

PROJECT MANAGEMENT

Consortium management tasks and achievements

The management team undertakes to organise all of the project meetings, teleconference and travel, both for the partners and for our External Advisory Group. We also maintain the PHAGOSYS website, hosted by the Centre for Integrative Systems Biology at Imperial College, and the PHAGOSYS wiki, which is an internal resource for the partners to share protocols, data, papers of interest, as well as a repository for the monthly teleconference minutes and presentations.

Problems which have occurred and how they were solved or envisaged solutions

Two tragic events affected the project during this first period. In the Autumn of 2008, shortly after the project commenced, the mathematician Professor Jaroslav Stark was diagnosed with cancer and went on long term leave; he died in June 2010. This meant that the mathematician at Imperial College was initially without supervision at a crucial stage of the project; this has led to some delays in progress on WP1. We have now recruited a new member to the consortium, Dr. Vahid Shahrezaei, a mathematician who is now supervising this part of the project.

The second tragic event was the death of Dr. Emmanuelle Caron in July 2009, after a short illness. This has had a profound effect on many members of the consortium, but particularly the research staff under her guidance in WP3. This has understandably led to some delays in progress. We have now recruited a new member to the consortium, Dr. Vania Braga, a cell biologist who is now leading WP3.

As a result of the loss of two of our colleagues to the consortium, and the delays in recruitment we propose to ask for a no-cost extension and to modify our timelines for the final period of the project. This is detailed in the **project planning and status** section below.

Changes in the consortium, if any

As discussed in the section above, we have had to recruit two new members to the consortium. At a management teleconference on 28 August 2009, we agreed to invite Dr. Vahid Shahrezaei and Dr. Vania Braga to join the consortium in work-packages one and three respectively. Dr. Caron had also been acting as deputy co-ordinator, and Prof. Jacques Neefjes was proposed and accepted to take on this role.

List of project meetings, dates and venues

- Warm-up meeting, Slovenia, 5-6 Feb 09
 - identified areas for harmonisation, and introduced the modellers to the biology
- Kick-off meeting, London, 16-17 Apr 09
 - agreed on protocols, progress updates from all

- Mid-term review, Dresden, 10-11 May 2010
 - progress updates from all and presentations to the External Advisory Group; discussion of first period report

Project planning and status

As reported in the management sections above the loss of colleagues and late start to some components of the project has delayed progress. This fact was also noted by our External Advisory Group, and is detailed in their report, which is appended to this document. On the basis of these recommendations we request a 6 month no cost extension to the project, in particular to allow WPs 1 and 4 to complete their deliverables.

Impact of possible deviations from the planned milestones and deliverables, if any

We do not plan to deviate from any of the planned milestones or deliverables in terms of their content, but some of the time-lines will need to be amended. An amended table is included below. In summary: two assay systems, rather than the one envisaged, have had to be developed and optimised for the *Salmonella* and *M. tuberculosis* systems, which has taken extra time. Therefore, the three deliverables indicated in the table have been delayed. The efforts at ICSTM in WPs 1 and 3 have been delayed due to the tragic deaths of two members of the team. Although we have in essence achieved the deliverables set for this time period, we feel considerably more could have been done had circumstances been different. Consequently we will delay the deliverables for the second period in line with the available budget and proposed no-cost-extension.

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Del. no.	Deliverable name	WP no.	Lead beneficiary	Estimated indicative person-months	Nature	Dissemination level	Delivery date (proj. month)
1.1	Initial Model	1	ICSTM	36	O	RE	12
2.1	High-throughput Imaging assay	2	MPICBG	12	O	RE	18
6.1	PHAGOSYS website	6	ICSTM	4	O	PU	12
1.2	Report on <i>Modelling phagocytosis</i> for website	1	JSI		R	PU	18
2.2	Predictive models of phagosome maturation	2	MPICBG	3	O	RE	18
2.3	Data array/ phagosome maturation	2	MPICBG	3	R	RE	18
2.4	Report on <i>Assay development and phagosome characterisation</i> for website	2	MPICBG		R	PU	18
3.1	Focused data array / uptake	3	ICSTM	18	R	RE	48 21
3.2	Report on <i>RNAi screens for uptake</i> for website	3	ICSTM		R	PU	18
4.1	Focused data array / pathogen survival	4	LUMC	72	R	RE	48 24
4.2	Report on <i>RNAi screens for maturation</i> for website	4	LUMC		R	PU	48 24
5.1	Data array/pathogen genes	5	MPIIB	36	R	RE	18
5.2	Report on <i>Manipulation of phagosome maturation by pathogens</i> for website	5	MPIIB		R	PU	18
4.3	Focused data array / phagosome maturation	4	NKI	30	R	RE	24 30
1.3	Revised Model	1	JSI	36	O	RE	24 27
3.3	Finalized data array / uptake	3	ICSTM	18	R	RE	36 39
4.4	Drugome array/ <i>Salmonella</i>	4	LUMC	24	R	RE	36 42
4.5	Finalized data array /pathogen survival and maturation	4	NKI	12	R	RE	36
4.6	Endocytosis array/ <i>M. avium</i>	4	MPICBG	12	R	RE	36
5.3	List of in vivo validated genes	5	MPIIB	36	R	RE	36
1.4	Final Model	1	JSI	36	R	RE	36 39
6.2	Provision of Final report	6	ICSTM	12	R	PU	36
TOTAL				400			

Any changes to the legal status of any of the beneficiaries, in particular non-profit public bodies secondary and higher education establishments, research organisations and SMEs

None

Development of the Project website, if applicable

The project website (<http://www3.imperial.ac.uk/cisbic/research/phagosys>), is hosted by the Centre for Integrative Systems Biology at Imperial College. We also have the PHAGOSYS wiki (<https://cisbic.bioinformatics.ic.ac.uk/phagosys/>), which is an internal resource for the partners to share protocols, data, papers of interest, as well as a repository for the monthly teleconference minutes and presentations. Validated protocols and reports will be moved from the wiki to the public website as appropriate.

