assessed automatically in 96 or 384-well plates, is now affordable by biotech and academic structures. Using HCS and phenotypic screens, we can discover small molecules that have dramatic effects on cells, traditionally achieved with biological agents (siRNA, peptides, proteins, antibodies...). For example liquinimod and fingolimod exert effects on immune cells that are comparable to LPS and monoclonal antibodies. Small molecules that bind specifically to bromodomains control the expression of specific genes. Another example of a therapeutic breakthrough is the launching of ivacaftor by Vertex, a small molecule modulator of the CFTR channel that is the first disease-modifying drug for cystic fibrosis. Also, small compounds are currently screened for cell reprogramming and stem cell differentiation, opening new avenues in regenerative medicine.

Breakthrough in analytics:

More and more, we see powerful analytical instruments (LC-MS, LC-MSMS, HR MS), leaving the area of specialized platforms to enter chemistry and biology labs. These mass spectrometers are controlled with user-friendly software. Thus, cheap, rapid and straightforward interpretation of data by the end user (chemists or biologists), favors broader uses, the acceleration of research and dialogue between the disciplines. Imaging techniques based on mass spectrometry have also become more common and accelerate our understanding of compound fate in organisms.

Powerful desktop computers:

While molecular modeling continues to require specific skills, protein visualization, idea generation through target visualization and enumeration of virtual libraries can now be realized on a desktop computer by the medicinal chemist himself. He can also perform complex sample analysis at his desktop, linked to spectrometers, computing and database servers. He learns by himself to observe biomolecules, to analyze data from complex experiments and interact in a productive way with computational chemists, analysts and biologists.

Consequences in drug discovery:

Downsizing: the small drug discovery lab. While expensive clinical development will surely remain the prerogative of large multinational corporations, rational drug design, target selection, medicinal chemistry can be performed by smaller teams, enabling real drug discovery and selection in academic labs and small "biotech" companies. Rational drug design has become more efficient.
Creative thinking made easier: as biomolecules and chemical compounds are becoming more and more comparable and appear to everyone as belonging to the same world, it is likely that the creative process will be easier in the coming years. Bisociation, a concept introduced by Arthur Koestler in 1964 to designate mental occurrences simultaneously associated with two habitually incomparable contexts, is considered the essential mechanism of creative thinking. We can be sure that creative thinking is now being facilitated in the community of chemists and biologists.
This may be reflected by the outstanding years 2010 and 2011 in terms of new drugs approved, including a large number of first-in-class drugs to treat severe diseases, such as vismodegib, a Hedgehog antagonist for advanced basocellular skin cancer, ivacaftor, a CFTR potentiator for cystic fibrosis, boceprevir and telaprevir, two inhibitors of the hepatitis C virus, to name a few which have been discovered by academics or small-size corporations.

Professor Benoît Déprez
Université de Lille 2
Institut Pasteur de Lille

Organic Synthesis Group

Dr Sébastien Papot, who is heading the local organizing team of the 48th RICT meeting, works within the Organic Synthesis Group directed by Professor Yves Blériot. This group belongs to the *Institut de Chimie des Milieux et des Matériaux de Poitiers* (IC2MP).

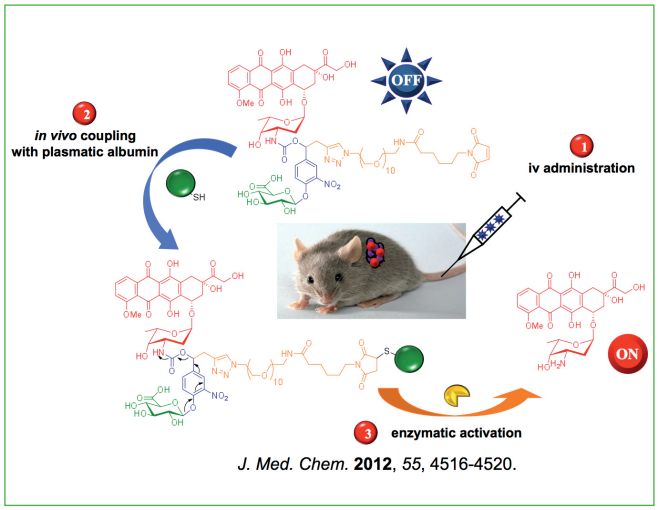
From left to right: *Romain Barat (Doctorant), Mikaël Thomas (MCU), Thibaut Legigan (Doctorant), Isabelle Opalinski (CR1), Zakariae Mellouki (M2),* ***Sébastien Papot (MCU)****, Brigitte Renoux (CR1), Clément Sanchez(M2), Jonathan Clarhaut (IR).*

