Initiative for Science in Europe ise:

Annex on
Boost collaborative basic research
to complete the Research & Innovation cycle in Pillar 2

To the ISE main recommendations on Horizon Europe and towards FP10

29.5.2024 (Version 1)

Boost collaborative basic research to complete the Research & Innovation cycle in Pillar 2

Throughout Horizon 2020 and currently in Horizon Europe, collaborative basic research has been marginalised, resulting in a gap in the Research and Innovation cycle.

In Horizon Europe and in the upcoming FP10, **Pillar 2** must be designed to achieve a **balanced participation from basic and applied research in addition to demonstration and innovation actions**. This would strengthen the effectiveness of the R&I cycle of the European research and innovation ecosystem by promoting a continuous exchange between advancement of knowledge and applications at different TRLs. Ultimately, this strategy will meet the needs of the industrial sector and private companies.

To help overcome the gap of collaborative basic research and complete the research and innovation cycle, ISE recommends **making collaborative basic research an intrinsic component of R&I Actions and introducing Research Actions** focussed on basic and applied research. This is particularly necessary to address Global Challenges. In this way an upward spiral would be created that is adding new knowledge in each round, elevating the innovation to the next higher level.

Annex to this recommendation: page

ISE main recommendations on Horizon Europe and towards FP10, 26.10.2023 Link

From ISE position on Horizon Europe, 12.7.2021:

The R&I cycle in pillar 2 of Horizon Europe

Pillar 2 of the upcoming framework programme is of utmost importance to tackle Global Challenges and enhance European Industrial Competitiveness. Since it constitutes a translational bridge between the Excellent Science and the Innovative Europe pillars, its actions should support basic and applied research together with the demonstration and innovation aspects in a balanced way. We envision this pillar as closure of the R&I cycle, where research and innovation outcomes grow through a positive feedback loop.

Recently, various works from ISE, LERU, Science Europe and EUA have suggested that the focus towards high Technology Readiness Levels (TRLs) in H2020 has caused a steady increase in support for applied research and demonstration actions, and a steep increase in support for innovation actions. Although we agree that increases for those actions were due, we notice that it has been unbalanced and that support for basic research has dropped dramatically. As a consequence, the Societal Challenges aspects in H2020 missed out on the benefits from projects feeding questions and knowledge between innovation and basic research. This has caused the weakening (and at times breaking) of the R&I cycle, thus slowing down (and at times hindering) the identification and deployment of ground-breaking solutions for current and future challenges.

This view is shared by a study from UNESCO (2017) reviewing approaches across the globe: *"the focus of scientific discovery has shifted from basic research to 'relevant' or big science, in order to solve pressing developmental challenges, many of which have been identified as SDGs [Agenda 2030] by the United Nations. [...] an adequate investment in* **both basic sciences and applied research and development (R&D)** *will be critical to reaching the goals of Agenda 2030"* (emphasis added). Applied to Europe today this requires a better balance in the support of research actions compared to innovation actions by completing and strengthening the R&I cycle.

LERU (2016) analysed H2020 Work Programmes from Societal Challenges and from Industrial Leadership regarding TRLs and found that there is a quantitative trend towards supporting higher TRLs in Societal Challenges, with peaks in TRLs 3-6 (2014-2015), moving to TRLs 4-6 (2016-2017). Early analyses made by ISE suggest that in 2018-2020 most peaks (except the transport challenge) moved even further to TRLs 5-7. Contrary to the Societal Challenges general trend, the trend in Industrial Leadership is moving from peaks in TRLs 4-6 (2014-15) to TRLs 3-5 (2016-2017 and 2018-2020). We find that while most Societal Challenges miss out on the benefits from basic and applied research, Industrial Leadership and the Transport Challenge show a more balanced distribution of TRLs and should be used as example for the Global Challenges in Horizon Europe.

While we see a high potential in bottom-up basic research in pillar 1, e.g., in the ERC and MSCA, we also believe that basic research contributions should be included in pillar 2 of HE to maximally benefit innovation within the R&I cycle. We acknowledge that there are dedicated Innovation Actions in pillar 2, complementing the innovation focus of pillar 3. Similarly, we call for dedicated basic and applied research actions in pillar 2, complementing the research focus on pillar 1. The unique position of pillar 2 to cover and thereby complete and strengthen the R&I cycle in a balanced way has the potential to

become one of the strengths of the Horizon Europe programme – a step change compared to H2020 (see, e.g., ISE 2016). In Appendix 2, we show a few examples of collaborative basic research.

Recommended action

- Make collaborative basic research an intrinsic part and occasional focus of R&I Actions. The EC's Implementation Strategy has as its first objective to maximise impacts and refers to level of TRLs in collaborative research. We strongly suggest providing funding that addresses Global Challenges through the encouragement of collaborative basic research as an intrinsic component and occasional focus of R&I Action projects. The collaborative work will sometimes emphasise basic and applied research and at other times the demonstration and innovation aspect. When all actions are considered together, they will end up supporting the four components in a balanced way.

This recommendation will have two additional positive impacts that we deem worth considering:

- Meets the needs of private companies by embedding programmatic basic research requirements in all clusters of pillar 2. Designing programmes with basic and strategic research will help meet the needs of private companies with limited in-house capacity for applied R&I. It will also help soften the lack of financial motivation for exploratory research that lays the groundwork for further improved innovation activities.

- Indirectly facilitates widening participation. Supporting projects encouraging basic and applied research that includes participants from EU-13. Enabling research groups across Europe to collaborate within the European Research and Innovation Programmes will advance economies across Europe, increase social stability, and help build a more inclusive and equal Europe.

LERU (2016):

16_08_LERU_The Strength of Collaborative Research for Discovery in Horizon2020.pdf

TRL analysis Horizon 2020 Work Programmes by LERU (2016) and ISE (2020 internal)

LERU (Figure 1) and ISE (Figures 2 and 3) analysed all H2020 Work Programmes from Societal Challenges and from Industrial Leadership regarding TRLs.
There is a quantitative trend towards supporting **higher TRLs in Societal Challenges**, with peaks in TRLs 3-6 (2014-2015), moving to TRLs 4-6 (2016-2017) and finally to TRLs 5-7 (2018-2020), which is missing out benefits from basic and applied research.
The trend in **Industrial Leadership** is moving towards the **lower / centre of TRLs**: with peaks in TRLs 4-6 (2014-15), moving to TRLs 3-5 (2016-2017 and 2081-2020), which is **more balanced and should be used as example for the Global Challenges in HE**.

While we see a high potential in bottom-up basic research in **pillar 1**, e.g. in the ERC, we also believe that basic research contributions should be included in **pillar 2** of HE to maximally benefit innovation within the R&I cycle. We acknowledge that there are dedicated Innovation Actions in pillar 2, complementing the innovation focus of pillar 3. Similarly, we call for dedicated basic and applied research actions in pillar 2, complementing the research focus in pillar 1. The unique position of pillar 2 to cover and thereby complete and strengthen the R&I cycle in a balanced way has the potential to become one of the strengths of the HE programme – a step change compared to H2020.

