

## **CASyM Newsletter #2**

**Content:** *Editorial, News, Guest Contribution, Events  
and Must Read section*

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## 1. Editorial

Promoting Systems Medicine and bringing together relevant stakeholders – CASyM’s first year of committed activity has just ended. This first year was a very busy one and with the current newsletter we would like to invite you to have a closer look at the events, which were organized by CASyM in 2013. This issue pays special attention to the additional workshops organized during the second half of 2013 complementing the two international conferences and the training tutorial, detailed in the previous newsletter.

In total approximately 400 experts, organized in 20 focused round table discussions, were consulted in 2013. The output of these consultation events can be downloaded as meeting reports from the [CASyM website](#) and represent the foundation of the proposed roadmap to Systems Medicine, which will soon circulate as a first complete draft version among CASyM’s associated partners as well as a selected group of stakeholders representing a broad expertise in relevant fields.

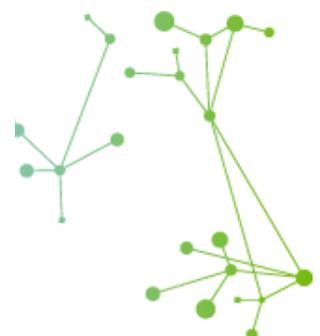
Next to this, members of our Steering Committee took the opportunity to promote CASyM and Systems Medicine in key presentations at different national as well as international events, for example the [ES:GC2](#) event in Brussels and the [ICSB2013](#) in Copenhagen.

We would also like to draw your attention to the guest contribution by Prof. Bernd Schreck from the German Center for Lung Research (DZL) at the Philipps University Marburg about: “Are we on our way to “Systems Physicians”?”.

Another important topic, which we would like to stress, is the “Vilnius statement” - a joint effort of the Virtual Physiological Human Institute, CASyM, Disciplus, INBIOMEDvision, Personal Health Systems Foresight and Avicenna as well as the IMI-eTRIKS Consortium on *in silico* medicine ([read more](#)). Since CASyM represents an open network, we will continue to put special emphasis on interacting with more initiatives and projects in the future to find synergies and to avoid duplication of efforts.

If you are interested in further CASyM activities or in Systems Medicine in general, please [register](#) at the [CASyM website](#) and contribute contents on its [blog space](#) or send us ideas and input on recent advances in Systems Medicine and how we can support Systems Medicine to bring it into everyday medical practice.

In summary, some very important milestones have been achieved during CASyM’s first year of funding:



## 2. CASYM WORKSHOPS AND MEETINGS

In order to develop the CASyM roadmap and to discuss relevant Systems Medicine topics, the CASyM consortium organizes concise workshop meetings dedicated to assess defined aspects of Systems Medicine and corresponding implementation strategies. Since the last newsletter release, the following workshops have taken place:

### 2.1 - The Road from Reactive Medicine to Proactive Systems P4 Medicine

On 25 June 2013 our partner EISBM (European Institute for Systems Biology & Medicine) organized the first methodological and technological workshop in Lyon, France, to discuss the requirements for a sustainable knowledge management as well as integration and sharing in translational research and Systems Medicine. External experts, CASyM members, and associated partners identified priority actions to tackle the existing challenges and opportunities in two parallel round table discussions:

- ▶ ROUND TABLE 1: Technological and infrastructure requirements for sustainable knowledge management
- ▶ ROUND TABLE 2: Ethical, legal and social issues in personal data protection and sharing

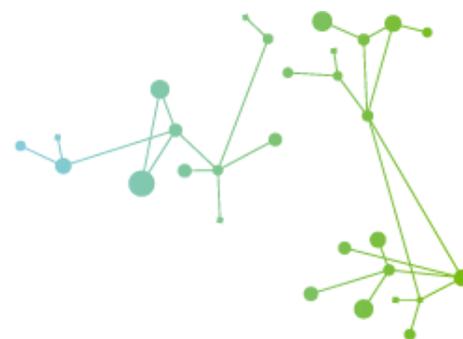
The workshop report can be downloaded [here](#).

### 2.2 - Strategic CASyM modelling workshop

It has been largely acknowledged in the biomedical sector that the number and complexity of available data related to patients, diseases, or therapeutics need novel approaches for their inclusion and, in the best case, for a comprehensive integration with scientific data and knowledge. The strategic CASyM modelling workshop, held on 11 June 2013 in Heidelberg, Germany, therefore dealt with the role of computational multiscale modelling in Systems Medicine. The participants identified main priorities and defined an action plan to develop the aspect of multiscale computational modelling for Systems Medicine in Europe to be integrated into the CASyM roadmap. The workshop report can be downloaded [here](#).

