PROJECT FINAL REPORT

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Project acronym: **INNOVCRETE**

Project title:

Unlocking the innovative capacity of multidisciplinary structural biology-driven research in Crete

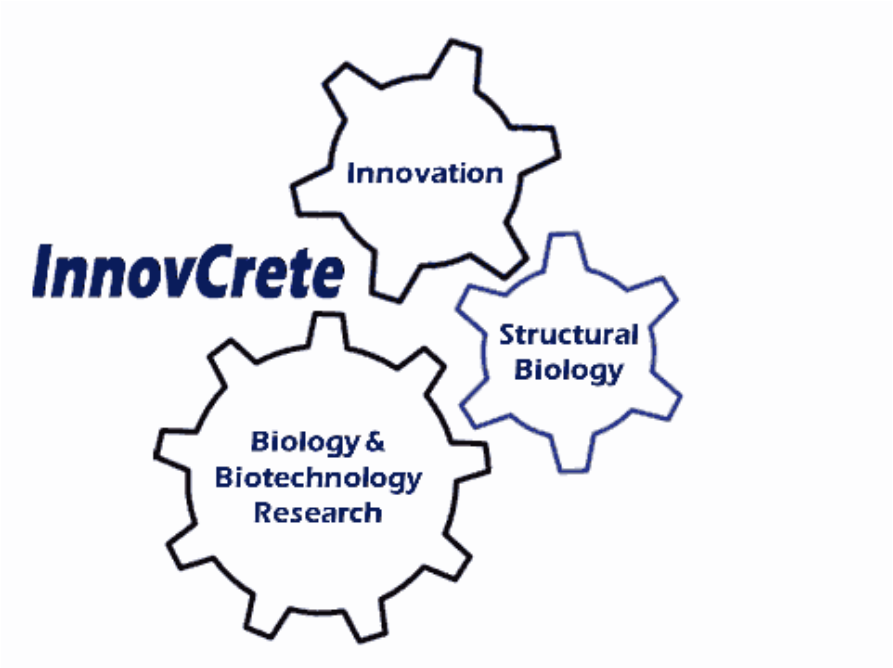
Funding Scheme: **Coordination and support action**

Period covered: from **1/11/2012** to **30/4/2016**

Name of the scientific representative of the project's co-ordinator, Title and Organisation:

Prof. M. Kokkinidis
IMBB/FORTH & University of Crete
Nikolaou Plastira 100 GR-70013, Heraklion, Crete GREECE
Tel: +30 2810 39114351
Fax: +30 2810 391101
E-mail: kokkinid@imbb.forth.gr

Project website address: **www.innovcrete.eu**



4.1 Final publishable summary report

Executive summary

Structural biology techniques are presently developing at an increasingly rapid pace. Whereas these disciplines have traditionally been tackled as single entities, this approach is no longer sufficient to gain a detailed and quantitative understanding of the dynamic structure and biological context of the cell. Structural biologists have now recognized the need and advantage of combining and integrating several different techniques to resolve a single biological problem in all its complexities. These advances and the incredibly fast rate of development constitute new challenges and opportunities with enormous innovation potential and defined the concept of the InnovCrete project.

The strategic interest in an integrated approach to structural biology-driven research and the promises it holds have been clearly recognized also in Crete. For this reason, the scientists of the Institute of Molecular Biology and Biotechnology (part of the Foundation for Research and Technology – FORTH) in Heraklion (Crete) have merged in the InnovCrete project their experience, knowledge, energy and enthusiasm, not only to strengthen their competence and innovative capacities, but also to sustain and enhance their perspectives in the European Research Area and to actively contribute to the strengthening of structural biology initiatives in Europe. InnovCrete aims to create an environment for high-profile structural biology research in Crete, to sustain scientific and technological excellence, and to significantly enhance the innovative capacity of biomedicine/biology, biotechnology and biomaterials research in Crete. Managed by IMBB and including top-tier European research establishments and facilities as partners, InnovCrete is a multi-disciplinary research platform for established and emerging techniques in structural biology, biochemistry, biomedicine and molecular biology. It supports key areas techniques opening up the study of important biological macromolecules in Crete, including important drug targets.

Access to state-of-the-art structural biology in Crete for both academia and SMEs has been only one facet of InnovCrete. Its workshops, conferences and exchanges, in partnership with world-leading academic organizations and SMEs, have promoted and developed innovative, integrated approaches to structural biology and established interdisciplinary network activities across Europe. InnovCrete has promoted excellence in skills development, and encouraged cross-border performance of research projects. It enhanced significantly the innovation capacity of FORTH and the Region of Crete as a whole, through efficient IPR management mechanisms, training in IPR and innovation management and the creation of a portfolio of exploitable results and infrastructures.

InnovCrete has attracted experienced and early-stage researchers and has helped retain some of the most innovative and creative structural and molecular biology professionals in the Region of Crete. It has achieved scientific breakthroughs that will spread the benefits of innovation in the Region of Crete and across the

European Union through strong links to scientific communities that share a passion for pushing the boundaries of existing scientific disciplines.

InnovCrete seeks also in future to increase the participation of its researchers to the EU RTD programmes. Its research is not be completely fundamental, but also contributes to solution of problems that are important for Crete, Greece and Europe as a whole in the areas of (a) Health-Biomedicine, (b) Agriculture/Food Security, (c) Biotechnology & Bio-inspired materials. Potentially exploitable results obtained in these fields are part of the technology portfolio of InnovCrete.

A summary description of project context and objectives

Structural biology is a branch of molecular biology concerned with the molecular structure of biological macromolecules such as proteins, DNA/RNA and viruses. Resolving a molecule's structure can give insights into the function of a molecule and eventually lead to drug targets, the development of new medicines, new bio-inspired nanomaterials etc. Structural biology and in particular the productivity of X-ray crystallography annd Free-Electron Lasers (FELs) is developing at an increasingly rapid pace. To determine the structure, proteins are usually crystallized, illuminated by X-rays, and the resulting diffraction pattern analyzed. This method of macromolecular crystallography is mainly carried out using X-rays generated at synchrotron facilities or conventional X-ray crystallographic facilities at structural biology laboratories. Furthermore the recent exciting demonstration of X-ray Free Electron Laser (XFEL) nano-crystallography has opened the door to a new era of structural biology. Apart from X-ray crystallography, structural biologists use many different techniques including Small Angle X-ray Scattering (SAXS), electron microscopy (EM), and a range of other biological/biomolecular imaging techniques. Whereas these disciplines have traditionally been tackled as single entities, this approach is no longer sufficient to gain a detailed and quantitative understanding of the dynamic structure and biological context of the cell. As each technique resolves structures at different resolutions and conditions, over the past few years, structural biologists have recognized the need and advantage of combining and integrating several different techniques to resolve a single biological problem in all its complexities. These advances and the incredibly fast rate of development provide new challenges and opportunities with enormous innovation potential. Synergies through the integration of structural biology with complementary research fields topic are turning into major **innovation engines** capable of meeting **European development concerns** and capable of sustaining **economic growth and employment** in Europe.

The strategic interest of structural biology-driven research and the promises it holds have been recognized as a clear thematic priority for development in Crete and created the basis for the **InnovCrete project**. For this reason, the **scientists of the Institute of Molecular Biology and Biotechnology (IMBB)** in Heraklion (Crete) and the wider academic community of Crete have merged in the project their experience and knowledge, so as to **sustain and enhance** their perspectives in the ERA and to actively contribute to the strengthening of

innovative structural biology based initiatives in Europe. The coordinating institute IMBB was founded in 1983 and is part of the Foundation of Research and Technology-Hellas (FORTH), one of the largest research centers in Greece. IMBB hosts approximately **30 research groups** and **160 scientists**. Over the years IMBB has been ranked as **the top Greek research centre in Biology**, across all fields of research, by international panels of experts appointed by the Hellenic Ministry of Development. IMBB now is recognized as one of the most productive and internationally esteemed research communities of southern Europe, thanks to its **high impact research results**. In this favourable environment, the InnovCrete project aims to become a dynamic hub of structural biology providing researchers in Crete access to an integrated infrastructure of cutting-edge technology and scientific expertise. We seek to provide strategic leadership for structural biology at a European level by promoting an integrated approach to technology and methodologies.

The aim of InnovCrete is to create an environment for **high-profile structural biology research** in Crete, to **sustain scientific and technological excellence** in Biomedical and Life Sciences and to significantly **enhance the innovative capacity** of biomedicine/biology, biotechnology and biomaterials research in Crete in areas that fall within major **priorities of the Innovation Union**. Managed by IMBB and including top tier partners in the EU, InnovCrete represents a **multi-disciplinary, multiscale research platform** for **established and emerging techniques** in structural biology.

InnovCrete comprises all IMBB Departments and supports **six key areas**: (1) macromolecular X-ray crystallography, (2) biological SAXS, (3) advanced biological imaging, (4) physicochemical techniques (MALLS, CD, EM etc) as well as (5) protein production/high-throughput crystallisation and (6) molecular modelling. One future goal of the InnovCrete project is to support very challenging structural biology projects at IMBB through the exploitation of XFELs.

