Coordinated Research Infrastructures Building Enduring Life-science services
- CORBEL -

Deliverable D4.1

Strategy for enabling user access within pilot use cases

WP4 – Community Driven Cross-Infrastructure joint research - Bioscience

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Contributing partner(s): MDC, UMCU, ICFO, CRG, BRFAA, HMGU, CIRMMP, CSIC, CNRS, SZN, FVB, VU/VUmc, DKFZ

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Content

Executive Summary

Within the first period of the CORBEL project, the goal of work package 4 (WP4) is to drive the development of shared services between European biological and medical science research infrastructures (BMS RIs) and to establish their maturity towards open user access. To accomplish this, we will employ use cases that follow defined pipelines covering a broad range of scientific research fields and involving expertise and techniques distributed across distinct RIs in several European countries. The RIs involved in CORBEL are currently at different operational stages with respect to their legal and functional development. This is reflected in their accessibility for external users. Whereas some RIs have already procedures in place that allow external scientists to get access to their core facilities, other RIs are still in the process of defining access procedures and establishing their service offers. Therefore, in CORBEL for the first time, eleven BMS RIs on the ESFRI roadmap (European Strategic Forum on Research Infrastructures) want to enable user access for projects that require combined advanced services across different infrastructures. This requires the definition of an appropriate strategy, which has been developed during the first month of the project.
This document presents the strategy for supporting user access within pilot use cases. After several meetings, WP4 partners agreed to apply a two-step process to identify well-suited pilot users and projects. Since most joint service pipelines need to be developed, tested and refined, BMS RIs partners have started to engage with a first generation of pilot users based on their pre-existing contacts. In a second step, an open call will be prepared and publicly advertised. This will provide not only high visibility for CORBEL and all involved BMS RIs, but also critical credibility to make the common services broadly established and openly accessible beyond the project duration.

Project objectives

This deliverable has contributed to the following objectives:

a) Start to establish an infrastructure platform that integrates services for life science and support scientific research projects that require joint services between different ESFRI BMS RIs

b) Start to build cross-ESFRI BMS infrastructure pipelines according to specific use case objectives:

- Use Case 1: A comprehensive approach to predicting and modeling the phenotypic implications of mutations and of genome-sequence, lifestyle and ambition differences between individuals, and to validate the predictions in in vivo models.

- Use Case 2: A comprehensive approach to determine and validate experimentally, model *in silico* and predict the pharmacological and toxicological effects of chemicals on biological model systems, based on information ranging from the 3D-atomic structures of compound target interactions and individual genomic information to the response of whole cell/organisms to those compounds.

- Use Case 3: A comprehensive approach to structure function analysis of the molecular machinery based on integrated access to structure determination methods of isolated protein complexes correlated with functional and *in situ* imaging methods and support the integration of the resulting data from the molecular to the cellular scale of biological organization in order to make functional

predictions that can be validated.

- Use Case 4: A comprehensive approach for access to harmonized marine metazoan developmental model databases, integrating genomic, transcriptomics, and morphological information, also through *in silico* models, and building on existing community resources.

Detailed report on the deliverable

Background

Work package 4 rationale

CORBEL meets the critical need in Europe to coordinate common activities, set up efficient interfaces and facilitate harmonised access to the infrastructures. It will establish a platform joining up the advanced capabilities, research facilities and services from individual BMS RI in response to the needs of user communities and supports the effective progression of complex research projects through two or more of the infrastructures involved.
The WP4, Community-driven cross-infrastructure joint research – Bioscience will ensure that scientific projects fully exploit the joined up potential of the 8 involved BMS RIs (BBMRI-ERIC, Elixir, EMBRC, Euro-BioImaging, EU-OPENSCREEN, Infrafrontier, Instruct, ISBE) through the development of scientific connectors in partnership with advanced users. Requirements, feedback and testing by the external partners will drive the development of shared services.
Four distinct use cases (UC), vetted by a process of cross-RI prioritisation cover all aspects of a bioscience translational pipeline: from novel model organisms to genotype-phenotype predictions, including nano to micro structure-function analyses of large protein complexes and predictive systems pharmacology.
In addition the key components of the shared platform: 1) Harmonised access policies, procedures, and portals (WP5), 2) Joint data management, exchange and integration services (WP6), 3) Common ELSI support and evaluation services (WP7), and 4) Shared Innovation support and industry partnership (WP8) will be established in response to the needs of users communities brought in via WP3 and WP4. Therefore, the definition of an appropriate and efficient strategy to enable user access within WP4 pilot use cases is crucial for the overall CORBEL project.
While each of the BMS RI is built on a solid platform anchored in their respective user communities, advanced research programs in the life sciences often need capabilities from multiple research infrastructures. Thus, it is critical to have effective processes to jointly engage with prospective users from the project planning and grant application stages to the execution of projects and the long-term sustainable management of research data.

Overview of WP4 use cases

Use Case 1: "Genotype-to-Phenotype analysis based on models and experimental data"
Leader Jutta Steinkötter, Max Delbrück Center for Molecular Medicine (MDC)

This first use case targets communities of life scientists who aim to relate genotype to phenotype. It will empower users to address main research topics such as systems and personalized medicine,

cancer, neurodegenerative and inflammatory diseases, precision biotechnology and modern non-recombinant agriculture with high impact for translational research in health and biotech industries. One of the greatest challenges in biomedical research is to predict disease risk and treatment outcomes for individuals, based on increasing genomic information. Personalized medicine aims to facilitate predictions about phenotypes of individuals (e.g. susceptibility to diseases or therapies), based on the analysis of complete genome sequences, functional genomic data, clinical assays and lifestyle parameters. Mathematical models of genotype-to-phenotype relations are generated by systems biologists to integrate genetic with molecular, physiological and imaging data. These models need to be available to researchers in biomedical areas handling biological samples or *in vivo* models, large data sets, screens, images and physiological data. Researchers in precision biotechnology fields (white, red, green and blue) will also benefit from the same type of model provision.