Specialized in the study of the reactivity of organic compounds, this group has a recognized know-how in the multi-step synthesis of highly value-enhanced and complex organic molecules, the reaction mechanisms implicated in these chemical transformations, in the extraction and exploitation of bioactive natural products as well as in their functionalization.

The group originated from the *"Synthèse et Réactivité des Substances Naturelles"* (SRSN) laboratory created in Poitiers in 1968 by Professor Jean-Claude Jacquesy. During the 1980's, this laboratory became specialized in synthesis in superacid media which, by use of superelectrophilic species, allows chemical transformations not possible employing "classical" organic chemistry. This study of the behavior of alkaloids under these conditions rapidly attracted the attention of Pierre Fabre Laboratories and resulted in a fruitful collaboration culminating in the development of a new anticancer drug, Vinflunine, a fluorinated derivative of an alkaloid extracted from the Madagascan periwinkle commercialized since 2009 under the name of Javlor®.

The current team has applied this historical theme of the use of superacid media in organic synthesis to two new research areas: glycochemistry and programmed molecular systems. Directed by Dr Sébastien Papot, the team will be housed in 2013 in a completely new laboratory (whose construction can be perceived in the background of Sebastien's group photo). Presently associate professor at the University of Poitiers, Sébastien has performed postdoctoral work at the University of Cork under the direction of Dr. A. R. Maguire as well as with Professor Gérald Guillaumet's group at the University of Orléans.

The subject which he is currently developing in Poitiers concerns the design of molecular systems composed of distinct units which coordinate to perform a complex task and represents a major challenge in organic chemistry. Such systems incorporate a program within their structure which will determine their behavior when interacting with external media. Applications go from the design of molecular systems programmed for the therapeutic targeting of anticancer agents to the development of artificial molecular motors.
A very recent example, illustrated in the scheme below, utilizes a prodrug which is bound covalently to plasmatic albumin and upon activation by glucuronidase liberates the cytotoxic agent.



J. Med. Chem. **2012**, *55*, 4516-4520.

This year has been very rich in events for Sébastien. A good scientist who is interested in prebiotic chemistry and tries to understand the origins of life by synthesizing certain elementary building blocks of life, he has in parallel experimented with a more classical (though evolutionarily more recent) approach which was validated a little over a month ago by the birth of Gaspar Papot.

Professor André Tartar
Université de Lille 2

UNIVERSITÉ DE POITIERS

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RENCONTRES INTERNATIONALES de CHIMIE THERAPEUTIQUE

INTERNATIONAL CONFERENCE ON MEDICINAL CHEMISTRY

JULY 4-6, 2012 | POITIERS, FRANCE

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SERVIER

Université de Poitiers

La Société de Chimie Thérapeutique (SCT): Activities of the French Medicinal Chemistry Society

The SCT was founded in 1966 with the objective of studying and encouraging research in all scientific and technical areas related to medicinal chemistry and of assisting in the communication of these research results. The SCT also has a fundamental role in initiating and maintaining scientific contacts, both national and international, with both public and private research groups as well as with other medicinal chemistry-oriented associations and federations.

Our major annual event is the organization of the Rencontres Internationales de Chimie Thérapeutique (RICT) which is enjoying this year it's 48th edition in Poitiers. These highly successful meetings bring together over 25 internationally recognized speakers from Europe, the USA and elsewhere who present their latest results in cutting-edge areas of drug design, from the discovery of new targets all the way to case studies with successful drug candidates. The presence of young scientists at these high-level meetings is particularly encouraged by way of low registration and housing fees as well as the possibility of presenting poster communications of their research results and attending career sessions. The two best posters are rewarded by a Vocational Prize, which will allow the awardees to attend the next RICT for free.

