IPAD-MD: Research Infrastructures for Phenotyping, Archiving and Distribution - Mouse Diseases Models

Deliverable 3.1 - Survey on European and International Research Agendas

(December 2015)

CONTENT

1. EXECUTIVE SUMMARY

- **IPAD-MD project**, **addresses global cooperation and coordination** between the INFRAFRONTIER Research Infrastructure, the IMPC and other complementary research infrastructures. **Engagement with a broad range of key stakeholders**, from user communities to funders, is of particular relevance to the IPAD–MD project
- In order to **provide an overview of the strategic research agendas** and the national, European and the global research policies relevant to IPAD-MD, a survey was conducted
- The survey was sent to thirty contact partners from both the **INFRAFRONTIER and the IMPC consortia** with a **response rate** of **60%**
- The current research areas of the INFRAFRONTIER and the IMPC Institutional partners are **Inflammation/Immunology** and **Metabolism** (61%), **Cancer** (56%) and **Rare and Neurodegenerative Diseases** (44%)
- The research areas in which INFRAFRONTIER and the IMPC should focus in the next five years (2020) are: **Metabolism** (61%), **Rare Diseases** (46%), **Ageing** and **Neurodegenerative diseases** (39%) and **Inflammation/Immunology** (33%)
- The survey was complemented with a **series of recommendations** in order to facilitate the **alignment between the INFRAFRONTIER and the IMPC** and **other research programmes and initiatives** herein selected
- **Partners of other programs and initiatives** of interest to INFRAFRONTIER and the IMPC and herein identify **should be included** in the planned **IPAD-MD Engagement workshops** as well as **in the Expert Group Meetings on Standards & Technology and Data & Resources**
- In order to increase the visibility of the resources and services offered by the INFRAFRONTIER and the IMPC **specific changes and improvements at the INFRAFRONTIER portal are suggested**

- **2. INTRODUCTION & OBJECTIVES**

IPAD-MD, a project funded under the European Union Horizon 2020 program**, addresses global cooperation and coordination** between the pan-European INFRAFRONTIER Research Infrastructure and complementary research infrastructures in America, Asia and Australia, contributing to the global effort of the IMPC, and with complementary research infrastructures and users in Africa. **It has a particular focus on involving the key stakeholders** (user communities such as the rare diseases community, industry, patient organisations, funders and policy makers) in shaping the resources and services provided by INFRAFRONTIER and the IMPC.

IPAD-MD will organise a **series of workshops that bring together representatives of the INFRAFRONTIER and IMPC research infrastructures and of their key stakeholders** to achieve three major objectives:

1. **Strengthen the coordination between the global research infrastructures in the field of the systemic phenotyping, archiving and distribution of mouse disease models**. A particular focus of IPAD-MD will be to improve global access to the common resources created by INFRAFRONTIER and the IMPC and to align the scientific strategy with international research agendas.
2. **Engage key international stakeholders to improve the resources and services offered by INFRAFRONTIER** and established in the context of the **IMPC**. Furthermore, IPAD-MD will involve funders and program agencies in the discussions about the future of the resources and services developed in INFRAFRONTIER and the IMPC.
3. **Coordinate globally the development of innovative technology solutions** for the improvement of the resources and services provided by INFRAFRONTIER and the IMPC.

Within the IPAD-MD project, the **WP3 - Engagement with Funders & Policy** is aiming at:

1. Providing an overview of the strategic research agendas and national, European and global research policies relevant to IPAD-MD
2. Providing thematic input to the IPAD-MD workshops

3. Ensuring the alignment of the scientific agendas of INFRAFRONTIER and the IMPC with national, European and international research agendas

In this context IPAD-MD **WP3 – Engagement with Funders and Policy** conducted a survey targeted at INFRAFRONTIER and IMPC partners, with the following objectives:

- **To list the current (2015) research areas of the Institutional partners** of the **INFRAFRONTIER and IMPC** Consortia
- **To survey the research areas in which INFRAFRONTIER and IMPC** consortia **should focus** in the coming five years **(2020)**
- **To identify the relevant programs and initiatives**, **to screen their scientific research agendas and to map out the relevant points of cooperation** between those and the INFRAFRONTIER and IMPC consortia
- **To provide recommendations and suggest specific steps in order to strengthen the cooperation** between other programs and initiatives and the INFRAFRONTIER and IMPC consortia
- **To identify the relevant stakeholders** of those programs and initiatives and **include them in the planned IPAD-MD Stakeholders workshops** and /or in the **Expert Group Meeting** as External Experts

3. RESULTS

3.1 Survey Results

- The survey was sent to thirty contact partners from both the **INFRAFRONTIER and the IMPC consortia** (Appendix – Table 1) over a period of 4 weeks (October - November **2015**).

- A total of eighteen answers were received, corresponding to a **response rate** of **60%**.

- To the question '*What is the current research priority of your institution*', **Inflammation/Immunology** as well **as Metabolism/Diabetes/Obesity** were selected by 61% of the respondents; **Cancer** was selected by 56% of respondents, whereas **Rare and Neurodegenerative Diseases** was mentioned by 44% of the respondents (See Figure 1, complete list can be found at Appendix, Table 2).

