



Rethinking research, understanding life, improving health



eisbm
European Institute
for Systems Biology & Medicine
A SYSTEMOSCOPE INSTITUTE



Mapping TOMORROW'S BIOLOGY & MEDICINE



World health players are confronted with major challenges: the persistent threat from infectious diseases, the emergence of new pathogens, the increasing prevalence of cancers and chronic diseases, and the limits of traditional treatments.

Despite spectacular progress in molecular biology, our knowledge of mechanisms underlying the development of diseases remains limited. At the same time, increased life expectancy has led to an uncontrolled explosion of healthcare expenditure. The pharmaceutical industry is thus struggling to bring innovative and cost-effective treatments to the market and society.

Recent years have seen the fast rise of systems biology, the next major step forward in biological research after the deciphering of the human genome. Systems biology represents a groundbreaking approach to overcome the current limitations of disease complexity and drug discovery. The development of systems biology will lay the foundation for a prospective medicine that will be predictive, personalized, preventive and participatory (4P-Medicine). Medicine will thus move from a reactive to a proactive mode focusing on wellness rather than on disease.

The European Institute for Systems Biology & Medicine aims to speed up the transfer of results obtained through systems biology approaches to industry and to routine patient care. It will do so by:

■ Studying life's complexity through a trans-disciplinary approach

Systems biology approaches will lead to deeper insights into the mechanisms of human diseases, enabling a more effective drug development process. New treatments will be adapted to the genetic make-up, food habits and health record of each individual through personalized diagnosis and follow-up.

■ Advancing research today to heal better tomorrow

Research programmes involving EISBM teams and partners have already led to significant progress, and opened new opportunities for therapy and diagnostics on the booming market of personalized medicine.

■ Boosting Europe's ambition to serve global public health

In close collaboration with the Lyonbiopôle world-class competitiveness cluster, EISBM will foster academy/industry partnerships during all phases of drug discovery, increasing regional, national and European competitiveness in the fields of infectious, non-communicable chronic diseases and cancers. This will play an important role in strengthening the biotechnology and pharmaceutical sectors, while improving public health in developed and developing countries equally.

Dr Charles AUFFRAY
EISBM Founding Director

We are delighted that Lyonbiopôle has taken the lead, with the support of all its affiliated academic research institutions, local authorities and industrial partners, to invite our colleague Dr Charles Auffray to establish the European Institute for Systems Biology & Medicine of the Systemoscope Consortium in the Rhône-Alpes region. EISBM is the new type of organization that France and Europe need to develop the full potential of this emerging field.

Both the Seattle Institute for Systems Biology and the Shanghai Centre for Systems Biomedicine will develop a special strategic relationship with EISBM, which will be greatly facilitated by the shared vision of Systems Biology & 4P-Medicine we have developed with Charles Auffray since we co-founded the Systemoscope Consortium.

We strongly believe that EISBM will contribute to the competitiveness of the health care sector in Rhône-Alpes, reinforce and accelerate innovation in the areas of biological products and vaccines, and bring France to the forefront of systems biology & medicine in the coming years.