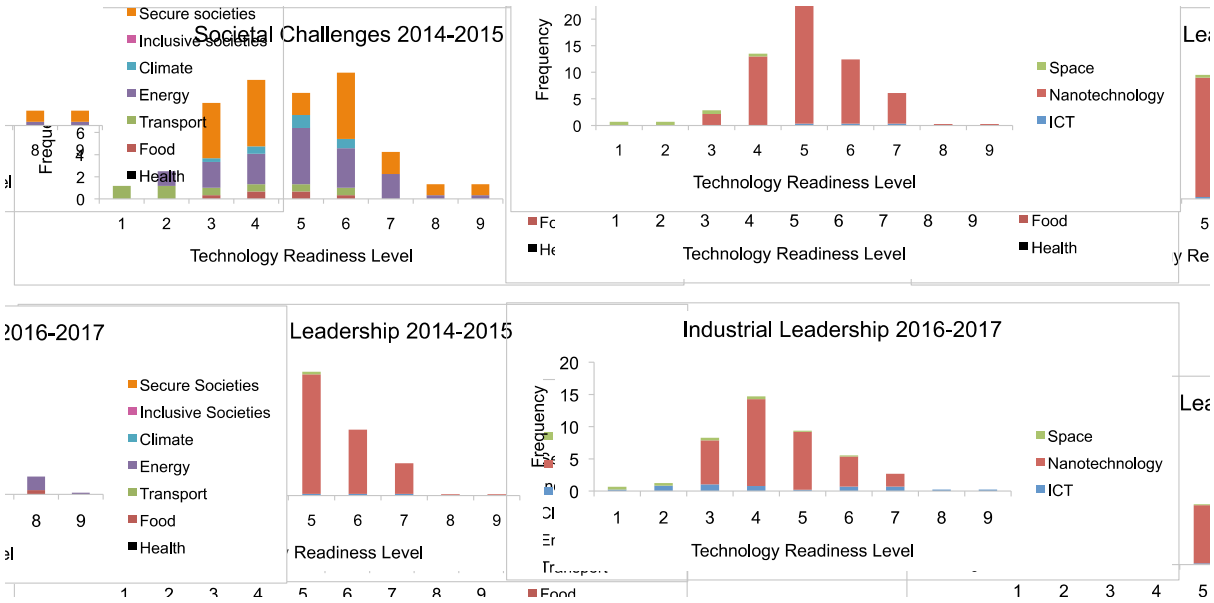

Figure 1 Use of TRLs in H2020 Work Programmes 2014 – 2017 (Source LERU 08/2016)

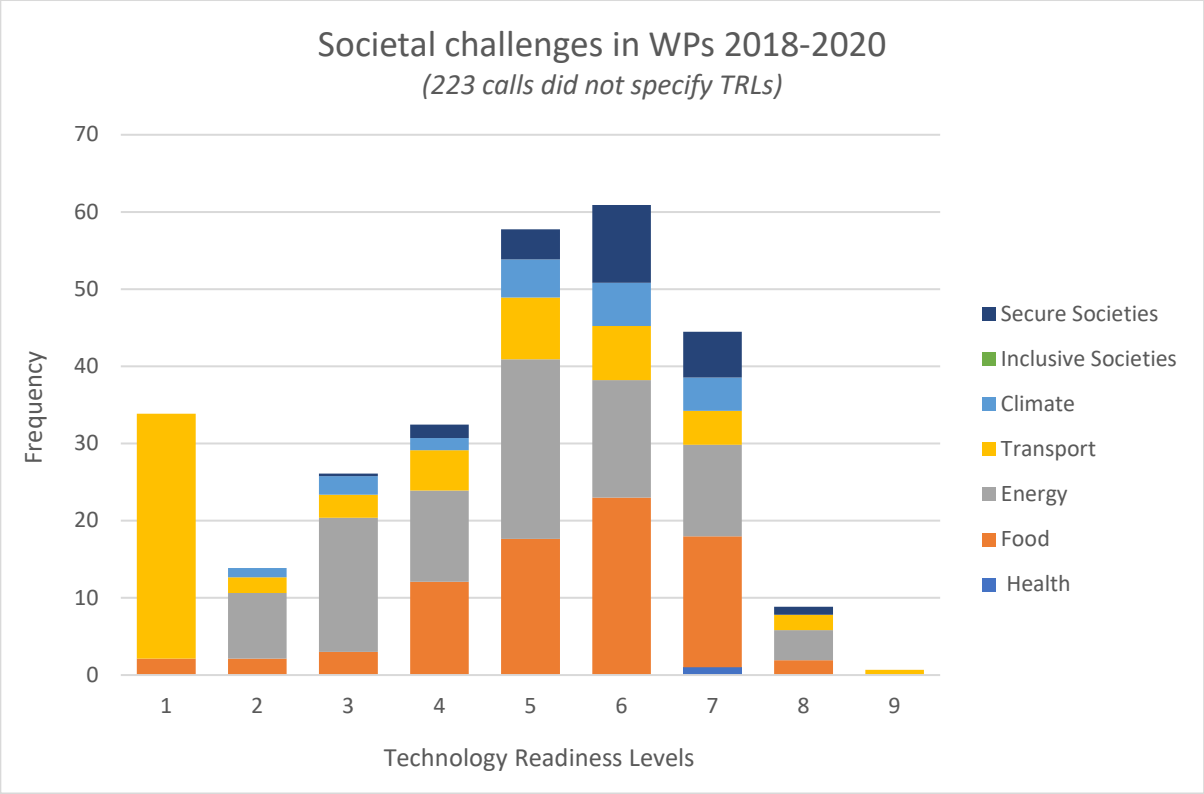

Figure 2 Use of TRLs in H2020 Work Programmes for Societal Challenges 2018 – 2020. Frequency is the number of calls which specified that TRL.