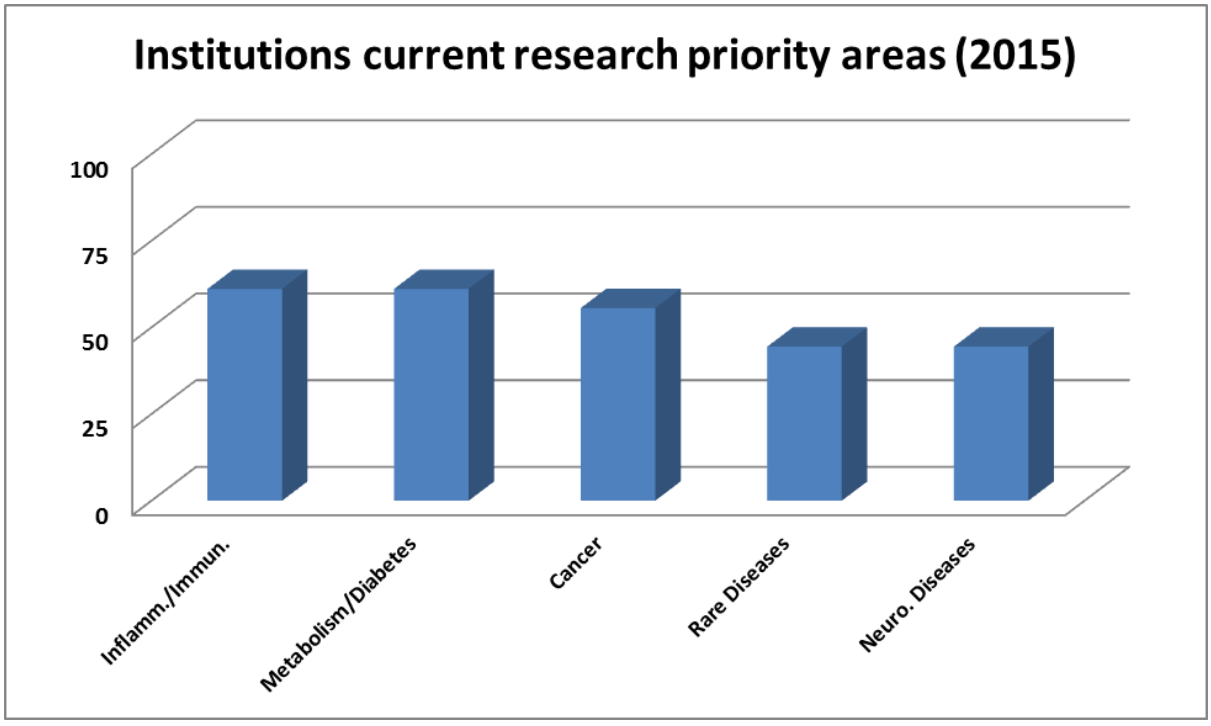

Figure 1. Five most selected current research areas by INFRAFRONTIER and IMPC partners Institutions (for the complete list see Appendix, Table 2).

- To the question '*In which research area should INFRAFRONTIER/IMPC focus in the next 5 years*', **Metabolism/Diabetes/Obesity** was selected by 61% of the respondents, **Rare Diseases** by 46% followed by **Ageing** and **Neurodegenerative diseases** both

with 39% of responses and **Inflammation/Immunology** with 33% of the responses (Figure 2, complete list can be found at Appendix, Table 3).