Installation and access to state-of-the-art structural biology for both academia and SMEs is only one aspect of the InnovCrete project. The InnovCrete workshops, conferences and secondments, in partnership with world-leading academic organizations and local/European SMEs, focus on promoting and developing innovative, integrated approaches to structural biology. By establishing and expanding interdisciplinary **network activiti**es across Europe, InnovCrete has promoted excellence in skills development, and encouraged cross-border performance of research projects and involvement in European Research Infrastructures. It furthermore **enhanced significantly the innovation capacity of IMBB in the area o structural biology-driven research** (molecular diagnostics, drug design, protein engineering, bio-nanomaterials etc) through the setting up of efficient **IPR management mechanisms**, **training in IPR and innovation management** and the creation of a **portfolio of exploitable results and infrastructures**. Through its contribution to the creation of **Structural Biology Clusters** InnovCrete has contributed to a broader innovation capacity building in the Region of Crete and the country as a whole. By catalyzing high quality **collaborative** research and through the upgrading of experimental facilities at IMBB, InnovCrete is in position to attract **experienced researchers** to Crete and help **retain the most innovative and creative structural biology professionals** of the country in the research

centres of Crete. Through this integrated approach we aim to achieve breakthroughs in structural biology that are not possible with the previous infrastructure and spread the benefits of innovation across the Region of Crete and across the European Union.

We also seek to increase the participation of its researchers to the EU RTD programmes. In this context a strategy has been developed through scientific exchanges and the organization of workshops, conferences and seminars, to increase the **visibility** of excellence of IMBB research in the diverse fields of structural biology and its applications and to ensure the sustainability of **strategic partnerships** with top international research establishments and local/European SMEs.

InnovCrete research is not completely fundamental, but also **contributes towards solving problems** that are important for the region of Crete, Greece and Europe as a whole; these problems are highly relevant to present and future EU RTD programmes, i.e. making European science more innovative and competitive with the rest of the world, contributing to an increase of the wealth of Europe, and helping to overcome major socio-economic problems. InnovCrete addresses major EU and local priorities by focusing on major challenges facing society e.g. food security, health, bio-inspired technologies etc. Based on the research excellence and creativity of the IMBB scientists, the following scientific areas have been identified as promising sources of innovative ideas that can be turned in the future into products and services that create growth and jobs: (a) Health-Ageing, (b) Food Security, (c) Biotechnology & Bio-inspired materials, (d) Development/exploitation of Innovative Methods and Technologies.

The ultimate long-term objective supported under the InnovCrete action (also after termination of EU funding) is to turn IMBB into a leading European Centre of Excellence in structural biology, firmly integrated within the ERA, with a pool of competent and highly competitive researchers who are responsive to socio-economic regional or European development needs and capable of catalyzing innovation and the establishment of novel spin-offs and SMEs in the Region of Crete and in Europe. The InnovCrete initiative meets therefore perfectly the key priorities of EU, national and regional development policies.

In summary, InnovCrete has established since 2012 a state-of-the-art coordinated and multi-scale infrastructure for the exploitation of key methods in the 21st century structural biology in Crete. InnovCrete can now provide instrumentation and expertise for applications in six areas of structural biology: (i) biological small angle X-ray scattering; (ii) macromolecular X-ray crystallography; (iii) biological/biomolecular imaging; (iv)physicochemical techniques; (v) protein production, physicochemical characterization and high-throughput crystallisation; and (vi) molecular modeling. InnovCrete also cooperates with several partnering organizations and transnational/national networks which complement the

infrastructure of IMBB and provide an integrated technology platform with all relevant methods in structural biology that are available in large-scale infrastructures.

A description of the main S&T results/foregrounds

InnovCrete: an integrating multidisciplinary project

The main result of the InnovCrete project is the establishment in Crete of a considerable scientific expertise in structural biology in combination with a state-of-the-art infrastructure, for the benefit of IMBB/FORTH scientists, the broader scientific community in Crete and several research oriented companies. The project has provided instrumentation and expertise in several areas: (i) biological small angle X-ray scattering; (ii) macromolecular X-ray crystallography; (iii) biological/biomolecular imaging; (iv) physicochemical infrastructure; (v) protein production, physicochemical characterization and high-throughput crystallisation; and (vi) molecular modeling. InnovCrete has also cooperated with several partnering organizations and transnational/national networks such as BioStruct-X, ESUO and Be/Opt-Xfel which complemented the infrastructure of IMBB by providing integrated technology platforms for all relevant methods in structural biology that are available in large-scale infrastructures.

With its instrumentation, networking and expertise, InnovCrete promoted multidisciplinary/multi-scale research, combining different methods and hybrid approaches. The research projects developed within the InnovCrete framework generate a significant potential for innovation at IMBB and considerable exploitation opportunities. This was clearly demonstrated by three projects which produced exploitable results for patent filing.

The InnovCrete projects are frequently very challenging and can be only tackled with the upgraded capacity for structural studies developed through InnovCrete. The creation of an integrated environment for protein production, characterization, crystallization and data collection has created bridges that efficiently link biology and biotechnology research at IMBB projects with structural methods.

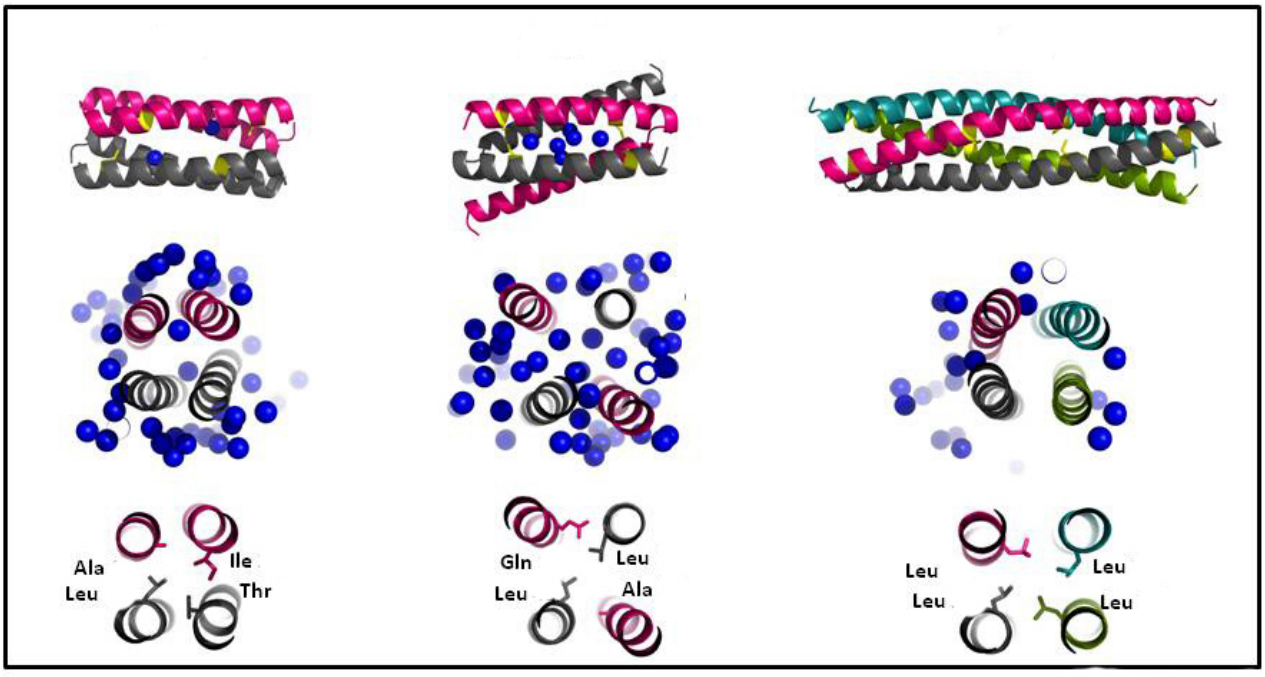
The S/T results of InnovCrete listed in the following are a selection among a large number of collaborative projects; however these provide at this stage the most promising opportunities for exploitation:

Re-engineering of the folding pathways of α-helical bundles, new self-assembly modes and bio-inspired materials.