The integration of services provided by the five BMS RIs involved in this use case (**BBMRI-ERIC**, **ELIXIR**, **Infrafrontier**, **Euro-BioImaging** and **ISBE**) will be implemented by pilot research projects, which aim to predict specific aspects of phenotypes from individual information. The five infrastructures will combine their services described in **Figure 1** and establish innovative pipelines to predict genotype-phenotype relationships based on models to integrate different types of experimental and biological data provided.

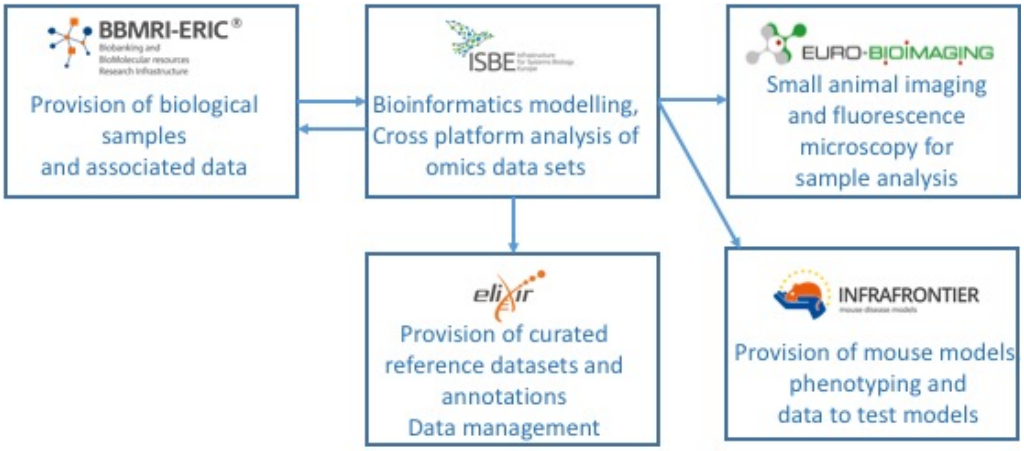

Figure 1: Use case 1 Infrastructures and services

For users from different scientific domains, who need integrated access to samples, imaging, data analysis and integration expertise, multi-level modelling and subsequent validation of data and predictions with *in vivo* models, the RIs and associated partner institutes will contribute to the following:

BBMRI-ERIC (BRFAA, Athens): provision of biological samples to be analyzed and provision of data together with the samples, in particular access to the Parkinson's Biobank: DNA samples, peripheral blood mononuclear cells, skin fibroblasts, serum, plasma and induced pluripotent stem cells (iPSCs) production and genomics, proteomics and computational services: biomolecular data, clinical records, pharmacology treatments, family history and environmental factors

ISBE (MDC, Berlin and VUA, Amsterdam): bioinformatics modelling, Omics cross-platform analysis, *in silico* integromics approach: model associated integration of genomic, transcriptomics, epigenomics, proteomics, metabolomics and physionomics data, for instance enabling the projection of SNP, DNA

sequence, deep RNA sequence and proteomics data onto genome map and dynamic models of different signaling networks, development of a "cell identifier tool" for cell-type prediction based on genomics data, model driven experimental design, data stewardship and standardization

ELIXIR (EMBL-EBI, Hinxton): provision of curated reference datasets and annotations, storage of data, innovative data management, interoperability activities (identifiers, semantic access and secure access to sensitive data)

Euro-BioImaging (CRG, Barcelona): mesoscopic imaging of fixed tissue (small animals, organs, etc.), multi-scale 3D and quantitative samples analyses

INFRAFRONTIER (HMGU, Munich): provision of mouse models and data to test/validate models, transgenic mouse model development, systemic phenotyping and access to EMMA repository (archiving/distribution)

Use Case 2: "Predictive systems pharmacology for safer drugs and chemical products"
Leader Bahne Stechmann, Forschungsverbund Berlin e.V. (FVB)

Chemical compounds are omnipresent in our daily lives as natural or synthetic products, be they drugs to treat diseases, pesticides to protect crops, food additives, metabolites and many more. Understanding how these chemicals affect biological processes has an important impact on a variety of research areas: for example, biologists from all life sciences interested in using chemicals as modulators of their biological system under study; chemists interested in identifying the biological activities of their isolated or synthesized chemical compounds; structural biologists interested in the experimental validation of drug leads against a defined macromolecular target (e.g. protein) and/or in the determination of the molecular basis of structure-activity relationships of chemical compounds interacting with their cellular targets; or systems biologists interested in probing their model systems (cell or animal) to validate their hypotheses or interested in understanding the pleiotropic effects of metabolites.
The aim of this use case is to build a seamless workflow with the experimental and virtual services of BMS RIs that contribute to the quantitative analysis, description and modelling of the effects of chemical substances on biological systems.
In use case 2, the six BMS RIs presented in **Figure 2** will combine their services and develop joint pipelines with a harmonized access for different "types" of researchers (e.g. cell or molecular biologists, chemists, systems biologist) who enter these pipelines via different research infrastructures and their associated partner institutes in CORBEL: **Elixir** (EMBL-EBI, Hinxton) **EU-OPENSCREEN** (FVB, Berlin), **Euro-BioImaging** (EMBL, Heidelberg), **Instruct** (CIRMMP, Florence), **ISBE** (VUA, Amsterdam), **Infrafrontier** (HMGU, Munich).