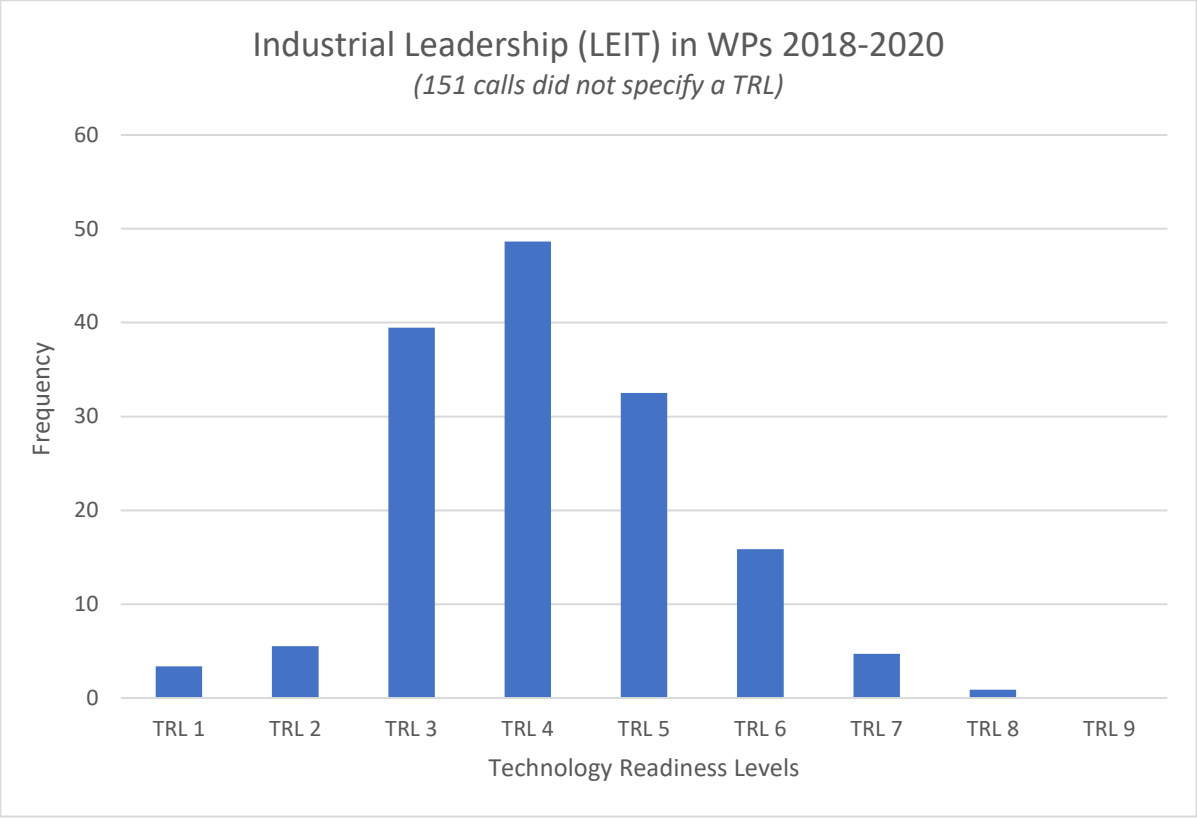

Figure 3 Use of TRLs in H2020 Work Programmes for Industrial Leadership 2018 – 2020. Frequency is the number of calls which specified that TRL.

ISE - Impact of former collaborative basic research at EU level

List of examples selected from various disciplines**:**

[as received] science discipline
Project title [acronym]

#1: Plant biology relevant to **crop improvement**
Genomics for Triticeae improvement [TriticeaeGenome]

#3: Plant biology relevant to **crop improvement**
Improvement of transgene expression and gene silencing in transgenic plants [Gene Silencing]

#4: Animal biology relevant to **human health**
Matrix Macromolecules in inflammation [INFLAMA]

#5: Human biology relevant to **human health**
Multiscale approach to the identification of molecular biomarkers in acute heart failure induced by shock [ShockOmics]

#6: Animal biology relevant to **human** health
Health and the Understanding of Metabolism, Aging and Nutrition [HUMAN]

#10: Chemistry relevant to **human** health
Integrating chemical approaches to treat pancreatic cancer: making new leads for a cure [PANACREAS]

#11: Plant biology relevant to **crop improvement**
Control of flowering time for sustainable and competitive agriculture and forestry [CONFLOW]

#13: **Medicine** – organ transplantation
The ONE Study - A Unified Approach to Evaluating Cellular Immunotherapy in Solid Organ Transplantation [The ONE Study]

#17: **Aeronautics**
Innovative Methodologies and technologies for reducing Aircraft noise Generation and Emission. [IMAGE]

#18: **Aeronautics**
Enhancing structural efficiency through novel dissimilar material joining techniques [SAFEJOINT]

#19: **Aeronautics**
Flow physics modelling – an integrated approach [FLOMANIA]

Initiative for Science in Europe ise:

ISE – Suggestions for broad call headings for collaborative basic research at EU level

List of examples for General heading per discipline to consider for future calls for collaborative basic research from various disciplines:

Cluster 1 - Health: Medical sciences:

Basic biological processes relevant to human health (from birth to healthy ageing)

e.g. Basic biological processes in bacteria relevant to antibiotics development and delivery for human health

e.g. Epigenetics driving determinants in early cancer development and detection

e.g. Biological and biomechanical research relevant to replacement, repair and regeneration of human tissues using medical devices with new and non-compromised chemistry; such as for oral, heart, or orthopaedics applications.

e.g. Biological research relevant to understand metabolic and cardiovascular diseases

Cluster 2 – Culture, Creativity and Inclusive Society: Social sciences:

Understanding social processes relevant to Democracies in danger

Breaking down the barriers to equality: Gender, Equality and ICT and AI.

Advancing Agenda 2030 and the role of Europe:

E.g. A meta-analysis and examination of the UN SDGs as to what is working, what Goals are being met, in advance of Agenda 2030.

E.g. Understanding Vaccine hesitancy in an age of Misinformation. Reasons for misinformation incl. education levels, social media channels, ethnicity, socio-economic & government responses.

Cluster 4 – Digital, Industry and Space: Physics sciences

Light pollution measurements for energy efficiency and environment: light and noise pollution measured from the International Space Station

Cluster 5 – Climate, Energy and Mobility: Aeronautic sciences:

Novel technologies, materials, sensors for mobility & aeronautics

e.g. Digitisation in design, manufacturing and operations for competitiveness and sustainability

e.g. Investigation of novel materials for enhanced performance of aircraft structures, especially using additive manufacturing and advanced hybrid structures

e.g. Investigation of novel sensors for embedded structural health monitoring systems in aircraft

e.g. Exploring future propulsion technologies, incl. electric, hybrid and H2 based systems.

e.g. Further progress in supersonic technologies

e.g. Materials for extreme conditions

Geographic sciences:

Identify the relative role of interactive processes to reduce uncertainties in environmental and earth system models

Engineering sciences:

Reduction of energy consumption and CO2 emissions

e.g. Electrification of energy intensive industries via microwave heating or other alternative electrical heaters.

e.g. Collectors as the heating source of energy intensive industries.

Cluster 6 – Food, Bioeconomy, Natural resources, Agriculture & Environment: Plant sciences:

Basic biological processes relevant to crop improvement and adaptation

e.g. Boosting crop resilience by understanding plant mechanisms to cope with climate change and pathogen pressure.

e.g. Basic biological processes in plants relevant to abiotic stress tolerance – drought, heat, cold, flooding etc.
e.g. Basic biological processes relevant to nutritional quality of plants for human diet and health – vitamins, secondary metabolites etc.
e.g. Understanding and improving plant photosynthesis as a system.
e.g. Basic biological processes relevant to quality traits of plants for bioeconomy – high value and staple products.

Animal sciences:

Basic biological processes relevant to animal wellbeing and improvement

Microbiological sciences

Basic biological processes relevant to microbiome improvement

ISE – Industry support for collaborative basic research at EU level

ISE invited companies and industry associations to express their support to boosting collaborative basic research to completing the R&I cycle in pillar 2 and creating an upwards R&I spiral with a Letter of Support.

List of Letters of Support already received (order as received):

Plantum, the Dutch plant breeders' association (> 250 companies) 27.02.2024
Plant sector:
Research performed at higher TRLs is based on a strong foundation of fundamental knowledge built up over many years. Thes past investments have proven of crucial importance in establishing multiple public-private initiatives, valorising this into products for farmers and consumers across Europe. Much of this knowledge pipeline is at risk of during up now that public investment in new fundamental (technical and biological) knowledge has been insufficient over the past years.