### 2.3 - CASyM/ICSB2013 training workshop - Should systems medical training be integrated for basic and clinical researchers?

This workshop was the second training event of CASyM and a central part of the educational activities to develop novel training concepts for the next generation of medical doctors and scientists in multimodal Systems Medicine approaches. The workshop was organized as a satellite event of the International Conference on Systems Biology (ICSB) on 3 September 2013 in Copenhagen, Denmark. The workshop report can be downloaded [here](#). Please note that this newsletter's [GUEST CONTRIBUTION](#) by Prof. Bernd Schmeck also elaborates on this topic.



## 2.4 - Towards a joint concept between National and European research & innovation programmes in systems (bio)medicine

The EC Health Directorate invited experts from the CASyM consortium and representatives of national funding bodies from across Europe for a workshop on 10-11 December 2013 in Brussels to discuss (i) common actions between different national/regional funding bodies of the Member States and (ii) which research activity is best performed on European level, including joint activities. The results of the discussions on joint national and European approaches to research and innovation programs in Systems Medicine will soon be released as a meeting report.

## 2.5 - 2<sup>nd</sup> Annual CASyM consortium meeting

On 9-10 December 2013 the second CASyM consortium meeting was taking place in Brussels. In this context, the current state of the work package activities, past and future tasks were discussed between the consortium members. Despite a very competitive project schedule with many comprehensive tasks, all major deliverables are on track to be achieved. As the major objective, the first road map draft was distributed among the consortium members before the meeting. It will be further refined based on the input of CASyM members and external experts (see also below for further information) before the document will be first published in mid-2014. Next to this, the CASyM partners discussed the opportunities and challenges of Horizon 2020 and agreed on a common strategy to tackle the dawning framework program.

On the second day of the meeting, CASyM achievements were discussed with representatives of the EC Health Directorate.

## 2.6 - Clinical needs in oncology and cardiovascular diseases, as drivers for a Systems Medicine approach

On 19-21 January 2014 our partner *The Department of Internal Medicine* of the University of Genoa, Italy organized a workshop, which focused on cancer and cardiovascular diseases as two pathologies with high relevance for Systems Medicine. European specialists for these two types of diseases were the prime target group of the workshop. In the following 4 Round table discussions the clinical needs of these diseases were discussed:

- ▶ ROUND TABLE 1: Methodologies and priorities in the implementation of Systems Medicine in Clinical Oncology
- ▶ ROUND TABLE 2: Methodologies and priorities in the implementation of Systems Medicine in Cardiovascular Medicine
- ▶ ROUND TABLE 3: Systems Medicine and personalized care in Oncology
- ▶ ROUND TABLE 4: Systems Medicine and personalized care in Cardiovascular Medicine

A meeting report is currently in preparation and will soon be published on the [CASyM website](#).



### 3. GUEST CONTRIBUTION

#### Prof. Bernd Schmeck: Are we on our way to “Systems Physicians”?



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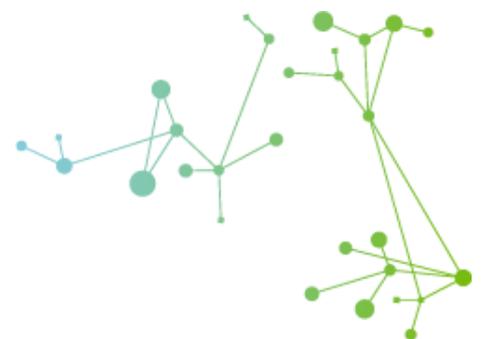
Systems Medicine has the potential to make medical care and practice more patient-centered, more (cost-) effective, more holistic, and reduce potential side effects. However, to develop and implement systems strategies in medicine, we do not

only need medical literacy in basic scientists performing Systems Biology, but also trained and experienced clinical practitioners. What challenges do we have to meet in on this way?

By definition, systems medicine involves the implementation of Systems Biology approaches in medical concepts, research and practice. This could be achieved by iterative and reciprocal feedback between data-driven computational and mathematical models as well as model-driven translational and clinical investigations.<sup>1</sup> Final outcomes could be examples of personalized medicine or the so- called 4P medicine (predictive, preventive, personalized and participatory)<sup>2</sup>.

