Brussels, 13 November 2018

COST 084/18

DECISION

Subject: **Memorandum of Understanding for the implementation of the COST Action "Innovation with Glycans: new frontiers from synthesis to new biological targets" (INNOGLY) CA18103**

The COST Member Countries and/or the COST Cooperating State will find attached the Memorandum of Understanding for the COST Action Innovation with Glycans: new frontiers from synthesis to new biological targets approved by the Committee of Senior Officials through written procedure on 13 November 2018.

MEMORANDUM OF UNDERSTANDING

For the implementation of a COST Action designated as

COST Action CA18103
INNOVATION WITH GLYCANS: NEW FRONTIERS FROM SYNTHESIS TO NEW BIOLOGICAL TARGETS (INNOGLY)

The COST Member Countries and/or the COST Cooperating State, accepting the present Memorandum of Understanding (MoU) wish to undertake joint activities of mutual interest and declare their common intention to participate in the COST Action (the Action), referred to above and described in the Technical Annex of this MoU.

The Action will be carried out in accordance with the set of COST Implementation Rules approved by the Committee of Senior Officials (CSO), or any new document amending or replacing them:

a. "Rules for Participation in and Implementation of COST Activities" (COST 132/14 REV2);
b. "COST Action Proposal Submission, Evaluation, Selection and Approval" (COST 133/14 REV);
c. "COST Action Management, Monitoring and Final Assessment" (COST 134/14 REV2);
d. "COST International Cooperation and Specific Organisations Participation" (COST 135/14 REV).

The main aim and objective of the Action is to INNOGLY rests on two pillars, each including two subtopics:
1) Glycan profiling in health and disease.
• Glycan-based correlations in developmental and cancer biology.
• Glycan dependent modulation of autophagy: cancer, lysosomal disorders, neurodegenerative diseases.
2) Glycan-based diagnostics and therapeutics.
• Glycan dependent fine tuning of immunity.
• Exploring the multifaceted roles of glycosaminoglycans.. This will be achieved through the specific objectives detailed in the Technical Annex.

The economic dimension of the activities carried out under the Action has been estimated, on the basis of information available during the planning of the Action, at EUR 60 million in 2018.

The MoU will enter into force once at least seven (7) COST Member Countries and/or COST Cooperating State have accepted it, and the corresponding Management Committee Members have been appointed, as described in the CSO Decision COST 134/14 REV2.

The COST Action will start from the date of the first Management Committee meeting and shall be implemented for a period of four (4) years, unless an extension is approved by the CSO following the procedure described in the CSO Decision COST 134/14 REV2.

TECHNICAL ANNEX

OVERVIEW

Summary
The aim of INNOGLY COST action is to build up a multidisciplinary group of researchers to address the same pioneering goal: Gaining new insight into the biological function of glycans in different biological contexts. INNOGLY will address two main topics:

1) **Glycan profiling in health and disease**, where studies will be more specifically focused on glycan-based correlations in developmental and cancer biology, and glycan dependent modulation of autophagy in cancer, lysosomal disorders and neurodegenerative diseases.

2) **Glycan-based diagnostics and therapeutics**, where INNOGLY investigators will focus on glycan dependent fine tuning of immunity, and the exploration of the multifaceted roles of glycosaminoglycans.

Within these topics, INNOGLY will foster the development of new glycan-based tools for diagnosis and treatment of diseases.

To this end, INNOGLY will bring together scientists working in the vast area of glycoscience and researchers of other scientific disciplines willing to mutual exchange of knowledge, skill and expertise. In this way, scientists who have never been involved in glycoscience can provide improvements and new tips by bringing their different points of view. The goal is to forge and foster collaborations among researchers, each of them spurred to pursue his own research interests, and to intermesh these interests with other colleagues in order to move forward new concepts, ideas and approaches to address glycan-related scientific challenges from new and wider perspectives. In addition, INNOGLY COST Action would provide the chance for young and smart researchers to get trained in the innovations of glycoscience and to find new career opportunities.

Areas of Expertise Relevant for the Action	**Keywords**
● Chemical sciences: Organic chemistry ● Biological sciences: Glycomics ● Basic medicine: Glycomics ● Basic medicine: Immunosignalling	● glycan profile ● glycan-based tools and biosensors ● immune modulation ● glycochemistry ● glycan-based polymers

Specific Objectives
To achieve the main objective described in this MoU, the following specific objectives shall be accomplished:

Research Coordination
● Develop a collaborative effort to achieve a common ground on the topics 1) Glycan profiling in health and disease, and 2) Glycan-based diagnostics and therapeutics, as well as the related subtopics.
● Develop glycan-based tools (nanometric and small molecules) to track glycosylation pathways and to dissect immunomodulatory functions.
● Foster progress in existing research projects.
● Develop biosensors to investigate glycan-protein interactions.
● Promote the synthesis of glycomimetics and glycan-based analogues of specific target epitopes.
● Develop glycan-based and glycan-integrated biopolymers.
● Improve manipulation and engineering of glycan-based systems.
● Develop straightforward methodologies to synthesize oligosaccharides and glycoconjugates.
● Develop glycoproteomic tools to image protein-specific glycosylation changes.