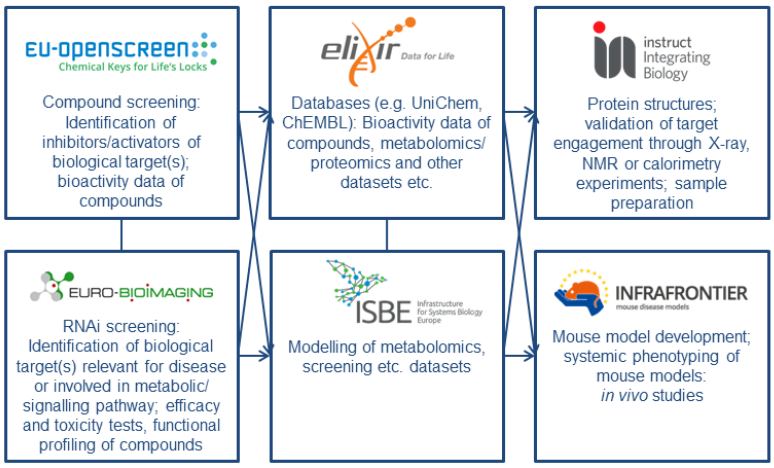

Figure 2: Use case 2 Infrastructures and services

One example for a project which makes use of such a pan-ESFRI pipeline is a cell or molecular biologist who conducts an siRNA screen in the framework of **Euro-BioImaging** and identifies one or more targets that are potentially relevant for a certain disease or are implicated in a specific metabolic/signalling pathway. Usually, these siRNA screens yield many potential 'hits' and it requires systems biology approaches, available through **ISBE**, to deconvolute these datasets derived from the RNAi screen and prioritize the potentially most relevant targets for follow-up experiments. **ELIXIR** offers databases, such as UniChem or ChEMBL, in which the user can retrieve information about compounds, which have been described to have an effect on the user's target-of-interest (e.g. commercially available inhibitors for this target-of-interest). If no inhibitor for the user's target-of-interest is available, **EU-OPENSCREEN** supports the user to screen for compounds, which are able to modulate the function of this biological target. Before these compounds can be used by the scientist as molecular 'tool' compounds (i.e. inhibitors), it is desirable to better understand the specificity of these compounds and their effect on so-called "off-targets". These efficacy and toxicity tests and general functional profiling studies of the compounds in living cells or tissue models (e.g. organoids) can be implemented with the support of **Euro-BioImaging**. The target engagement of these compounds needs to validated by compound through X-ray, NMR or calorimetry experiments (or a combination thereof), which are provided by **INSTRUCT.** Ultimately, the scientist studies the compound/target in a (disease-relevant) mouse models which are provided by **Infrafrontier.**
As this example shows, the pan-ESFRI pipeline in Use case 2 will contribute to early drug discovery by providing the necessary tools, instrumentation and expertise for the identification and validation of novel targets.

Use Case 3: "Structure-function analysis of large protein complexes – from nano to micro"
Leader Jan Ellenberg, European Molecular Biology Laboratory (EMBL)

A central challenge to understand the molecular mechanisms of health and disease is to understand how the structure of protein complexes and organelles gives rise to their function. The central underpinning of rational therapy design is that understanding the atomic and molecular structure of life's machinery allows to predict their function and interfere with it. However, it is clear that this process requires an integrated approach that combines high-resolution structure determination of isolated protein complexes with validation of the structure, interactions and, ultimately, their functions in a physiological context *in situ*. Only by directly combining *in vitro* and *in situ* imaging methods can structure be determined in its functional context and the predicted function be

validated. The main research topics that will be supported are in line with EU funding strategy, including systems medicine, disease mechanisms etc. Moreover, there is imminent impact for pharmaceutical applications and drug design, as well as imaging technology innovation and image data sharing through the development of new standards.

Ideal pilot projects for this use case would be those that are already up and running, and have reached a point at which usage of additional cutting-edge technologies and/or support for data integration across scales would make a difference and add value to the project outcome. In return, to enable the building of sustainable and satisfactory services for the future, pilot users are expected to provide feedback on the services and to work in close collaboration with all infrastructure staff involved. It is a high priority to make the flow of experiments as smooth as possible along the service pipelines of different techniques and research infrastructures.

In this regard, the BMS RIs **Euro-BioImaging**, **INSTRUCT**, **ISBE** and **ELIXIR** will establish an integrative access and service pipeline to the following technologies:
Euro-BioImaging (EMBL Heidelberg, UMCU Utrecht, ICFO Barcelona): Correlative light-electron microscopy, super-resolution microscopy, functional imaging methods, image data standards and repositories.
ELIXIR (EMBL-EBI, Hinxton): Interlinked data repositories for image data types with different resolution.
INSTRUCT (CSIC, Madrid): Molecular resolution EM, EM image data standards, atomic-level 3D structural and interaction information, software tools for data integration together with ELIXIR.
ISBE (DKFZ, Heidelberg): Quantitative analysis, data integration and modeling for functional predictions.