Leroy HOOD, MD, PhD
PRESIDENT
Seattle Institute for
Systems Biology

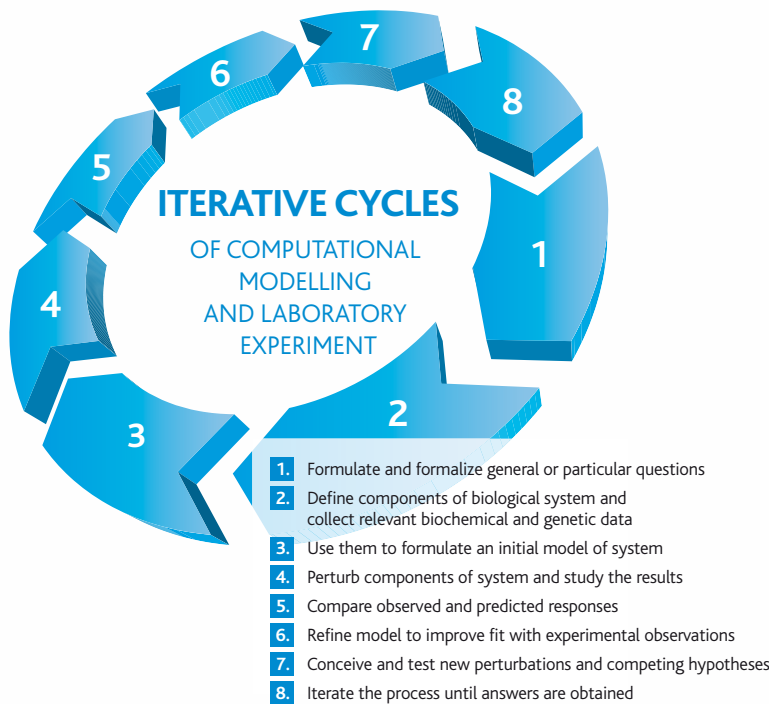


Zhu CHEN, MD, PhD
DIRECTOR
Shanghai Centre
for Systems
Biomedicine



Understanding LIFE'S COMPLEXITY

■ through trans-disciplinary research



EISBM: focusing on 4P-Medicine development

- **PREDICTIVE**
able to determine the probability of an individual contracting certain diseases by examining his or her biological make-up;
- **PREVENTIVE**
able to develop appropriate preventive measures and drugs for individuals, based on their potential health problems;
- **PERSONALIZED**
able to tailor treatments to individuals;
- **PARTICIPATORY**
with the active participation of patients.

