



Euro-BioImaging

European Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences

WP7 Access to innovative light microscopy technologies

Guidelines for Proof-of-Concept Studies – High Throughput Microscopy

EMBL

July 2011

The Advanced Light Microscopy Facility (ALMF) at EMBL Heidelberg provides advanced light microscopy and image analysis services for all of EMBL's scientific groups and external visitors predominantly from EMBL Member States. At the EMBL Advanced Light Microscopy Facility (ALMF), we have had 207 external visitors during the period from 2006 to 2010, using 29 different imaging platforms.

See the ALMF homepage at: http://www.embl.de/almf/almf_services/ for more detailed information.

The enclosed report contains the guidelines used at the ALMF to evaluate and run visits by external scientists who wish to use the high throughput microscopy possibilities at EMBL.

We suggest that the principles that have guided the EMBL ALMF visiting scientist program can be used as guideline for the establishment and running of Euro-Biolmaging access to high throughput microscopy.

1 Guidelines for scientific visits to the ALMF conducting high throughput microscopy projects

1.1 General outline of the project schedule

1. The scientist interested to conduct a high throughput microscopy project in the ALMF contacts informally the head of the facility to enquire the feasibility to conduct the project in the ALMF, to explore the possibilities for a scientific host and to estimate the approximate project costs.
2. After positive response from the ALMF head, the visiting scientist, scientific host and ALMF staff establish a project milestone plan (see Appendix 1).
3. The scientist submits a formal but concise application to the ALMF including the formal agreement of the scientific host and ALMF head and the developed project milestone plan (see 1.2. for an application template).
4. The project application is evaluated on a scale from 1 -10 by written procedure (email) by a board of EMBL scientists representing the different scientific disciplines of EMBL, the head of the ALMF committee and ALMF and the proposed scientific host at EMBL. (see 1.3. for an evaluation template)
5. After positive project evaluation the scientist is invited to visit the ALMF and conduct the project work. Timelines are arranged according to the project ranking (average score of the board evaluation). Highly ranked projects may be considered to start earlier than lower ranked ones. Due to space and personnel constraints no more than three external visitors are accepted to work in the ALMF at any time and scientific hosts (except for the head of the ALMF) typically accept only one external visitor at a time. The ALMF makes every effort to host the scientist as soon as possible after application to maintain scientific competitiveness.
6. The logistics of the visit (e.g. accommodation, travel, shipment of reagents) should be arranged with ALMF staff, scientific host and the administrative assistant of EMBL's visitor programme.
7. The project work is conducted in the ALMF supported by the scientific host's laboratory.
8. After project completion, the scientist summarizes the project results and in a short report (typically one page) and provides standardized feedback on various issues of his/her stay (see 1.4 for a report template).

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9. In the post visit period the scientist will inform the ALMF when the results obtained at EMBL are published in scientific journal(s) with appropriate mention of ALMF support in the acknowledgement section of the article. This is included in ALMF visitor reports.

1.2 Application Guidelines

The formal application of the scientist to the ALMF should be concise and typically not exceed two pages and include the following items:

1. A short CV of the applicant.
2. A short scientific project description containing the following information:
 - Project title
 - Scientific background of the project
 - Description of work proposed to be conducted at the ALMF
 - Importance of the project for the overall research of the scientist
 - Expected results
 - **A milestone plan of the project with clear deliverables and routes for exit if the milestones are not achieved.**
3. Further information requested
 - Equipment/technology that is envisaged to be used
 - Approximate costs of the project (e.g. based on equipment usage hours and reagents; needs to be estimated consulting the head of ALMF and scientific host)
 - Previous experience of the applicant in light microscopy techniques (in particular the one that he/she intends to use at the ALMF)
 - Biological hazards associated with the project
 - Approval of the scientific host at EMBL (could be head of ALMF)
 - Estimation of the time to be spent at EMBL (preferred starting and ending dates should be proposed according to the milestone plan).
 - Agreement to acknowledge the ALMF in publications resulting from data obtained during the visit.
 - Approval of the scientists home institution supporting the visit to the ALMF

1.3 Evaluation Guidelines

The project application will be evaluated according to the following criteria (scale 1 to 10, 1=lowest, 10=best mark). Evaluations should be concise and typically not exceed one page:

1. *Scientific excellence*

- What is the significance/importance of the project in comparison with international standards in the field?
- What is the relevance/contribution of the project to the scientist's overall scientific work/interests?
- Are the project's results likely to be included in future scientific publications?
- What is the scientific quality of the scientist or home laboratory?