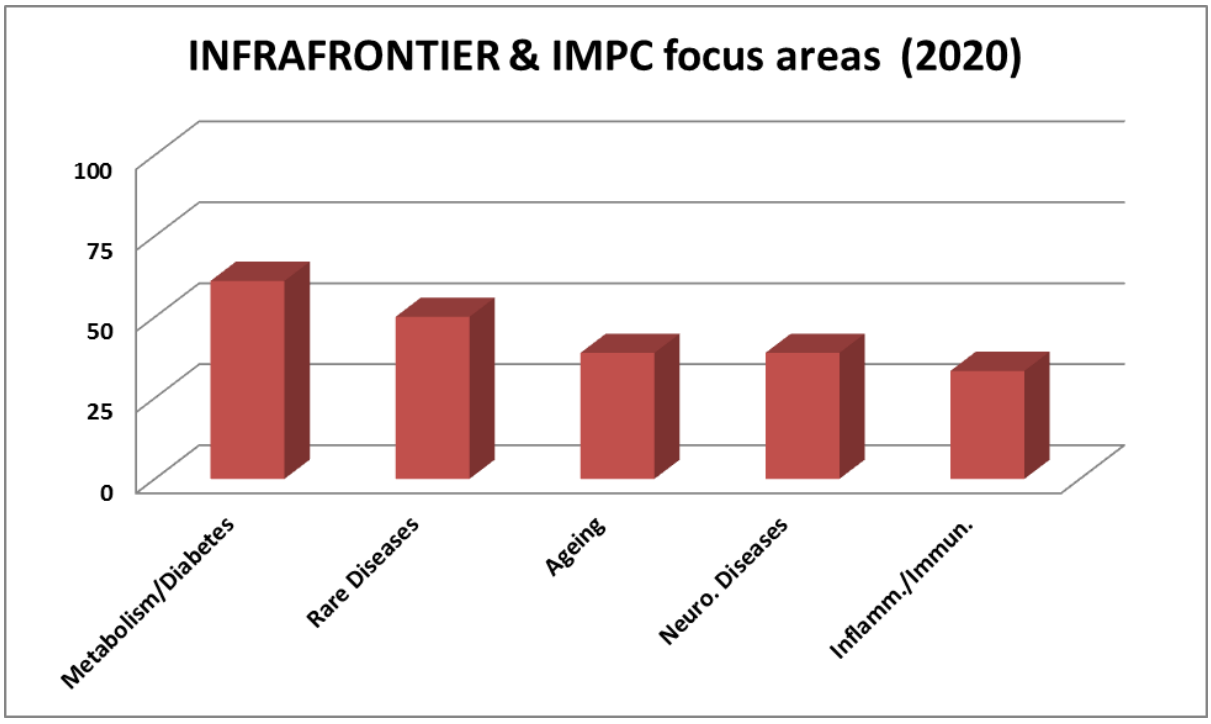

Figure 2. Five most selected areas in which INFRAFRONTIER and the IMPC consortia should focus on the next 5 years (for the complete list see Appendix, Table 3).

- Based on the results of the survey, a selection of initiatives and programs whose goals are complementary to the INFRAFRONTIER and the IMPC was performed (Table 1). This selection is targeted mainly European funded programs and initiatives, and where applicable, consortia with common partners to INFRAFRONTIER. Marie S. Curie Actions were not considered as within the scope of this report.

Table 1: Complementary programs and research initiatives in the five selected areas in which INFRAFRONTIER and IMPC should focus on the next five years (2020)

Research Area	Program
Ageing	• COST Mouse Age • ShArm • ERIBA

Research Area	Program
Inflammation / Immunology	• BT Cure IMI
Metabolism/Diabetes/Obesity	• IMI Diabetes Platform (DIRECT, IMIDIA, SUMMIT)
Neurodegenerative Diseases	• JPND • New Meds IMI
Rare Diseases	• IRDiRC • ERA-Net E-Rare

DIRECT-IMI=Diabetes Research on patient stratification – Innovative Medicines Initiative; **ERIBA**=European Research Institute for the Biology of Ageing; **IMIDIA-IMI**=Improving beta-cell function and identification of diagnostic biomarkers For treatment monitoring in diabetes - Innovative Medicines Initiative; **IRDiRC**=International Rare Diseases Research Consortium; **NKI-MCCA**=Netherlands Cancer Institute-Mouse Clinic for Cancer and Ageing; **JPND**=EU Joint Program-Neurodegenerative Disease Research; **ShArm**=Shared Ageing Research Models; **SUMMIT-IMI**=Surrogate markers for micro- and macro-vascular hard endpoints for innovative diabetes tools - Innovative Medicines Initiative

AGEING

- Three European funded research initiatives were found in the area of Ageing (Cost MouseAge, ERIBA and ShArm) [Figure 3]
- **COST MouseAge** aims at forming a multidisciplinary network to reach consensus on ways to test preclinical interventions in aged mice
- **ERIBA** gives emphasis on basic research in order to advance the understanding in the biology of age
- **ShArm** focus providing access to aged mouse models to the scientific community and thereby to promote the sharing of mouse models and mouse age tissue
- While COST MouseAge and ShArm focus exclusively in mouse as animal models ERIBA includes other models organisms, the mouse as animal model is mostly used at the Mouse Clinic of Cancer and Ageing (MCCA).