Capacity Building

● Bridge the gap between scientific communities with complementary knowledge and common interests in glycan-related topics.
● Set up a platform for early career researchers.
● Help early career researchers to access and build new networks.
● Disseminate the results to foster new researchers (with a special focus on Inclusiveness Target Countries) to join the glycoscience community.
● Facilitate engagement between key players and stakeholders of the glycoscience community across Europe.
● Enhance public communication to boost promotion of glycoscience within the mainstream of biological sciences.
● Lead to increased funding opportunities for R&D.

TECHNICAL ANNEX

1. S&T EXCELLENCE

1.1. CHALLENGE

1.1.1. DESCRIPTION OF THE CHALLENGE (MAIN AIM)

'Cinderella's coach is ready'. This is the title of the introduction of the Special Issue on Carbohydrates and Glycobiology published in 2001 in Science. Therein, the authors indicated: ''…The chemistry and biology of carbohydrates has been a Cinderella field: an area that involves much work but, alas, does not get to show off at the ball with her cousins, the genomes and proteins...'. Thus, the call for glycoscientists was clear: arousing the interest of researchers to explore the amazing world of glycans, a topic poorly explored and also highly complex and in continuous evolution. Undoubtedly, both simple and complex glycans are ubiquitous in all living organisms and are key mediators of molecular recognition phenomena. They are directly involved in many physiological events, such as cell migration and tissue generation during embryogenesis, they underlie the pathophysiology of many diseases and play crucial roles in pathogen-host interactions especially at the first stage of infections. The structural complexity and the faster evolution of glycans along with the intricacy of their structural analysis and identification, however, has kept glycans away from mainstream research in medical and life science for decades. Indeed, although glycans are relevant building blocks in living organisms, the interest and consequently the knowledge about glycans has not been as prominent as the one of the other macromolecules.

Initially, in an era in which the high variability of the glycosylation processes complicated the assessment of the functions that glycan structures could mediate, only general theories were developed. Since then, the information regarding the biological roles of glycans has vastly expanded and the initial theories, even associated with limited evidence, glimpsed what would be the relevant discoveries in the understanding of the "glycan code". The last two decades saw great strides in this field. For example, it was recognized that human genetic disorders are linked to defects in glycosylation. Furthermore, a better understanding of the 'storage disorders' allowed to define that the dysregulation of a single glycosidase results in severe diseases. The multiple roles of terminal glycans in glycoproteins were elucidated by employing glycan-specific animal lectins. However, many questions still remain without an answer and a series of new discoveries have opened new intriguing scenarios that need to be explored. The close collaboration between scientists with different specific expertise is key to address this.

The challenge and the major innovation of INNOGLY (INNOvation with GLYcans: new frontiers from synthesis to new biological targets) is to support new strategies to investigate the fundamental roles played by the "glycan code" in biology. Many topics detailed in this COST Action have already been the subject of previous and current studies centred on the biological role and mechanism of action of glycans. However, they are usually confined within well-defined boundaries in highly specific fields and investigated by restricted pools of scientists with similar background. It is well established that a multidisciplinary approach merging many different expertise is the best way to tackle complex and multifaceted scientific challenges. It is difficult, however, to find suitable "platforms" capable of hosting a multidisciplinary team of scientists with diverse background in related but well distinct fields, such as biology, chemistry and physics, in order to achieve a wider, overall perspective.

These challenges have been recognized in the last five years by the international community as a priority area as demonstrated by the building up of glyco-consortia and the publication of papers and reports with a common claim: the understanding and the exploitation of glycoscience to pave the way for new and innovative area of research. Specifically, INNOGLY rests on two major pillars, each of them broken down into two main subtopics:

1) **Glycan profiling in health and disease**.

• Glycan-based correlations in developmental and cancer biology.

• Glycan dependent modulation of autophagy: cancer, lysosomal disorders and neurodegenerative diseases.

2) **Glycan-based diagnostics and therapeutics**.

• Glycan dependent fine tuning of immunity.

• Exploring the multifaceted roles of glycosaminoglycans (GAGs).