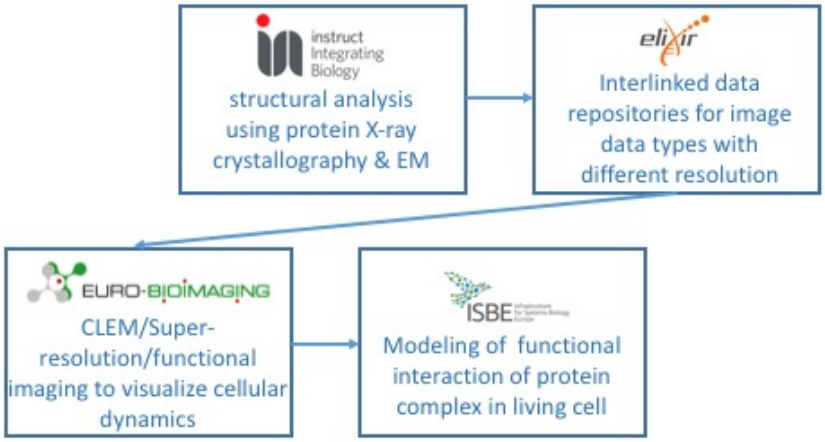

Figure 3: Use case 3 Infrastructures and services

Use Case 4: "Marine Metazoan Developmental Models for Biomedical research – from predictive integrated databases to functional testing"
Leader Evelyn Houliston, Centre National de la Recherche Scientifique (CNRS)

Advances in the understanding of many fundamental biological processes are hampered by their inaccessibility to experimentation in traditional animal model species, ethical considerations concerning research on vertebrates and particularly mammals, and incomplete linkage to data analysis pipelines, data integration and predictive models. Marine species have long proved powerful

models for understanding many cellular phenomena including the gene regulatory networks underlying cellular and developmental transitions, fertilization, cell division, differentiation, stem cell biology, morphogenesis, regeneration, ageing and physiological responses. The advent of high-volume low-cost 'omics approaches, along with major improvements in imaging and functional genomics technologies, and a vast increase in computer power, has opened a potential goldmine of novel model species covering the vast range of animal biodiversity. With this use case we aim for a complementary set of selected marine metazoan models for developmental and cell biology: 1) To set up integrated databases combining sequence and imaging data via pipelines linking EMBRC-ERIC, Euro-BioImaging, EMBL-ELIXIR and ISBE as user-friendly entry portals for both established and new users. 2) To provide access to biological material as well as functional genomics and imaging capabilities for testing and exploitation of these models in selected pilot user test cases.

EMBRC, ELIXIR and Euro-BioImaging will work together to develop pipelines to establish harmonized marine metazoan developmental model databases integrating genomic, transcriptomic and morphological data. The database suite will build on existing community resources (genome, gene expression and imaging data) from the EMBRC partners and their collaborators, notably P. Lemaire (Montpellier) who developed the aNiSEED database framework for ascidian development (http://www.aniseed.cnrs.fr).

The database will cover 3 marine models characterized by complementary modes of embryogenesis: amphioxus (*Branchiostoma lanceolatum*), sea urchin (*Paracentrotus lividus*) and jellyfish (*Clytia hemisphaerica*). These species form a complementary and powerful set of experimental model species. The database suite will serve a central curated repository and will allow a wide user base in biological and biomedical sciences to explore in silico the potential of alternative models to address specific biological questions.

The initial genome browser should be in place by October 2017, amphioxus (*Branchiostoma lanceolatum*) will be first integrated to the ENSEMBLE archives, followed by the jellyfish (*Clytia hemisphaerica*) and finally by the sea urchin (*Paracentrotus lividus*). Elixir will provide help developing harmonizing standards, nomenclature, data integration and database interoperability. In parallel an ontology working group will be established in collaboration with WP6 in order to establish a standardized ontology for all three of the models. Once the genome browser has been established, spatial expression and imaging data will be verified and gathered to add to the database in a second phase.

During year 1 and year 2 of the CORBEL project a simplified pipeline will be proposed: access to the Marine stations of the EMBRC network and the EMBL for acquisition and processing of imaging data and the use of the marine organisms and facilities for experimentation

Once the first version of the database in on line (month 24), a more elaborated pipeline including multiple RI's (**Figure 4**) will be proposed to the test users:

EMBRC (CNRS/UPMC, Villefranche, USTAN, St Andrews and SZN, Naples): marine organisms and facilities for experimentation, 4D imaging, database information

Euro-BioImaging (EMBL Heidelberg): combined access to advanced imaging and some marine model species at EMBL, Pipelines for acquisition, processing and integration of imaging data into databases

EU-OPENSCREEN (FVB, Berlin): identification of users with needs of assay systems with particular characteristics accessible in marine models (e.g. cilia beating, chromosome disjunction…)

ISBE (VUA, Amsterdam): access to and data-integration with computational models of marine organisms

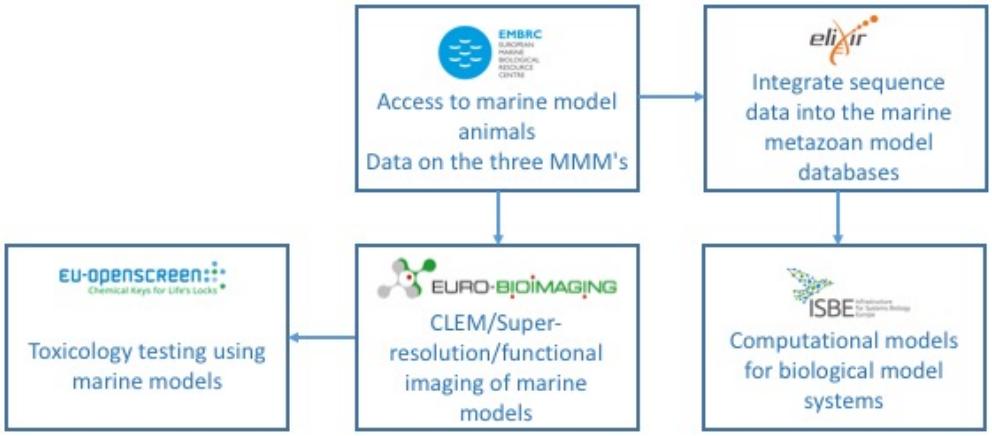

Figure 4: Use case 4 Infrastructures and services

Description of Work

A two-step strategy for enabling user access within pilot use cases

In this deliverable, we aim to develop a strategy that will allow user access to the BMS infrastructure services for the pilot use cases. We have decided to apply a two-step process that will enable us to identify suitable pilot projects, ensure sufficient technical support and appropriate resource and time allocation for each pilot user and will nevertheless provide unbiased and open access to scientific expertise and facilities.