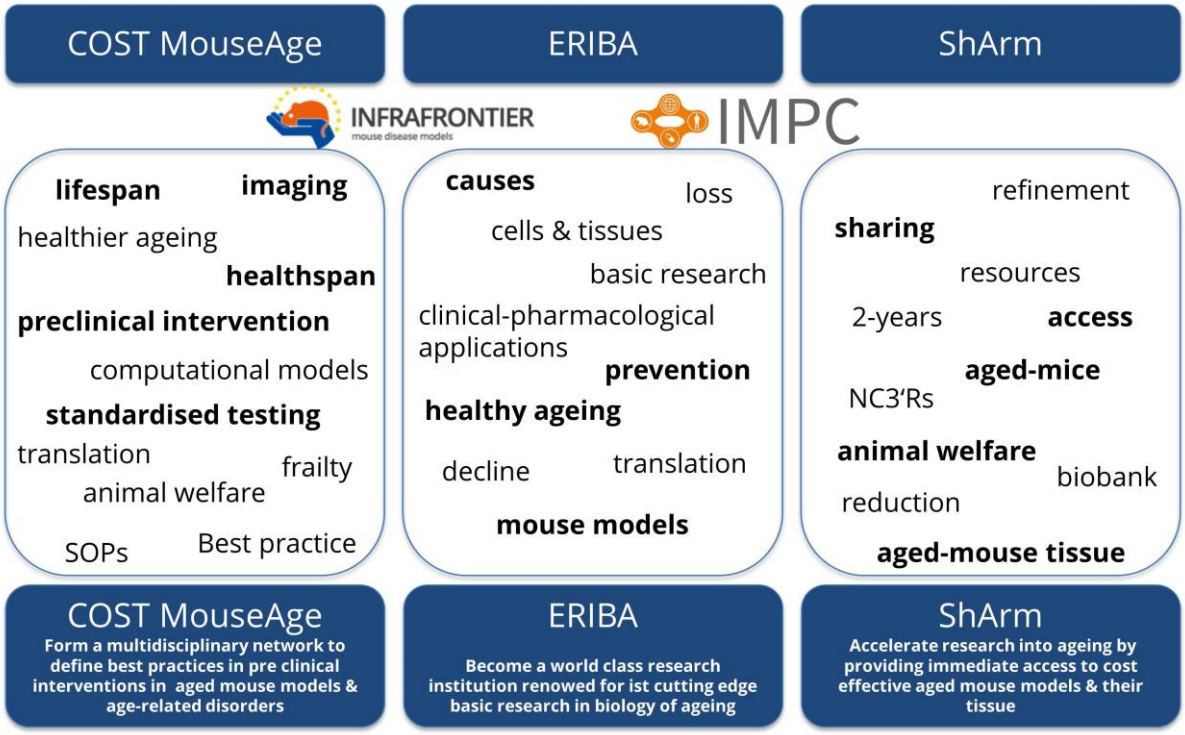

Figure 3. Word clouds derived from analyses of the Memorandum of Understanding of COST MouseAge and Aims & Objectives of the ERIBA and ShArm Initiatives (sources: http://www.mouseage.eu/; http://www.umcg.nl/EN/Research/ERIBA/; https://www.sharmuk.org/; adapted from word cloud generator tool: https://www.jasondavies.com)

IMMUNOLOGY/INFLAMATION

- One program was identified in the Immunology and Inflammation research area: Be The Cure for Rheumatoid Arthritis - Innovative Medicines Initiative [Figure 4]
- **Be The Cure for Rheumatoid Arthritis - Innovative Medicines Initiative** aims at bringing together academic rheumatology research and research in pharmaceutical companies in Europe to further broaden the knowledge of disease causing factors and disease progression in Rheumatoid Arthritis

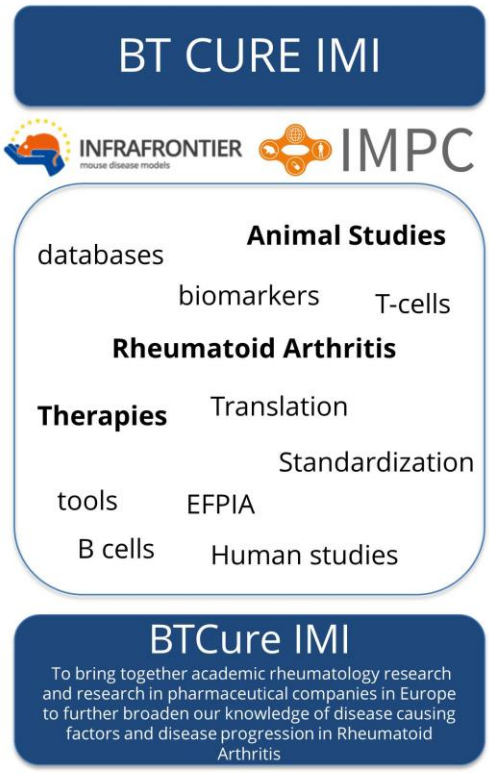

Figure 4. Word cloud derived from analyses of the goals of BTCure IMI (Source: http://btcure.eu/about-be-the-cure/, adapted from word cloud generator tool: https://www.jasondavies.com)

METABOLISM

- Three programs were identified in the Metabolism research area: **Direct IMI**, **IMIDIA IMI** and **SUMMIT IMI** [Figure 5]. The three initiatives form the IMI Diabetes Platform.
- **Direct IMI**, Diabetes Research on patient stratification – Innovative Medicines Initiative, intends to identify novel biomarkers and to define subtypes with rapid diabetes developments and progression as well as altered response to diabetes treatment.
- **IMIDIA IMI,** Improving beta-cell function and identification of diagnostic biomarkers for treatment monitoring in diabetes - Innovative Medicines Initiative, aims at improving beta-cell function and identification of diagnostic biomarkers for treatment monitoring in diabetes

- **SUMMIT IMI**, Surrogate markers for micro- and macro-vascular hard endpoints for innovative diabetes tools - Innovative Medicines Initiative, aims at discovering, developing and qualifying potential markers for diabetic patients

