Stairway to Excellence
Cohesion Policy and the Synergies with the Research and Innovation Funds

Example of Synergies

Molecular scissors for double stranded RNA
- International Institute of Molecular and Cell Biology (IIMCB)

Poland

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Executive Summary
The resourceful combination of funding from national sources with Structural Funds (SF) and Framework Programme 7 (FP7) allowed the research team of Prof. Janusz Bujnicki to make breakthrough discoveries and identify a new enzyme, which helps cut double stranded RNA as "molecular scissors", making RNA suitable for DNA-like analyses. An FP7 ERC Proof of Concept grant was used to further elaborate the technology, ensure the IPRs protection and conduct market analysis, which helped identify a suitable commercial partner, with whom the Institute now collaborates in a nationally funded technology commercialisation project.

Type of synergies
- Upstream activities
- Sequential and parallel funding

S&T field targeted by the synergies
- Biotechnology
- ICT

The views expressed are purely those of the author and may not in any circumstances be regarded as stating an official position of the European Commission.
1. INTRODUCTION

The case presented in the following sections is one of the examples of synergies provided by the ‘Stairway to Excellence’ project in which different sources of funding have been combined to amplify the R&I investments and their impact on the economy and wider society.

As described in the guide ‘Enabling synergies between European Structural and Investment Funds, Horizon 2020 and other research, innovation and competitiveness-related Union programmes’, synergies can be achieved through:

- **Sequential (or successive) funding** that use funds in separate projects built on each other;
- **Parallel funding** that use funds in separate projects complementing each other;
- **Simultaneous/cumulative funding** that brings together Horizon2020 and ESIF funds in the same project aimed at achieving greater impact;
- **Alternative funding** that reorients FP7/Horizon 2020 projects that were positively evaluated, shortlisted, but not funded given the limited budget, towards Structural Funds impact.

The combination of sources of funding is used to address two types of activities:

- **Upstream activities** build the appropriate capacities to perform research. They can be capacity building in physical capital (construction or improvement of research infrastructures, purchasing equipment, (including IT equipment and connections), data storage capacities), innovation infrastructures (LivingLabs, FabLabs, Design factories, etc.) and social capital (assistance for building networks, clusters and consortia).
- **Downstream activities** are focussed towards the market and the creation of economic value. They can be applied to research, development and demonstration activities, technology transfer and adoption; technology and innovation audits to identify potential demand for RDI results; proof-of-concept funding; pilot lines for first production; and pre-commercial procurement projects. There can also be activities to support the improvement of the innovation eco-system in a territory.

2. CONTEXT

The research programme started with a nationally-funded project, concerning restriction enzymes for RNA (2007-2010). The scientists discovered a previously unknown activity of BsMiniIII enzyme, which could cleave double stranded RNA (dsRNA) molecules as molecular “scissors”. The discovery of BsMiniIII dsRNase activity suggested the way for analysing RNA in ways analogous to DNA sequence analysis.

The research team benefited from parallel investments in the research infrastructure of the Institute, financed from SF (2009-2015), which helped develop computational services to support novel methods and algorithms for research projects, as well as the dissemination of the outcomes of work by Prof. Bujnicki’s team to the wide scientific community.

In 2010, Prof. Bujnicki was awarded a grant based on the SF support measure “TEAM”, offered by the Foundation for Polish Science, to model RNA and protein-RNA complexes from sequence to structure to function, using a combination of laboratory and bioinformatics efforts (2010-2014). The scientific outputs included new bioinformatics techniques for analysing RNA interactions with selected types of ions and molecules. The project was complemented by the FP7 ERC Starting Grant, which focused on other types of RNA modelling (2011-2015). Framework Programme (FP) funding allowed the team to characterise in detail the dsRNase activity of BsMiniIII enzyme, initially funded by the ‘Stairway to Excellence’ project.

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discovered in the nationally-funded project. RNA molecules relay genetic information between DNA and proteins, regulate processes occurring in cells and constitute the genetic material of viruses causing influenza, rabies, Ebola and AIDS.

The development of a RNA cleaving method was welcomed by the scientific community and an article published in “Nucleic Acid Research” was distinguished by the journal as a “Breakthrough Article”. The Researchers patented their invention and used the FP7 ERC Proof of Concept grant (2013) to support its commercialisation. Co-operation was established with a domestic company A&A Biotechnology, and the consortium uses a nationally-funded grant (2015-2018) to further optimize the previously discovered or engineered enzymes and develop technological products.