1.1.2. RELEVANCE AND TIMELINESS

After a slow start in the early 1990, an international effort of many investigators has resulted in truly interdisciplinary collaborative efforts worldwide, which have organized resources and techniques to elucidate and dissect the human glycome and to detect efficient approaches to regulate physio- and pathological processes mediated by glycans. To date, core glycomics facilities, consortia and shared labs that allow the access to specialized technologies have been built up both in EU countries (e.g. Glycoscience Laboratory, IBCarb network, ESF Euroglycoforum, EUROCarbDB, Copenhagen Center for Glycomics) and in non-EU countries (e.g. Consortium for Functional Glycomics, Emory Comprehensive Glycomics Core, Glycotechnology Core Resource, Alberta Glycomics Center, Institute of Glycomics, Japan Consortium for glycobiology, Human Disease Glycomics/Proteome Initiative). Given the huge number of such initiatives, this list cannot be exhaustive but it is a clue of the great level of interest and attention of the scientific community on glycans and related glycoscience. Moreover, a series of excellent roadmaps on glycoscience have been published in the last five years. A representative group of European Glycoscientists were in charge of a review on how glycoscience can contribute to the European Bioeconomy. In particular, they published a report 'A roadmap for Glycoscience in Europe' (initiative coordinated by ESF Euroglycoforum, IBI Carb network and European Science Foundation) wherein key areas of opportunities for glycoscience have been identified, and promoted the formation of trans-European coordinated research programmes based on open innovation partnerships between academia and industry. Besides the follow up of the EU roadmap, the so-called Metrology for Carbohydrates (CarboMet, https://carbomet.eu/) has been funded within the Coordination and Support Action of Horizon2020. It brings under the same umbrella glycoscientists from academia and industry to ensure full engagement of the glycoscience community across Europe to identify the current state of the art and in particular future innovation and technological challenges in carbohydrate metrology (https://carbomet.eu/). Recently, pioneering projects within the ERC Advanced grant as well as Innovative Training Network for young researchers have been funded to high level glycoscientists. The COST scheme has recognized the value of this research field and an excellent COST Action CM1102 'Multivalent Glycosystems for Nanoscience MultiGlycoNano' was recently concluded. Moreover, in 2012 the National Research Council (NRC) of the National Academies, published a report entitled Transforming Glycoscience: A Roadmap for the future. The committee in charge of this report consisted of a group of highly prominent glycoscientists coming from different fields such as chemistry, biology, medicine, and computer science who worked together to assess the importance and impact of the glycan code by exploring the landscape of current research. This effort identified the challenges that would need to be addressed to enable the field to move forward. Subsequently, in 2016 a working group convened by National Heart, Lung, and Blood Institute (NHLBI) composed of glycoscientists and experts coming from diverse disciplines published the report 'Training the next generation of biomedical investigators in glycosciences' in The Journal of Clinical Investigation wherein they suggested a promotion of the so-called "glycoscience desert" by exploiting targeted training programs. Of note, The Programs of Excellence in Glycosciences (http://pegnac.sdsc.edu/) sponsored by NHLBI is a reliable and exciting way to further this goal. This venture has achieved a resounding success by developing programs of supervised research training with the aim of bringing young, smart and promising researchers into this still poorly explored research

field. More recently, the journal Nature dedicated a paper titled 'Sweet success' on glycobiology, wherein the high-impact of glycoscience and the growing prospects for researchers to find career opportunities are highlighted.

1.2. OBJECTIVES

1.2.1. RESEARCH COORDINATION OBJECTIVES

The major objective of INNOGLY is to promote the communication and exchange of knowledge between glycoscientists and researchers working in scientific areas which, although different from glycoscience, are closely related with the topics selected in the present Action. The outcome of this sharing of know-how and synergism of expertise within the network will enable INNOGLY to improve the existing knowledge among these topics, by looking at them from different perspectives.

• Develop a collaborative effort to achieve a common ground on the topics 1) Glycan profiling in health and disease, and 2) Glycan-based diagnostics and therapeutics, as well as the related subtopics.

• Develop glycan-based tools (nanometric and small molecules) to track glycosylation pathways and to dissect immunomodulatory functions.

• Foster progress in existing research projects.

• Develop biosensors to investigate glycan-protein interactions.

• Promote the synthesis of glycomimetics and glycan-based analogues of specific target epitopes.

• Develop glycan-based and glycan-integrated biopolymers.

• Improve manipulation and engineering of glycan-based systems.

• Develop straightforward methodologies to synthesize oligosaccharides and glycoconjugates.

• Develop glycoproteomic tools to image protein-specific glycosylation changes.

1.2.2. CAPACITY-BUILDING OBJECTIVES

• Bridge the gap between scientific communities with complementary knowledge and common interests in glycan-related topics.

• Set up a platform for early career researchers.

• Help early career researchers to access and build new networks.

• Disseminate the results to foster new researchers (with a special focus on Inclusiveness Target Countries) to join the glycoscience community.

• Facilitate engagement between key players and stakeholders of the glycoscience community across Europe.

• Enhance public communication to boost promotion of glycoscience within the mainstream of biological sciences.

• Lead to increased funding opportunities for R&D.

1.3. PROGRESS BEYOND THE STATE-OF-THE-ART AND INNOVATION POTENTIAL

1.3.1. DESCRIPTION OF THE STATE-OF-THE-ART

1) Glycan profiling in health and disease. In this regard, INNOGLY will focus on: i) Glycan-based correlations in developmental and cancer biology; ii) Glycan dependent modulation of autophagy: cancer, lysosomal disorders and neurodegenerative diseases.