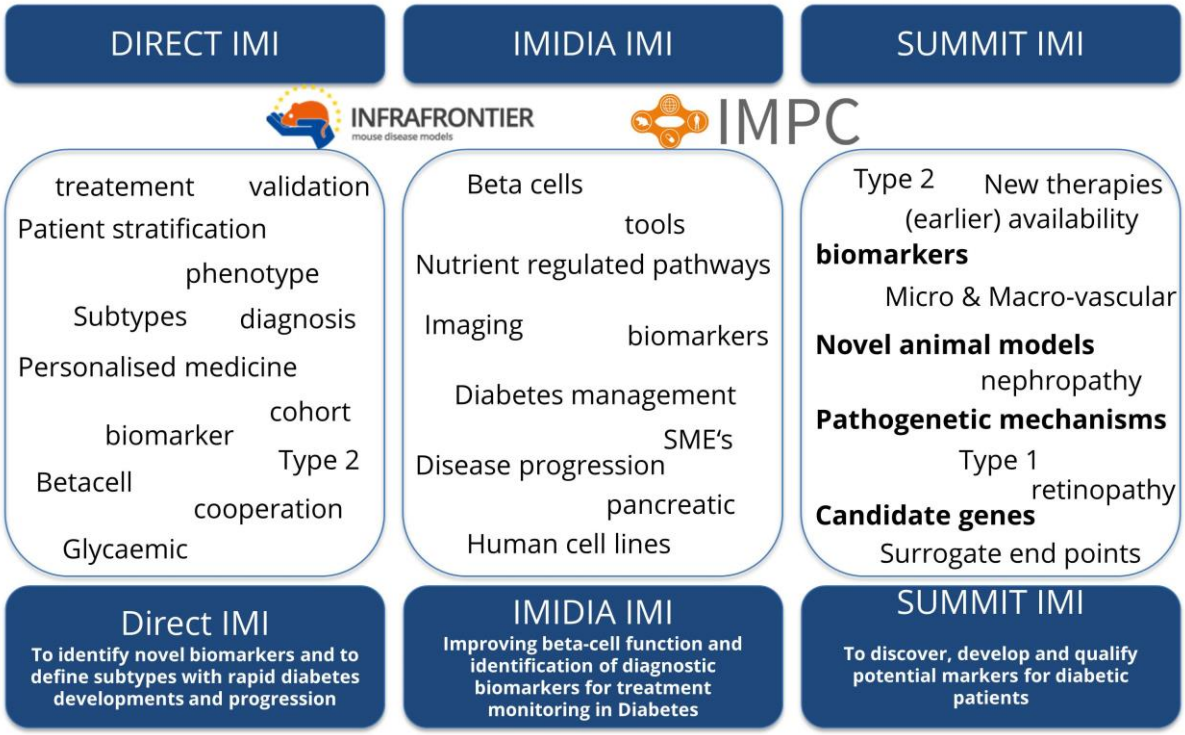

Figure 5. Word clouds derived from analyses of the goals and objectives of DIRECT IMI, IMIDIA IMI and SUMMIT IMI (Source: http://www.direct-diabetes.org/; http://www.imidia.org/; http://www.imi-summit.eu/; adapted from word cloud generator tool: https://www.jasondavies.com)

NEURODEGENERATIVE DISEASES

- Two programs were identified in the Neurodegenerative disease research area: **JPND** and **New Meds IMI** [Figure 6]
- **JPND**, Joint Program-Neurodegenerative Disease Research, intends to identify the origins of the neurodegenerative disease and understand the diseases mechanisms and models, so that a better disease definition and diagnosis can be provided and progress in treatment can be achieved
- **NewMeds IMI**, Novel methods leading to new medications in depression and schizophrenia- Innovative Medicine Initiative, proposes to find new methods for the development of drugs for schizophrenia and depression

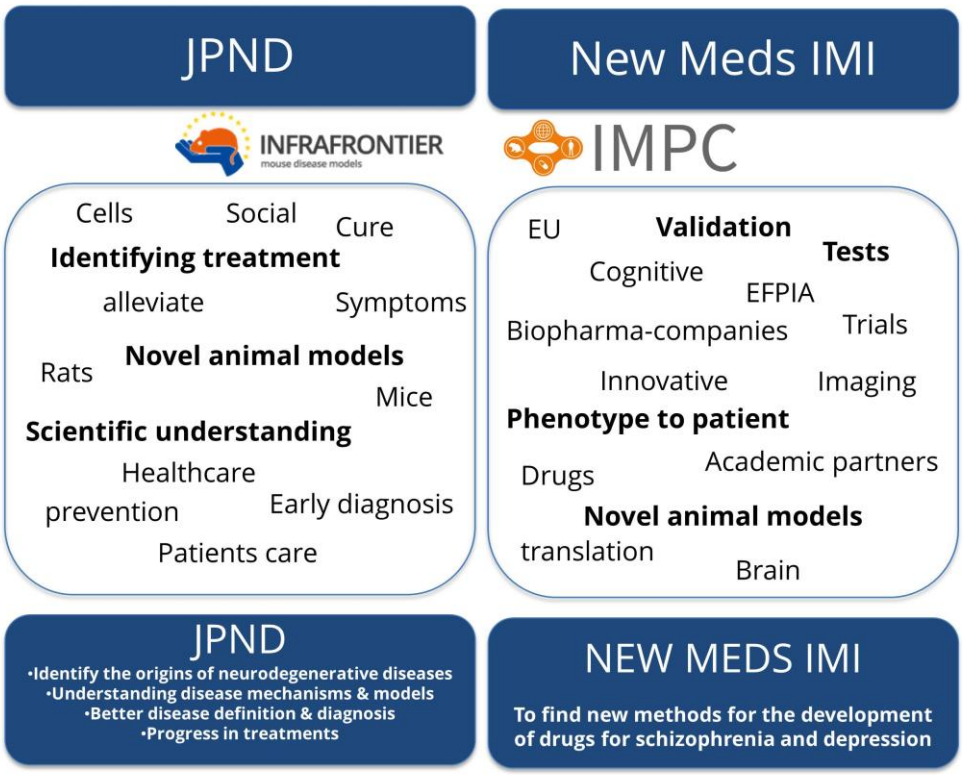

Figure 6. Word clouds derived from analyses of the Strategic Agenda of the JPND and objectives of New Meds IMI (Sources http://www.neurodegenerationresearch.eu/; http://www.newmeds-europe.com/; adapted from word cloud generator tool: https://www.jasondavies.com)