3. IMPLEMENTATION

The synergies covered by this case include sequential funding for a comprehensive, multi-annual research programme, based on SF, FP and national sources, covering the entire innovation cycle, with basic and applied research, technology demonstration, IPR protection and development of products. Parallel funding was used to supplement FP7 projects and establish the critical mass needed for ambitious empirical research. The projects generated substantial know-how, patentable inventions and bioinformatics solutions, as well as international recognition of the Polish research team. The synergies were enabled by the availability of dedicated support measures, complementing FP7, based on SF and state budget. Factors limiting the synergies included: relative complexity of implementation of SF-based projects compared with FP, and problems with attracting foreign postdocs due to the uncompetitive remuneration of researchers in Poland. The synergies and the projects involved in the synergies will be detailed in the following sections.

Figure 1 maps the project chronologically, the research activities of the organisation and the type of funding. It aims to give a picture of relations between projects revealing planned or unplanned dependencies (synergies) between projects and their source of funding.

Figure 1: Diagram of chronology of the main projects involved in synergies
**Added value / complementarities created by the synergies**

- Covering the entire innovation cycle, including basic and applied research, technology demonstration, IPR protection and development of technological products thanks to the synergies between different funding sources
- Continuous funding for a comprehensive research programme, with its subsequent stages - projects funded from separate sources - narrowing focus to finally develop highly innovative technological solutions
- Generation of substantial know-how, patentable inventions and bioinformatics solutions
- International recognition for scientific excellence
- Interdisciplinary approach, combining research in bioinformatics and biochemistry
- Ability to establish and maintain a large, world class research team
- Opportunity to attract Polish scientists returning from foreign research stays
- Establishment of ICT infrastructure including equipment, software and databases, which can also be used in future research projects, including publicly available bioinformatics solutions available to other researchers in Poland and abroad.

**Mechanisms facilitating the synergies**

- Creativity of researchers and project management specialists, capable of identifying and combining multiple sources of financing
- Existence of a dedicated office supporting R&D project management at the Institute with competent experts
- Availability of support measures directly complementing FP7 funding in Poland (“TEAM” and “IDEAS PLUS” programmes)
- National co-funding for FP- and SF-based R&I projects carried out by public research organisations.

**Main problems encountered in implementing the synergies**

- Complexity of application, implementation and reporting for SF-based projects compared with ERC or state-funded R&I grants
- Restrictive SF regulations concerning eligible costs, preventing some possible synergies
- Inefficiency of public procurement procedures in R&I projects, delaying project-related purchases and leading to sub-optimal decisions
- Challenges in finding suitable business partners for commercialisation of research results
- Support schemes tend to focus on measurable outputs of projects, not on stimulating scientific excellence - even though certain important discoveries could translate into a single patent and subsequent scientific article, which nevertheless generates a scientific breakthrough
- Funding for ICT research infrastructures is usually interpreted as establishing large data processing centres, while smaller-scale, more targeted investments such as in-house computational facilities have less opportunities for funding
- Problems in attracting foreign postdocs as members of the research team due to rivalry with the leading Western academic centres.

**Suggestions to improve the synergies**

- Strengthening long-term strategic R&I planning at both national and EU levels
- Stronger focus on quality rather than quantity in R&I funding - breakthrough results require long research efforts and might not be attained without combining multiple funding sources
- The need for a stronger recognition of researchers who secure external R&I funding and successfully complete projects in Poland’s science system
- The need to ensure comparable remuneration of researchers funded by H2020 projects across the EU to attract foreign scientists to Poland and stop the brain drain of Polish researchers
Deepening science-industry dialogue and collaboration, while appreciating their different motivations to pursue R&I projects
Streamlining SF procedures and modalities to more closely resemble standards adopted by FP7/H2020
The establishment of dedicated funding calls for beneficiaries of SF or FP support measures to ensure sequential funding for their projects across the entire innovation cycle.

Main motivations in implementing the synergies
- Securing funds to ensure the continuity of R&I programme throughout subsequent stages of the innovation cycle
- Building up on successes achieved and further elaborating deliverables from previously completed projects.

Facilitating mechanisms for the take up of the scientific results
- International Institute of Molecular and Cell Biology employs experts supporting researchers in administrative, legal and financial matters on a permanent basis in addition to specialists funded from project budgets
- Institutional funding allocated to scientific organisations based on regular assessments, taking into account research excellence, provides the bottom line for the Institute’s operations and is supplemented by dedicated grants from multiple sources
- Funding for the promotion of research results, IPR protection and commercialisation secured thanks to a careful selection of specific, well-targeted support measures on national and EU levels
- IPR regulations facilitating institutional ownership of scientific inventions and availability of dedicated national funding for international IPR protection.

Impact on the regional / national economy
- The scientific reputation of the Institute in the global field of biotechnology
- Development of an innovative technology, which has the potential to generate successful export products for Poland
- Pursuit of the science-industry collaboration to commercialize the technology
- The establishment of a world class research team and ensuring the continuous research involvement of the team members
- The reintegration of experienced Polish scientists, returning from research stays at leading Western universities.
Figure 2 aims to position projects according to the activities they cover; from upstream (infrastructures, equipment, research activities) to downstream related activities (innovation, knowledge transfer, access to market).