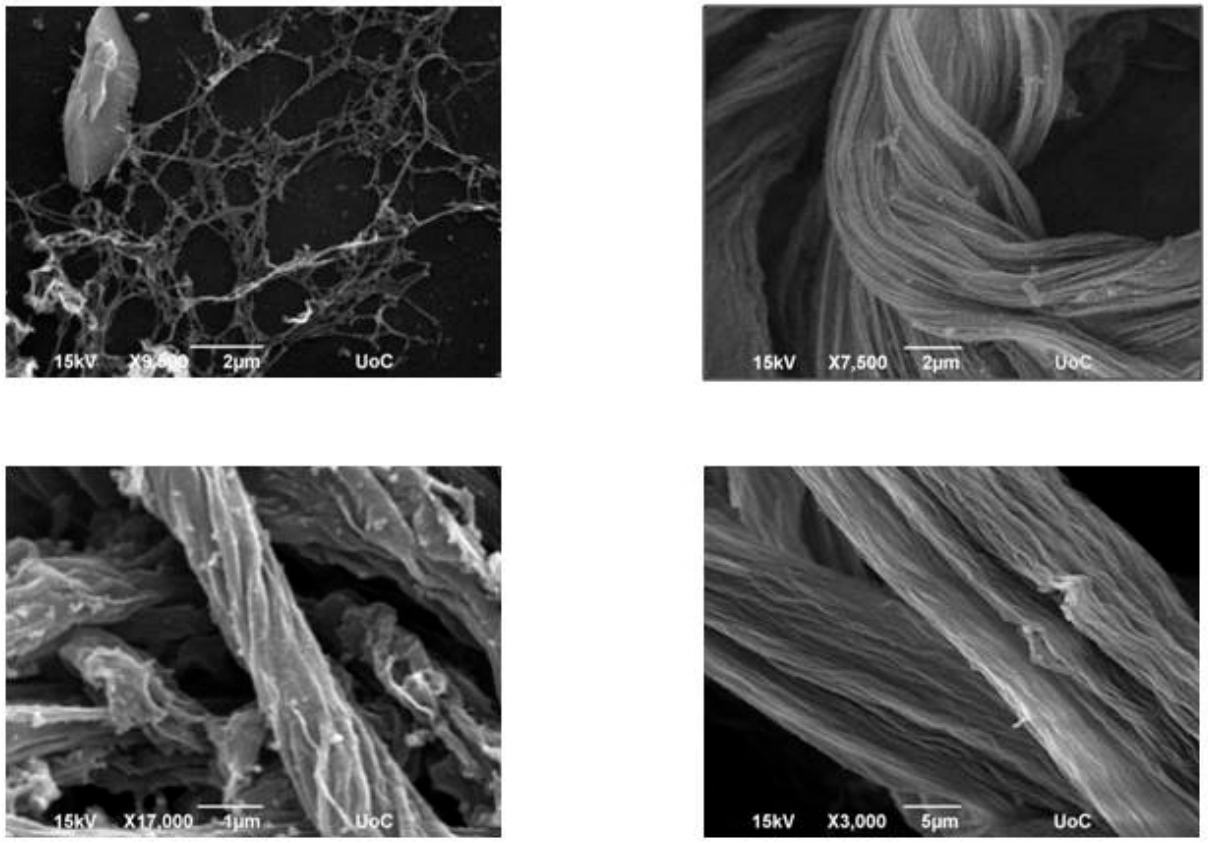
In the framework of InnovCrete project we elucidated the folding pathways of Rop protein, a paradigm of the 4-α-helical motif (Amprazi *et al.*, 2014, PNAS).

Subsequently we re-designed helical bundles as building blocks for novel biomaterials (fibres, hydrogels etc) and characterized their properties by biophysical (Size- Exclusion Chromatography, Circular Dichroism, FTIR) and structural methods (protein crystallography, SAXS, electron Microscopy). In addition, we explored the implications of the "decoration" of the resulting constructs (helical scaffolds, fibres, hydrogels) with selected enzymatic domains, initially endonucleases. We found that the chimeric enzymes not only retain the activity of the attached endonucleases, but if different domains are attached and the geometries of the scaffolds are taken into account, novel, highly specific endonuclease activities can be developed. These chimeric enzymes have a vast spectrum of potential applications, e.g. in genome modifications and gene therapy. Due to the structural plasticity of helical proteins, we were able to develop highly stable helical scaffolds that are suitable for the development of enzymes that remain active in extremely harsh environments.

Two scaffold-based protein engineering approaches are at the stage of patent filing for a) novel enzyme engineering methods and b) engineering of novel bio-inspired materials.



Structures of engineered helical proteins which reveal the structural plasticity of helical bundle motifs, a property which we exploited for the engineering of bio-inspired materials



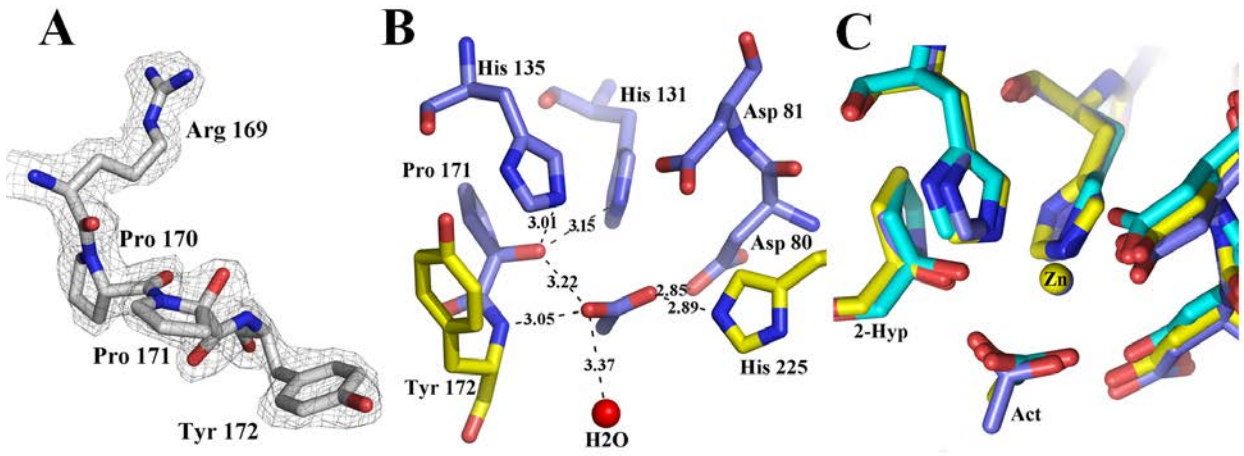
Functionalized fibres carrying novel restriction endonuclease specificities. The assembly of the fibres has been designed on the basis re-engineered helical bundle proteins

Discovery of unusual post translational modifications associated with bacterial pathogenicity mechanisms

Posttranslational hydroxylation of proline (Pro) side chains has a key role in collagen biosynthesis, plant cell wall architecture and regulates critical cellular signaling and degradation processes. Its full extent has yet to be established, as its occurrence is probably significantly broader than previously perceived. Its role in various diseases and new therapies is only recently becoming clear. On the other hand, Pro hydroxylation in bacteria is largely unexplored.

We discovered a so far unknown Pro hydroxylation activity which occurs in active sites of polysaccharide deacetylases (PDAs) from bacterial pathogens, targeting the protein backbone to produce 2-hydroxyproline (2-Hyp). Crystallographic studies complemented by mass-spectrometry and mutagenesis reveal details for the Pro→2-Hyp conversion which is possibly autocatalytic, modifies with high specificity a conserved Pro, and utilizes the same active site and one of the catalytic residues as the deacetylation reaction. The origin of the oxygen of the hydroxyl group of 2-Hyp is molecular oxygen. By

providing additional hydrogen bonding capacity, Pro hydroxylation alters the active site creating a more favourable environment for transition state stabilization, and thus potentially enhancing deacetylase activity. Although our results classify this process among the few examples of active site "maturation", it is atypical by being an intrinsic, backbone modifying activity, rather than an enzyme-catalyzed, side-chain modifying one. Our results pave the way for more detailed studies to explore the extent of 2-Hyp occurrence in eukaryotic and prokaryotic proteins as well as its implications in protein folding, stability and catalysis. More sophisticated concepts for PDA catalysis could improve our understanding of how Pro C_α hydroxylation affects defensive mechanisms of bacterial pathogens. Finally this work promises the development of novel antibiotics that target the maturation of PDA active sites in pathogens such as *B. anthracis*, *B. cereus* etc.



Crystal Structures of PDAs A) Detail of a 2Fo-Fc electron density map of Bc1960 calculated at 2.5σ and showing the presence of a 2-Hyp residue at position 171 B) View of the active site of Bc1960, showing the metal binding triad (residues Asp81, His131, His135), the catalytic Asp (Asp80) and 2-Hyp (Pro171). Note the closeness of the -OH group of 2-Hyp to the active site. The hydrogen bonding network which includes the active site acetate molecule (Act) and the amido group of residue Tyr172 which has a key role in the deacetylation reaction is also shown. C) Superposition of the active sites of Bc1960, Bc0361and Bc0330 showing also the position of the divalent metal.

Studies of the Type III secretion system of plant pathogens

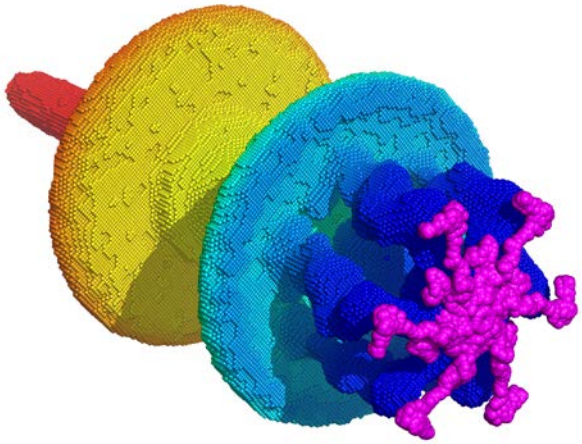
Pseudomonas syringae pathovars infect over 40 important crops worldwide and were deemed the most important bacterial plant pathogens. Infection involves gaining access and adapting to the plant's apoplast, proliferation, secretion of type three helper proteins (T3H) and injection (translocation) of type three effector proteins (T3E) into plant cells via the Type Three Secretion System (T3SS). Translocated effectors can abrogate the plant immune defense, likened to switching off the burglar alarm. The plant tissue environment triggers a genetic pathogenesis program in *Ps*, which critically involves the expression of T3SS

core genes, T3H as well as T3E genes. Plant tissue factors triggering *Ps* pathogenesis are poorly defined. The RNA polymerase activators HrpR-HrpS and one of their targets, the extra-cytoplasmic sigma factor HrpL are key transcription factors controlling all T3SS, T3H and T3E genes. HrpR-HrpS are negatively regulated by HrpV, whose activity is suppressed by HrpG. HrpJ of Ps is a protein of regulatory function and a secretion/translocation substrate itself; it is known to control the secretion of T3H and translocators, as well as the translocation of T3E, playing an additional role inside the plant following its translocation, which is suppression of host immunity.