Therefore, key components of CASyM are e.g. the development of multidisciplinary training and professional dissemination concepts, creating and shaping a sustainable European community of Systems Medicine.<sup>3</sup> At the CASyM ICSB2013 training workshop and the Ljubljana CASyM course 2013, important issues have been discussed and goals have been defined<sup>4</sup>: (i) Systems Medicine should span all aspects of medical education as a framework for integration of all (pre-) clinical disciplines. (ii) Systems-Medicine-facilitated courses of “traditional” topics should aim at understanding complex topics with the help of dynamic systems approaches and (visualization-based) gadgets. (iii) Research physicians and clinical practitioners should be educated more thoroughly in statistics, bioinformatics, and -omics technologies, and should be open-minded for the use of Systems Biology modelling for medical purposes. (iv) Software should be adapted for intuitive usage by clinicians.

Tasks we have to meet on the way to physicians with literacy in and probably affinity to systems medicine start during medical school: The Bologna Process should in principle lead to a medical education consisting of a Bachelor focused on natural sciences and a Master in clinical medicine. On the other hand, new concepts e.g. in Germany aim on a 6-year programme starting with clinics on the first day, focussing on “problem-orientated learning”, i.e. signs and symptoms, rather than patho-physiological systems (cancer, proliferation, inflammation etc.). Whether this is compatible with or in favour of Systems Medicine-oriented training might be doubted. In addition, many European countries face a shortage in physicians, especially in the field of general practitioners. This has motivated representatives of health insurance companies, political parties, and patient organisations to demand a faster and less “science-oriented” medical education. The desired result would be an increased output of practitioners that can recognize the most frequent signs and symptoms and prescribe a standardized and established



therapy. Moreover, the aforementioned shortage in physicians leads in many countries to i) a high and still increasing workload for physicians, and ii) a significant disparity between basic researchers and clinical practitioners in terms of income as well as the possibility to get tenured positions. Consequently, in many areas, it becomes increasingly more difficult to find medical students or practitioners, which are willing and/or able to take an interest in or participate in new (scientific) developments. Very often, young clinicians that would be ideal candidates to become “systems physicians”, both as researchers and practitioners, are nowadays forced to and rewarded for fast, standardized and unquestioned application of (observational-)”evidence-based medicine”.

In conclusion, besides the development of Systems-Medicine-facilitated courses of “traditional” and integrative topics, we should focus on two additional goals: i) To increase the awareness for the mid- and long-term benefits of this way among students, academic teachers, and clinicians, but also representatives of health insurance companies, political parties, and patient organisations. ii) To give both medical students and young physicians a framework and protected area to train and participate both in the development and application of systems-based strategies. In the end, we absolutely need their positive input and enthusiasm. As first steps in this direction, the Systems Biology Platform<sup>5</sup> of the German Center for Lung Diseases at the Philipps-University Marburg is implementing a facultative curricular course in Systems Medicine for medical students and students in the Master-programme “human biology”. It will start in 2014 and grants 6 ECTS credit points. The course covers modules on clinical medicine & pathophysiology, molecular regulatory circuits & technology, as well as statistics, bioinformatics & modelling. In addition, the platform offers a clinician scientist programme for young physicians in cooperation with the University Medical Center Marburg. It provides training in Systems Medicine and free time for own research.

#### References:

1. European Commission workshop “From Systems Biology to Systems Medicine”, 2010
2. Sobradillo P, Pozo F, Agustí A. P4 medicine: the future around the corner. Arch Bronconeumol. 2011;47:35
3. CASyM report: European Systems Medicine road-map discussions – Coordinating Systems Medicine across Europe, Brussels, November 2012.
4. CASyM ICSB2013 training workshop report - Should systems medical training be integrated for basic and clinical researchers? - Copenhagen, Sep. 2013
5. [www.i-lung.de](http://www.i-lung.de)

## 4. THE CASYM ROAD MAP: CURRENT STATUS AND FUTURE PLANS

Major tools for CASyM to prepare the proposed road map are expert driven conferences and workshops with focused round table discussions. In 2013 the CASyM consortium organized a series of such events to describe short-, medium- and long-term priority issues for a European wide Systems Medicine approach. The output of these events are all summarized in specific event reports ([read more](#)) and represent the framework for the proposed road map, which presently exists in its first complete draft version.