The SCT also organizes every year smaller but high-profile one-day meetings, generally in Paris. The first of these, which takes place in the autumn (« Journée d'automne »), is focused on a particular theme in medicinal chemistry and brings together over half a dozen speakers, all specialists in that year's theme. In the spring, the SCT joins forces with the Organic Chemistry Division of the French Chemical Society (SCF) and the National Academy of Pharmacy (ANP) to organize a one-day meeting combining talks by internationally renowned speakers from all three disciplines. The SCT also awards a prize destined to encourage research in medicinal chemistry by a young scientist (less than 36 years old) who has already shown proof of his or her scientific talents. These two meetings are open to all after simple registration but with minimal or no registration fees.

The SCT's continuous encouragement of students in medicinal chemistry is demonstrated by the organization of the Young Scientists Day (Journée Jeunes Chercheurs, JJC), which is held every winter. This year's meeting, the 19th of its kind, actually took place over two days in view of the meeting's increasing success. The JJC allows young scientists motivated by a career in medicinal chemistry to present oral and poster communications (whose quality is rewarded by prizes), attend round tables on career orientation, participate in facsimile job interviews and interact with more senior scientists also invited to the meeting. It is a great opportunity for students and postdocs to become immersed in the medchem world and share thoughts, ideas and aspirations with their fellow budding scientists.

In its desire to acknowledge science of the highest calibre, the SCT also attributes every year the Mentzer and the Ehrlich Prizes, two prestigious awards recognizing seminal work conducted in the area of medicinal chemistry by a scientist or his research group. This work will be presented in a plenary lecture by each prizewinner at the RICT meeting of that year.
Finally, in an effort to widen its horizons and those of its members, the SCT maintains an active membership in the French Federation for Chemical Sciences (FFC) and the European Federation of Medicinal Chemistry (EFMC). The SCT is also an editorial partner of the European Journal of Medicinal Chemistry. We thus encourage you to submit manuscripts in all fields of medicinal chemistry for publication in this increasingly high-impact international journal.

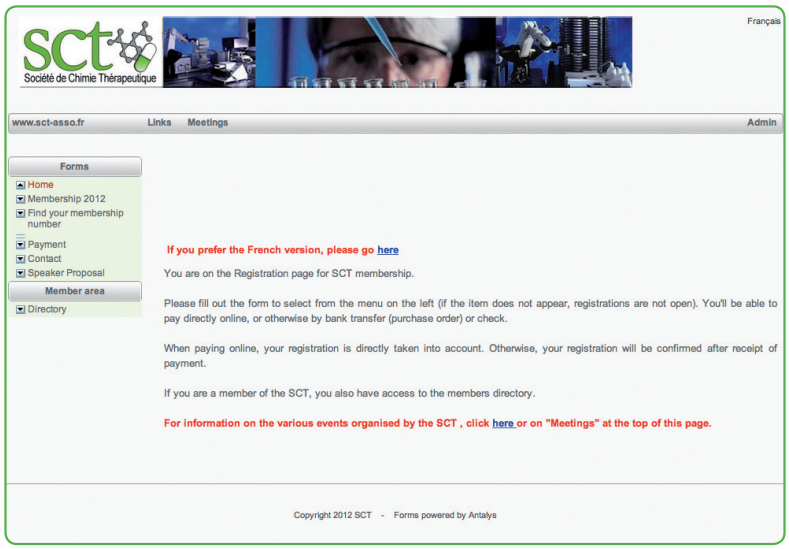
Please feel free then to visit our website (http://www.sct-asso.fr/) where you can be informed of the programs and details of our different meetings, of the prizes we award as well as register online to become a member of the SCT (which we strongly urge you to do), make speaker proposals for upcoming meetings, become informed of job possibilities and keep track of our various other activities.

Dr Robert H. Dodd
SCT President

SCT: Website and Social Networks

www.sct-asso.fr

The SCT website has been designed as a platform presenting the activities of the Society as well as a relay of communication between members. You have access to the News and Events directly from the homepage. You will find information about the society, meetings, prizes, job offers, texts and links proposed by SCT members. You can also add information by contacting us at communication@sct-asso.fr.