BASF, agriculture – chemical company 06.03.2024
Plant & chemistry sectors:
To help overcome the gap of collaborative basic research and complete the research and innovation cycle, we support ISE's recommendation to make collaborative basic research an intrinsic component of R&I Actions and introducing Research Actions focussed on basic and applied research. This is particularly necessary to address Global Challenges. In this way an upward spiral will be created that is adding new knowledge in each round, elevating the innovation to the next higher level.
Ultimately, this strategy will meet the needs of the industrial sector and private companies.
Help farmers sustainably increase the yields and quality of their crops to feed a growing world population by increasing agricultural productivity in a sustainable manner.
The BASF Innovation Center Gent has been actively involved in many multi-disciplinary and collaborative research programs funded or supported by the EU in the past, which have been of great benefit to our innovation potential.

FIDE, Federation of the European Dental Industry (> 550 companies) 13.03.2024
Medical sector:
FIDE considers the need for scientific research fundamental to accelerate innovation and to develop new, less invasive materials and medical devices in Europe.
Basic research is a requisite for industries to get insight into knowledge and help large companies and in particular SMEs to be at the forefront and increase their competitiveness.
Most companies cannot afford to do such research themselves. Basic research must be carried out by public entities to allow for unexpected findings which can be captured and transferred only by industries and businesses with the necessary know-how and investment capacity.
To our understanding collaborative basic research is an integral part of the research and innovation cycle.
Regulatory matters such as the European Medical Device Regulation (use of nanotechnology), the EU Mercury Regulation …and related activities benefit from scientific research, the results of which contribute significantly to meeting the new challenges for better quality service to citizens in terms of dental health.

PLOCAN Oceanic Platform Canarias 19.3.3024
Marine sector - renewable energy, food production

Bayer AG, agriculture & pharmaceutical company 22.03.2024
Plant & pharma sectors:
The unique position of pillar 2 to cover and thereby complete and strengthen the R&I cycle in a balanced way has the potential to become one of the strengths of the Horizon Europe programme creating a step change towards FP10.
We support ISE's recommendation to make collaborative basic research an intrinsic component of R&I Actions and introducing Research Actions focussed on basic and applied research.

Evektor, important aircraft manufacturer in Czech Republic 22.03.2024
Aircraft sector:
We support ISE's call for dedicated basic and applied research actions in pillar 2, complementing the research focus on pillar 1.
Evektor has already been part of consortium of PARASOL and NEPIT projects with Marie Sklodowska-Curie Actions since we have seen these activities beneficial.
In addition, we agree with the Initiative for Science in Europe, that policy makers need to improve the innovation framework to attract companies investing in Europe today and in future.

INDUCIENCIA, Spanish Science Industry Technology Platform 25.03.2024
Physics sector
INDUCIENCIA is formed by close to 200 members, where more than 60% are companies, with a big number of SMEs (more than 100), 25% of knowledge generation institutions (research facilities, universities, research institutes, technological centres…) and public authorities among others.

INEUSTAR, Spanish Science Industry Association 25.03.2024
Physics sector
INEUSTAR, is a Spanish association of industrial companies dedicated to conception, design, construction, exploitation and maintenance of the scientific instruments and facilities. INEUSTAR's mission is to contribute to the progress of science and technology, as well as to the strengthening of the innovation. Our focus is on the collaboration between companies and academia in all the different stages of knowledge/technology generation, paying special attention in the collaboration from early research stages (TRL2-3), fostering and promoting Public-Private Partnerships and knowledge transfer activities in all facilities, projects and scientific programs along the world.
Even though INEUSTAR is an association formed by Spanish organizations, our vision and market are global and it exists an effective collaboration with multiple research facilities, industrial associations and public authorities throughout Europe and across the world.

Siemens AG 08.04.2024
Digital, Mobility, Energy, Healthcare, Building sectors

ISE - Impact of former collaborative basic research at EU level – examples:

– example 1: Plant biology relevant to crop improvement

Project: Genomics for Triticeae improvement

Acronym: TriticeaeGenome

Call: FP7, Theme 2, Food, Agriculture and Fisheries, and Biotechnology, KBBE-2007-1-2-02, "Genomics for cereal improvement for food, feed and non-food uses."

This project will assemble the knowledge required, and use modern breeding techniques, including genetic engineering, to produce cereal crops (from the Triticeae tribe) with improved composition and characteristics that will satisfy the proven needs of consumers, processors and producers. In addition to developing new knowledge in the areas of genetics and genomics, the project will build on existing resources inside and outside Europe. To assure dissemination and transfer of the results, industrial, farmers' and consumers' representatives should be included from the project's inception. Participation in international genomics programmes and collaboration with ICPC target countries is encouraged. Funding scheme: Large collaborative project. Expected impact: The project will enable Europe to assume a clear leadership role in Triticeae genomics, thus producing a competitive advantage in the global market.

Budget: € 7 500 000, of which EU € 5 300 000

Period: 01.06.2008 – 31.05.2015

Partners: 17 partners from 9 countries (INRA coordination, Schulman a WP leader)

Summary: TriticeaeGenome was developed as a main contribution to the international consortia's efforts to construct physical maps of barley and hexaploid wheat for improving plant breeding, accelerate gene and QTL (Quantitative Trait Locus) isolation, and to set up the foundation for future genome sequencing. It aimed at delivering novel information and tools to breeders and scientists based on a better understanding of organization, evolution, and function of Triticeae genomes.

Report: https://cordis.europa.eu/docs/results/212/212019/final1-212019-1160184-tg-final-publishable-summary-report-v2-with-logo-figures-and-partners-list.pdf

Impact: **TriticeaeGenome unlocked the genomes of two economically crucial crops—barley and wheat—and provided the foundations for basic and applied discoveries until the present day and beyond**. The pan-genomes currently underpinning basic research from evolution to cell biology, as well as accelerating breeding in the cereals, directly stem from work within the project. Publicly available BAC libraries were generated, together with minimal tiling paths, for each chromosome, enabling the genome assembly projects that followed. Integrated physical maps for 1AS, 1AL, 1BS, 1BL, 3B, 3DS, and 3DL of wheat and 1H and 3H of barley were generated, together with high-density maps, enabling many genes to be fine mapped and some to be positionally cloned. These included two Mendelian loci (YrH52, cul4) and three QTLs underlying fungal disease resistance, yield and quality traits (PV-QTL, QYld-idw, QSng.sfr). The wheat Yr15 was positionally cloned, revealing the tandem kinase—pseudokinase family as a new class of disease resistance genes. Diversity sets were assembled, enabling genome-wide association analyses for heading date, grain yield and plant height, for which known and new chromosomal locations underlying these traits were identified. New bioinformatics annotation pipelines were developed.

***Information by** Alan Schulman / LUKE / FI, 30.8.2023*

Impact of collaborative basic research at EU level **– example 3:** Plant biology relevant to crop improvement

Project: Improvement of transgene expression and gene silencing in transgenic plants

Acronym: Gene Silencing

Call: FP5, Quality of Life and Management of Living Resources, QLK3-2000-00078

This proposal aimed at exploiting plant-specific gene silencing mechanisms to develop new strategies for the prevention of transgenic silencing and for the controlled use of gene silencing for the inactivation of endogenous genes and gene families in crop plants. The project combined novel basic research elements with the application of these results in modern agriculture for the benefit of the consumer and European industry, as it was expected to develop strategies for a safe and reliable use of a commercially highly important technology.