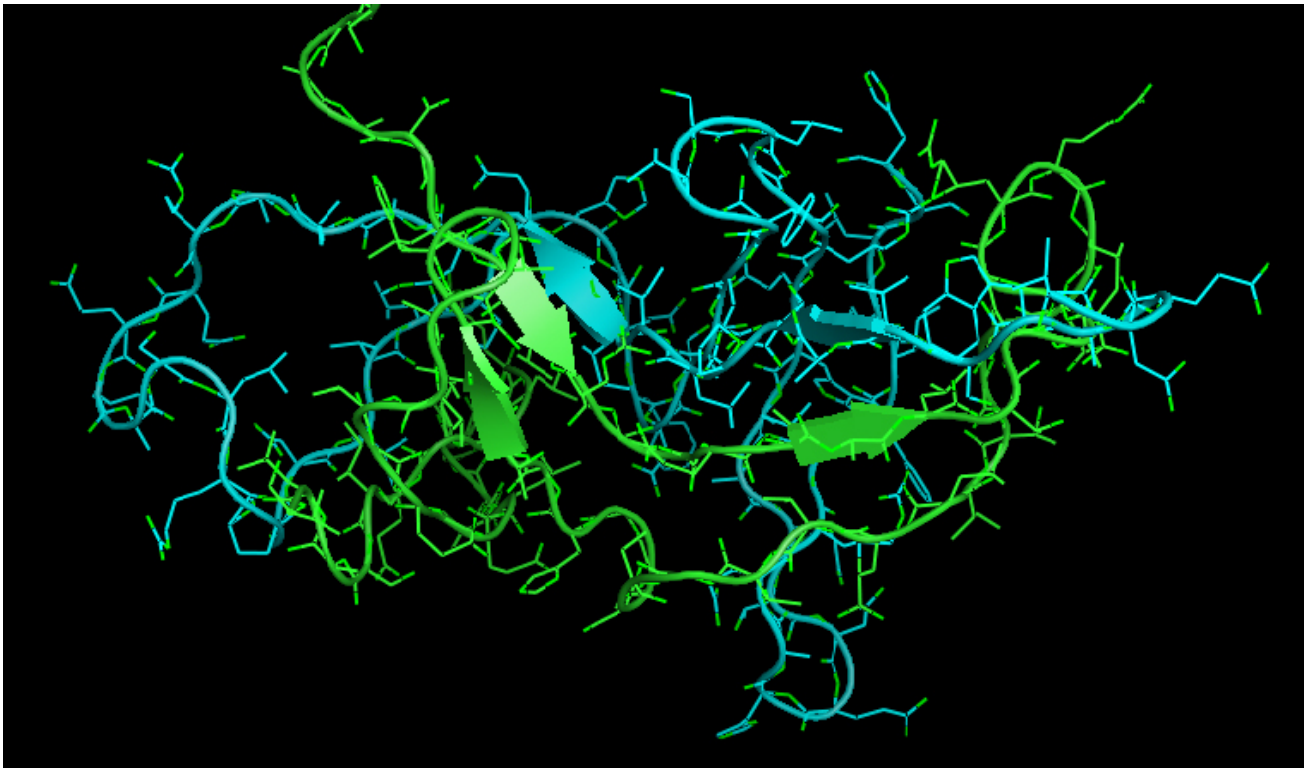
We found that HrpJ directly binds to HrpG-HrpV complex, acting possibly as a modulator of the transcriptional activity of HrpRS, coupling transcriptional control and T3SS-mediated secretion. We have identified the existence of HrpG-HrpV, HrpG-HrpJ, HrpG-HrpV-HrpJ complexes both from *Pseudomonas syringae* pv. phaseolicola (*Pph*) and *Erwinia amylovora* (*Eamy*), using co-expression and co-purification strategies. We employed multi-angle light scattering to determine the molecular weight and molar ratio of the HrpG-HrpV-HrpJ reconstituted complex from *Eamy*, which was found to be around 76 kD (1:1:1 complex). Structural studies involving small-angle X-ray scattering have shown that the HrpG-HrpV-HrpJ complex is a particle similar to the determined structures of the respective complexes coming from animal pathogenic bacteria (YopN-SycN-YscB in *Yersinia*). Full expression analysis with quantitative real time PCR conducted in wild type *Pph* as well as in *hrpG*, *hrpV* and *hrpJ* mutants showed that HrpGV and HrpJ exert opposite function during T3SS activation; while HrpG-HrpV seem to suppress T3SS expression, HrpJ activates it. Ongoing data analysis of a full secretome analysis coupled to mass spectrometry in wild type *Pph* and *hrpG*, *hrpV* and *hrpJ* mutants will reveal the differences in the repertoire of secreted substrates for each strain that will allow us to determine the role of the complex and its subunits to regulation of T3SS secretion.

A range of proteins and complexes from the type III secretion system such as HrpE, HrpG, HrpV, HrpJ, HrcQAc, HrcQBc from different bacteria was analysed structurally with the help of protein crystallography and SAXS.

This work promises the development of novel antimicrobial agents that target key elements of the Type III pathogenicity mechanism.



HrpE dummy atom model (magenta) from SAXS docked on the cytoplasmic side of the EM derived model of the Shigella injectisome.



Crystal structure of the complex of the conserved Type III secretion system proteins $HrcQ_A$, $HrcQ_B$ *from the plant pathogen P. syringae* pv phaseolicola.

Technologies for molecular diagnostics

These activities focus on two main research areas: the study of biomolecules conformation and of conformational changes induced by ligand binding and the coupling of such conformation-sensing events to the study of DNA molecules for molecular diagnostic purposes. During the last three years we showed several examples where biomolecular conformation was elucidated in a fully quantitative manner using acoustic wave devices and our newly developed model. Specifically, we showed the ability to detect acoustically multiple DNA targets by using a single probe; we studied with the acoustic device and AFM the structure of an intrinsically disordered protein, and changes upon its structure upon potassium binding; we also proved the hydrodynamic nature of DNA acoustic sensing by providing experimental evidence to back up our theoretical predictions. The use of acoustic wave devices for the quantitative determination of protein molecular weight was also published, while work on the characterization of the structure of calmodulin using the combined QCM/ellipsometry instrument is under development and will soon be published. **In addition, the application of the above concepts to molecular diagnostics was described in a patent application, submitted to the UK patent office.**

The potential impact (including the socio-economic impact and the wider societal implications of the project so far) and the main dissemination activities and exploitation of results

Although IMBB has consistently demonstrated in the past its capacity for excellence in research and innovation, there is every expectation that its international competitiveness, and innovative capacities will be **improved significantly through the InnovCrete project**. The project has been in a relatively short time able to catalyze innovations in the areas of Health & Biomedicine, Biotechnology and Bio-inspired nanomaterials. These will contribute to **regional, national and European economic growth and quality of life**, making a contribution in **lifting Greece from its present economic downturn**. Although these innovations originated **from research projects that were already in progress at IMBB**, **they could be only achieved through the involvement of the InnovCrete technology platform**. On the other hand, the project has also **developed through networking considerable and beneficial synergies** to other ongoing national activities (see WP6); these initiatves have already received national funding and will significantly promote innovation in biomedicine, biology and biotechnology in Greece, thus becoming engines for regional & national economic development. Key elements are thus gathered to make InnovCrete a scientific and economic success: the **project is sustainable** beyond the lifetime of REGPOT funding, and its scientific strategy and concepts are very **innovative**.

Better integration of InnovCrete in the European Research Area as a whole

The collaboration of the InnovCrete teams with **EU academic partners that are renowned internationally for their expertise** on all aspects of the project and the **involvement of research-intensive SMEs** offer the ideal synergy to turn the InnovCrete consortium into a leading European Centre of Excellence for structural biology, **firmly integrated within the ERA**. The involvement of high-profile partners in the rigorous seminars, conferences, trainings and workshops programme of InnovCrete, along with professional dissemination activities, has led to a **broad recognition of the InnovCrete project and IMBB in the EU** and a **stable integration in ERA**, thus considerably contributing to the InnovCrete impacts.

One further InnovCrete impact is the establishment of **long-term strategic partnerships** with its partners. This is reflected in activities aiming at the joint preparation of applications for EU funding, joint training activities (WP2), establishment of networks and interdisciplinary communities (BIOSTRUCT-X, BE/OPT XFEL, ESUO) etc. There is a high probability that these interactions will lead to bilateral research projects through EU funded and other programmes (INSTRUCT-EL has already received funding), producing joint innovation and training activities beyond the lifetime of the InnovCrete project. All innovations directly or indirectly resulting from InnovCrete (e.g. in the fields of **gene therapy, drugs development, new bio-inspired materials, understanding of diseases and ageing, food security** etc) meet major socio-economic

and scientific development needs of the Region of Crete, the country and Europe, are consistent with Innovation Union priorities and **will have a significant long-term impact in the ERA**.

The **international exposure, inflow of knowledge, the new technologies and methodologies, the new and upgraded instrumentation, along with the recruitment of a dynamic group of experienced researchers and the implementation of a career development plan** has created a scientific culture in Crete which will be beneficial for the professional development of the research staff. Key elements in the ERA integration of InnovCrete are also the workshops, practical courses and conference programme of the project (WP4), which **created a European tradition of excellent scientific meetings organized in Crete**. This in turn will bring **recognition of InnovCrete and IMBB among ERA scientists as a premium partner for collaborations**.