Recently we improved functionalities at **http://www2.sct-asso.fr** by adding the possibility to become a member of the SCT and to take part at SCT meetings by filling out online forms. You can then conveniently pay online with a credit card or later by check, bank transfer, or purchase order. You can also retrieve your membership number required to pay the reduced fee for SCT organized meetings (such as RICT). As a member, you have access to the directory with the coordinate of all members that have accepted to share their address. The SCT is also happy to consider your speaker proposals for next meetings, simply by filling out the available form which you can find by clicking "Speaker Proposal".

SCT is also present on the 2 most popular social networks, **LinkedIn** and **Facebook**.
You can become a **"Com. Committee SCT"** relation on LinkedIn and a member of the "RICT - International Conference on Medicinal Chemistry" and "SCT - Journées Jeunes Chercheurs" groups.
On Facebook, make **"Societe Chimie-therapeutique"** a friend of yours and become a member of "RICT - International Conference on Medicinal Chemistry" and "Journées Jeunes Chercheurs" groups. You will thus be permanently connected to the SCT and its members and you will be informed of News and Events organized by the SCT. RICT and JJC speaker profiles and sponsors will be made immediately available to you and you will be alerted to new job offers.

RICT on LinkedIn

RICT on Facebook

The Communication of the SCT
Dr Frédéric Schmidt, Institut Curie, & **Dr Terence Beghyn**, Université de Lille 2

The five awards attributed each year by the SCT

All the information can be reached on the website: **www.sct-asso.fr**

1. The Mentzer prize for medicinal chemistry (Sponsored by Laboratoires Pierre Fabre)

This prestigious award is attributed every year to an eminent scientist for outstanding results in the discovery and/or the selection of new drugs

2. The Ehrlich lecture (Sponsored by Janssen Cilag)

This prestigious award is attributed every year to an eminent scientist or a research team for outstanding results in the discovery of bioactive natural products or discovery of new drugs inspired by natural products.
During the RICT's meeting the winners of these two traditional prizes (Mentzer and Ehrlich) will present their results.

3. SCT prize for young medicinal chemist (Sponsored by Laboratoires Servier).

This award ("Prix d'encouragement à la recherche en Chimie Thérapeutique") is for researcher no older than 36.
The recipient of the prize is invited to give a talk at the spring meeting co-organized by the SCT, the French Society for Chemistry and the French Academy of Pharmacy.

4. Best poster Award for young medicinal chemist (Sponsored by Laboratoires Servier).

Two prizes are offered each year for the best two posters presented by young researchers at the RICT. The recipients are invited to deliver a talk at the SCT fall meeting which usually takes place in November.

5. Camille Wermuth prize (Prestwick Chemicals and SCT)

Each year a medicinal chemistry book is selected and given to Young Medicinal Chemist following oral or poster communications.

The two grants attributed each year by the SCT

1. Grants for conferences

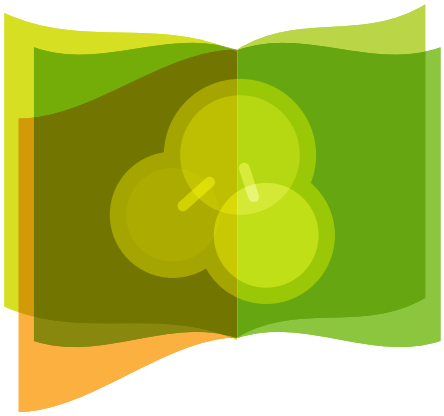
Several grants are offered each year for young medicinal chemists to attend meetings such as the ACS (American Chemical Society) meeting and RICTs.
These grants are attributed to following the Young Medicinal Chemist who presented the best talk and the best posters.
Other grants to attend meetings are also given at the RICTs following the poster presentation.

2. Grants for research (sponsored by laboratories Servier)

Each year a call for project is launched by Servier. The SCT announce the subject of the call for project and organize the selection of the applications.
This year's subject was: "Alzheimer Disease: Search for an agent interfering with protein misfolding and spreading".
One or two project are selected each year by a Jury that includes Scientist from Servier and from the SCT. The grants cover a PhD (3 years) or a Post-Doc position (2 years).