RARE DISEASES

- In the Rare Diseases area, two initiatives were found: **IRDiRC** and **ERA-NET: E-Rare** [Figure 7]
- **IRDiRC** the **International Rare Diseases Research Consortium** aims at, by the year 2020, delivering 200 new therapies for rare diseases and means to diagnose most rare diseases
- **ERA-NET E-Rare** focuses on extending and strengthening the transnational cooperation on rare diseases. Specifically E-Rare 3 (2015-2019) is promoting the use of European Research Infrastructures by the rare disease research community

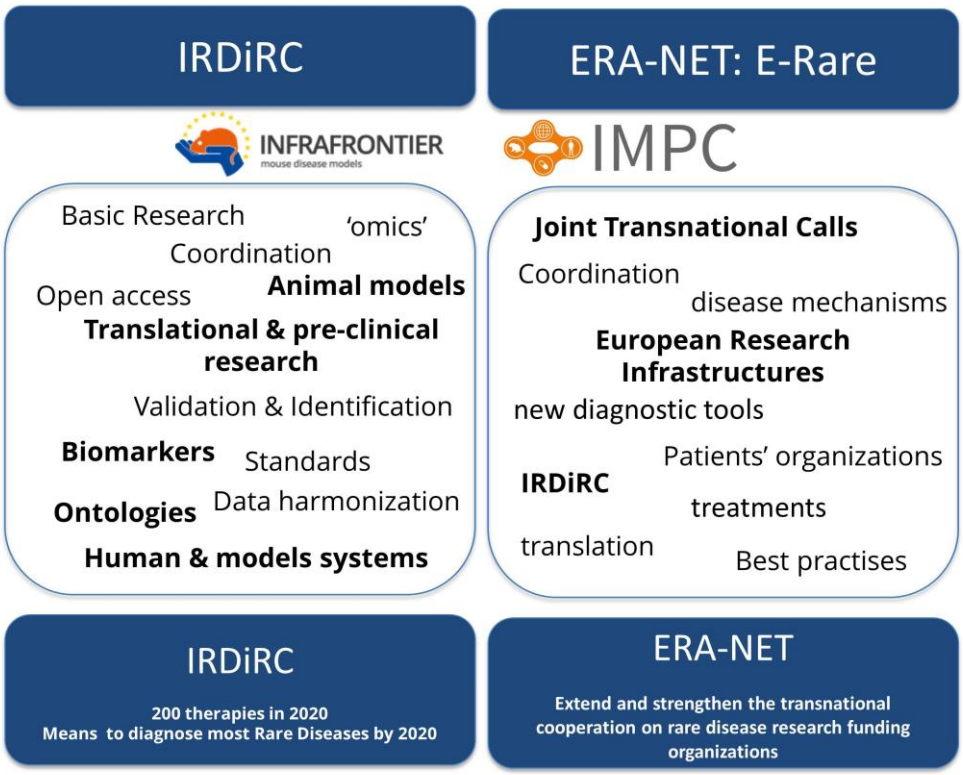

Figure 7. Word cloud derived from analyses of IRDiRC Policies & Guidelines and ERA-NET E-Rare IMI (Sources http://www.irdirc.org/goals/; http://www.erare.eu/; adapted from word cloud generator tool: https://www.jasondavies.com)

4. RECOMMENDATIONS

In the all the research areas selected, **strong cooperation** and **coordination** should be sought with other existent initiatives/programs.

4.1 AGEING

- Direct link to INFRAFRONTIER portal should be implemented at the COST MouseAge. A short description of the infrastructure available at INFRAFRONTIER should be provided by the IPAD-MD management team, so that the potential users can easily and promptly be directed to it.

- Currently (December 2015) COST MouseAge is coordinating a survey regarding the infrastructure needs in Europe (direct links: http://www.mouseage.eu/news/coordinating-infrastructure-needs-europe and http://goo.gl/forms/KPsOK0wwzZ. INFRAFRONTIER will participate in the survey and IPAD-MD management team should collect and distribute the results among INFRAFRONTIER and IMPC partners.

- Selection and depiction of existent mouse models of age should be implemented at the INFRAFRONTIER web portal, e.g., as a sub-section at the EMMA strain list, to ease out the search and to promote the use of aged mouse models to the broader user community (in cooperation with ShArm)

- Promotion of the use of mouse repositories as means to reduce the number of animals and refinement of tests should be pursed together by INFRAFRONTIER and ShArm, by means of a 'White Paper on advantages of use of mouse repositories from animal welfare and economic point of view'. This action should also be integrated with the IPAD-MD Cross-Cutting Theme: Animal Welfare (IPAD-MD WP8)

- The Coordinator/key partners of the COST MouseAge as well as ERIBA Research Groups using mice as animal model (e.g. *Gene regulation in ageing and age-related diseases*, *Laboratory of Quantitative Epigenetics*,) should be included in the IPAD-MD Stakeholders workshops and/or as external experts in the Expert Group Meeting in Standards & Technology as well as Data & Resources

4.2 IMMUNOLOGY/IMFLAMMATION

- Both the academic and industry partners at the BTCure IMI should be included in the IPAD-MD Stakeholder Engagement workshops (e.g., IPAD–MD Industry & Innovation workshop, 2016 and IPAD-MD Final Workshop 2019), in order to share information, best practices and increase awareness of the INFRAFRONTIER and the IMPC services and resources.
- INFRAFRONTIER should get further information on the validation of the final Standard Operation Procedures (SOPs) of the three mouse models for Rheumatoid Arthritis (CIA, CAIA and TNFTg mouse models) generated within the *Animal Studies* Work package of BT CURE IMI. Next steps on the validation process could be obtained by the BSR Fleming, a common partner INFRAFRONTIER and BT Cure IMI.
- Better promote and integrate the Immuno-therapy and Immuno-Oncology research areas within the INFRAFRONTIER web portal, together with INFRAFRONTIER and IMPC partner CIPHE, Centre D'Immunophenomique, France