**Figure 2: Diagram of the complementarities of the funds in the knowledge triangle / flow**

- **National Project 1:** “New tools for analysis and manipulations of nucleic acids” (MNiSW, 2007-2010)

- **SF Project 1:** "Biocentrum Ochota" (POIG 2.3), 2009-2015

- **FP Project 1:** “RNA+P=123D” (FP7 ERC SG), empirical research of RNA sequence-structure-function relationships (2011-2015)

- **National Project 2:** “RNA+P=123D” (IDEAS FOR POLAND), parallel funding to ERC SG (2011-2015)

- **National Project 3:** “Development of new products for biotechnological industry based on innovative RNA cleaving technology” (PBS, 2015-2018), technology commercialisation with A&A Biotechnology

- **SF Project 2:** "Modelling of RNA and protein-RNA complexes from sequence to structure to function" (POIG TEAM), 2010-2014

- **FP Project 2:** eRNAses (FP7 PoC) (2012), technology demonstration, IPR protection, market analysis

**Research** (Research Infrastructures, facilities, Research activity etc.)

**Training** (Continuous professional training, PhD fellowships etc.)

**Innovation** (Knowledge dissemination, knowledge transfer events, funding of the KTOs etc.)
4. RELATED PROJECTS

Name of the nationally funded project: “New tools for analysis and manipulations of nucleic acids: restriction enzymes acting on RNA and DNA-RNA hybrids”

- National funding scheme: “Research & Development Projects” (MNISW, Ministry of Science and Higher Education)
- Budget: 1,000,000 PLN (~ 0.23m EUR)
- Time frame of the project: 2007-2010
- Main objectives and type of costs covered: The project initiated Prof. Bujnicki’s comprehensive research efforts focused on identifying and engineering the so-called restriction enzymes for RNA, i.e. enzymes that could cut RNA strains in ways similar to widely known methods of cleaving DNA. In the course of the project, the research team discovered a previously unknown activity of BsMiniIII enzyme, namely the ability to cleave double stranded RNA (dsRNA) molecules as molecular "scissors". The discovery of BsMiniIII dsRNase activity suggested the way for analysing RNA in ways analogous to DNA sequence analysis. The team has also engineered a chimeric enzyme capable of cleaving specific RNA sequences in RNA/DNA hybrids. These initial discoveries have concluded the nationally-funded project and have led to further research plans that were subsequently pursued in SF and FP funded projects. The project budget included expenditures on research equipment, consumables (laboratory materials), salaries and conference trips.

Name of the SF PROJECT: “Biocentrum Ochota - IT infrastructure for development of strategic directions of the biology and medicine”

- SF funding scheme: Operational Programme Innovative Economy, 2.3 (Investments in ICT infrastructure of science)
- Budget: 4,834,300 PLN (~ 1.15m EUR)
- Time frame of the project: 2009-2014
- Main objectives and type of costs covered: The project involved the establishment of ICT research infrastructure and the development of computational services supporting novel methods and algorithms for other projects in IIMCB. The research efforts included setting up hardware/software system and the development of new software. Project outputs included a new database front-ends and web servers. The efforts were synergistic with other grants, including ERC and TEAM, and helped disseminate new methods developed in these grants to the wide scientific community. The project budget covered research infrastructure, software licences, and personnel cost and training.

Name of the SF PROJECT: “Modelling of RNA and protein-RNA complexes from sequence to structure to function”

- SF funding scheme: “TEAM” (Operational Programme Innovative Economy POIG, support measure 1.2 – FNP, Foundation for Polish Science)
- Budget: 2,200,000 PLN (~ 0.5m EUR)
- Time frame of the project: 2010-2014
- Main objectives and type of costs covered: The project involved the establishment of a database system and ontologies describing RNA modifications, accompanied by the elaboration of RNA modelling methods, related bioinformatics tools as well as techniques for predicting RNA interactions with metals, molecules and proteins. The research efforts combined laboratory work with software development. It contributed to the establishment of a publicly available MODOMICS database, maintained by the Institute, describing RNA modification pathways. The scientific outputs included new bioinformatics techniques for analysing RNA interactions with selected types of ions and molecules. The project was complemented by the ERC Starting Grant, which was initiated a year after the SF project and focused on other types of RNA modelling. Both approaches were used in combination in subsequent scientific experiments, and individual analytical methods from one project were
applied in the other to strengthen the results (e.g. a benchmark used to develop the “MinkoFit3D” method from SF project was also used to test the “PyRy3D” method from FP project), and ERC funding was used to continue selected elements of SF project. Foreign internship of one of research team members helped acquire and transfer know-how related to novel research techniques, which proved useful for the project, and the project included co-operation with leading foreign scientists for specifically identified research tasks. The project budget covered research equipment, consumables, salaries and international mobility.