Other companies are strongly encouraged to propose calls for project!

Professor Hervé Galons
Université de Paris Descartes



European Journal of Medicinal Chemistry

Published under the auspices of the French Société de Chimie Thérapeutique (SCT)

Editor-in-Chief: **Prof. Hervé Galons**
Honorary Editor-in-Chief: **Prof. Olivier Lafont**

More than 2000 papers are submitted each year and approximately 700 are published.

The European Journal of Medicinal Chemistry is a global journal that publishes studies on all aspects of medicinal chemistry:

- organic synthesis;
- biological behavior;
- pharmacological activity;
- drug design;
- …

The impact factor of EJMC (3.1) is one of the best of all medicinal chemistry journals.

The "Journées Jeunes Chercheurs" (JJC)

The SCT has always striven to ensure that its various activities include young scientists and the *Journées Jeunes Chercheurs* (JJC), which it traditionally organizes during the first week of February, confirms this tendency as shown by the increasing importance of this event.

This meeting, now held over two days, brings together close to 250 participants coming from every part of France as well as from several European and North African francophone universities. In 2012, over 20 oral communications were presented by PhD students and postdocs allowing them to share their latest research results while the presentation of over a hundred poster communications during a convivial evening of wine-tasting allowed for close personal exchanges.

The topics presented covered every aspect of modern research in medicinal chemistry: structure-activity relationships, ADMET, chemical biology, chemoinformatics, imaging, physical chemistry, biolabeling and diagnostic tools, drug vectorization, nanotechnologies, natural products, synthetic methodology, etc. Three plenary lectures were also presented by the well-known scientists Dr Eric Doris (CEA-Saclay), Dr Dominique Lesuisse (Sanofi) and Professor Jean Martinez (IBMM, Montpellier), thereby contributing to the scientific excellence of this meeting.

Finally, in keeping with the JJC tradition, presenters of the best oral communications were awarded prizes which will allow them to attend the national 2012 American Chemical Society meeting to be held next August in Philadelphia while authors of the best poster communications have been invited to present their posters at the 48th RICT meeting in Poitiers next July.

A second important facet of the JJC concerns the future careers of doctoral students. Individual one- hour meetings are thus organized with representatives of human resources from major pharmaceutical firms as well as from smaller biotechs and start-ups in which simulated interviews are held and recommendations given in writing an effective CV. A round-table is also held allowing debate around themes important for future employment such as creation of a company, working in a small company and advice for obtaining a first job.

This year, these XIXth JJC were held on the site of Biocitech in Romainville (on the periphery of Paris) with the avowed intention of bringing together two worlds that only rarely intermingle: the academic world, in which the great majority of doctoral students evolve, and the world of small biotech companies where most of these students will eventually find employment. This new partnership, the result of fruitful exchanges between the SCT and the President of Biocitech, Jean-François Boussard, will hopefully be a long-term one. It will allow establishment of valuable contacts for young scientists, offering them a different vision of the research career that they will be undertaking in the coming years. Thus, the JJC now benefits from an exceptional environment for its future development.

The organizers of the JJC wish once again to acknowledge the SCT for its support and unfailing engagement toward young scientists. They also thank all the companies that have provided human and financial support (Genepep, e-novalys, Alfa Aesar, Borochem, Galapagos, Biotage, Brucker, Büchi, Chem-X Infinity, Flamer Technologies, OriBase Pharma, Mutabilis, Iris, Sanofi, Servier, TCI Europe, Prestwick Chemical and Roche) as well as Biocitech for their warm hospitality. They give you rendezvous next February, once again at Biocitech, and they promise to continue to innovate in the coming years.

Dr Luc Demange
Université de Paris Descartes

CEREP PROFILE

Cerep is an internationally recognized provider of preclinical drug discovery services for in vitro pharmacology, in vitro ADME-Tox & in vivo pharmacokinetics ensuring solutions which are faster and cost-effective. These services focus on identifying the most promising drug candidates at early stages thus eliminating those compounds likely to fail in development.