Upgrading the RTD capacity and capability

The InnovCrete project has considerably upgraded the RTD capacity of IMBB in key areas of structural biology. This upgrade has been achieved a) through the significant **strengthening of the human potential** by means of the recruitment of experienced researchers (WP1) and b) the **acquisition / upgrade of scientific equipment** which put InnovCrete at **a level comparable to very high European standards** (WP3). The international exposure of InnovCrete scientists through the workshops/conferences programme, the improved skills for the preparation of grant applications (through special training courses) and activities for **IP management, technology transfer and commercialization** (WP5, WP6) will in near future **catalyze increased external funding, which will be very beneficial for the continuous upgrading of the RTD capacity and capability and the quality of research in Crete.** These improvements will be also very helpful for strategic research planning of individual research groups; at the level of IMBB as a whole, they will result in **more focused research projects** and a **better critical mass of researchers** capable of tackling challenging structural biology-driven projects.

Improved research capacity for increased contribution to regional economic and social development

InnovCrete has a strong involvement in regional initiatives (Agro-Food Cluster), will stay part of the *Smart Specialization Strategy for the Region of Crete*, the program for the development of the *Knowledge complex/Key Enabling Technologies* in Crete, and will further promote the establishment of national Clusters in Structural Biology.

Improved skills for participation in EU programmes

In order to improve the skills and know-how in the field of H2020 participation, workshops/practical courses on funding opportunities (WP5) and on IP and innovation management (WP6) have been organized. These offered training in grant application writing, research project management, including dissemination, commercialization etc. Equipped with these new scientific and managerial skills, the scientists from the

Region of Crete will be much more capable of taking part in international competitive funding and European research collaborations. In addition, participation in EU projects is enhanced through the strategic partnerships (WP2, WP6) and the rigorous exchange programme. The upgraded RTD capacities will enhance the recognition of InnovCrete among leading European research groups as an excellent partner for EU programme proposals with specialist know-how and modern instrumentation.

Improved innovation potential

Crete is a particularly fertile ground for innovation in structural biology-driven research, as it includes the highest density of researchers in Life Sciences, and the two top rated research and academic institutions of the country (IMBB/FORTH and UOC). The RTD reinforcement through InnovCrete will produce applications for the biomedical, biotechnology and the bio-inspired materials sectors. Examples of such progress are **new gene therapy tools based on gene replacement without the need for integrative gene therapy vectors, new antibacterial drugs, novel bio-inpired materials such as hydrogels and fibres with dimensions in the nano- to micro-scale region etc**.

3.2 Spreading excellence, exploiting results, disseminating knowledge

The InnovCrete members have a commitment to **knowledge dissemination** and have used their existing networks, within academia, industry, policy and public administration to spread the information about InnovCrete activities, research achievements and regional development initiatives (WP5). Beyond that, longstanding relations with their colleagues in academia and the industrial sector in the EU and worldwide have been used to disseminate knowledge and scientific results and to strengthen the image of IMBB as a centre of excellence in structural biology research. In addition to classical dissemination tools (publications, TV, radio, newspapers), **state-of-the-art electronic means** (the InnovCrete web site, social media, see WP5), and **communication materials** (brochures, flyers, posters, etc.) have presented the project at the largest possible public front (details in WP5).

The diffusion of information to the **scientific community** has been transmitted through the publication of scientific articles in peer-reviewed journals and presentations as well as posters at national and international scientific conferences. To achieve an even higher recognition, InnovCrete has hosted in Crete the **series of international conferences and workshops** (WP 4) which significantly increased the impact of the project.

In the context of "excellence spreading", regional training workshops and courses for skills training (on research funding, IP and innovation management, WP 4 & WP6) **have been open to scientists from UOC or other Cretan research institutions** (in addition to InnovCrete members). InnovCrete has also spread excellence and increased the impact of the project by providing **access to its new equipment to other research groups for their own research.**

With regard to the innovation and results exploitation dimension of InnovCrete, specific measures have been used for identifying potential partners and sources of finance for commercialization:

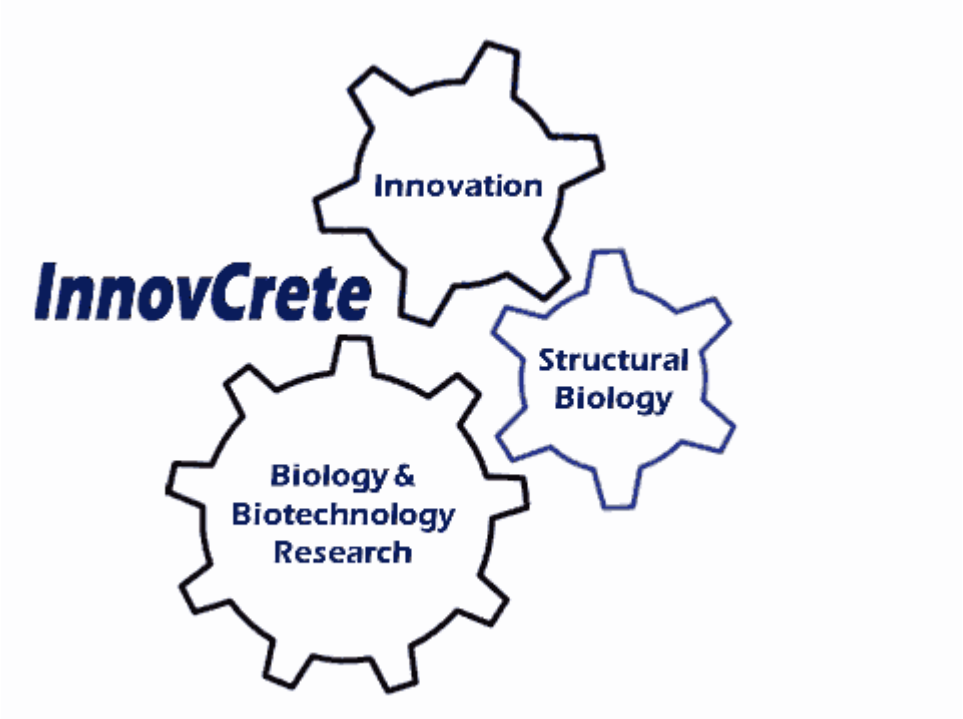
- Creation of an IPR/Technology Transfer Helpdesk for PR management
- Creation of a portfolio of exploitable results
- Participation in the largest international promotional and partnering events
- Collaboration with companies
- Organization of company missions to IMBB.
- Participation in Technology Transfer Brokerage Events

The address of the project public website, if applicable as well as relevant contact details.

www.innovcrete.eu

Prof. M. Kokkinidis
IMBB/FORTH & University of Crete
Nikolaou Plastira 100 GR-70013, Heraklion, Crete GREECE
Tel: +30 2810 39114351
Fax: +30 2810 391101

e-Mail: kokkinid@imbb.forth.gr



4.2 Use and dissemination of foreground

Section A (public)

TEMPLATE A1: LIST OF SCIENTIFIC (PEER REVIEWED) PUBLICATIONS, STARTING WITH THE MOST IMPORTANT ONES										
NO.	Title	Main author	Title of the periodical or the series	Number, date or frequency	Publisher	Place of publication	Year of publication	Relevant pages	Permanent identifiers[1] (if available)	Is/Will open access[2] provided to this publication?
1	Structural plasticity of 4-alpha helical bundles exemplified by the puzzle-like molecular assembly of the Rop protein	M. Amprazi et al	Proceedings of the National Academy of S ciences of the United States	Vol. 111/I ssue 30	National Academy of Sciences	USA	2014	11049-54		yes
2	Tag1 deficiency results in olfactory dys function through impaired migration of m itral cells	G.G. Bastakis et al	Development	Vol. 142	Company of Biologist s Ltd	UK	2015	4318-28		
3	MicroRNAs for Fine-Tuning of Mouse Embryonic Stem Cell Fate Decision throug h Regulation of TGF-# Signaling	Ch. Hadjimichael et al.	Stem cell reports	Vol. 6	Cell Press	USA	2016	292-301		
4	On the Hydrodynamic Nature of DNA A coustic Sensing	A.Tsortos et al.	Anal. Chemistry	Vol. 88	American Chemical Society	USA	2016	6472-6478		
5	Monitoring structural	P. Mateo-Gil et al.		Vol. 52	Royal	UK	2016	6541-44		

[1] A permanent identifier should be a persistent link to the published version full text if open access or abstract if article is pay per view) or to the final manuscript accepted for publication (link to article in repository).