Driving a paradigm shift in the practice of biology

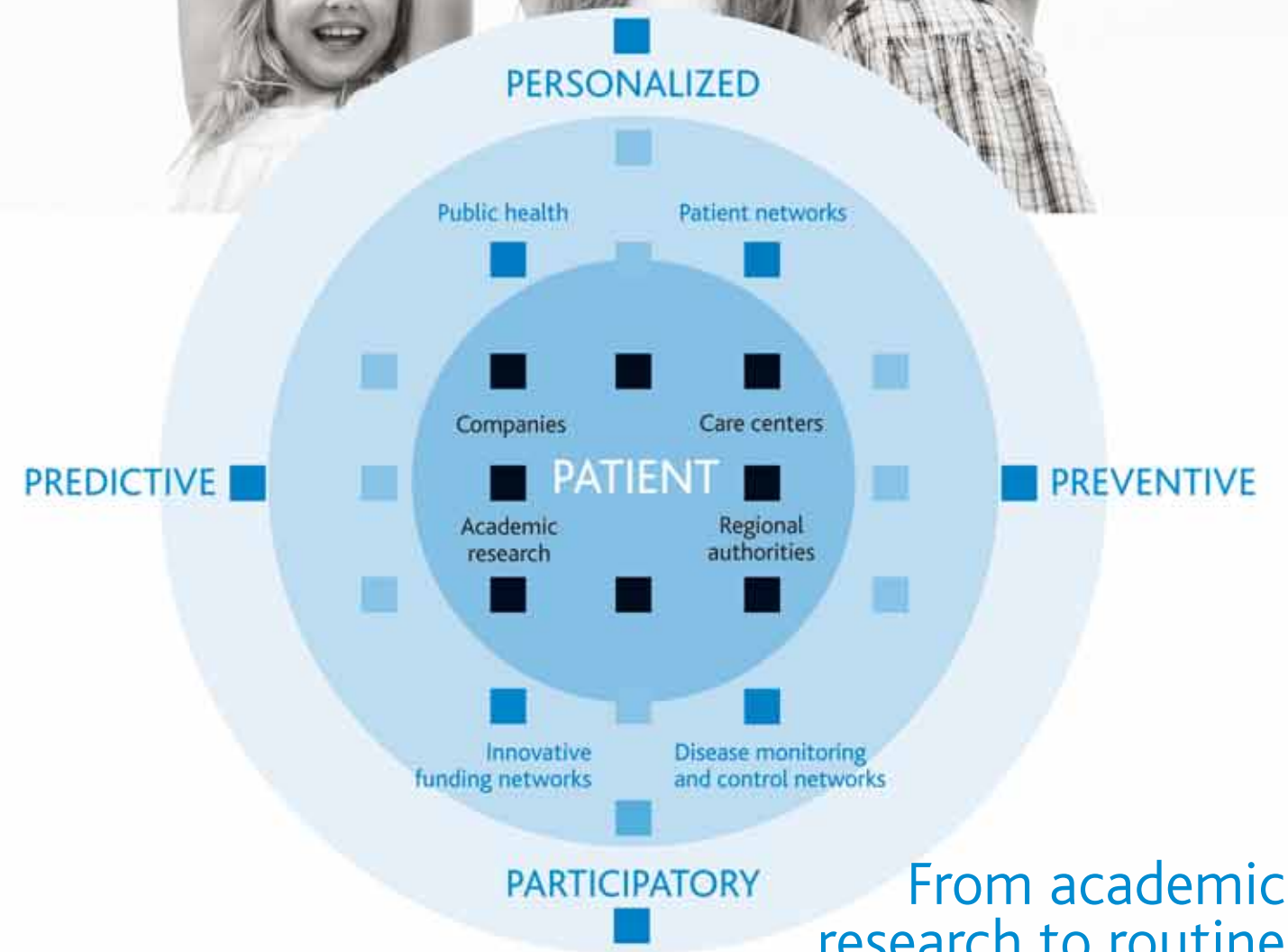
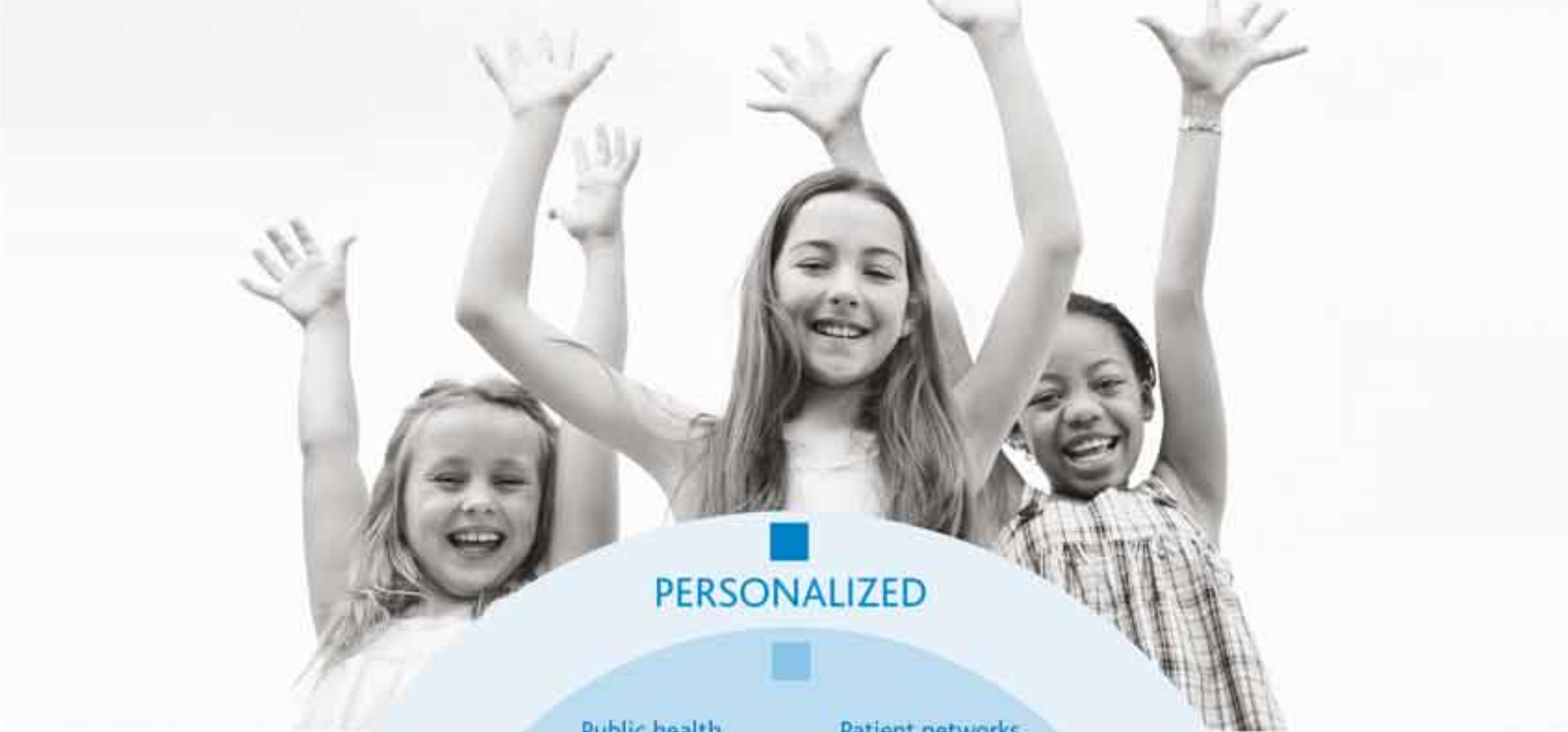
Understanding and managing complexity is one of today's greatest challenges for all scientific and engineering disciplines.