For many years, Cerep has developed unique know-how based on technologies of in vitro screening and profiling using its proprietary BioPrint® database, which allows the modeling of clinical effects of drug candidates from their molecular properties.

Cerep technologies provide services to more than 460 pharmaceutical and biotechnology companies worldwide, including most of the top pharmaceutical firms. Moreover, the strength of Cerep services also arises from in-house production of biological materials.

Added to sites in France and in US, Cerep has opened labs in Shanghai and thus become a partner more close and convenient to locations where compounds are synthesized and drug candidates are optimized, again reducing turnaround time for data generation and delivery to discovery teams.

Cerep's success has been earned through providing consistent, high quality data – resulting in Cerep's renowned reliability - wherever screening is performed.

Link to contact: sales@cerep.com | www.cerep.com

BIO*alternatives*

BIO*alternatives* SAS is a Contract Research Organization specialized in cellular and molecular pharmacology. The company provides services to support the early stages of drug discovery in a wide range of areas of expertise (immuno-inflammation, dermatology, neurobiology, tissue inflammation, morphogenesis, cell metabolism, stress, aging) as well as to support the claim substantiation of healthcare compounds.

BIO*alternatives* is involved in the main steps of preclinical development:
- model & assay development, biological target or biomarker identification & target validation,
- Hit to lead process,
- High Content Screening, cell based assays, profiling and functional assays for the proof of concept and the lead validation.

BIO*alternatives*' added value comes from its experience in managing R&D studies using a wide range of in vitro models. The company mainly uses human primary, secondary cell cultures and in-house developed reconstructed tissues. The company focus is to assay compounds within a tissue or in vivo-like context close to physiological relevant conditions in order to decrease future in vivo or clinical attrition rate.

The company uses and offers access to a dedicated up-to-date technology platform:
- High Content Analysis platform (Imaging system, flow cytometry, time-laps video),
- Transcriptome analysis (RT-qPCR, PCRarray, Affymetrix for whole transcriptome),
- Cell & Tissue culture platform for cell isolation, purification, sorting, cloning, transfection,
- Multiformat plate readers for absorption, densitometry, fluorescence (including FRET), luminescence, radioactivity.

The company is also involved in the analysis of biological samples (cell extracts, RNA, embedded tissues).
Based on a large panel of more than 400 validated assays and with 16 years of experience, the company is a leader of customized biological solutions and designs every day focused approaches and suitable solutions for individual client projects.

BIO*alternatives* was founded in 1996 by Dr. François-Xavier BERNARD and Dr. Alain DEGUERCY in order to develop alternative methods to animal testing. The company is located 20 km from Poitiers where 40 people work in a 700 square meter laboratory. The company provides services to more than 200 customers worldwide.

Link to contact: jne@bioalternatives.com / add@bioalternatives.com | www.bioalternatives.com

@rtMolecule - Chemical custom synthesis

@**rtMolecule** specializes in the custom synthesis of milligram to gram quantities of **stable isotope labelled** materials, **metabolites** and **reference standards**. We mostly work for the bioanalytical departments of CROs and pharmaceutical companies, and we are familiar with the quality standards and internal procedures needed to meet their requirements. We also provide reference materials for environmental (pollutants) and agricultural purposes.

Stable isotope-labeled compounds

With the advent of LC/MS technologies, it has become much easier to detect and quantitate drugs and drug-related materials in biological matrices. This evolution of LC/MS technology has created an opportunity to make greater use of stable isotope-labeled compounds as the primary means of detecting and quantitating compounds from preclinical and clinical pharmacokinetic stdies.

Metabolites

Quantitative bioanalysis would be required from the early identification of metabolites in preclinical testing, in toxicokinetic analysis and during human clinical trials. The need to provide quantitative metabolite information early in human trials, requires the synthesis of reference standards, as well as the development and validation of numerous bioanalytical methods.

Chemical synthesis expertise in a wide range of drug discovery fields:

In addition to Custom Synthesis we are also engaged in production of screening compounds and building blocks. We pride ourselves on the preservation of the secrecy and confidentiality of our customer's proprietary information, which is protected by a confidentiality disclosure agreement.