[2] Open Access is defined as free of charge access for anyone via Internet. Please answer "yes" if the open access to the publication is already established and also if the embargo period for open access is not yet over but you intend to establish open access afterwards.

	changes in intrins ically disordered proteins using QCM-D: application to the bacterial cell division pr otein ZipA				Society of Che mistry					
6	Side-chain interactions in the regulatory domain of human glutamate dehydrogenase determine basal activity and regulation	V. Mastorodemos et al.	J. Neurochem.	Vol. 133	Blackwell Publishing	UK	2015	73-82		
7	HrpG and HrpV proteins from the Type III secretion system of Erwinia amylovora f orm a stable heterodime	A.D. Gazi et al.	FEMS Microbiology Letters	Vol. 362	Blackwell Publishing	UK	2015	1-8		
8	The benefit of the European User Co mmunity from transnational access to nat ional radiation facilities	E. Barrier et al.	Journal of Synchrotron Radiation	Vol. 21	IUCr	UK	2014	638-39		No
9	Assessment of In-Depth Degradation of Ar tificially Aged Triterpenoid Paint Varni shes Using Nonlinear Microscopy Tec hniques	G. Fillipidis et al.	Microscopy and Microanalysi s	Vol. 21	Cambridge University Press	UK	2015	510-517		
10	The detection of multiple DNA targets with a single probe using a conformation-sensit ive acoustic senso	A.Tsortos et al.	Chemical Communicatio ns	Vol. 51	Royal Society of Chemistry	UK	2015	11504-507		
11	Quantitative determination of protein mo lecular weight with an acoustic sensor; significance of specific	K. Mitsikakis	The Analyst	Vol. 139	Royal Society of Chemistry	UK	2014	3918		

	versus non-specific binding									
12	Imaging ectopic fat deposition in caenor habditis elegans muscles using nonlinear microscopy	M. Mari et al.	Microscopy Research and Technique	Vol. 78	Wiley-Liss Inc	USA	2015	523-28		
13	Models of Rate and Phase Coding of Place Cells in Hippocampal Microcircuits	Cutsuridis V	Hippocampal Microcircuits : A comput ationa l modeller's resource book	Vol. 2	Springer	USA	2016	6347		
14	Simplified compartmental models of CA1 pyramidal cells of theta-modulated inhibition effects on spike timing-dependent plasticity	Cutsuridis V. et al.	Hippocampal Microcircuits : A comput ationa l modeller's resource book	Vol. 2	Springer	USA	2016			
15	The peptide Z-Aib-Aib-Aib-L-Ala-OtBu	Gessmann R. et al.	*Acta Crystallogr.*	C70	IUCr	UK	2014	405-407		
16	The achiral tetrapeptide Z-Aib-Aib-Aib- Gly-OtBu	Gessmann R. et al.	*Acta Crystallogr.*	C70	IUCr	UK	2014	1046-49		
17	Zn-substituted pseudoazurin solved by S/Zn-SAD phasing	Gessmann R. et al.	*Acta Crystallogr.*	F71	IUCr	UK	2015	19-23		
17	The crystal structure of Z-Gly-Aib-Gly-Aib-OtBu	Gessmann R. et al.	*J. Pept. Sci.*	21	IUCr	UK	2015	476-479		
18	Biophysical and enzymatic properties of aminoglycoside adenylyltransferase AadA6 from *Pseudomonas*	Papadovasilaki et al.	*Biochem. Biophys. Rep.*	4	ELSEVIER		2015	152-157		

	aeruginosa									
19	Persistent draining crossover in DNA and other semi-flexible polymers: evidence from hydrodynamic models and extensive measurements on DNA solutions	M.L. Mansfield et al.	J. Chem. Physics	143	AIP Publishing		2015	124903		

TEMPLATE A2: LIST OF DISSEMINATION ACTIVITIES								
NO.	Type of activities[3]	Main leader	Title	Date/Period	Place	Type of audience[4]	Size of audience	Countries addressed
1	*Conference*	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	CTSB-HeCrA7	18-21/9/2014	FORTH, Crete	Scientists, Industry, media	110	ALL
2	*Conference*	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Advances in Structural biology with FELs	20-22/4/2016	FORTH, Crete	Scientists	60	ALL
3	Workshop	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Horizon2020 training	6/5/2014	FORTH, Crete	Scientists, Industry	30	EU
4	Workshop	FOUNDATION	Research Funding	14/4/2016	FORTH,	Scientists,	30	ALL

[3] A drop down list allows choosing the dissemination activity: publications, conferences, workshops, web, press releases, flyers, articles published in the popular press, videos, media briefings, presentations, exhibitions, thesis, interviews, films, TV clips, posters, Other.

[4] A drop down list allows choosing the type of public: Scientific Community (higher education, Research), Industry, Civil Society, Policy makers, Medias, Other ('multiple choices' is possible).

		FOR RESEARCH &TECHNO-LOGY HELLAS	Opportunities		Crete	Industry		
5	Workshop	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Innovation capacity building	30/10/2015	FORTH, Crete	Scientists, Industry, media	30	ALL
6	Workshop	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Innovation Mana-gement/awareness	20/10/2015	FORTH, Crete	Scientists, Industry	30	ALL
7	Workshop	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Financial Instrument s for Research Funding 2014-2020	31/3/2014	FORTH, Crete	Scientists, Industry	72	ALL
8	Workshop	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Patenting Inventions	28/11/2013	FORTH, Crete	Scientists, Industry	70	ALL
9	Workshop	FOUNDATION FOR RESEARCH &TECHNO-LOGY	Optical and acoustic methods for analyzing protein-protein interactions	16/2/2015	FORTH, Crete	Scientists	30	ALL

		HELLAS						
10	Flyers	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS		28/10/2014 (other leaflets for 2012-2016 see www.innovcrete.eu / leaflets.html)	FORTH, Crete & world-wide distribution	Policy makers, civil society, Scientists, Industry, media	600+	ALL
11	Website	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	www.innovcrete.eu	1/3/2013	FORTH, Crete & world-wide distribution	Policy makers, civil society, Scientists, Industry, media	-	ALL
12	Poster presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	CTSB-HeCrA7, Nanostructures and Crystal Structure of Di-Phe in Tetra hydrofuran	19/9/2014	FORTH, Crete	Policy makers, Scientists, Industry, media	110	ALL
13	Poster presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Faraday Discussion 166: "Self-assembly of biopolymers" , Turning Helical Bundles into Fibrils Via Redesign of Folding Pathways	14/9-24/9/2013	Bristol, UK	Scientists		ALL
14	Articles published in the popular press	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Reports on InnovCrete	2012-2015	Crete	Policy makers, Scientists, Industry, media		ALL
15	Oral presentation	FOUNDATION	WORKSHOP	10/4/2014	EIE-Athens	Scientists,	50+	ALL

		FOR RESEARCH &TECHNO-LOGY HELLAS	"STRATEGIC PIPELINE PLANNING"			industry		
16	Social media	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Reports on InnovCrete	2012-2015	Crete	Policy makers, Scientists, Industry, media		ALL
17	Oral Presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	MLCB/MLSB worskshop, Neural Information Processing Society (NIPS),	Dec 12-13, 2015	Montreal, Canada	Scientists		ALL
18	Oral Presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Hippocampal Spring Research Conference	June 5-9, 2015	Taormina, Sicily, Italy	Scientists		ALL
19	Poster presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Current Trends in Structural Biology & 7th International Conference of the Hellenic Crystallographic Association	September 2014	Heraklion, Crete	Scientists		ALL
20	Poster presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY	Current Trends in Structural Biology & 7th International Conference of the Hellenic Crystallographic	September 2014	Heraklion, Crete	Scientists		ALL

		HELLAS	Association					
21	Poster presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	24th Annual Meeting of the German Crystallographic Society (DGK)	March 2016	Stuttgart University, Germany	Scientists		ALL
22	Poster presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	10th Conference, Hellenic & Italian Biomaterials Societies (Book of Abstracts, P#18)	26-28 November, 2015	NHRF, Athens, Greece	Scientists		ALL
23	Oral presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	International Workshop on Acoustic & Electrochemical Methods in the study of affinity interactions at surfaces (AEMIS) ("Acoustic devices as a powerful tool for biophysics and molecular diagnostics")	20 June 2015	Bratislava, Slovakia	Scientists		ALL
24	Oral presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Nokia 'International Open Innovation Challenge' and Nokia 'Growth Partners' – Investor Finland, Fair, Helsinki,	9-11 November 2015	Helsinki, Finland	Industry, media, scientists, others		ALL
25	Poster presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	4th International Conference on BioSensing Technology (**"**Maintaining protein's native conformation upon surface immobilization by using DNA as an anchor molecule: a study employing a QCM-D	10-13 May 2015	Lisbon, Portugal,	Industry, scientists		ALL

			biosensor ”)					
26	Poster/ oral presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	15th UBRC Conference, “Characterizing macromolecular size and shape in solution: comparison between numerical models and empirical data for DNA”	10 April 2015	Utah State University/ Bingham Research Centre, Vernal, UT, U.S.A	Scientists		ALL
27	Oral presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	InnovCrete Workshop on Acoustic & Optical Systems for Studying Biomolecular Interactions “Extracting structural information for biomolecules from acoustic data”	16-18 February 2015	Heraklion, Crete, Greece	Scientists		ALL
28	Oral presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	61st AVS International Symposium, section: Fundamentals & Method Development of QCM, “Full experimental proof of the relationship between the intrinsic viscosity of DNA and the acoustic ratio of SAW and TSM sensors (Book of Abstracts, p. 204)	9-14 November 2014	Baltimore, MD, U.S.A	Scientists		ALL
29	Oral presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	61st AVS International Symposium, section: Fundamentals & Method Development of QCM, “Characterization of the conformation of linker-suspended proteins at surfaces through acoustic ratio measurements”, (Book	9-14 November 2014	Baltimore, MD, U.S.A	Scientists		ALL

			of Abstracts, p. 204)					
30	Oral presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Surface Acoustic Wave Sensor Symposium , "The role of SAW devices in clinical and diagnostic platforms"	30-31 October 2014	Vienna, Austria	Scientists		ALL
31	Oral presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	1st Event on Science, Supporting Business: Mature Technologies, "Method for food-borne pathogen detection"	17 July 2014	Hellenic Ministry of Foreign Affairs, Athens, Greece	Policy makers, civil society, scientists, media		ALL
32	Oral presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	International Symposium on Acoustic Sensors in Analytical & Biophysical Studies "Acoustic signal analysis for biophysical studies"	29-30 August 2013	FORTH, Heraklion, Crete, Greece	Scientists		ALL
33	Poster presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	International Symposium on Acoustic Sensors in Analytical & Biophysical Studies "Characterization of protein adsorption through acoustic ratio measurements"	29-30 August 2013	FORTH, Heraklion, Crete, Greece	Scientists		ALL
34	Workshop	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Computational Sciences in Drug Discovery	30-June-2014	FORTH, Heraklion, Crete, Greece	Scientific comm unity (higher education, Research) Media		ALL
35	Press releases	FOUNDATION FOR	(see periodic reports)	2012-2016	FORTH, Heraklion, Crete, Greece	Policy makers,		ALL