Systems biology represents a move from a reductionist approach to an integrative research strategy designed to tackle the complexity of biological systems and their behaviour at all levels of organization - from molecules, cells, tissues and organs to organisms in their changing environment. It seeks to understand how the individual components of a biological system interact in time and space to determine its functioning in normal and perturbed conditions. The knowledge obtained through systems approaches thus focuses primarily on function rather than on structure.

Mixing expertise under one roof

Systems biology allows integration of a large amount of global genome, transcriptome, proteome and metabolome data, collected with high-throughput measurement platforms, and of other relevant quantitative biological, environmental and medical data. The aim is to build and inform predictive multi-scale models ranging from the molecular to the organ and organism levels.

Success relies on integrated and standardized experimental and software platforms for data collection and analysis, visualization, simulation, hypothesis generation and testing, as well as on the integration of a wide range of expertise from various disciplines: physics, chemistry, mathematics, informatics, engineering, epistemology, history of sciences, law, ethics.



From academic research to routine patient care



Advancing research today

HEALING TOMORROW

EISBM teams and partners are already engaged in a wide range of national, European and international research programmes, some of which have already provided new insights into the mechanisms of various chronic diseases, including cancer, asthma and allergy.

Key expected benefits

- Enabling improved early stage disease identification - allowing more effective societal and individual interventions.
- Better prediction of therapeutic efficacy and safety - reducing time, cost, and failure rate of clinical trials.
- Enhanced resolution of disease populations into explicit sub-phenotypes thereby improving therapeutic specificity - personalizing therapy.
- Optimizing monitoring of disease progression or improvement - using models as next generation biomarkers.

European and international research programmes

The development of the U-BIOPRED platform for Unbiased BIOmarkers for the Prediction of REspiratory Disease outcomes, supported until 2014 by the joint Innovative Medicines Initiative (IMI) of the European Union and the European Federation of Pharmaceutical Industry Associations (EFPIA), represents an ambitious attempt to identify the functional and regulatory pathways that play central roles in respiratory pathophysiology, starting with severe asthma, through an integrative systems approach. Global precompetitive research collaboration between the academic, industrial and patient organization partners of the U-BIOPRED consortium is expected to produce a step change in respiratory medicine, and avenues for better treatment. Data and discoveries will be made public according to established European Union policy. U-BIOPRED has been set up to serve as a generic collaborative platform for other companion projects, three of which have been funded recently by the European Union.

MeDALL (Mechanisms of the Development of ALLergy), aims to generate novel knowledge on the mechanisms of initiation of allergy and to propose early diagnosis, prevention, and targets for therapy. A novel phenotype definition and an integrative translational approach are needed to understand how a network of molecular and environmental factors can lead to complex allergic diseases. A stepwise, large-scale, and integrative approach will use a network of complementary expertises in allergy, epidemiology, allergen biochemistry, immunology, molecular biology, epigenetics, functional genomics, bioinformatics, computational and systems biology.

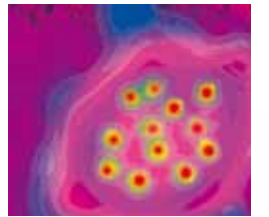
Two other companion projects are supported in the context of the Virtual Physiological Human Programme, in which EISBM partner teams are involved:

- the AirPROM consortium for predicting outcomes of airway diseases through patient-specific computational modelling,
- the Synergy-COPD consortium which is developing a modelling and simulation environment for systems medicine with specific focus on chronic obstructive pulmonary disease.