2. *Feasibility of the project*

- Is the project feasible to be successfully conducted in the ALMF?
- **Is the milestone plan and project exit routes realistic?**

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- Are the technologies available at the ALMF appropriate to address the posed question(s)?
 - Does the applicant have sufficient specific training for the experiments to be conducted, or will he/she be able to acquire the skills in the timeframe of the proposed project?
 - Are the estimated project costs reasonable and can they be covered by the scientist?

If any of the three questions above are evaluated as not feasible or insufficient (ranking as "1") the project will be rejected.

3. Others

- Will the applicant benefit in the post-visit period from the project (e.g. by the training received, results obtained, scientific networking started, be able to apply for his/her own grant)?
- Does the applicant need to conduct the research at the ALMF (or could he/she conduct the work in another place that is closer by his home laboratory, or more qualified for the specific application)?

1.4 Reporting Guidelines

1.4.1 Reporting and management during the project

Project meetings will be held according to the milestone plan to discuss whether the respective milestone could be achieved. If necessary, the timelines of the project and milestone plan will be adapted accordingly, or the project will be terminated. Participants (also via teleconference) of these project meetings are: The scientist(s) conducting the project, the project supervisor at the home institution, the scientific host at EMBL, and the ALMF staff involved in the project. A brief meeting report is generated by the meeting participants for documentation of the progress of the project.

1.4.2 Reporting after project completion

After project completion the scientist is asked to report on the scientific results obtained, the impact the results have on his/her future work, the quality of the scientific, technical and logistic support from the ALMF and EMBL (if feasible scale 1 to 10, 1=lowest, 10=best mark). Reporting should be concise and typically not exceed one page:

- Type of instruments used
- Satisfaction concerning given advice and information on usage of most appropriate imaging instrument(s)
- Satisfaction concerning logistic support at the facility (office space, computing, libraries, accommodation)
- Satisfaction concerning technical support to make best use of the imaging instrument(s)
- Satisfaction concerning scientific support to set up the experiments and interpretation of results
- Rating of scientific impact of imaging infrastructure usage on the project
- Satisfaction concerning administrative support

- Summary on project results which were achieved by using ALMF instrument(s)
- List of publication(s) containing project results based on using ALMF instrument(s)

APPENDIX 1**Example for a high throughput microscopy project milestone plan****Project title:**

Identification of protein kinases/phosphatases with a role in Golgi structure and function

Aims of the project:

A human kinome and phosphatases targeting siRNA library will be screened for siRNAs that interfere with the morphology of the Golgi complex in a high-throughput laser scanning confocal-microscopy-based time-lapse assay. Identified hits will be further tested to interfere with the ER to Golgi transport of ts-O45-G by high throughput time-lapse spinning disk microscopy.

Estimated project duration:

In total the project is expected to last for 15 months. The total time spent in the ALMF is estimated to be around 9 months.

Milestone plan:

MS1 (M6): Reagents

Establishment of a stable HeLa cell line expressing dsRed-H2B and GFP- GAnINacT2.

This work will be conducted at the home institution.

Risk assessment and exit routes

If the establishment of the cell line fails the project will be terminated. If it is delayed, following milestones will be delayed accordingly.

MS2 (M7): Laboratory assay

Establishment of the laser scanning microscopy based time-lapse imaging conditions for Golgi and H2B. (on ALMF screening microscope). Important feasibility controls include Golgi fragmentation kinetics after nocodazole treatment and unperturbed cell cycle progression of untreated cells under the imaging conditions.

Risk assessment and exit routes

If the establishment fails the project will be terminated. If it is delayed, following milestones will be delayed accordingly.

MS3 (M10): High throughput microscopy assay

Establishment of automated high throughput image acquisition conditions such that existing image analysis (available for Golgi analysis in the ALMF) procedure will be able to score well known Golgi phenotypes (siRNA targeting PLK1, GM130, GMAP210).

Risk assessment and exit routes

If the establishment fails the project will be terminated. If it is delayed, following milestones will be delayed accordingly.

MS4 (M12): Pilot screen

Completion of a pilot screen testing for 20 siRNA known to affect Golgi morphology using the developed high throughput assay.

Risk assessment and exit routes

If the establishment fails the project will be terminated. If it is delayed, following milestones will be delayed accordingly.

MS5 (M14): High throughput screen

Completion of the siRNA screen testing a human kinase and phosphatase library (available at ALMF) for effects on Golgi morphology using the developed high throughput assay. The screen will comprise three successfully analysed replicates.

Risk assessment and exit routes

If this fails the project will be terminated. If it is delayed, following milestones will be delayed accordingly.

MS6 (M15): Secondary screen

Completion of the siRNA screen testing the primary hit siRNAs in a secretory transport assay (ts-O45-G) well established in the ALMF.

Risk assessment and exit routes

If this is delayed, following milestones will be delayed accordingly.