Budget: € 3 743 431, of which EU contributed € 2 550 688

Period: 01.01.2001 – 31.12.2003

Partners: 11 partners from 7 countries (coordination at the University of Leeds)

Summary: Soon after the first generation of transgenic plants, the potential of the technology for research and application was obvious, while it became evident that, especially after the integration of multiple transgene copies or their homology with endogenous genes, diverse epigenetic processes could result in reversible, but somatically or meiotically stable gene inactivation, summarized under the term "gene silencing". Based on two previous collaborative networks, the consortium of QLK3-2000-00078 consisting of previous members as well as new groups with complementary expertise addressed the molecular basis of the process. Combining diverse plant and fungi model organisms, crop plants and different approaches, the consortium discovered several components and fundamental principles of different, though interconnected pathways.

Report: *Can't find a final report*

Impact: **The consortium made ground-breaking discoveries about the role of transgene structure, intron content, copy numbers, or promoter features.** A major success factor was further the application of forward and reverse genetic screens to identify the genes that encoded different epigenetic regulators components. Combined with molecular methods it was possible to describe mechanisms that were modifying either the DNA methylation or other chromatin features of the affected genes (transcriptional silencing) or the stability of their transcripts (post-transcriptional silencing). The discovery of small RNAs and their feedback on DNA methylation and chromatin at the target genes opened new avenues for understanding the complexity of gene silencing. **The findings were the basis for following projects aiming to understand the interplay between epigenetic changes and plant development, stress responses, and defense mechanisms.** Many young scientists were involved in the research, could participate in the regular, always stimulating meetings and continued their career afterwards in academia and industry. The success of the consortium is documented in numerous high-scoring publications, acknowledging the support of the project. Just some examples from the different labs: DOI 10.1046/j.1365-313x.2000.00793.x; DOI 10.1007/s11032-006-9001-x; DOI 10.1128/MCB.25.9.3793-3801.2005; DOI 10.1093/nar/gkh530; DOI 10.1073/pnas.202380499; DOI 10.1016/S0014-5793(04)00280-7; DOI 10.1016/j.cub.2004.04.037; DOI 10.1126/science.1063051; DOI 10.1146/annurev.cellbio.21.122303.114706

Information by *Ortrun Mittelsten Scheid / GMI / AT, 20.11.2023*

Impact of collaborative basic research at EU level **– example 4:** Animal biology relevant to human health

Project: Matrix Macromolecules in inflammation

Acronym: INFLAMA

Call: FP7-PEOPLE - Specific programme "People" implementing the Seventh Framework Programme of the European Community for research, technological development and demonstration activities (2007 to 2013)

Diagnosis and treatment of inflammatory-related diseases remains a clinical challenge. An international consortium has searched for therapeutic solutions to inflammation in the biochemistry of tropical animals. Study of the role of carbohydrates, glucomics, is highlighting their importance in health and disease. The extraordinary complexity of carbohydrates, ranging from simple single molecules to huge polymers, has so far hampered the progress of analytical methodologies.To advance the field of glucomics, the EU-funded INFLAMA (Matrix macromolecules in inflammation) project assembled a network of research labs – 'gluco-net' – for carbohydrate research.

Budget: € 183.600 of which EU € 151.200

Period: 01.12.2011 – 30.11.2014

Partners: 4 partners from 4 countries (Unins, Passi leader)

Summary: Key scientific activities of the project included the delineation of the mechanisms of hyaluronan synthesis in cell cultures of human smooth muscle cells and endothelial cells following inflammatory stimulation. The scientists also evaluated the expression of all the genes involved in the hyaluronan biosynthesis pathways.INFLAMA research results shed light on the molecular mechanisms involved in the anti-inflammatory, antithrombotic and antimetastatic effect of unique heparin analogues isolated and characterised by the researchers. In vitro models have elucidated hyaluronan synthesis. Signalling mediated by proteoglycans demonstrated the importance of macromolecules on cell membranes during inflammation-triggered stimuli. Studies used the tropical sea squirt Styela plicata, which in the presence and absence of TNFalpha resulted in complex changes in inflammatory cytokine and adhesion molecule expression. The induced inflammatory response was considerably reduced by S. plicata heparin treatment.

Report: https://cordis.europa.eu/docs/results/247/247516/final1-final-doc-2.pdf

Impact: In the 36 months of the program the scientists involved worked applying the techniques necessary for the glycosaminoglycans purifications and all analyses were correctly carried out sharing techniques procedures. Another important aspect was addressed in this project related to the O-GlcNAcylation. In fact **it was demonstrated that several enzymes involved in biological processes are regulated by O-GlcNAcylation** and this process seems to be related to hexosamine pathway, one of the metabolic markers of diabetes and a pro inflammatory condition. An important achievement was obtained by the study on glycans purified from adult specimens of the ascidians Styela plicata, Asidia nigra, collected in Rio de Janeiro at Guanabara Bay. **A critical sulphation pattern was identified in heparin sulphate chains of membrane proteoglycans. The cancer model demonstrated the critical function of this proteoglycan in cancer development and invasiveness.** INFLAMA results have featured in no less than 54 peer-reviewed papers, conference presentations and international meetings.

Information by *Alberto Passi / ITA / IT, 30.9.2023*

Impact of collaborative basic research at EU level **- example 5:** Human biology relevant to human health

Project: Multiscale approach to the identification ofmolecular biomarkers in acute heart failure induced by shock

Acronym: ShockOmics

Call: Type of funding scheme: SME-targeted Collaborative Project (small or medium-scale focused research project)

Work programme topics addressed: HEALTH.2013.2.4.2-1

The proposal is structured around the following Scientific Questions: i) What are the fundamental cellular and molecular mechanisms for acute HF following systemic inflammation induced by shock? ii) What are the cellular responses that shock causes in the myocardium, in terms of gene expression regulation,protein synthesis, metabolic alterations? iii) What are the circulating biomarkers of acute HF? iv) What is the relationship between such biomarkers, the biochemical parameters, and the hemodynamic measurements, which are routinely available in EDs, ICUs, and ORs? v) What are the exact regulatory points in the cascade, which could become targets for a cardioprotective therapy against shock? vi) Based on the answers to the previous questions, how can we design new technologies for the prevention of life threatening events in critically ill patients, and how can innovative multiscale monitoring techniques be implemented so that therapies are delivered as efficiently as possible?

Budget: € 6 703 316,95, of which EU € 5,174,001.00

Period: 01.10.2013 – 30.09.2017

Partners: 10 partners from 6 countries (Politecnico di Milano coordination, Tedeschi a WP leader)

Summary: The management of hemodynamic stability in shock patients is of paramount importance in the intensive care unit (ICU). New, cutting edge knowledge is necessary to overcome the shortcomings of available therapies, which are targeted to reduce symptoms of shock and multiple organ failure. However, they are unable to target the root cause or to act at the “beginning of the cascade”, because of the lack of a model explaining the molecular basis of shock-induced tissue injury and ensuing multiple organ failure.