Initial results of systems biology

The group led by Zhu Chen in Shanghai developed a systems approach in collaboration with the team of Charles Auffray to investigate the dynamic functional changes occurring during the differentiation of human leukemia cells induced by exposure to retinoic acid and arsenic salt. This combination of small molecules, inspired by Western and Eastern medical traditions, has demonstrated efficacy in the treatment of acute promyelocytic leukemia. This study delivered insights into the synergistic molecular mechanisms that promote death of the cancer cells, resulting in a high-quality disease-free survival in most patients.

At the Institute for Systems Biology in Seattle, Leroy Hood and his colleagues have pioneered systems approaches to a variety of biological and medical problems. They developed the first comprehensive predictive model for transcriptional control of physiology in a free living cell, deciphering the adaptation of halophilic bacteria to their changing hypersaline environment, and opening the way for engineering of this biological process. Using a systems approach to prion disease in a mouse model, they identified the molecular networks perturbed in these neurodegenerative diseases, suggesting novel avenues for their treatment. Leveraging the exponential increase in the power of DNA sequencing, they demonstrated that a systems genetics analysis of the genome of two parents and their two children could identify the genes involved in two diseases without resorting to large populations.



Bright business prospects for the bio-health sector

The booming market for personalized medicine in the United States is already worth \$232 billion, and it is projected to grow by 11% per year. The market for a more personalized approach to health and wellness will grow to as

much as \$452 billion by 2015. Market opportunities extend beyond drugs and devices to also include demand for high-tech storage and data-sharing, as well as low-technology products and services aimed at consumers heightened awareness of their own health risks. The core diagnostic and therapeutic segment of the market is

estimated to be worth \$24 billion, and is expected to grow by 10% annually to reach \$42 billion by 2015*.

EISBM will particularly seek to boost innovation and business development on three segments: biologicals, vaccines and diagnostic tests.

* Source: PricewaterhouseCoopers, "The Science of Personalized Medicine Translating the Promise into Practice", December 2009.



EISBM A EUROPEAN AMBITION

■ to serve global public health

Leveraging world-class talents and expertise

The European Institute for Systems Biology & Medicine will be an independent foundation operating under the aegis of the Lyon Scientific Foundation, with affiliations to the research and higher education institutions, hospitals, industrial companies and regional authorities involved in the Lyonbiopôle world-class competitiveness cluster.

EISBM seeks donations for an initial endowment of 50 million Euros. It intends to collect resources over the next 10 years from public and private, national and international sources to provide a consolidated budget of 15 million Euros per year.

The founding faculty of senior scientists will be extended over time to twelve junior and senior leading international investigators.

A cross-disciplinary founding team



■ **Charles AUFFRAY**
Biologist
CNRS Research Director
Founding Director



■ **Dominique CHARRON**
Clinician and Biologist
Laboratoire Jean Dausset
Hôpital Saint Louis
Paris office



■ **Chantal RABOURDIN-COMBE**
Biologist
Université Claude Bernard
Université de Lyon



■ **Vincent LOTTEAU**
Biologist
Inserm Research Director
Université de Lyon



■ **Françoise ARGOUL**
Chemist and Biophysicist
CNRS Research Director
Ecole Normale Supérieure
Université de Lyon



■ **Christophe PISON**
Clinician and Biologist
Université Joseph Fourier
Hôpital Albert Michallon
Grenoble office



■ **Vitaly VOLPERT**
Mathematician
CNRS Research Director
Institut Camille Jordan
Université de Lyon

A public health mission: developing new tools to improve patient care

■ **Gaining a better understanding of infectious diseases, non-communicable chronic diseases and cancers** through the development of a cross-disciplinary environment where biologists, pharmacists and physicians will work together on long-term joint projects. Chemists, computer scientists, engineers, mathematicians, physicists, epistemologists, historians and lawyers, economists and ethicists, will help them in the design, prototype and use of innovative platforms for large-scale integrative biology (genomics, transcriptomics, proteomics, metabolomics, imaging, phenotyping).