Since the start of the CORBEL project, several meetings have taken place that were intended as platform to discuss among WP4 partners the strategy for enabling user access. During the WP4 kick-off meeting in Heidelberg on October 13th 2015, the access policy for CORBEL pilot projects was determined.

1. The technical feasibility of a user pilot project (e.g. the technical requirements and the match of services by participating RIs) has to be evaluated and approved by the involved RIs in the particular use case. This evaluation also entails the value of the suggested project as a demonstration project for the common RI services.
2. Each pilot project has to engage the service of a minimum of two, preferably three or more participating RIs to be acknowledged as a good demonstration project.
3. To facilitate the use of RI services, the in-depth consultancy of users is not only crucial during the pilot use cases, but considered one of the most important results of CORBEL.
4. Pilot users shall be external users of the RI service providers, i.e. in the framework of CORBEL they should not access those RI services which are hosted at the legal entity that they are affiliated with.
5. The cost model is defined by the respective RI. If possible in the frame of the allocated CORBEL resources, access to the RI services should be free of charge for pilot users.

Following further discussions among WP4 partners via conference calls and e-mail conversations, a final decision regarding the strategy was taken, which could be presented at the CORBEL kick-off meeting in Hinxton on November 19th 2015. The commonly agreed strategy of the use case leads was the decision to apply a two-step process for identifying pilot user projects:

1) With immediate start, each use case establishes the common service pipelines and identifies 2-3 initial pilot users = 'VIP users'

2) In parallel, WP4 will prepare an open call for pilot users to be run in summer 2016 = 'CORBEL users' to be served starting autumn 2016

Strategy for VIP user access

During the first phase of CORBEL, the interaction between RIs and the timely coordination of booking schedules between facilities need to be established. Procedures how to interact and work closely together within the same project have to be defined and it is expected that users will have to overcome some technical or administrative hurdles in the beginning. On the other hand, the first generation of users of the CORBEL infrastructure services will benefit from very close interactions with CORBEL RIs, premium support by facility staff and continuous exchange between all relevant parties involved in an experimental pipeline. Direct and personal contacts are therefore deemed most relevant at this initial stage, which lead to the idea of the 'VIP user'.

The first contact with prospective VIP users was established via pre-existing relations between WP4 partners and external scientists working in relevant research fields. Depending on the organization of each use case, user engagement was achieved either in the framework of a workshop that brought together representatives of all RIs involved in the respective use case and interested scientists or by other means such as e-mail conversations and phone conferences. Partners of UC1, UC2 and UC4 opted to organize workshops, which were held during the first two weeks of February. UC3 partners decided to engage with users via bilateral communication tools. Following a general introduction about the CORBEL project and the proposed services and thereafter an expression of interest by the researchers, more detailed information about infrastructure technologies and access procedures was provided. WP4 managers are currently organizing in-depth bilateral discussions between prospective VIP users and infrastructures members to further define the technical needs and scientific expectations of the proposed projects.

In the following step, supported by WP4 managers, VIP users will be asked to write a short and concise project proposal for CORBEL documentation (see Annex for template). This reference document will be filled in with additional information whenever this becomes available. The feasibility of the proposed projects will be approved or declined by the requested infrastructures. Projects engaging the services of a minimum of two participating RIs will be selected as suitable VIP projects as officially announced in the milestone MS27.