Report: https://www.shockomics.deib.polimi.it/?page_id=165

Impact: **The ShockOmics project focused on the molecular triggers of acute heart failure in association to shock, in the presence of uncontrolled proteolytic activity, in order to identify inflammatory mediators and markers which are activated in shock and novel targets for the delivery of new therapies**. In this framework, several biosample and data sources were integrated by clinical records. Analyses spanned all omics technologies (metabolomics, proteomics, peptidomics, and transcriptomics) and omics outcomes were integrated with clinical indexes and parameters relevant to cardiovascular (CV) regulation from hemodynamic monitoring. Artificial intelligence and data-mining methods were applied to work out risk prediction algorithms. Therapeutic advancements were pursued starting from the “autodigestion hypothesis”, which focuses on the detrimental proteolytic effects from digestive enzymes leaking from the intestinal compartment via the wall damaged by the ongoing shock. This pushed to confirm previous experiments on rats both in the same species and in the swine shock models. The latter experiments asked to further develop technologies for intestinal infusion through the naso-gastric access beyond the pylorus by a dedicated infusion line and smart control pumps.

***Information by** Gabriella Tedeschi / Lodi- Milan / IT, 02.10.2023*

Impact of collaborative basic research at EU level **- example 6:** Animal biology relevant to human health

Project: Health and the Understanding of Metabolism, Aging and Nutrition

Acronym: HUMAN

Call: HEALTH.2013.2.1.1-1: Functional validation in animal and cellular models of genetic determinants of diseases and ageing processes. FP7-HEALTH-2013-INNOVATION-1.

Intense research identified around 4,000 single nucleotide polymorphisms (SNPs) associated with human age-related diseases such as metabolic disorders. The evolutionary distance of most animal models from humans represents a major limitation for the functional validation of these SNPs. To overcome these difficulties, HUMAN will generate mouse models carrying human hepatocytes or pancreatic β-cells from either primary cells (hepatocytes) or induced pluripotent stem cells (iPSCs). This innovative approach offers the unique possibility of studying the function of genetic risk variants associated with metabolic diseases in an integrated living system (the mouse body), but within human-derived organs, i.e. liver and pancreas. We will test the effect of different nutritional regimes (e.g. high fat diet, caloric restriction), to disentangle the complex molecular mechanisms and circuitry across organs (e.g. hypothalamus-liver axis) which lead to pathology.HUMAN will generate iPSCs biobanks and comprehensively manage all associated information. HUMAN is uniquely situated to drive innovation towards a better knowledge of the genetic basis of human metabolic diseases, thereby contributing to healthier aging of European citizens.

Budget: € 16,154,075.44 of which EU € 11,994,553.00

Period: 01.10.2013 – 30.09.2018

Partners: 17 partners from 8 countries (Karolinska Institutet KI, coordination)

Summary: HUMAN carry out large-scale multi-centre metabolic phenotyping of humanised animal and cellular models. Based on genotype, metabolic and healthy longevity phenotypes, fibroblasts from donors were selected. These cells were induced into pluripotent stem cells for further differentiation to hepatocytes or pancreatic β-cells for humanisation of mice.. Researchers made significant progress towards generating the mouse models with humanised liver or pancreatic β-cells in the first project period. After obtaining ethical approval as well as completing material transfer agreements and generating new standard operating procedures, fibroblast cell lines required for induced pluripotent stem cell production were shipped to partner laboratories and induction started. Scientists also genotyped several liver cell samples to identify donors with the highest number of risk or protective alleles. Also, they determined that FRGN mice with humanised liver are a better model for studies of human metabolism than the FRG mice with humanised liver.

Report: https://cordis.europa.eu/project/id/602757/reporting

Impact: **The research activities and the results generated by the HUMAN consortium have a great impact on different levels in the study of longevity, development of metabolic syndrome, on the physiological regulation of metabolisms, and on the cross talk between the brain and gut**. A significant contribution to the need for generation of animal models that recreated the human condition is the prove that the humanised liver mice, were able to reproduce the negative outcome of the first clinical trials in human in which a nuclear receptor was targeted in the liver. The work of HUMAN may thus positively shorten the time between discovery and implementation into clinical care, by showing a way how already in a pre-clinical stage predict the outcomes of phase 2 clinical trials.
The results achieved from the analysis of humanised mouse livers highlighted human genotype-associated changes in the function of the human hepatocytes with involvement of metabolic and cellular organisation processes.

Information by *Maurizio Crestani/UNIMI/IT, 03.10.2023*

Impact of collaborative basic research at EU level – example 10: Chemistry relevant to human health

Project: Integrating chemical approaches to treat pancreatic cancer: making new leads for a cure

Acronym: PANACREAS

Call: FP7-HEALTH-2010-two-stage

Pancreatic ductal adenocarcinoma (PDAC) causes 34000 deaths in the EU every year. Conventional cancer treatments have no impact on it and the search for new therapeutics is mandatory. We propose to build a team with clinicians, translational cancer researchers, chemists, and two pharmaceutical enterprises, to synthesize and implement new drugs for PDAC. These drugs will be validated using genetically engineered PDAC mouse models established at the Center for Integrated Oncology in Bonn. By creating and exploring diverse classes of compounds capable of arresting tumor growth and of interfering with its metastatic spread, this project will deliver a high number of new molecules with potential as anticancer therapeutics. In particular, our consortium will produce new indoleamine 2,3-dioxygenase-2 inhibitors, galectin-3 inhibitors, edelfosine analogues, inhibitors of the Hippo signaling pathway, alpha-mannosidase inhibitors, SIRT6 inhibitors, and therapeutics acting by synthetic lethality. For compounds with strong proof-of-concept activity, our consortium will perform the Investigational New Drug (IND)-Enabling Studies, with the goal of delivering a new drug ready to be tested clinically by the end of the project. The PANACREAS project is meant to help find better treatments for PDAC, boost research on this form of cancer in the EU, and open new avenues for scientific and technological innovation.

Budget: € 3 899 823,25, of which EU € € 2 965 207,00

Period: 01.03.2011 – 29.02.2016

Partners: 11 partners from 5 countries (UNIVERSITATSKLINIKUM BONN coordination, Bruzzone a Unit PI)

Summary: The PANACREAS project proposed to build a multidisciplinary team to synthesize, implement and test new drugs for PDAC. These drugs were meant to work through diverse and novel modes of action, targeting oncogenic pathways, mutated tumor suppressors and aberrant biological functions which still lack clinically applicable inhibitors. The most promising structures identified during the project have been validated for their therapeutic potential in the UKB laboratory, using an established genetically engineered PDAC mouse models and orthotopic PDAC xenografts.

Report: https://cordis.europa.eu/docs/results/256/256986/final1-final-report-an.pdf

Impact: The PANACREAS team recruited clinicians, translational cancer researchers, chemists and pharmaceutical industry partners. In an integrated effort, they worked to synthesise and test drugs for PDACs that target various oncogenic pathways. **Assays, models and in silico research was carried out to identify inhibitors of various tumour suppressors such as Yes-associated protein (YAP) or enzymes (SIRT6, IDO2, and alpha-mannosidase) that may be implicated in PDAC pathogenesis**. Compounds identified and active in PDAC models include: a kinase inhibitor interfering with YAP, edelfosine analogues, new galectin inhibitors. The most promising compounds identified during the project will be validated for their therapeutic potential using an established genetically engineered PDAC mouse model and orthotopic PDAC xenografts. Strong anticancer activity by any of these drugs will give the green light for their future testing in clinical studies and hopefully for their clinical application.