■ **Bridging the gap between academia and the biotechnology and pharmaceutical industries**

- by fostering the development of partnerships on experimental, mathematical and computational technologies with technology providers and emerging small innovative companies;
- to help **developing diagnosis and therapeutic applications accessible to clinicians and patients.**

Capitalizing on the dynamic scientific, medical and industrial environment of Rhône-Alpes

Headquartered in Lyon-Gerland, at the heart of the Charles Mérieux campus, EISBM will highly benefit from the valuable competences of its academic and industrial partners within the Lyon and Grenoble international competitive clusters in the fields of biological, medical and technological research. At the crossroads between the various research, education and technology transfer components of the Rhône-Alpes region, EISBM will also leverage emerging initiatives in Lyon and Grenoble and play a key role in increasing the international exposure of regional research.

EISBM is developing as a joint venture with Lyonbiopôle representing the Rhône-Alpes research and higher education institutions, local and regional authorities, industrial partners and small and medium companies.

Building open global partnership models

It will be extended through joint projects with major European universities and a network of systems biology and medicine centres worldwide.

EISBM research programmes

The EISBM teams will develop innovative systems approaches through national and international public-private partnerships with academic, clinical and industrial groups to understand key biological functions, such as the control of energy metabolism or immune defenses and their perturbations in the major diseases that impact human health.

EISBM will devote a significant part of its activities to the systems biology of infectious diseases, targeting viral hepatitis, pulmonary nosocomial and communitary bacterial infections. EISBM is fostering the formation of a world-wide alliance to combat the major non-communicable chronic diseases listed by the World Health Organization (cardiovascular diseases,

cancer, chronic respiratory diseases and diabetes) as representing, together with rheumatologic diseases and neurologic disorders, the predominant health problems of the 21st century.

Expected outcomes

EISBM will implement cutting-edge experimental and computational methodologies in support of systems approaches to fundamental biological questions, focusing on overcoming the hurdles encountered for multi-scale integration across multiple levels of biological organization, a current challenge for the field.

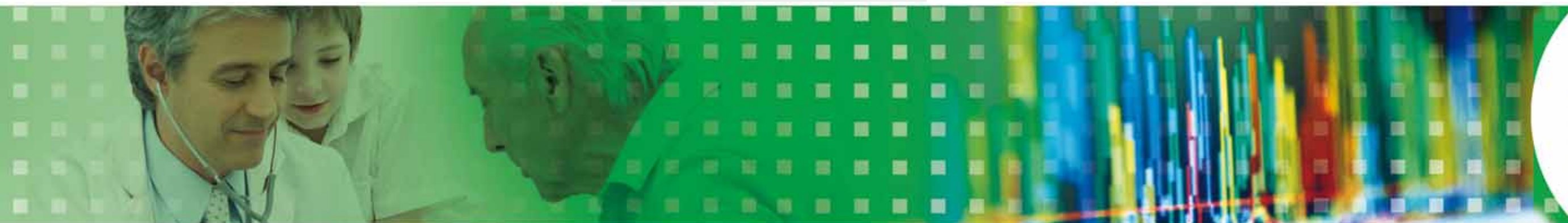
By sustaining the development of systems 4P-Medicine, EISBM will provide novel insights into the mechanisms of prominent diseases, and propose novel diagnostic and therapeutic options that will be developed by its industrial partners for implementation through integrated care.



With the launch of the European Institute for Systems Biology & Medicine, Europe greatly strengthens its role in leading research and applications of the systems approach. Charles Auffray and his colleagues will have the full support of those of us working on the Human Physiome Project of the International Union of Physiological Sciences. EISBM is an important initiative and will have undoubted benefits for the future of health care in Europe and beyond.