R&D Support services include:

We can provide the synthesis of compounds within a particular class of molecules selected by the customer. Specialized expertise is offered in the following fields: steroids, indoles, alkaloids, sugars, fatty acids, terpenoids, amino acid derivatives…
@rtMolecule offers an original method to generate potential drug-candidates prepared following our knowledge of functional group reactivities in superacidic media. We have significant experience and expertise in the synthesis of fluorinated organic molecules. For example the synthesis of amino fluorinated building locks.

Link to contact: fabien.zunino@artmolecule.fr | www.artmolecule.eu

BioCydex - Chemical custom synthesis

BioCydex was founded in 2002 to develop specialized cyclodextrin-enabled products and provide innovative drug delivery systems to the pharmaceutical, biotech and bioengineering. We provide solutions and technologies which when implemented radically improve the conditions of drug administration and its effectiveness.

We are active in major therapeutic fields: organ transplantation, ophthalmology, oncology and diagnostics. Delivery of active principles is assured by our patented technology: Vectipharm®, Solvamax® or Proteosol®.

We offer an integrated and innovative galenic platform. Particularly, BioCydex places its competence and expertise at the disposition of its industrial partners with the aim of developing their small or large molecules rendered unexploitable due to problems associated with stability, solubility and bioaccessibility.

Concurrently, we develop our own products. The most advanced is a molecular complex, under the trademark Vectisol®, which can be directly supplemented to organ, tissue and cell-line preservative solutions. During renal transplant, there is a spectacular reduction in the delay in the reestablished graft function in the presence of Vectisol® (urination, creatinin levels,. . .). In addition, fibrosis and cellular atrophy were drastically reduced confirming the protective effect of Vectisol® during ischemia and reperfusion.

BioCydex has been also supplying modified cyclodextrins since a decade and offers an integrated cyclodextrin based biotechnology platform.

Link to contact: Tel.: +33 549 453 640 | www.biocydex.net

SGS Life Science Services

WHEN YOU NEED TO BE SURE SGS

SGS Life Science Services is one of the European leaders in bioanalytical services, with over 25 years of experience and operating a GLP compliant laboratory in Poitiers. Pharmaceutical and biotech companies of all size have chosen us as their preferred bioanalytical partner. SGS has the expertise to both develop assays from scratch (including immunoassays) and to support large scale routine sample analysis, from preclinical to clinical studies.

SGS Poitiers (Cephac) has established a strong reputation bringing scientific expertise and high quality analysis for the international development of New Chemical Entities (NCE), but also of New Biological Entities (NBE).

Services

SGS Poitiers (Cephac) can provide bioanalytical testings for drug development from early to late phase:

- Method Transfer, Development, Optimisation and Validation
- PK Bioanalysis (small molecules, biopharmaceuticals)
- PD Bioanalysis (biomarkers)
- Immunogenicity testing
- Cell-Based Assays

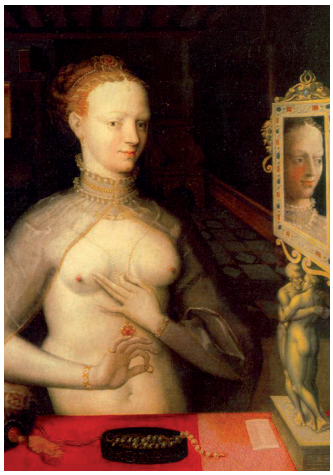
Mass Chromatographic Method Department offers a large expertise for method development, validation and quantification of NCEs, biomarkers and peptides in biological fluids (plasma, urine, tissues,..) from preclinical and clinical studies. Exploratory studies in early phases are also performed. This department is equipped with 18 LC-MS/MS and Ultra-Fast-LC systems (UFLC), including the latest instruments, UPLC-MS/MS Xevo TQS (among the most sensitive on the market). These Xevo-TQs instruments are of interest for peptide and protein quantification and will also help to improve NCEs/Biomarkers limits of quantification.