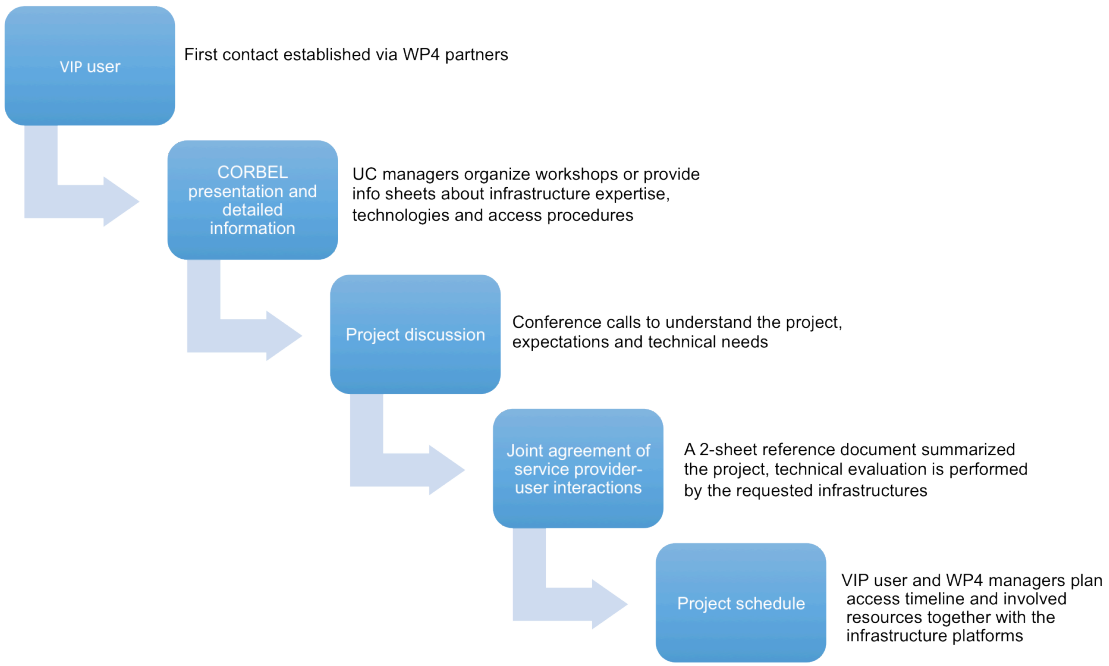

Figure 5: Engagement process with VIP users

Strategy for the open call

Instead of selecting pre-identified users for the pilot projects, an open call offers the possibility to raise awareness about the mission of CORBEL and the services that will be accessible. The benefits of high publicity and visibility of the BMS RIs and CORBEL are apparent in light of the agreed goal to establish sustainable common services under the CORBEL framework that remain accessible for researchers after project conclusion, and to attract broad user communities. Through the open call, scientists will have the chance to participate as pilot users in WP4 use cases. The open call preparation and procedure have been defined by WP4 partners as follows. The major elements comprise:

- Public advertisement (e.g. in high-impact journal(s) such as Nature) (supported by WP2)
- Provision of a clear set of service definitions from all infrastructures
- Smart and easy-to-understand presentation of all use case service pipelines on the CORBEL website to attract external “naïve” users (supported by WP2)
- A short (~2 page) project template for users to describe their request of service access
- Evaluation of submitted user proposals (development of access procedure in open call supported by WP 5)
- i) Technical feasibility (including data management with WP6)
- ii) Scientific merit (independently reviewed)
- Survey of user and provider experience, outcome and impact (diffusion with WP2)

CORBEL users will access UC pipelines following a procedure similar to the one for VIP users. However, instead of pre-identifying users and addressing them personally, all scientists are approached unbiased. The publications advertising the open call serve as channels to the CORBEL website, where all relevant information is displayed publicly. WP4 managers provide an information sheet that summarizes more detailed information about available services and access procedures.

For an in-depth project discussion, the WP4 managers set up a conference call with interested researchers to understand their project, technical needs and scientific expectations. Thereafter, CORBEL open call applicants are asked to draft a short project proposal by filling out a 2-sheet document provided as template. Based on this project proposal, the technical evaluation and subsequently approval or decline of the suggested project is performed by the requested facilities. In case of acceptance of the project, the UC lead informs the user about the successful evaluation. As a final step, future users and WP4 managers plan access timelines and resources involved together with the infrastructures to ensure that the project can be accomplished in a reasonable time frame.

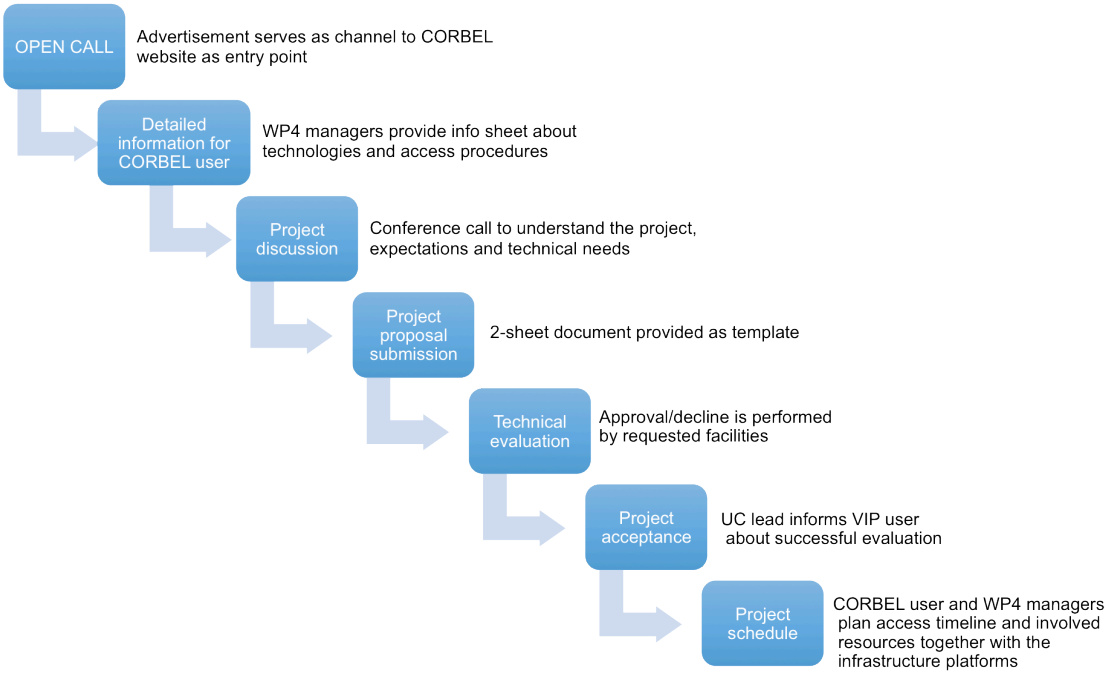

Figure 6: Open call procedure for CORBEL users

As we cannot predict the outcome of this open call in terms of the number of users who will become interested in CORBEL services, we have to anticipate that application numbers might exceed the maximal capacity of RI facilities. In this case, we will implement an additional evaluation step based on scientific merit, which will allow the prioritization of project proposals. Candidate users will be informed about this potential measure on the CORBEL homepage. The open call for WP4 UCs will be offered independently of WP3 (Community Driven Cross-Infrastructure joint research – Medical), but via close interaction on the level of WP leads and WP managers, collaboration between WPs whenever applicable will be ensured.