		RESEARCH &TECHNO-LOGY HELLAS				civil society, scientists, media		
35	web	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	(see periodic reports & www.innovcrete.eu)	2012-2016	FORTH, Heraklion, Crete, Greece	Policy makers, civil society, scientists, media		ALL
37	Web/social media	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	https://www.facebook.com/ #!/innovcrete	2013-2016	FORTH, Heraklion, Crete, Greece	Policy makers, civil society, scientists, media		ALL
38	Conference/ TT Brokerage Events	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	BIO EUROPE 2014	Nov.3-5, 2014	Frankfurt, Germany	Industry, Policy makers, civil society, scientists, media	>150	ALL
39	Conference/ TT Brokerage Events	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Successful R&I in Europe 2014- 6th European networking event	30-31 October, 2014	Duesseldorf, Germany	Industry, Policy makers, civil society, scientists, media	>150	ALL
40	Conference/ TT Brokerage Events	FOUNDATION FOR RESEARCH &TECHNO-	Successful R&I in Europe 2015- 7th European networking event	5-6 November, 2015	Duesseldorf, Germany	Industry, Policy makers, civil	>150	ALL

		LOGY HELLAS				society, scientists, media		
41	Poster presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	CTSB-HeCra7 Nanostructures and Crystal Structure of Di-Phe in Tetra hydrofuran	19/09/2014	FORTH-Crete	Scientists	110	ALL
42	Oral presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Structural Plasticity and Structural Conservations to the Extreme in 4-alpha-helical Bundles	18/06/2015	Patras, Greece	Scientists		ALL
43	Oral presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Euromar 2013 ProteinPredict: A novel method for the prediction of the active site of the protein	30/6-5/7/13	Hersonissos, Crete, Greece	Scientists		ALL
44	Poster presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	CTSB-HeCra7, Exploring the self-assembly of α-helical superstructures	19-21/9/2014	FORTH-Crete	Scientists	110	ALL
45	Poster presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	SAS2015 , Structure of the E.coli cell cycle regulator 6S non-coding RNA and its complex with RNA polymerase	13-18/09/2015	Berlin, Germany	Scientists		ALL
46	Poster presentation	FOUNDATION	3rd FAST-DOT SUMMER	28/9-2/10/2015	Anissaras,	Scientists		ALL

		FOR RESEARCH &TECHNO-LOGY HELLAS	SCHOOL “PHOTONICS MEETS BIOLOGY”, Non-linear imaging techniques visualize the lipid profile of C. elegans		Crete, Greece			
47	Poster presentation	FOUNDATION FOR RESEARCH &TECHNO-LOGY HELLAS	Faraday Discussion 166: “Self-assembly of biopolymers” , Turning Helical Bundles into Fibrils Via Redesign of Folding Pathways	14/9-24/9/2013	Bristol, UK	Scientists		ALL

Section B (Confidential)
Part B1

TEMPLATE B1: LIST OF APPLICATIONS FOR PATENTS, TRADEMARKS, REGISTERED DESIGNS, ETC.					
PATENT	YES		GB 1511687.4	MEASUREMENT OF ANALYTE WITH AN ACOUSTIC WAVE SENSOR	FORTH
PATENT	YES		FILING IN PREPARATION	HELICAL SCAFFOLDS FOR BIOINSPIRED MATERIALS	FORTH
PATENT	YES		FORTH	HELICAL SCAFFOLD BASED ENZYMES	FORTH

Part B2

Type of Exploitable Foreground[5]	Description of exploitable foreground	Confidential Click on YES/NO	Foreseen embargo date dd/mm/yyyy	Exploitable product(s) or measure(s)	Sector(s) of application[6]	Timetable, commercial or any other use	Patents or other IPR exploitation (licences)	Owner & Other Beneficiary(s) involved
General advancement of knowledge	NEW DETECTION METHOD FOR STRUCTU-RAL CHANGES OF BIOMOLE-CULES	YES		ULTRA-SENSITIVE ACOU STIC DIAGNOSTIC PLAT FORMS	MEDICAL INDUSTRIAL		PATENT FILED	FORTH
General advancement of knowledge	NEW CONCEPT FOR HYDROGE L & FIBRES ENGINEE-RING BASED ON HELICAL PEPTIDES	YES		NEW MATERIALS	MEDICAL INDUSTRIAL		PATENT FILING IN PREP.	FORTH
General advancement of knowledge	NEW CONCEPT FOR ENZYME ENGINEE-RING BASED ON	YES		NEW ENZYMES	MEDICAL INDUSTRIAL		PATENT FILING IN PREP.	FORTH

[19] A drop down list allows choosing the type of foreground: General advancement of knowledge, Commercial exploitation of R&D results, Exploitation of R&D results via standards, exploitation of results through EU policies, exploitation of results through (social) innovation.

[6] A drop down list allows choosing the type sector (NACE nomenclature) : http://ec.europa.eu/competition/mergers/cases/index/nace_all.html

Type of Exploitable Foreground[5]	Description of exploitable foreground	Confidential Click on YES/NO	Foreseen embargo date dd/mm/yyyy	Exploitable product(s) or measure(s)	Sector(s) of application[6]	Timetable, commercial or any other use	Patents or other IPR exploitation (licences)	Owner & Other Beneficiary(s) involved
	HELICAL SCAFFOLDS							

A patent entitled “Measurement of analyte with an acoustic wave sensor” was filed in the UK under application number GB 1511687.4. The patent involved an innovative approach regarding analyte detection by taking into account differences in the hydrodynamic volume of biomolecules/liposomes in order to enhance the acoustic wave sensor response. These changes, which reflect changes in the structure of the bio-matter, were exploited for the development of ultra-sensitive acoustic diagnostic platforms related to DNA detection in the range of attomole.

Two more patents on a) bio-inpired materials and b) the engineering of novel enzymes for biomedical and biotechnology applications (e.g. gene therapy and plant biotechnology) - both based on protein scaffold concepts refined in the InnovCrete project - are in the process of getting filed with the Hellenic Industrial Property Organisation (OBI). OBI has already performed for each patent a third party search, which revealed the absence of any overlapping patents internationally.

4.3 Report on societal implications

A General Information *(completed automatically when **Grant Agreement number** is entered.*	
Grant Agreement Number:	316223
Title of Project:	**Unlocking the innovative capacity of multidisciplinary structural biology-driven research in Crete**
Name and Title of Coordinator:	Prof. Michael Kokkinidis

B Ethics	
1. Did your project undergo an Ethics Review (and/or Screening)? • If Yes: have you described the progress of compliance with the relevant Ethics Review/Screening Requirements in the frame of the periodic/final project reports? Special Reminder: the progress of compliance with the Ethics Review/Screening Requirements should be described in the Period/Final Project Reports under the Section 3.2.2 *'Work Progress and Achievements'*	***No***
2. Please indicate whether your project involved any of the following issues (tick box) :	***YES***
RESEARCH ON HUMANS	
• Did the project involve children?	No
• Did the project involve patients?	No
• Did the project involve persons not able to give consent?	No
• Did the project involve adult healthy volunteers?	No
• Did the project involve Human genetic material?	No
• Did the project involve Human biological samples?	No
• Did the project involve Human data collection?	No
RESEARCH ON HUMAN EMBRYO/FOETUS	
• Did the project involve Human Embryos?	No
• Did the project involve Human Foetal Tissue / Cells?	No
• Did the project involve Human Embryonic Stem Cells (hESCs)?	No
• Did the project on human Embryonic Stem Cells involve cells in culture?	No
• Did the project on human Embryonic Stem Cells involve the derivation of cells from Embryos?	No
PRIVACY	
• Did the project involve processing of genetic information or personal data (eg. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction)?	No
• Did the project involve tracking the location or observation of people?	No
RESEARCH ON ANIMALS	
• Did the project involve research on animals?	No
• Were those animals transgenic small laboratory animals?	No
• Were those animals transgenic farm animals?	No
• Were those animals cloned farm animals?	No
• Were those animals non-human primates?	No
RESEARCH INVOLVING DEVELOPING COUNTRIES	
• Did the project involve the use of local resources (genetic, animal, plant etc)?	No
• Was the project of benefit to local community (capacity building, access to healthcare, education etc)?	No
DUAL USE	

• Research having direct military use	No
• Research having the potential for terrorist abuse	No

C Workforce Statistics

3. Workforce statistics for the project: Please indicate in the table below the number of people who worked on the project (on a headcount basis).