Some of the most significant biological roles of glycans have been elucidated by studying alterations in glycosylation pathways in genetically altered model systems and in human genetic disease. Indeed, defects in glycosylation pathways and/or genetically altered glycosylation patterns in vertebrate cell lines are powerful tools to shed light on many complex glycan biosynthetic pathways and, at the same time, they are often correlated with severe diseases and congenital pathologies. On the other hand, glycans by themselves may also act as signaling molecules internal to a given species. An in-depth understanding of these phenomena is expected to have a significant impact on public health due to the development of new therapeutic approaches.

i) Glycan-based correlations in developmental and cancer biology. There is a large body of evidence showing that glycans play crucial roles in all phases of development by promoting embryonic cell migration and proliferation, through modulation of the signaling properties of protein receptors embedded within or attached to the cell membrane. In this regard, an emerging concept suggests that the cell functions and processes that are indispensable for embryonic development are also essential for cancer progression. In the last two decades, this concept has driven cancer biology and developmental biology to “walk hand in hand”. In particular, relevant papers on the emerging role of the hedgehog signaling pathway in cancer, and the use of oncofetal antigens (*e.g.* O-glycosylated oncofetal fibronectin and the carcinoembryonic antigen) as markers for cancer diagnosis, have been published. More recently, the structural analogy between GAGs expressed by placenta and GAGs expressed on some cancer cells has been demonstrated.

ii) Glycan dependent modulation of autophagy: cancer, lysosomal disorders and neurodegenerative diseases. Autophagy is a survival-promoting pathway which plays a crucial role in cell biology. It is in charge of the capturing, degradation, and recycling of intracellular proteins and organelles in lysosomes. Thus, it plays an important role in protein and organelle quality control. In this framework, the genetic lysosomal storage disorders, such as the Gaucher disease, are caused by accumulation of nondegraded glycans in lysosomes due to the deficiency of a single lysosomal glycosidase. Recent studies highlight the importance of glycoconjugates in the regulation of autophagy, including glycosylation of cytoplasmic proteins (by O-GlcNAc transferase, OGT) and glycoconjugates in the extracellular environment. These diverse glycoconjugates may exert a stimulatory or inhibitory effect in a broad range of physiologically relevant conditions. For example, OGT through catalysing the attachment of GlcNAc to specific serines/threonines of proteins, is associated with numerous biological processes such as transcription, cell cycle progression, autophagy, stress response and nutrient sensing. Furthermore, it has been demonstrated that although autophagy in some contexts suppresses tumorigenesis, in most instances it facilitates tumorigenesis. Cancer cells can also upregulate autophagy to survive micro environmental stress and to increase growth and aggressiveness. On the other hand, autophagy deficiency is known to contribute to the pathogenicity in many neurodegenerative diseases. Therefore a better knowledge of the specific roles played by glycoconjugates in autophagy is a challenge that needs to be addressed.

2) Glycan-based diagnostics and therapeutics. INNOGLY will focus on: i) Glycan dependent fine tuning of immunity; ii) Exploring the multifaceted roles of glycosaminoglycans (GAGs).

All cell types express on their surface a dense, often highly conserved array of glycan structures (the so-called glycocalyx) which is tissue-, species- and cell-type specific, wherein carbohydrates are combined with other biomolecules such as proteins and lipids (glycoproteins and glycolipids). Beyond other crucial roles for cell survival (i.e. ensuring its mechanical stability and affording protection against infective microorganisms), all these glycoforms are key mediators of fundamental molecular recognition phenomena, including cell-cell interactions, cell-extracellular matrix (ECM) interactions, and ligand-receptor interactions. In this scenario, it became evident that specific recognition of a unique glycan could mediate an equally specific and critical biological role, and that modulation of the recognition event could be achieved by using carbohydrate-based drugs or carbohydrate targeting molecules.

i) Glycan dependent fine tuning of immunity. Significant alterations of the cellular glycoform(s) occur during differentiation and glycans could serve as specific cell markers and cellular differentiation biomarkers. Indeed, altered glycosylation patterns on malignant cell surfaces suggested specific roles in cancer progression, and interferes with the development of cancer immunotherapy. On the other hand, glycoforms expressed on pathogen surfaces have been identified as pathogen-associated molecular patterns (PAMPs). They are recognized by pattern recognition receptors (PRRs), such as some C-type lectin receptors and Toll-like receptors (TLR), on antigen presenting cells (APCs), triggering their uptake and processing into peptide fragments which are eventually presented by major histocompatibility complex (MHC) class II molecules to T lymphocytes, a critical process in the transition from innate to adaptive immunity. APCs, such as dendritic cells (DCs), provide a crucial bridge between the innate and adaptive responses, and they are responsible for the fundamental discrimination between self/non-self antigens. It is generally accepted that there is a common mechanism based on APC biology underlying the immune tolerance and the activation of the immune defence, and the different glycoforms exposed on self/non-self antigens' surface play an essential modulatory role. In addition, changes in the glycosylation pattern of circulating immunoglobulin-G (IgG) antibodies occur in autoimmune disease, and the extent of changes correlates with the disease severity. Cracking this 'sugar code' holds tremendous promise for deciphering disease mechanism and for immune modulation.