Eventually, users interested in CORBEL services will use the homepage as first entry point to the project. Therefore, the set-up and content of the CORBEL homepage is of uttermost importance. It should provide a clear and extensive overview about the mission and the services of CORBEL as well as a description of example pipelines. Depending on user needs, additional pipelines could be established to include projects not covered by the already existing pipelines. Similarly and naturally only in agreement with the involved infrastructures, it is envisaged that users could have the possibility to request access to services provided by other BMS RI nodes than the WP4 partner institutes. Users are informed that CORBEL offers open (but not free of charge) access to the most advanced technologies in Europe. Internet links to all RIs homepages will be displayed, allowing the user to acquire further information about the different RIs and their respective fields of expertise, strengths and technologies. In addition, contact details of the WP4 managers are provided as they

can be addressed for additional support and guidance. Thereby, an 'experienced' user – one who has prior experience with the requested RIs or knows which RIs he would like to use – can access the RI directly via the CORBEL homepage. 'Naïve' users seeking further advice, however, have the possibility to consult the WP4 managers. Via establishing personal contact, the WP4 managers can provide support and guidance on how to choose the most suitable RIs.

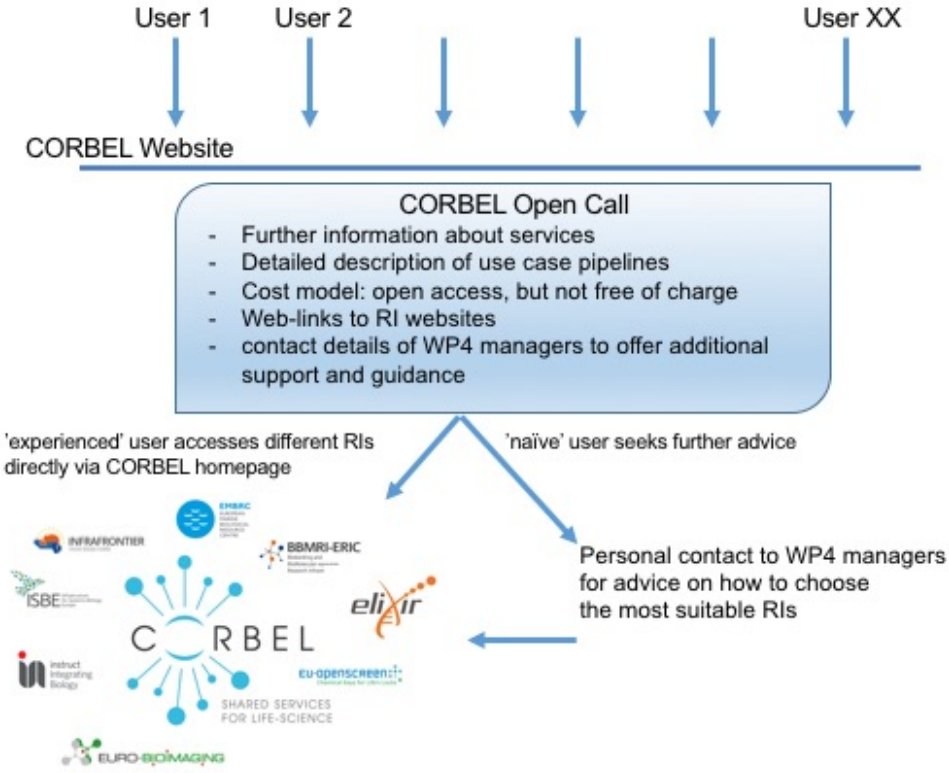

Figure 7: The CORBEL homepage, entry point of WP4 open access procedures

Next steps

Work with the VIP users

During the first two weeks of February, WP4 partners involved in use case 1 and 2 have organized workshops with prospective VIP users and infrastructure representatives. The aims of these meetings were to 1) introduce the organisation and objectives of CORBEL, the objectives of WP4 and in particular their respective use case, 2) introduce the scientific projects of the invited pilot users and 3) discuss how the RIs could collectively support the pilot users in the implementation of their research projects.

Most of the invited users have already accessed/are currently using services provided by one of the infrastructure partners (for instance EU-OPENSCREEN or ISBE) and are interested in accessing other infrastructures. The next steps to help them moving on from one infrastructure to another/several others are currently identified and will be precisely defined via bi-lateral discussions that will enable to fill in the project reference document.

After the workshops, we can already anticipate a need for flexibility with respect to the service providers that will be involved in the pipelines under development. VIP users have indeed expressed interest in services provided by infrastructures involved in other use cases than the one for which

they were approached and/or even infrastructures involved in WP3. Similarly some VIP users would like to request services from RI central offices or other nodes than the actual WP4 partners. Therefore we propose that use case managers adapt the VIP project template document presented in Annex for each selected VIP projects according to pilot user needs, of course in agreement with the involved RIs.

Use case 1 is of interest for various users, including cell and systems biologists, biologists working on translational medicine such as neurobiologists, immunologists and clinicians. Four VIP users will access UC1 pipelines in the next months:

- Dr. Jonas Busch (Charité, Berlin), urologist, works on systems medicine in kidney cancer and address the question why patients with this disease respond differently to drug therapy approaches and how tumor stem cells affect these responses
- Prof. Angelika Eggert (Charité Berlin), specialised physician for paediatric oncology and haematology, leads a project aiming at identifying core signalling networks controlling hallmarks of cancer in highly aggressive neuroblastoma which lead to treatment failure and relapse based on integration and computational analysis of various OMICs data sets
- Prof. Giorgos Hadjigeorgiou (University of Thessaly, Vólos), neurologist and neuroscientist in the field of epidemiology of Movement Disorders, Neurodegenerative Diseases and other Neurological Disorders, performs genetic association studies in particular of Parkinson's disease
- Prof. Marieke van Ham (Sanquin, Amsterdam), immunologist, studies personalized medicine of autoimmunity and allergy and targets detrimental antibody formation