Information by *Santina Bruzzone / UNIGE / IT, 06.10.2023*

Impact of collaborative basic research at EU level **– example 11:** Plant biology relevant to crop improvement

Project: Control of flowering time for sustainable and competitive agriculture and forestry

Acronym: CONFLOW-QLRT-2000-01412

Call: FP5-Life Quality programme. This project aimed to develop widely applicable genetic tools that allow the genetic control of flowering for the purpose of containment of transgenes, as well as the fine-tuning of flowering time in agriculturally important crops and trees. Biological containment of transgenes via flowering control (non-flowering) is aimed at crops where the vegetative parts are harvested, for example, forage grasses, sugar beet and certain vegetables. The fine-tuning of flowering, either acceleration or delay, allows existing crop varieties to be harvested at the optimal time and exploited in new geographical areas or in response to long-term changes in climatic conditions and land-use policy.

Budget: € 2-3M?

Period: January 2001 – August 2004

Partners: Eight academic + two commercial partners from 8 countries (DLF Trifolium (DK) coordination, Claus Andersen as coordinator)

Summary: Partners were involved in the identification of novel flowering time regulators (activators and repressors) from Arabidopsis and subsequently examined the functional conservation of these novel and known flowering regulators in a number of crops (e.g. rice, sugar beet, Lolium) and woody species (citrus, birch, poplar). Flowering regulators involved in the vernalisation pathway were used in crops to obtain non-flowering sugar beet and *Lolium perenne*. Non-flowering ryegrass were generated with a chemically inducible switch to induce flowering upon demand for the purpose of seed production. In parallel, a risk assessment analysis was performed of the effectiveness and stability of the biological containment through controlled experiments with non-flowering ryegrass under different environmental conditions. Inducers of flowering were used as a proof-of-concept to obtain transgenic early flowering poplar and citrange trees that flower after a few months instead of the normal 10-15 years.

Report: ?

Publications Key publications: #1. Levy Y. et al. Multiple roles of Arabidopsis VRN1 in vernalization and flowering time control. Science 297, 243. (2002). #2. Searle I.R. and Coupland G. Induction of flowering by seasonal changes in photoperiod. EMBO J. 23 (6): 1217-22. (2004).

Impact: **CONFLOW delivered a genetic toolbox with flowering regulators that can be exploited in crops and trees to induce or suppress flowering or generate crops that do not respond to changes in environment (e.g. photoperiod or vernalisation).** The prevention of flowering in crops and forest trees is a major target for the industry and relevant for vegetables (e.g. lettuce), field crops (e.g. sugar beet, ryegrass) and trees to improve quality, production and wood formation. Early flowering crops can dramatically impact the breeding process. For trees, breeding is severely hampered by a life cycle of 5-20 years, but with the current flowering toolbox, this can be substantially accelerated. For the breeding industry it is extremely important to bring new cultivars onto the market a.s.a.p. Therefore, they are developing 'speed-breeding' protocols, also for annual and biennial crop species, making use of flowering inducers and trigger flowering by optimal environmental conditions. The tools developed to fine-tune flowering time will help to make it predictable, even under unforeseeable environmental fluctuations (e.g. weather conditions), and help to adapt new and existing varieties and crops to their location and changing climate. Nowadays, with the new developments in gene editing (CRISPR/Cas) it is possible to modify gene expression very precisely and with a set of inducers and suppressors of flowering in hand we can now direct flowering in both ways.

Information by *Gerco Angenent / Wageningen UR/ NL, 15.01.2024*

Impact of collaborative basic research at EU level – **example 13:** medicine – organ transplantation

Project: The ONE Study - A Unified Approach to Evaluating Cellular Immunotherapy in Solid Organ Transplantation

Acronym: The ONE Study

Call: FP7-HEALTH - Specific Programme "Cooperation": Health, Call ID: FP7-HEALTH-2010-single-stage.
The ONE Study applies the novel concept of cell therapy to human clinical organ transplantation. This cooperative project aims at developing and trialling various immunoregulatory cell products in organ transplantation recipients, allowing a direct comparison of the safety, clinical practicality and therapeutic efficacy of each cell type. The central focus of the ONE Study project is to:

- Produce and manufacture distinct population of haematopoietic immunoregulatory cells,
- Comparatively study the tolerogenic characteristics of these regulatory cell types;
- Test these cell therapy products side by side in a clinical trial living donor renal transplant recipients.

The health economics of cell therapy as a new medical technology is another essential aspect of the ONE Study work program that will be fully evaluated. True viability of the proposed new cellular treatments will depend not only on their clinical benefit, but also on an acceptable health-economics profile. The project had 6 working packages, 4 more related to applied research and 2 (WP5 and WP 6) to basic research. WP5 dealt with comparative characterization of cell products and WP 6 with new cell populations with tolerogenic potential.

Budget: Total cost € 14 629 391,35; Grant agreement ID: 260687

Period: 1 November 2010 to 31 October 2017

Partners: 15 partners from 5 countries (coordination: Prof. Geissler, Regensburg)

Summary: **We uniquely delivered meaningful and reliable information about regulatory cell therapy to the organ transplantation community**; for instance the description of both T cell and monocyte-derived cell products and details of immune regulatory cell properties. Based on The ONE Study, the UK group has already initiated a randomised trial called the TWO Study with their polyclonal Treg cell product (ISRCTN11038572), and other ONE Study partners (Massachusetts General Hospital: NCT03577431 and UCSF Medical Center: NCT02188719) are doing trials in transplant recipients with cell products used in The ONE Study. Opening the way to these and other more advanced clinical trials was the unifying philosophy of The ONE Study.

Report: https://cordis.europa.eu/project/id/260687/reporting

https://pubmed.ncbi.nlm.nih.gov/?term=Regulatory+cell+therapy+in+kidney+transplantation+lancet&sort=date

Impact: Regulatory cell therapy is achievable and safe in living-donor kidney transplant recipients, and is associated with fewer infectious complications, but similar rejection rates in the first year. Therefore, **immune cell therapy is a potentially useful therapeutic approach in recipients of kidney transplant to minimise the burden of general immunosuppression.**

Information by *Birgit Wittl and Christine Bayer, University Hospital Regensburg, DE, 27.2.2024*

Impact of collaborative basic research at EU level – **example 17:** aeronautics

Project: Innovative Methodologies and technologies for reducing Aircraft noise Generation and Emission.

Acronym: IMAGE

Call: H2020-EU.3.4. - SOCIETAL CHALLENGES - Smart, Green And Integrated Transport (MG-1.10-2015 - International cooperation in aeronautics with China)

Budget: 3.6 M€ (1.8 M€ from EU + 1.8 M€ from China)

Period: 2016 - 2019

Partners: 22 partners (12 EU partners + 10 Chinese partners)

Summary: The project, IMAGE (Innovative Methodologies and technologies for reducing Aircraft noise Generation and Emission), aims at investigating experimentally and numerically innovative airframe and engine noise-reduction technologies and, in a systematic conjunction, to develop robust numerical and experimental methodologies of addressing these technologies. Airframe noise is addressed by tackling landing gears and high-lift devices, and engine noise through its fan component. Fundamental investigations of three key control strategies are carried out: plasma actuation, turbulence screens and innovative porous materials, on a platform of three configurations, relevant to airframe and aero-engine noise generation and control, including a wing mock-up, tandem cylinder and engine-fan duct. Beyond this, IMAGE explores further the installation effect of aeroacoustic engine-jet/wing interaction, as well as low-noise concepts and optimal noise actuation methods by means of aeroacoustic optimization.
The overall objectives of the IMAGE project are: (1) to investigate innovative control technologies and strategies that are able to effectively manipulate airframe and engine noise in terms of suppression of noise generation and propagation; (2) to understand the physical mechanism of noise control and reduction in deployment of these technologies; (3) to improve current methodologies and technologies in aero-acoustic measurements and numerical analysis; (4) to investigate low-noise concepts with minimum or null penalty for aerodynamic performance, loads and cost; (5) to reinforce at European level the EU-China collaboration and mutual understanding in dealing with global environmental problems in relation to aircraft noise emission footprint.