ii) Exploring the multifaceted roles of glycosaminoglycans (GAGs). Glycosaminoglycans (GAGs) are major ECM components and in the cellular milieu are found either free (hyaluronan, HA) or bound to protein cores of proteoglycans (PGs). These macromolecules are variously associated with surfaces of all mammalian cell types and are involved in a number of essential cellular events, such as embryogenesis, cell growth, adhesion and migration, viral invasion as well as the processes of tumour onset, growth and metastasis. For example, HA can bind with the CD44 receptor on the cell surface and provide cellular attachment. Many cancer cells overexpress such receptors and therefore, can be accurately targeted. Moreover, GAGs are known inhibitors of proteinases, proteolytic enzymes required for matrix remodelling and for modulating cell signalling via matrix constituents. This aspect is especially important since proteinases contribute to all stages of the metastatic cascade, thereby suggesting a multiple role of GAGs in cancer development and progression. Finally, the biological activity of most signalling proteins, including cytokines, chemokines (involved in immunity and inflammation) and growth factors (involved in cell growth and differentiation) are regulated by GAGs, such as heparan sulfate (HS), to which they bind. GAGs play also a critical role in maintaining the structural integrity of the nervous system through their many effects on neurons, glia, inflammatory cells and other cell types. Thus GAGs are key players of a large number of neurodegenerative diseases termed protein-folding disorders (PFDs) which include Parkinson, Alzheimer's, and Creutzfeldt-Jakob neurodegenerative diseases. In particular, GAGs can interact, *inter alia*, with Tau protein and α-synuclein protein, which are crucially involved in Alzheimer's and Parkinson's diseases, respectively. For example, it has been suggested that cellular accumulation of α-synuclein is a major cause of Parkinson's disease. Some lysosomal GAGs inhibit the protease cathepsin D, responsible of α-synuclein degradation, causing the neurotoxic accumulation of the protein.

Recently, GAGs hold great promise in the emerging field of biomaterials. Indeed, GAGs offer shock absorbance in several tissues. For example, keratan sulfate (KS), a highly charged GAG, has crucial roles in maintaining the corneal hydration and mechanical strength. Being utterly degradable inside the body, it is reasonable to assume that biomaterials prepared from ECM-derived GAGs will have the utmost potential for regenerative medicine applications. In this regards, glycans have been recently employed for the construction of glycan-based or glycan-integrated biocompatible polymers. This is a rapidly expanding field, providing very sophisticated biomaterials which find wide application for tissue (re)generation and engineering to replace or repair tissue that has been damaged through disease or trauma.

1.3.2. PROGRESS BEYOND THE STATE-OF-THE-ART

1) Glycan profiling in health and disease. In order to gain more insight into this topic and related subtopics, INNOGLY will forward the development of i) smart and reliable glycan-based tools; and ii) biosensors.

Altered levels and distributions of cell surface glycans as well as glycan binding proteins (lectins) are biomarkers of pathological conditions like infection and malignancy, but they also occur during various

phases of embryonic development, suggesting a key involvement and similar roles of glycans in two seemingly well separated fields like developmental biology and cancer biology. Indeed, embryos arise from a single cell and undergo rapid growth involving cell migration and cell-cell interactions. Moreover, the Warburg effect, as the result of the metabolic impairment of the oxidative phosphorylation, has been recently identified as a hallmark for both cancer and embryonic development. INNOGLY proposers will collect and share information concerning post-translational modifications and metabolic pathways occurring in fetal and cancer development. In this way, INNOGLY members, as well as the whole scientific community, will benefit from this extensive body of knowledge which allows to establish specific correlations among these two proliferative events. Moreover, as the same features of embryonic development are seen in the context of cancer, INNOGLY will promote the use of many of the experimental tools employed to study embryogenesis for studying cancer. Different innovative approaches will be boosted within this COST Action to gain insight on the role that glycosylation plays in cancer development and progression and on the molecular mechanisms controlling alterations of glycosylation that are important in the process of carcinogenesis. Indeed, the detailed molecular and biochemical characterization of specific glycosyltransferases directly related to the generation of Tumour Associated Carbohydrate Antigens (TACAs) will give an important contribution to assess changes and biological roles of carbohydrate epitopes in development and cancer stages. Moreover, specific carbohydrate-based technologies as well as different *in vitro* and *in vivo* models that allow the functional analysis of glycans in cancer, angiogenesis and immunomodulation will be employed within INNOGLY. The identification of disease-associated biomarkers has been the ground of many studies since several years, and while progress has been established, this is still a challenge and a huge unmet need. In this regard, INNOGLY will employ expertise in NMR spectroscopy and mass spectrometry and related cutting edge facilities available in academic and industrial partners for the characterisation at high-resolution of protein-glycan interactions. Additionally, the implementation of novel, sensitive and robust biosensors, such as smart saccharide-based nanomaterials with improved stimuli sensitivity, molecularly imprinted biopolymers (MIP), and bespoke microfluidic devices, will be promoted for fine detection of a variety of carbohydrate biomarkers, as well as to study effects of defective O-glycosylation during vertebrate development. INNOGLY will be also devoted to investigate the connection between autophagy and diseases associated with a dysregulation of this pathway, such as cancer, lysosomal disorders and neurodegeneration. Several lines of evidence indicate that glycans are the bridge: their signalling from the ECM converges on autophagy and autophagy related genes are regulated by glycosylation. In addition, oligosaccharide exposure in the cytosol has been reported to trigger an autophagic response. The sharing of expertise and know-how within the INNOGLY consortium will drive an in-depth study of the molecular details bridging glycans, autophagy and diseases, and of the regulation and mechanism of this intriguing clearance pathway.