Responding to the trend of the pharmaceutical industry, SGS invested in the growing department of Biomarkers and Biopharmaceutical Testing to offer a wide range of services from testing small peptides, through big molecules and recently the opening of the cell biology laboratory (BSL2+). Bioanalytical work covers testing of both endogenous (Biomarkers) and drug products (PK assays) with application at all stage of the development. Key platforms we are using for running our assays are: spectrophotomer readers for ELISA assays, Luminex and MSD readers for conducting multiplexed Immunoassays, FACS system for flow cytometry analysis of cells and other systems for testing enzymatic activities. Depending on the intended application, analytical methods can either be used after simple qualification or can be fully validated.

Link to contact: Tel.: +33 1 76 63 20 16 | www.sgsgroup.fr

A MOMENT OF HISTORY

Diane de Poitiers and the elixir of youth.



According to historian, in her age, Diane de Poitiers (1499-1566), the unique daughter of Jean de Poitiers, was probably the most beautiful and the most healthy woman of France. She became notorious as the latter's favorite of the king Henry II of France (1519-1559) although she was twenty years older than him [1].

She married young (15 years old) with Louis de Brezé, seigneur d'Anet who was thirty-nine years her senior. When her husband died in 1534 in Anet, Diane adopted the habit of wearing the colours of black and white for the rest of her life as she is represented in the famous painting of François Clouet.

On the other hand, in 1533, the futur king of France, Henri II married Catherine de Medicis. Diane and Catherine were actually related to one another, being both descendants of the *La Tour d'Auvergne*. Indeed, to Catherine, Diane was an intrusive elder cousin as well as a rival. Diane de Poitiers would remain Henri's lifelong companion, and for the next 25 years she would be the most powerful influence in his life. Despite wielding such power over the king, Diane's status depended on the king's welfare, and his remaining in power. In 1559, when Henri was critically wounded in a jousting tournament, Queen Catherine de Medicis assumed control, restricting access to him. Immediately thereafter, Catherine de Medicis banished Diane from Chenonceau to the Château de Chaumont. She stayed there only a short time, and lived out her remaining years in her castle in Anet, Eure-et-Loir.

At the end of the winter 1566, she suddenly falled ill and died at the age of sixty-six. In accordance with her wishes, and to provide a resting place for her, her daughter completed the funeral chapel built near the castle of Anet. During the French Revolution, her tomb was opened and her remains thrown into a mass grave.

In 2008, during an archaeological dig in the cemetery of Anet, skeletons were excavated near a monument to Diane de Poitiers. Diane de Poitiers remains were identified from the other skeletons by some physical particularities (arthritic lesions, ante mortem tooth lose, consolidated tibia and fibula fractures…) for which Ambroise Paré treated her.

The most surprising became from analysis of Diane's hair which have been preserved at the castle. Coupled mass spectrometry showed a great concentration of gold in these hairs and Diane's hair diameter was around 65 µM instead of 80-90 µM. Hair thinning is relevant from a symptom of chronic gold intoxification and Diane is known to have undergone a long course of gold treatment hoping it was an elixir of youth. Gold was also discovered in the putrefaction fluid deposits.

Gold's supposed powers of regeneration go back to antiquity. Pliny the Elder (AD 23-79) describes the preparation of two remedies using gold and their therapeutic properties. In the 13th century, alchemists like Michael Scot, Roger Bacon, and Arnaud de Villeneuve wrote about "Aurum potabile"—drinkable gold—and how to obtain it. Drinkable gold was also well known in the 16th century French Court, and Alexandre de la Tourette dedicated his book on the subject to King Henri III. In the 17th century, many doctors and chemists like Jean Beguin and Christophe Glaser published gold recipes, including drinkable gold, in their chemistry manuals.

Authors of the paper expected chronic intoxication in Diane's case [2], which would explain the high levels of gold in the hair compared with gold residues in other tissues which was relatively low. They believe that she drank gold, which is compatible with Brantôme's report [3] in order to remain young enough. Brantôme saw her "at almost seventy years of age, beautiful of face, also fresh and also pleasant as she had been at thirty years of age…"

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Sources
[1] http://en.wikipedia.org/wiki/Diane_de_Poitiers
[2] P. Charlier et al. Fatal alchemy. Brit J Med 2009; 339: 1402.
[3] Brantôme, Vie des dames illustres, françaises et étrangères (ed Moland) Garnier frères, 1868.

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