Use of foreground and dissemination activities during this periods (if applicable).

- A number of partners have given talks on PHAGOSYS related work, including:
- Brian Robertson is co-editing a book entitled *The Systems Biology of Micro-organisms*, which will include contributions from this and other EU funded projects. He also given talks on the systems biology of phagocytosis at Imperial College on 14 December 2009 and at the Society for General Microbiology meeting in Edinburgh on 30 March 2010.
- Jacques Neefjes gave two seminars on related work at Imperial College London on 11 November and 14 December 2009. He also presented his work at LUMC in Leiden. The NKI, LUMC and MPICBG labs were visited by members of the JSI lab for in depth discussion on integrating the experimental data into the systems biology models. Image data and calculated features from siRNA screens performed at the NKI and MPICBG labs were exchanged with the JSI lab for further analysis.
- Rico Barsacchi gave a talk entitled "A cell based assay to identify novel therapeutic targets of *M. tuberculosis* infection" to the "Cell Based Assay" meeting in Cologne, Germany on 8th June 2010.
- In the first half of the project, Saso Dzeroski gave a variety of talks related to the content of the PHAGOSYS project. In particular he gave an invited talk on "Inductive Process Modelling for Systems Biology" at the workshop "Inductive Process Modelling" held at the ECML/PKDD 2008 Conference, and a tutorial (on inductive queries and constraint-based data mining, including equation discovery) at the Discovery Science 2008 Conference. He has given talks at partner institutions (Imperial, LUMC, MPI-CBG) and institutions outside the PHAGOSYS consortium (University of Bari and Naples; Fondazione Bruno Kessler, Trento; German Cancer Research Center, Heidelberg; European Bioinformatics Institute, Hinxton), mostly on the topic of equation discovery for systems biology.
- Saso Dzeroski co-organized MLSB-2009, *The Third International Workshop on Machine Learning in Systems Biology*, held in Ljubljana, Slovenia on September 5-6 2009. Two posters

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describing work from the PHAGOSYS project were presented. The workshop attracted more than 60 participants, had 6 invited talks, 12 oral presentations and 22 posters.

Co-ordination activities during the period in question, such as communication between beneficiaries, possible co-operation with other projects/programmes etc.

From the outset we recognised the need for the modellers to familiarise themselves with the experimental biology side of the project. To that end there have been a series of visits by the modellers to the partner institutes carrying out the experimentation.

Visits to Partner institutes

Dr Barbara Szomolay (Imperial College) visits to:

IJS, Ljubljana, 5-6 September 2009

NKI, The Netherlands, 7 September 2009

MPI-CBG, Dresden, 27-30 September 2009

Prof Saso Dzeroski (IJS) visits to:

MPI-CBG, Dresden, 8-10 November 2009

Imperial College London, 10-13 November 2009, 22-23 March 2010

NKI/LUMC, The Netherlands, (with Ivica Slavkov) 28-31 March 2010

Prof Jacques Neefjes (NKI) visits to

Imperial College London, 11 November 2009, 14 December 2009

The MPI-CBG is collaborating with the Swedish company Cellaxes in order to establish electroporation-based transfection protocols in 384-well format, using their high throughput platform Cellaxes HT.

Monthly Teleconferences

Each month one of the work-packages updates the rest of the consortium on their progress; slides (circulated in advance) are presented, with questions and comments from the participants. Minutes, as well as the presentation, are placed on our wiki.

We have had discussion with one of our External Advisory Group members, Prof. Ulrich Schaible, about collaborative work on modelling the impact of mycobacterial lipids on intracellular trafficking.

A modelling workshop was held at MPI-CBG 10th to 12th May 2010

The modellers and experimentalists (from JSI, Imperial College, LUMC, TUD and MPI-CBG) discussed and presented their biological questions, screening results and modelling outputs to define the necessary next steps for better quality modelling and for a more effective scientific interaction between the two disciplines (modelling and biology). IJS, IC, TUD and MPI-CBG modellers discussed and presented their most recent work regarding a novel generic modelling

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approach for simulating biological data (the biological paradigm used as a starting point is the Rab conversion in the endocytosis pathway). The sessions and participants are detailed below.

SESSION A- Analysis of large scale datasets from functional cell based-assays

IJS, Ljubljana participants:

Saso Dzeroski, Dragi Kocev, Bernard Zenko, Ivica Slavkov, Darko Aleksovski, Valentin Gjorgjioski

LUMC, Leiden participants:

Nigel Savage, Tom Ottenhoff THM, Kees Korbee

MPI-CBG, Dresden participants:

Rico Barsacchi, Varadha Sundaramurthy, Marc Bickle, Nikolay Samusik

SESSION B - Equation Discovery Track

Ljubljana participants:

Ljupco Todorovski, Katerina Taskova, Aneta Trajanov, Darko Cerepnalkoski

Imperial College:

Vahid Shahrezaei, Barbara Szomolay,

MPI-CBG:

Yannis Kalaidzidis, Roberto Villaseñor, Giovanni Marsico, Perla del Conte-Zerial, Lilla Farkas

TUD: Lutz Brusch