On the whole, the implementation of this COST Action is expected to promote the development of new, smart and reliable diagnostic tools (nanometric, polymeric and small molecules) to track different glycosylation pathways and to correlate changes of glycosylation patterns with pathologic events. This would bring a significant progress in the field of biological sciences and medicine through better definition of glycans' role in cell biology, under both physiological and pathological conditions.

2) Glycan-based diagnostics and therapeutics. In order to gain more insight into this topic and related subtopics, INNOGLY will support innovative approaches i) to investigate the immunomodulatory functions of glycans; ii) to study the role of GAGs-proteins interactions in cancer and neurodegenerative diseases; and iii) to develop glycan-based and glycan-integrated biopolymers.

Within this COST Action the role of glycans as modulators of innate and adaptive immune responses will be investigated. New chemical tools based on innovative nanomaterials as mimicking system for in vitro and in vivo studies to dissect this immunomodulatory function will be developed. Nanomaterials as biosensors for the detection of anti-carbohydrate antibodies will be also investigated as new tools for diagnosis of pathologic events. In addition, in many infections (particularly in those induced by bacteria, fungi and many clinically important parasites), the antibody response is dominated by anti-carbohydrate antibodies rather than anti-protein/peptide because glycan-antigens are highly immunogenic and abundant on the glycocalyx and in secretions that are exposed to the host. For many infections the development of specific diagnostic tests remains an ongoing challenge regarding sensitivity and specificity. Therefore, the sensitive detection of antibodies specific to pathogen-derived glycan antigens justifies the development of diagnostic tests for specific infections. A well-known bottleneck for this development has been that single glycan-antibody interactions are of relatively low affinity and in the natural context of the pathogen, glycans are normally presented as a dense array of multivalent structures to generate high affinity molecular interactions. In the past, chemical strategies

have been developed to conjugate glycan-antigens to proteins, polymers and dendrimers to increase the antigen valency, improve the affinity and avidity of antibody binding and consequently also the sensitivity of detection. INNOGLY will promote the design and preparation of a new generation of nanometric carbohydrate-based tools to detect anti-carbohydrate antibodies in a sensitive and specific way to further explore this read-out as specific biomarkers to follow/detect an infection (or cancer).

The complex and dynamic interplay between GAGs and a vast array of ECM proteins as well as membrane receptors and lysosomal enzymes is a crucial biological step that contributes to the pathophysiology of cancer and neurodegenerative diseases. INNOGLY will promote the investigation in more detail of these close correlations by focusing on the role of GAGs. In particular, the mission of this COST Action is also to forward the study of the structural, functional and recognition role of GAGs within proteoglycans by means of advanced technologies and facilities available in the research institutes involved. Indeed, it was demonstrated that Raman micro-spectroscopy and NMR-based methods allow recording of the discrete GAG profiles of individual live cells making feasible its use for cell screening purposes. This method can potentially be utilized for identifying specific molecular signatures of GAGs as a marker of cancer progression in tissues. This is important as during tumor progression there is a remodelling of PG glycosylation of both cell surfaces and the ECM, among others, through heparanase action. Heparanase is an enzyme that cleaves PG HS-side chains, thus strongly modulating various regulatory pathways, including the bio accessibility of HS-binding growth factors and cytokines. Additional challenges are i) a deeper understanding of the role of glycosylation of proteins involved in neurodegenerative diseases (*e.g.* Tau protein), and ii) the interactions of amyloid proteins (*e.g.* α-synuclein) with glycolipids embedded in the plasma membranes. Advances in this field are urgently needed since they would pave the way for elucidating the onset and progression of such diseases, and for the definition of new innovative therapeutic approaches. On the whole, significant advances are expected within this COST Action by combining structural, analytical (*e.g.* mass spectrometry, high-resolution NMR spectroscopy and theoretical analysis) and cutting-edge biological approaches (advanced cellular models and relevant clinical samples), with the aim to better understand the structure-activity relationships of these interactions and investigate their biological function, especially in terms of cancer progression and neurodegenerative diseases.