Type of Position	Number of Women	Number of Men
Scientific Coordinator	-	1
Work package leaders	3	4
Experienced researchers (i.e. PhD holders)	13	16
PhD Students	2	2
Other	12	10

4. How many additional researchers (in companies and universities) were recruited specifically for this project?	**0**
Of which, indicate the number of men:	0

D Gender Aspects

5. Did you carry out specific Gender Equality Actions under the project?

○ Yes
○ No

6. Which of the following actions did you carry out and how effective were they?

		Not at all effective				Very effective	
❑	Design and implement an equal opportunity policy	○	○	○	○	○	n.a.
❑	Set targets to achieve a gender balance in the workforce	○	○	○	○	○	n.a.
❑	Organise conferences and workshops on gender	○	○	○	○	○	n.a.
❑	Actions to improve work-life balance	○	○	○	○	○	n.a.
○	Other:	n.a.					

~~**7. Was there a gender dimension associated with the research content – i.e. wherever people were the focus of the research as, for example, consumers, users, patients or in trials, was the issue of gender considered and addressed?**~~

~~○ Yes- please specify~~

~~○ **No**~~

E Synergies with Science Education

8. Did your project involve working with students and/or school pupils (e.g. open days, participation in science festivals and events, prizes/competitions or joint projects)?

○ ~~Yes- please specify~~

○ No

9. Did the project generate any science education material (e.g. kits, websites, explanatory booklets, DVDs)?

○ Yes- please specify website, www.innovcrete.eu

○ No

F Interdisciplinarity

10. Which disciplines (see list below) are involved in your project?

○ Main discipline[7]: 1.5
○ Associated discipline[7]:1.3
○ Associated discipline[7]:4.1

G Engaging with Civil society and policy makers

11a Did your project engage with societal actors beyond the research community? *(if 'No', go to Question 14)*

○ **Yes**
○ No

11b If yes, did you engage with citizens (citizens' panels / juries) or organised civil society (NGOs, patients' groups etc.)?

○ No
○ **Yes- in determining what research should be performed**
○ Yes - in implementing the research
○ Yes, in communicating /disseminating / using the results of the project

[7] Insert number from list below (Frascati Manual).

11c In doing so, did your project involve actors whose role is mainly to organise the dialogue with citizens and organised civil society (e.g. professional mediator; communication company, science museums)?	○ ○	**Yes** No

12. Did you engage with government / public bodies or policy makers (including international organisations)

- ○ No
- ○ Yes- in framing the research agenda
- ○ Yes - in implementing the research agenda
- ○ **Yes, in communicating /disseminating / using the results of the project**

13a Will the project generate outputs (expertise or scientific advice) which could be used by policy makers?

- ○ Yes – as a **primary** objective (please indicate areas below- multiple answers possible)
- ○ **Yes – as a secondary objective (please indicate areas below - multiple answer possible)**
- ○ No

13b If Yes, in which fields?

Agriculture		Energy		Human rights	
Audiovisual and Media		Enlargement		Information Society	
Budget		Enterprise		Institutional affairs	
Competition		Environment		Internal Market	
Consumers		External Relations		Justice, freedom and security	
Culture		External Trade		Public Health	
Customs		Fisheries and Maritime Affairs		Regional Policy	
Development Economic and Monetary Affairs		Food Safety		Research and Innovation	
		Foreign and Security Policy		Space	
Education, Training, Youth		Fraud		Taxation	
Employment and Social Affairs		Humanitarian aid		Transport	

13c If Yes, at which level?

- ○ Local / regional levels
- ○ National level
- ○ European level
- ○ International level

H Use and dissemination

14. How many Articles were published/accepted for publication in peer-reviewed journals?	**19**
To how many of these is open access[8] provided?	
How many of these are published in open access journals?	
How many of these are published in open repositories?	
To how many of these is open access not provided?	**1**
Please check all applicable reasons for not providing open access:	
❑ publisher's licensing agreement would not permit publishing in a repository ❑ no suitable repository available ❑ no suitable open access journal available ❑ no funds available to publish in an open access journal ❑ lack of time and resources ❑ lack of information on open access ❑ other[9]: ……	

15. How many new patent applications ('priority filings') have been made? *("Technologically unique": multiple applications for the same invention in different jurisdictions should be counted as just one application of grant).*		**1 & 2 in preparation**
16. Indicate how many of the following Intellectual Property Rights were applied for (give number in each box).	Trademark	**0**
	Registered design	**0**
	Other	**0**
17. How many spin-off companies were created / are planned as a direct result of the project?		**0**
Indicate the approximate number of additional jobs in these companies:		**0**

18. Please indicate whether your project has a potential impact on employment, in comparison with the situation before your project:

- ❑ Increase in employment, or
- ❑ Safeguard employment, or
- ❑ Decrease in employment,
- ❑ Difficult to estimate / not possible to quantify

- ❑ In small & medium-sized enterprises
- ❑ In large companies
- ❑ None of the above / not relevant to the project

19. For your project partnership please estimate the employment effect resulting directly from your participation in Full Time Equivalent (*FTE = one person working fulltime for a year*) jobs:	*Indicate figure:* *39*

[8] Open Access is defined as free of charge access for anyone via Internet.
[9] For instance: classification for security project.

Difficult to estimate / not possible to quantify	❑

I Media and Communication to the general public

20. As part of the project, were any of the beneficiaries professionals in communication or media relations?

○ **Yes** ○ No

21. As part of the project, have any beneficiaries received professional media / communication training / advice to improve communication with the general public?

○ **Yes** ○ No

22 Which of the following have been used to communicate information about your project to the general public, or have resulted from your project?

❑	**Press Release**	❑	**Coverage in specialist press**
❑	**Media briefing**	❑	**Coverage in general (non-specialist) press**
❑	**TV coverage / report**	❑	**Coverage in national press**
❑	**Radio coverage / report**	❑	Coverage in international press
❑	**Brochures /posters / flyers**	❑	Website for the general public / internet
❑	DVD /Film /Multimedia	❑	Event targeting general public (festival, conference, exhibition, science café)

23 In which languages are the information products for the general public produced?

❑	Language of the coordinator	❑	**English**
❑	Other language(s)		

***Question F-10*:** Classification of Scientific Disciplines according to the Frascati Manual 2002 (Proposed Standard Practice for Surveys on Research and Experimental Development, OECD 2002):

FIELDS OF SCIENCE AND TECHNOLOGY

1. NATURAL SCIENCES

1.1 Mathematics and computer sciences [mathematics and other allied fields: computer sciences and other allied subjects (software development only; hardware development should be classified in the engineering fields)]

1.2 Physical sciences (astronomy and space sciences, physics and other allied subjects)

1.3 Chemical sciences (chemistry, other allied subjects)

1.4 Earth and related environmental sciences (geology, geophysics, mineralogy, physical geography and other geosciences, meteorology and other atmospheric sciences including climatic research, oceanography, vulcanology, palaeoecology, other allied sciences)

1.5 Biological sciences (biology, botany, bacteriology, microbiology, zoology, entomology, genetics, biochemistry, biophysics, other allied sciences, excluding clinical and veterinary sciences)

2 ENGINEERING AND TECHNOLOGY

2.1 Civil engineering (architecture engineering, building science and engineering, construction engineering, municipal and structural engineering and other allied subjects)

2.2 Electrical engineering, electronics [electrical engineering, electronics, communication engineering and systems, computer engineering (hardware only) and other allied subjects]

2.3. Other engineering sciences (such as chemical, aeronautical and space, mechanical, metallurgical and materials engineering, and their specialised subdivisions; forest products; applied sciences such as

geodesy, industrial chemistry, etc.; the science and technology of food production; specialised technologies of interdisciplinary fields, e.g. systems analysis, metallurgy, mining, textile technology and other applied subjects)

3. MEDICAL SCIENCES

3.1 Basic medicine (anatomy, cytology, physiology, genetics, pharmacy, pharmacology, toxicology, immunology and immunohaematology, clinical chemistry, clinical microbiology, pathology)

3.2 Clinical medicine (anaesthesiology, paediatrics, obstetrics and gynaecology, internal medicine, surgery, dentistry, neurology, psychiatry, radiology, therapeutics, otorhinolaryngology, ophthalmology)

3.3 Health sciences (public health services, social medicine, hygiene, nursing, epidemiology)

4. AGRICULTURAL SCIENCES

4.1 Agriculture, forestry, fisheries and allied sciences (agronomy, animal husbandry, fisheries, forestry, horticulture, other allied subjects)

4.2 Veterinary medicine

5. SOCIAL SCIENCES

5.1 Psychology

5.2 Economics

5.3 Educational sciences (education and training and other allied subjects)

5.4 Other social sciences [anthropology (social and cultural) and ethnology, demography, geography (human, economic and social), town and country planning, management, law, linguistics, political sciences, sociology, organisation and methods, miscellaneous social sciences and interdisciplinary , methodological and historical S1T activities relating to subjects in this group. Physical anthropology, physical geography and psychophysiology should normally be classified with the natural sciences].

6. HUMANITIES

6.1 History (history, prehistory and history, together with auxiliary historical disciplines such as archaeology, numismatics, palaeography, genealogy, etc.)

6.2 Languages and literature (ancient and modern)

6.3 Other humanities [philosophy (including the history of science and technology) arts, history of art, art criticism, painting, sculpture, musicology, dramatic art excluding artistic "research" of any kind, religion, theology, other fields and subjects pertaining to the humanities, methodological, historical and other S1T activities relating to the subjects in this group]

2. FINAL REPORT ON THE DISTRIBUTION OF THE EUROPEAN UNION FINANCIAL CONTRIBUTION

This report shall be submitted to the Commission within 30 days after receipt of the final payment of the European Union financial contribution.

Report on the distribution of the European Union financial contribution between beneficiaries

Name of beneficiary	Final amount of EU contribution per beneficiary in Euros
1.	
2.	
Total	