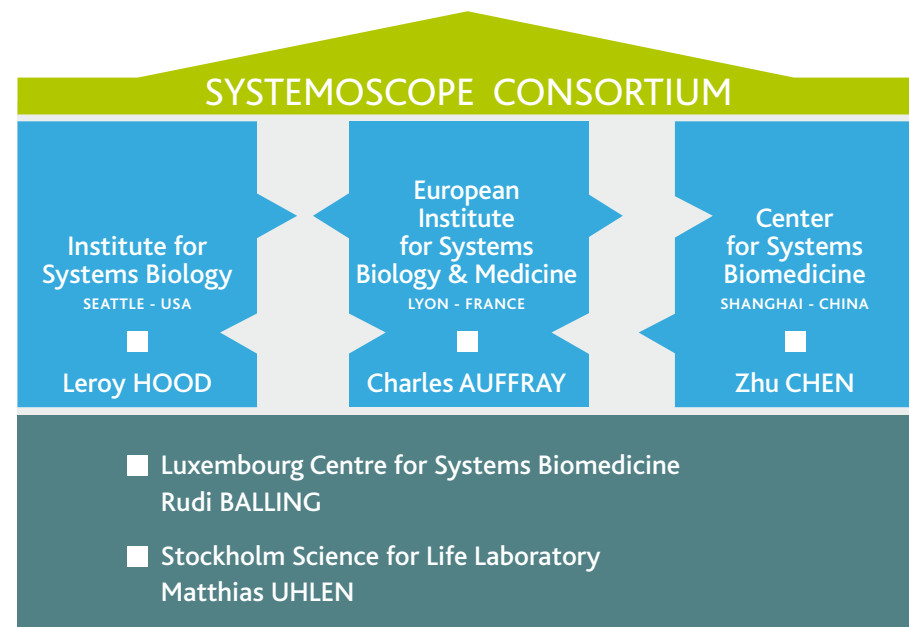
Denis NOBLE

President, International Union of Physiological Sciences ■ Director of Computational Biology, Oxford University



Bridging the gap between ACADEMIA & INDUSTRY

■ Systemoscope Consortium



With the common aim of sharing knowledge to speed up progress, key players in the field of systems biology & medicine across Europe, Asia and the USA have decided to form a strategic alliance and unite their efforts.

The Systemoscope International Consortium embodies a shared vision of systems biology and 4P-Medicine.

It was founded in 2002 by Dr Charles Auffray (France), Prof. Zhu Chen (China) and Prof. Leroy Hood (USA).

The aim of the Consortium is to foster systems approaches in biology and medicine based on public-private partnerships and to bring the tools of functional genomics and the results of systems biology from the laboratory to the patient.

EISBM is the core European component of the Systemoscope Consortium.

Pioneering SYSTEMS BIOLOGY & MEDICINE

■ by supporting EISBM

A range of options are open to support the foundation and development of EISBM

SPECIAL PARTNER

This label qualifies you to take part in EISBM activities as a founding member and to act as our ambassador.

MAIN PARTNER

Contributions will first be directed to the recruitment of qualified staff and faculty and the purchase of adequate equipment. On the long term, they will also support research projects coordinated by EISBM.

Operating under the umbrella of a public interest foundation according to French law, EISBM will deliver gift receipts eligible for 66 to 75% tax reduction on donations. This offers the guarantee of a safe legal framework for fund management.

ENDOWMENT

An initial endowment of 50 million Euros will be consolidated from the small individual "citizens of the world" contributions and the large donations from wealthy individuals and corporations.

EISBM is yours, will work with you, for you.



CONTACTS: www.eisbm.org

Charles AUFFRAY
EISBM Founding Director
cauffray@eisbm.org

Pascale TURMEL
EISBM Project Manager
pturmel@eisbm.org

Bruno MOUGIN
EISBM Industrial Partnerships
bmougin@eisbm.org

Myriam PLEYNARD
Financial Manager
Fondation Partenariale Lyon 1
Tel: + 33 (0)6 03 53 03 67
myriam.pleynard@lyon1fondation.org