INNOGLY will support also the development of advanced biopolymers. For example, several chemically crosslinked GAG hydrogels are currently available, however, with only limited applications in the clinic. In most cases, such hydrogels are employed as injectable materials. Within this COST Action, the potential of GAGs beyond their use as delivery vehicles will be explored. Degradable HA-based hydrogels with suitable bio-instructive cues can be prepared to be used as an in vivo patch to support the migration, proliferation and differentiation of endogenous progenitor cells. The swelling and degradation of such hydrogels can be controlled by altering the degree of chemical crosslinking and incorporation of bioinert polymers, such as PEG (polyethylene glycol) or PVA (polyvinyl alcohol). Thus, INNOGLY will provide a platform to exchange expertise that will be highly valuable to develop a technology where GAGs can be used in novel approaches.

1.3.3. INNOVATION IN TACKLING THE CHALLENGE

To the best of our knowledge, INNOGLY provides an unprecedented opportunity to form a network of scientists with highly diverse expertise, brought together to tackle common challenges in the vast field of glycosciences. Given the multiple roles that glycans play in many research areas, only a cooperative interdisciplinary approach carried out by a pool of scientists with diverse and specific expertise may lead to better understand the structure, function and mechanism of action of carbohydrates and glycoconjugates. To achieve such an ambitious goal, it is necessary to bring together experts from different fields, including biochemists, biophysicists, (nano)material scientists, structural and cellular biologists, medical biotechnologists, immunologists, analytical, medicinal, computational, and synthetic organic chemists. Indeed, joining experts in developmental biology with experts in cancer biology is crucial to gain new insights into correlations of the glycosylation pattern changes in cancer and embryonic development. To this end, the collaboration with biosensor developers to detect the glycosylation patterns is of paramount importance. Likewise, experts in glycobiology will interact with teams addressing GAGs and their multiple roles in development, repair, defence mechanism and disease, as well as with scientists studying the role of glycoconjugates in the connection between autophagy and several diseases associated with a dysregulation of this pathway. Moreover, the collaboration with analytical chemistry experts in NMR spectroscopy and mass spectrometry will be key for the characterization of protein-glycan interactions and detection of novel

saccharide-based biomarkers. Synthetic organic chemists will provide synthetic oligosaccharides and/or glycomimetics to be employed as models to study their roles in different biological contexts in collaboration with the partners with large expertise in advanced biological models. Therefore INNOGLY will foster knowledge exchange by developing a joint research agenda around glycoscience-related topics of major scientific and socio-economic relevance.

1.4. ADDED VALUE OF NETWORKING

1.4.1. IN RELATION TO THE CHALLENGE

The added value of INNOGLY is the team. It consists of a multidisciplinary group including researchers coming from the glycoscience community and experts of the afore-mentioned research fields, willing to mutual exchange of knowledge, skill and expertise to address the same pioneering goal: Gaining new insight into the biological function of glycans in different biological contexts. INNOGLY aims at supporting such a highly multidisciplinary network and aspires to become a common “umbrella” where scientists with multiple diverse and complementary skills and expertise are fostered to meet others speaking the same scientific language. Thus, the goal is to forge collaborations among researchers, each spurred to pursue his/her own research interests, and to intermesh these interests with other colleagues in order to move forward new concepts by exploiting their proper expertise. A major outcome that could emerge from this COST Action is the opportunity to look from different perspectives at specific scientific “puzzles” involving different disciplines but having glycans as the common denominator. These achievements could only be reached within the INNOGLY innovative collaborative multidiscipline context. Finally, the multidisciplinary nature of the INNOGLY team will help to improve the visibility of glycoscience to industry and the society as a whole.

1.4.2. IN RELATION TO EXISTING EFFORTS AT EUROPEAN AND/OR INTERNATIONAL LEVEL

The European Union pays special attention to research in glycoscience (see section 1.1.2.). In a time of such great ferment there is the need for initiatives like the one proposed by this Action. INNOGLY is a golden opportunity to transfer knowledge. Indeed, INNOGLY aims at giving a valuable contribution to the disclosure of the still unknown roles of glycans by exchange of know-how between a multidisciplinary and complementary group of researchers. Thus, the idea is to instil the passion for this research field to researchers, especially young investigators, who have never been involved in glycoscience. As a consequence, they can provide improvements and new tips by bringing their different point of view. Moreover, this COST Action will encourage the interactions with already funded actions, such as COST Action CA15138 ‘European Network of Multidisciplinary Research and Translation of Autophagy knowledge’, the COST Action BM1406 ‘Ion Channels and Immune Response toward a global understanding of immune cell physiology and for new therapeutic approaches’ and the COST Action CA16122 ‘Biomaterials and advanced physical techniques for regenerative cardiology and neurology’.