4.2 METABOLISM

- The local synergies available at the INFRAFRONTIER partner level for instance with HMGU, Germany and UAB, Spain in the metabolic disease area can be used to bring forward the INFRAFRONTIER and IMPC resources and services.
- Due to the fact that both IMIDIA and SUMMIT IMIs are programs that were already concluded, the IPAD-MD management team should seek contact in order to be informed about IMIDIA and SUMMIT IMIs final reports and recommendations
- The academic and industry partners of the IMI diabetes platform should be included in the planned IPAD-MD Stakeholder Engagement Workshops

4.3 NEURODEGENERATIVE DISEASES

- The resources and services available at the INFRAFRONTIER and the IMPC should be made more visible within the JPND, both by direct contacts from INFRAFRONTIER partners (e.g. ICS, France) and by including JPND members in the IPAD-MD Stakeholders Workshops: Engagement with Funders and Policy
- The outcomes of the IMI 2 (Calls 6- 7) under the topic 'Big Data for better outcomes' in the neurodegenerative diseases area should be monitored

4.4 RARE DISEASES

- Both the Chair of the IRDIRC Steering Committee is member in the INFRAFRONTIER–I3 Advisory Board and the INFRAFRONTIER Coordinator and the INFRAFRONTIER and IMPC partners were members of the Working Groups on Models Systems and on Ontologies and Rare Disease Prioritization. Therefore, the level of cooperation between INFRAFRONTIER and IRDiRC has been mainly met at the contact level
- INFRAFRONTIER contributes indirectly to the IRDiRC objectives by seeking synergies and specific collaborations with E-Rare program (s. ERA-NET E-Rare)
- A landing page at INFRAFRONTIER portal targeted at the Rare Diseases community, in which a description of mouse models of rare diseases developed by the INFRAFRONTIER partners should be included.
- Improvement in the current link between EMMA strain list and OMIM database
- Collect the needs and requirements of Patients Organizations at European (e.g. EURORDIS) and INFRAFRONTIER partners level (e.g. France CERBM-ICS; Spain UAB)
- The results of the 7th E-Rare Joint Transnational Call for European Research Projects on Rare Diseases (E-Rare-3 JTC, February 2015) should be assessed by the IPAD-MD management team. Information regarding the number of projects, which specific areas within the rare diseases and which are the participating Institutions should be collected and distributed among INFRAFRONTIER and the IMPC partners.
- Seek synergies with other ESFRI projects that cooperate with E-Rare in the pre-clinical area (e.g. EATRIS).

5. CONCLUSIONS & GENERAL RECOMMENDATIONS

- A notification service informing the INFRAFRONTIER/EMMA users when a mouse line of interest to a specific research area is deposited at EMMA should be developed and implemented at INFRAFRONTIER portal
- A data mining tool should be developed and implemented at the INFRAFRONTIER portal so that the number of publications and specific research areas targeted can be monitored and the INFRAFRONTIER and IMPC resources are made more visible to the users

- Outcomes and implementation description of these recommendations should be yearly monitored, and its progress should be reported to the IPAD-MD partners. In addition a summary of its achievements should be included in IPAD-MD D3.2 Report on Alignment of Scientific Strategies

6. REFERENCES

Ageing

- COST Mouse Age – Memorandum of Understanding (2014); [http://www.mouseage.eu/]
- ERIBA [http://www.umcg.nl/EN/Research/ERIBA/Paginas/eriba.aspx]
- Shared Ageing Research Models; [www.sharmuk.org/about-us/our-goals]

Drug Development/Diagnostics/ Personalized Medicine

- Innovative Medicines Initiative – The Right prevention and treatment for the right patient at the right time , Strategic Research Agenda for IMI2 (2014)
- Science Europe - Medical Sciences Committee: How to Transform Bug Data into Better Health (2014); [www.scienceeurope.org/scientific-committees/Medical-sciences/publications-of-the-medical-sciences-committee]
- European Science Foundation – Personalized Medicine for the European Citizen (2012); [www.esf.org]
- Per Med – Shaping Europe's Vision for Personalized Medicine (2015); [www.ibbl.lu/personalised-medicine/personalised-medicine-consortium/]

Metabolism

- [http://www.direct-diabetes.org/]
- [http://www.imidia.org/]
- [http://www.imi-summit.eu/]

Neurodegenerative Diseases

- JPND Research Strategy - Tackling the challenge of Alzheimer's and other neurodegenerative diseases in Europe (2012) [www.neurodegenerationresearch.eu/initiatives/jpnd-alignment-actions/animal-and-cell-models/]
- Report of the JPND Action Group – Experimental models for neurodegenerative diseases (2014), [www.neurodegenerationresearch.eu/initiatives/jpnd-alignment-actions/animal-and-cell-models/]

Rare Diseases

- International Rare Diseases Research Consortium - Policies & Guidelines (2013); [www.irdirc.org/wp-content/uploads/2013/06/IRDiRC_policies_24MayApr2013.pdf]

- E-Rare ERA-Net (2015); [www.erare.eu/objectives]