REFERENCE SCIENTIFIC PUBLICATIONS

- Zheng, P.Z., Wang, K.K., Zhang, Q.Y., Huang, Q.H., Du, Y.Z., Zhang, Q.H., Xiao, D.K., Shen, S.H., Imbeaud, S., Eveno, E., Zhao, C.J., Chen, Y.L., Fan, H.Y., Waxman, S., Auffray, C., Jin, G., Chen, S.J., Chen, Z. and Zhang, J. (2005) *Systems analysis of transcriptome and proteome in retinoic acid/arsenic trioxide-induced cell differentiation/apoptosis of promyelocytic leukemia*. Proc. Natl. Acad. Sci. USA 102:7653-7658. PMID: 1589460.
- Graudens, E., Boulanger, V., Mollard, M., Mariage-Samson, R., Barlet, X., Grémy, G., Couillault, C., Lajémi, M., Piatier-Tonneau, D., Zaborski, P., Eveno, E., Auffray, C. and Imbeaud, S. (2006) *Deciphering cellular states of innate tumor drug responses*. GGenome Biology 7:R19. PMID: 16542501.
- De Chasse, B., ... Vidal, M., André, P., Rabourdin-Combe, C. and Lotteau, V. (2008) *Hepatitis C virus infection protein network*. Mol. Syst. Biol. 4 :230. PMID: 18985028.
- Bonneau, R., Facciotti, M.T., Reiss, D.J., Schmid, A.K., Pan, M., Kaur, A., Thorsson, V., Shannon, P., Johnson, M.H., Bare, J.C., Longabaugh, W., Vuthoori, M., Whitehead, K., Madar, A., Suzuki, L., Mori, T., Chang, D.E., Diruggiero, J., Johnson, C.H., Hood, L. and Baliga, N.S. (2007) *A predictive model for transcriptional control of physiology in a free living cell*. Cell 131:1354-1365. PMID: 18160043.
- Auffray, C., Chen, Z. and Hood, L. (2009) *Systems medicine: the future of medical genomics and healthcare*. Genome Med. 1:2. PMID: 19348689.
- Volpert, V. and Petrovskii, S. (2009) *Reaction-diffusion waves in biology*. Phys Life Rev 6:267-310. PMID: 20416847.
- Auffray, C. (2009) *Sharing knowledge: a new frontier for public-private partnerships in medicine*. Genome Med. 1:29. PMID: 19341500.
- Milani, P., Chevereau, G., Vaillant, C., Audit, B., Haftek-Terreau, Z., Marilley, M., Bouvet, P., Argoul, F. and Arneodo, A. (2009) *Nucleosome positioning by genomic excluding-energy barriers*. Proc. Natl. Acad. Sci. USA 106:22257-22562. PMID: 20018700.
- Hwang, D., Lee, I.Y., Yoo, H., Gehlenborg, N., Cho, J.H., Petritis, B., Baxter, D., Pitstick, R., Young, R., Spicer, D., Price, N.D., Hohmann, J.G., Dearmond, S.J., Carlson, G.A. and Hood, L.E. (2009) *A systems approach to prion disease*. Mol. Syst. Biol. 5:252. PMID: 19308092.
- Auffray, C., Charron, D. and Hood, L. (2010) *Predictive, preventive, personalized and participatory medicine: back to the future*. Genome Med. 2:57. PMID: 20804580.
- Auffray, C., Adcock, I.M., Chung, K.F., Djukanovic, R., Pison, C. and Sterk, P. (2010) *An integrative systems biology approach to understanding pulmonary diseases*. Chest 137:1410-1416. PMID: 2052565.
- Roach, J.C., Glusman, G., Smit, A.F., Huff, C.D., Hubley, R., Shannon, P.T., Rowen, L., Pant, K.P., Goodman, N., Bamshad, M., Shendure, J., Drmanac, R., Jorde, L.B., Hood L. and Galas D.J. (2010) *Analysis of genetic inheritance in a family quartet by whole-genome sequencing*. Science 328:636-639. PMID: 20220176.
- Navratil, V., de Chasse, B., Rabourdin-Combe, C. and Lotteau, V. (2011) *When the human viral infectome and disease networks collide: towards a systems biology platform for the aetiology of human diseases*. BMC Syst. Biol. 5:13. PMID: 21255393.
- Bousquet, J., Anto, J., Auffray, C. ... Pison, C. et al. (2011) *MeDALL (Mechanisms of the Development of ALLergy): an integrated approach from phenotypes to systems medicine*. Allergy Epub Jan 24. PMID:21261657.

EISBM ■ headquarters: Lyon Gerland ■ 50 avenue Tony Garnier ■ 69007 Lyon - France
■ www.eisbm.org



eisbm
European Institute
for Systems Biology & Medicine
A SYSTEMOSCOPE INSTITUTE