Report: https://cordis.europa.eu/project/id/688971

https://cordis.europa.eu/project/id/688971/reporting

Impact: The project, IMAGE, focusing on “Innovative methods and numerical technologies for airframe and engine noise reduction”, targeted for reducing aircraft noise generation in line with Flightpath2050. The project has concluded a **comprehensive understanding of the physical mechanisms concerning flow-induced airframe and engine-fan noise generation, propagation and control,** and of further improvement of beam-forming technology and noise source identification in aero-acoustic experimental analysis. The experiment has generated well-documented database, supporting the development of numerical modelling and simulation methodologies for reliable validation and verification. With technical synthesis and industrial assessment, the noise control methods have been optimized and made **steps towards potential industrial use, and the methodologies developed have formed a robust part of advanced tools in industrial practice**.

Information by *Helge Pfeiffer helge.pfeiffer@kuleuven.be & Elena Jasiūnienė elena.jasiuniene@ktu.lt, 11.4.2024*

Impact of collaborative basic research at EU level – **example 18:** aeronautics

Project: Enhancing structural efficiency through novel dissimilar material joining techniques

Acronym: SAFEJOINT

Call: FP7-NMP-2012-SMALL-6

Budget: 4 093 335 € (EU contribution € 3 130 477,00)

Period: 1 January 2013 - 31 December 2015

Partners: 9 partners from 7 countries

Summary: The objective of the project - to develop novel techniques for metal to metal and metal to composite joining as well as developing novel techniques for the non-destructive inspection and evaluation of such joints to enhance confidence to designers and end-users of hybrid structures of them through life safe performance. There is a high demand for the design of lightweight energy efficient structures for transport applications to meet CO2 emissions targets set worldwide. To achieve this, designers have introduced the concept of "hybrid" structures where two or more lightweight materials are used each possessing unique properties that when joined together result in high performance lightweight structures that would not have been possible if a single material was used. This approach requires the development of joining techniques for materials with fundamentally different physical properties that will ensure the safe and reliable transfer of load between the constituent materials.

Report: https://cordis.europa.eu/project/id/310498/reporting

Impact: Enhancing structural efficiency in aeronautics. **Joining of dissimilar materials has been a challenge in various industrial applications** and over the years methods and technologies to improve joining as well as methods to reliably inspect those joints have **constantly been sought by industry**. SAFEJOINT has made a **significant progress** in this respect **by developing innovative technologies that enhance the joining strength of dissimilar materials and reliable inspection techniques.** The project has generated significant interest in both the research community and industry, demonstrating its impact by generating new and innovative ideas and approaches.

Information by *Helge Pfeiffer helge.pfeiffer@kuleuven.be & Elena Jasiūnienė elena.jasiuniene@ktu.lt, 11.4.2024*

Impact of collaborative basic research at EU level – **example 19:** aeronautics

Project: Flow physics modelling – an integrated approach

Acronym: FLOMANIA

Call: EU FP5-GROWTH - Programme for research technological development and demonstration on "Competitive and sustainable growth 1998-2002" (1.1.3.-4. - Key Action New Perspectives in Aeronautics)

Budget: 5.21 M€

Period: 2002 - 2004

Partners: 17 partners

Summary: The primary objective of the FLOMANIA (Flow physics modelling as an industrial requirement) project was to provide the Europe. Aerospace Industry with a mechanism to exploit substantial advances made on the research side in the area of modelling and simulating turbulent aerodynamic flows. This is the key towards reliable integration of CFD into multidisciplinary methods and involves: (1). Establish of reliability, robustness and accurate knowledge of the limitations of currently used algebraic, one and two equation, eddy viscosity, models. (2). Generate the validated integration of new non-linear and EARSM models in industrial aerodynamic CFD codes and, as the major aim, generate the validated integration of full DSM models in industrial codes. (3). Extend these implementations to the new generation of unstructured solvers, including the analysis of their impact on adaptivity. (4). Create the industrial transition process towards DES, representative of the next generation of turbulence modelling. (5). Establish the limits of validity of various model generation for industrial applications. (6). Ensure a high level of focused technology transfer in implementation strategies of turbulence models into the industrial codes.

Report: https://link.springer.com/book/10.1007/978-3-540-39507-2

Impact: The FLOMANIA project targeted the development of robust, reliable and accurate turbulence models for RANS (URANS) applications (with effort on both structured/unstructured /hybrid meshes and methods). Through the project work, a set of **existing weaknesses in turbulence modelling were overcome** by closing the gap between currently available RSM and industrially used 2-equ. models. The project **pioneered upstream research** taking into account DES method(s) for validation and for evaluating range of validity of RANS methods.
The project was considered an early initiative to **group the experts in research and CFD developer in Europe, to transfer their advanced knowledge to aeronautical industry in a controlled, objective-oriented way.**

Information by *Helge Pfeiffer helge.pfeiffer@kuleuven.be & Elena Jasiūnienė elena.jasiuniene@ktu.lt, 11.4.2024*

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Members of the ISE Horizon Europe Working Group

Martin Andler – President, ISE
Fernanda Bajanca – King's College London & children's hospital in France; former Chair, MCAA
Sandra Bendiscioli – Head of Policy, EMBO
Simon Clark – Policy Officer, EGU
Sebastian Dahle - Assistant professor at University of Ljubljana; President, Eurodoc
Monica Dietl – Executive coordinator, ISE
Maria Górna – Researcher at University of Warsaw, MCAA
Bruno Goud – Researcher emeritus, Institute Curie, EMBO
Gian Maria Greco – Professor at University of Macerata, Chair MCAA
Chloe Hill – Policy officer, EGU
Roland Imhoff – Professor at Gutenberg University Mainz, EASP
Elena Jasiuniene - Professor at Kaunas University of Technology, EASN
Kostas Kontis – Professor at University of Glasgow, EASN
Mariluz Martínez Marco - External consultant EU affairs, EPS
Karin Metzlaff – *Chair of the Working Group* - Executive director, EPSO
Helge Pfeiffer – Assistant professor at KU Leuven, EASN
Enrique Sánchez, *Vice-chair of the Working Group* – Policy officer, EPS
Gottfried Schmalz – Professor at University of Regensburg, PER-IADR
Martina Tekavec-Bembic - Senior Professional Associate at National Institute for Biology, SI EPSO
Mauro Torti – Professor at University of Pavia, FEBS
Carolina Varela – Policy Officer, ICoRSA
Melita Vidacovic – Full Research Professor at University of Belgrad, FEBS

For inquiries, please contact:
Karin Metzlaff – karin.metzlaff@epsomail.org
Enrique Sánchez – enrique.sanchez@eps.org
Monica Dietl – monica.dietl@initiative-se.eu

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