Other

- G7 – Group of Senior Officials on Global Research Infrastructure Progress Report (2015); [www.bmbf.de/en/group-of-experts-is-to-issue-a-report-on-global-research-infrastructures-1433.html]
- Science Europe – Joint Statement by SE, CEASER, EARTO, LERU to take action on working in partnership in achieving the European Research Area (2015); [www.scienceeurope.org/uploads/PublicDocumentsAndSpeeches/joint-statement-17072012_en-2.pdf]
- Science Europe - Science Europe Roadmap (2013), [www.scienceeurope.org/scientific-committees/Medical-sciences/publications-of-the-medical-sciences-committee]

7. APPENDIX - SURVEY

Dear INFRAFRONTIER/IMPC partners,

In the remits of the IPAD-MD project we are conducting a **very short survey** aiming at identifying and mapping the different policy programs relevant to INFRAFRONTIER and IMPC.

With the results of this survey we will get a more accurate view on the existing overlaps in the strategic research agendas of INFRAFRONTIER/IMPC and other research programs and identify areas where further complementary should be sought.

The survey will not take longer than three minutes of your time and we will be grateful for a large participation!

Please fill in the 3-question survey until **06 November 2015**, following the link below:

https://www.surveymonkey.com/r/NYSJ5TL

Many thanks in advance,
With best wishes,

The IPAD-MD team

Q1 What is the current research priority area of your Institution (multiple choice possible)

□ Ageing

□ Big Data and data driven research

□ Cancer

□ Drug development/ Diagnostic test development/ Personalized Medicine

□ Metabolism/Diabetes/Obesity

□ Gnotobiology/ Microbiota

□ Neurodegenerative Diseases

□ Rare Diseases

□ Other (please specify)

Q2: In which research area(s) should INFRAFRONTIER/IMPC focus in the in the next 5 years? (multiple choice possible)

□ Ageing

□ Big Data and data driven research

□ Cancer

□ Drug development/ Diagnostics test development/ personalized medicine

□ Metabolism/Diabetes/Obesity

□ Microbiome

□ Neurodegenerative Diseases

□ Rare Diseases

□ Other (please specify)

Table 1. List of INFRAFRONTIER and IMPC partners contacted to answer the survey

INFRAFRONTIER & IMPC partners	
Australian Phenomics Network	Australia
Biomedical Sciences Research Center "Alexander Fleming"	Greece
Catholic University Leuven	Belgium
Centre d'Immunophénomique	France
Centro Nacional de Biotecnologia – Consejo Superior de Investigaciones Cientificas	Spain
Consiglio Nazionale delle Richerche	Italy
European Molecular Biology Laboratory – European Bioinformatics Institute	United Kingdom
Helmholtz Centre for Infection Research	Germany
INFRAFRONTIER GmbH/Helmholtz Center Munich	Germany

INFRAFRONTIER & IMPC partners	
Institute Clinique de la Souris	France
Institute of Molecular Genetics	Czech Republic
Instituto Gulbenkian de Ciencia	Portugal
International Mouse Phenotyping Consortium	United States of America
Karolinska Institute	Sweden
Korea Mouse phenotyping Consortium	Korea
Mouse Biology Program – University of California Davis	United States of America
MRC Harwell	United Kingdom
Nanjing University	China
National Institutes of Health	United States of America
Netherlands Cancer Institute	The Netherlands
Riken BioResource Center	Japan
Technical University Vienna	Austria
Tel Aviv University	Israel
The Jackson Laboratory	United States of America
Toronto Center for Phenogenomics	Canada
TSE Systems	Germany
Universitat Autonoma de Barcelona	Spain
University of Copenhagen	Denmark
University of Oulu	Finland
Welcome Trust Sanger Institute	United Kingdom

Table 2. List of the current research area within INFRAFRONTIER and the IMPC partners

Research Area	Answer (%)
Ageing	39
Big Data & Data-driven research	33
Cancer	56
Drug development & Personalized medicine	28
Gnotobiology/Microbiota	33
Inflammation/Immunology	61
Metabolism/Diabetes/Obesity	61
Neurodegenerative Diseases	44
Rare Diseases	44
Other: Development of gene therapy approaches	6
Other: Epigenetics	6
Other: Genetics of human diseases – equally serving all the research areas listed	6
Other: IMPC Mouse generation & phenotyping	11
Other: Infections Diseases, Influenza	6
Other: The Institute is multidisciplinary in biological and biomedical science, including in addition to the above: theoretical biology experimental evolution, development and cell cycle regulation	6

Table 3. List of the research areas in which the INFRAFRONTIER and IMPC partners should focus in the next 5 years

Research Area	Answer (%)
Ageing	39
Big data & Data-driven research	22
Cancer	22
Drug development & Personalized medicine	33
Gnotobiology/Microbiota	17
Inflammation/Immunology.	33
Neurodegenerative Diseases	39
Rare Diseases	50
Other: Development of gene therapy approaches	6
Other: Improving predictive value of pre-clinical mouse models	6
Other: Mouse generation (from IKMC), phenotyping & gene editing technologies (but should not compete with for profit service providers)	11
Other: We have selected the broad areas of dealing with large datasets and the application of genomic approaches to support personalize/precision medicine. However, all the other research areas listed would equally benefit from the application of large scale, well curated genome-phenome datasets to personalized medicine.	6