Since CASyM is an open network, we will seek input from all relevant stakeholders for the opportunity to guide the further development of the current road map document. It is therefore a great pleasure for the CASyM consortium to invite all associated partners to critically review the first draft of the CASyM road map and to provide opinions, suggestions, comments and remarks. Each of the associated reviewers will be listed by name in the actual document when the road map will be officially published on the CASyM website ([www.casym.eu](http://www.casym.eu)) by mid-2014.

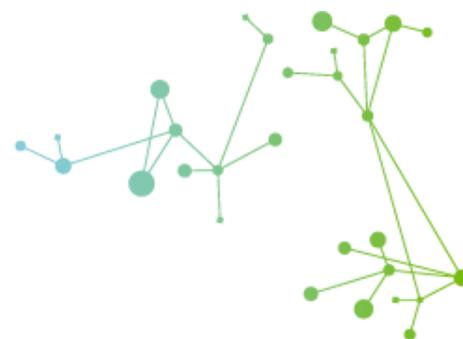
So, if you would like to engage in the CASyM road map discussion, feel free to join CASyM through our [website](#) and become a road map reviewer.

## 5. “MUST READS”: IMPORTANT PUBLICATIONS IN SYSTEMS MEDICINE

In this section, we are presenting current publications in Systems Medicine. The publications are recommendations of the CASyM partners and arbitrarily ordered. A more comprehensive list of important and interesting publications in Systems Medicine can also be accessed [here](#) via the CASyM website. Please feel free to submit additional recommendations to [m.kirschner@fz-juelich.de](mailto:m.kirschner@fz-juelich.de) or [clemens.ostrowicz@uni.lu](mailto:clemens.ostrowicz@uni.lu) or at the [CASyM Blog](#) space.

### Recent

- ▶ A Generally Applicable Translational Strategy Identifies S100A4 as a Candidate Gene in Allergy. **Bruhn, S et al.**: *Sci. Transl. Med.* (2014) / ([more](#))
- ▶ From Nonalcoholic Fatty Liver Disease to Hepatocellular Carcinoma: A Systems Understanding. **Rozman, D**: *Digestive Diseases and Sciences*, Springer Science+Business Media New York (2014) / ([more](#))
- ▶ Why Model? **Wolkenhauer, O**: *Frontiers in Physiology* (2014) / ([more](#))
- ▶ The Role of Theory and Modelling in Medical Research. **Wolkenhauer, O**: *Frontiers in Physiology* (2013) / ([more](#))
- ▶ Multiscale Cancer Modelling and In Silico Oncology: Emerging Computational Frontiers in Basic and Translational Cancer Research. **Stamatikos, GS et al.**: *J Bioengineer & Biomedical Sci.* (2013) / ([more](#))
- ▶ A circadian clock transcription model for the personalization of cancer chronotherapy. **Li, X-M et al.**: *Cancer Res.* (2013) / ([more](#))
- ▶ Systems medicine: helping us understand the complexity of disease. **Vandamme, D et al.**: *QJM* (2013) / ([more](#))
- ▶ Pediatric systems medicine: evaluating needs and opportunities using congenital heart block as a case study. **Tegnér J and Abugessaisa I**: *Pediatric Res.* (2013) / ([more](#))
- ▶ The Vilnius statement on in silico medicine research in Europe. **VPH Institute, and of the Discipulus, INBIOMEDvision, PHS Foresight, CASyM, and Avicenna (2013)**: [Statement](#) (PDF)



## 6. SELECTED UPCOMING EVENTS

- ▶ CASyM academic/industry interaction workshop, Lyon 10 April, 2014
- ▶ CASyM training tutorial: Modelling Tools for Pharmacokinetics and Systems Medicine, Stuttgart 18 May, 2014  
This tutorial is part of the 20th International Symposium on Microsomes and Drug Oxidations **but can be booked independently of the congress** ([registration form](#), pdf).
- ▶ The first Systems Biology and Systems Medicine School, including CASyM tutorial sessions, Como 21-27 September, 2014

Please check the website regularly for updates on our [events section](#).

## 7. ACKNOWLEDGEMENTS

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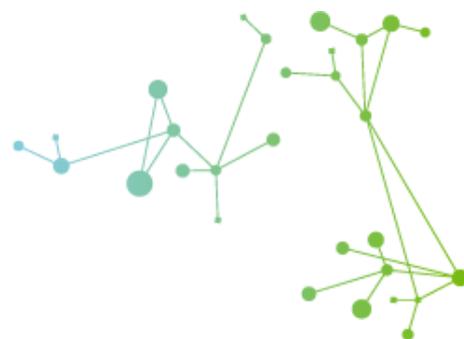
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