Name of the FP PROJECT: “RNA+P=123D – Breaking the code of RNA sequence-structure-function relationships: New strategies and tools for modelling and engineering of RNA and RNA-protein complexes”

- FP funding scheme: ERC Starting Grants
- Budget: 1,500,000 EUR
- Time frame of the FP funded project: 2011-2015
- Main objectives and type of costs covered: The project involved the development of methods for 3D modelling and structure prediction of RNA, in particular of very large RNA molecules, in ways analogous to 3D modelling of proteins to facilitate interpretation of data encoded in gene sequences. It built upon the outcomes of previous, nationally funded projects, by testing and improving prototype tools. The efforts involved also the establishment of new ways of assessing the RNA structure model quality and benchmarking various modelling methods, and experimental verification of models with biotechnological and medicinal applications. In the course of the project, the research team characterised in detail the dsRNase activity of BsMiniIII enzyme, initially discovered in the previously described nationally-funded project. RNA molecules relay genetic information between DNA and proteins, regulate processes occurring in cells and constitute genetic material of viruses causing influenza, rabies, Ebola and AIDS. Unsurprisingly, the development of a RNA cleaving method was welcomed by the scientific community and the article “Sequence-specific cleavage of dsRNA by Mini-III RNase”, published in January 2015 in “Nucleic Acid Research”, was distinguished by the journal as “Breakthrough Article”. Before publishing the results, researchers filed priority application in the Polish Patent Office and initiated the international patenting process. The project results were presented at numerous conferences, seminars and guest lectures. Apart from the molecular “scissors” for RNA, the project yielded other results, described in multiple dozens of scientific publications, presented at international conferences and protected by another patent application. The project budget included expenditures on: laboratory equipment, consumables (materials used for experimental research), salaries of researchers and international visits including participation in scientific conferences. The salary of the team leader, prof. Janusz Bujnicki, was covered in 50% from the ERC grant, with the other half funded from the Institute’s budget, while other members of the research team were either fully remunerated from the project budget or combined with funding from other grants.

Name of the nationally funded project: “Breaking the code of RNA sequence-structure-function relationships: New strategies and tools for modelling and engineering of RNA and RNA-protein complexes”

- National funding scheme: “IDEAS FOR POLAND” (FNP, Foundation for Polish Science)
- Budget: 640,000 PLN (~ 0.15m EUR)
- Time frame of the project: 2011-2015
- Main objectives and type of costs covered: Additional funding for ERC Starting Grant beneficiaries, offered by the non-public Foundation for Polish Science, which complemented the FP7 funding to generate critical mass in empirical research projects. The project budget included expenditures on scholarship, supplementing the salaries from ERC grant.
**Name of the FP PROJECT: “eRNAses - Engineered Sequence-Specific RNases: New reagents for RNA biotechnology”**

- FP funding scheme: ERC Proof of Concept
- Budget: 149,970 EUR
- Time frame of the FP funded project: 2013
- Main objectives and type of costs covered: The project carried over results from the ERC Starting Grant in order to develop a proof of concept, related to cutting RNA sequences using the BsMiniIII enzyme and by the RNase-ZnF hybrid enzyme by finishing the prototypes’ development and carrying out their validation. It also helped protect intellectual property, conduct market research and establish relations with a suitable industrial partner to pursue technology commercialisation. The findings confirmed that the enzyme can indeed be used for producing RNA molecules, applicable among others in cell biology and thus potentially useful in nanotechnologies, as well as diagnostic and therapeutic techniques. The commercialization part of the project resulted in initiating co-operation with a specialist high-tech company A&A Biotechnology from Gdynia, Poland. The project budget included expenditures on laboratory research and professional services related to IPR protection and market analysis.

**Name of the nationally funded project: “Development of new products for biotechnological industry based on innovative RNA cleaving technology”**

- National funding scheme: “PBS” – Applied Research Programme (NCBIR, National Centre for Research and Development)
- Budget: 3,466,441 PLN (~ 0.8m EUR)
- Time frame of the project: 2015-2018
- Main objectives and type of costs covered: The project builds on the successful results of the previously described nationally, SF and FP funded projects and focuses on optimisation of previously discovered or engineered enzymes to make them useful in practice, as well as includes commercialisation of results of these efforts. It will be carried out jointly by the Institute and its corporate partner, A&A Biotechnology. The ongoing efforts are expected to generate novel products, based on the molecular “scissors” for double stranded RNA. The project budget includes: research equipment, consumables, salaries and external services, with co-funding component by the private sector company.