The pipelines proposed for Use case 2 will be relevant for a variety of different users, including cell biologists, chemists, pharmacologists, and biochemists.
Six VIP-users will access these pipelines in the next months:

- Prof. Margarida Amaral (University of Lisbon) studies CFTR mutations and their implication on CFRT function and intracellular traffic which is often underlying cystic fibrosis
- Prof. Walter Birchmeier (MDC Berlin) studies Wnt/beta-catenin and Gab1/Shp2 signaling
- Claus Scheidereit (MDC Berlin) works on signal transduction processes that activate the inducible transcription factor *nuclear factor-κB* (NF-κB) as well as regulatory mechanisms that control the activity of NF-κB in the nucleus
- Prof. Stefan Laufer, pharmacologist and medicinal chemist (University of Tübingen), develops selective protein kinase inhibitors
- Prof. Franz Bracher, pharmacologist and chemist (LMU München) develops selective inhibitors of protein kinases
- Prof. Ian Wilson, biochemist (Imperial College London), studies drug metabolism and molecular toxicology

UC3 partners have established contacts with several prospective VIP users and received first positive responses. In a next step, the prospective projects will be discussed with users and infrastructure members.

UC4 partners have organized a workshop mid-February to define the main features of the database that will be built based on a survey of the main user requirements. The development of the database being a priority, the engagement with VIP users will probably start later.

Open call preparation

In parallel with the work in progress with VIP users, WP4 managers will further define the process of the open call. They will prepare the information that will be communicated on the CORBEL homepage with the support of WP2, provide project proposal template for the submission of user application and work closely with WP5 to develop access procedures for the technical and scientific evaluation.

References

Abbreviations

BBMRI-ERIC: Biobanking and BioMolecular resources Research Infrastructure
BMS RIs: Biological and Medical Science Research Infrastructures
BRFAA: Biomedical Research Foundation of the Academy of Athens
CORBEL: Coordinated Research Infrastructures Building Enduring Life-science services
CNRS: Centre National de la Recherche Scientifique
CRG: Centre for Genomic Regulation
CIRMMP: Consorzio Interuniversitario Risonanze Magnetiche di Metallo Proteine
CSIC: Agencia Estatal Consejo Superior de Investigaciones Cientificas
DKFZ: Deutsches Krebsforschungszentrum
EMMA: European Mouse Mutant Archive
EMBL-EBI: European Molecular Biology Laboratory-European Bioinformatics Institute
EMBL: European Molecular Biology Laboratory Heidelberg
ESFRI: European Strategy Forum on Research Infrastructures
FVB: Forschungsverbund Berlin e.V.
HMGU: Helmholtz Zentrum München für Gesundheit und Umwelt
ICFO: Fundacio Institut de Ciencies Fotoniques
INSTRUCT: Instruct Academic Services Limited
ISBE: Infrastructure for Systems Biology in Europe
MDC: Max Delbrück Center for Molecular Medicine
UMCU Utrecht: Universitair Medisch Centrum Utrecht
USTAN: University of St Andrews
VUA: Vrije Universiteit Amsterdam
WP: Work Package
SZN: Stazione Zoologica Anton Dohrn

Delivery and schedule

The delivery is delayed: yes

WP4 comprises many partners and extensive discussions were necessary to develop the appropriate strategy, which is crucial for all forthcoming actions. The development of a consensus strategic approach well suited for each use cases was prioritize over on time submission.

Adjustments made

NA

Appendices

Appendix 1

CORBEL VIP user

Project reference template (example for a UC3 pilot project)

1. Please provide the following information:

First Name	
Last Name	
E-Mail	
Organization (University/ Institute/Department	
Address	
ZIP/Postal code	
City	
Country	

2. Please provide a short (max. 200 words) CV highlighting your expertise in the field and cite 3 relevant publications

3. Please provide a short description of your scientific project using the following division:

Project Title	
Introduction/ Scientific Background (max. 200 words)	

Description of work proposed to be conducted at CORBEL facilities (max. 300 words)	
Expected results summarized in max. 5 points	1. 2. 3. 4. 5.

4. Please indicate the technologies and services that are envisaged to be used.

Euro-BioImaging		Yes/no
EMBL Heidelberg	- Functional imaging methods - Correlative light-electron microscopy - Image data standards and repositories in collaboration with ELIXIR and EMBL-EBI	
UMCU Utrecht	- Correlative light-electron microscopy	
ICFO Barcelona	- Super-resolution microscopy	
ELIXIR		
EMBL-EBI, Hinxton	- Interlinked data repositories for image data types with different resolution	
INSTRUCT		
CSIC Madrid	- Molecular resolution EM - EM image data standards - Atomic-level 3D structural and interaction information - Software tools for data integration together with ELIXIR.	
ISBE		
DKFZ Heidelberg	- Quantitative analysis - Data integration and modeling for functional predictions	

5. Please indicate the approximate duration for the use of RI facilities:

Facility No 1: (insert name) Duration in weeks:
Facility No 2: (insert name) Duration in weeks:
Facility No 3: (insert name) Duration in weeks:
Etc.

This information can also be filled in after consultation with all facilities.

6. Please indicate which additional services at the respective BMS RI you would request:

List of additional resources that can be requested at Point 6:
Instruments
Technical assistance to run instrument
Methodological setup (e.g. design of study protocol and standard operation procedures)
Training in infrastructure use
Probe preparation
Animal preparation
Animal facilities
Wet lab space
Server Space
Data processing and analysis
Training workstations
Training seminar room

7. Please indicate which additional BMS RI services you would request if applicable:

ex: access to EU-OPENSCREEN or ECRIN services, etc.