2. IMPACT

2.1. EXPECTED IMPACT

2.1.1. SHORT-TERM AND LONG-TERM SCIENTIFIC, TECHNOLOGICAL, AND/OR SOCIOECONOMIC IMPACTS

The long term scientific perspective of this Action is focused on research fields where the role of glycans in several health-related issues needs to be explored in detail and exploited for medical applications, from diagnostic to therapies. Two major investigation lines have been selected: 1) glycan profiling in health and disease, and 2) glycan-based diagnostics and therapeutics. They share common grounds in the developments of accessible new tools and technologies that would make glycosciences (i) less complex, (ii) easily available, and (iii) affordable for any chemistry, biochemistry,

biomedical or biotechnological investigator. Easier understanding and adaptation to different systems, as well as integration with genomic and proteomic databases, constitute short-term perspectives. These should increase our understanding of biological function resulting in: (i) improving manipulation and engineering of glycan-based systems, and (ii) enhancing the quest for biomarkers. Glycoscience is central to many disciplines (chemistry, biochemistry, microbiology, medicine, physiology, developmental biology, material science and computational science). Any progress in the process of acquiring and sharing data in an optimal timescale will benefit a large scientific and technological audience, and translates in training and education. The agreement on appropriate instruments, protocols and methodologies will promote the ad hoc production of glycomics data and drive relevant companies to standardization with carbohydrate derivatives. The glycomics market is rapidly expanding and currently its largest share is in academic research institutes. This illustrates that glycomics remains to be fully exploited as novel technology by the industry. The major barrier hampering the entry of industries in this research area is the lack of tools and standard procedures. The design of this Action addresses the urgent need for fast, efficient and reproducible carbohydrate analysis which can be used not only as discovery tools but also for quality control of carbohydrate-based products, such as foods, biopharmaceuticals or cosmetics, as well as processing carbohydrate-based feed stocks and developing more effective disease diagnostic kits and better targeted/personalized medicine.

2.2. MEASURES TO MAXIMISE IMPACT

2.2.1. PLAN FOR INVOLVING THE MOST RELEVANT STAKEHOLDERS

The range of stakeholders is wide, from academic research institutes and organisations, to pharmaceutical, nutraceuticals and biotechnological companies, and further to patient organizations. It also includes manufacturers and vendors of glycomics enzymes, kits, reagents and instruments. In its current application phase INNOGLY involves representatives from academic research institutes and organisations, covering the areas of chemistry, medicine, pharmacy, nutrition, biology and biotechnology, material science and bioinformatics. Some of the proposers are already involved in EU-funded initiatives. Liaising with these on-going initiatives will facilitate engagement between key players and stakeholders of the glycoscience community across Europe. After the second year, a meeting will be organized for representatives of the EU private sector and full Action participants, in order to present the results and consult for technology transfer. This will provide a forum for public-private collaboration leading to submissions of joint research proposals or other translational actions.

2.2.2. DISSEMINATION AND/OR EXPLOITATION PLAN

Dissemination of results is a key objective, and target audiences fall into three categories. (i) Academic and industrial researchers active in the fields of glycoscience and glycotechnology at large, who will be the immediate beneficiaries of the research output; (ii) European and national policy makers who can capitalise on the initial results of the Action as they formulate funding strategy and calls for proposals; (iii) the general public, including high school and undergraduate students, who could benefit from proper and currently lacking education in glycoscience and glycotechnology. A series of actions will be organized: (i) scientific publications and review articles reporting results of cooperative work; (ii) Working Group meetings including joined meetings with other Actions having complementary objectives; (iii) Action workshops with external expert speakers and lectures at national/international conferences; (iv) Training School events towards learning and exploiting novel findings; (v) lectures at host institutions given by undergraduate and postgraduate fellows; (vi) public engagement in science events; (vii) Action website with public engagement pages, overview of each WG and links to public results; (viii) contributions to training actions on internet (e.g., glycobiology and glycochemistry e-learning course, glycopedia.eu). INNOGLY will benefit from the input of members already involved in H2020 programmes. Members of the Management Committee and Working Groups while attending other scientific meetings will act to promote collaboration with complementary programmes and avoid possible redundancy. Related to intellectual property (IP) strategy and patents, the Action aims at providing opportunities for collaborative work but will not interfere at the IP stage other than encourage participants to take the necessary steps to protect their inventions.

2.3. POTENTIAL FOR INNOVATION VERSUS RISK LEVEL

2.3.1. POTENTIAL FOR SCIENTIFIC, TECHNOLOGICAL AND/OR SOCIOECONOMIC INNOVATION BREAKTHROUGHS

INNOGLY will contribute to accelerate the dissemination of knowledge on the roles of glycans in various biological contexts where the post translational protein glycosylations play crucial functions. In addition, INNOGLY will contribute to the development of improved glycan-based diagnostic and therapeutic tools. Due to such ambitious goals, INNOGLY is a high-risk initiative, according to the "no risk, no gain" slogan. INNOGLY partners, however, firmly trust in the strength and potential of this Action, as all proposers are highly motivated and determined to integrate their efforts and expertise to achieve the main objectives. Indeed, the Action proposers are truly confident that the innovations promoted by INNOGLY will have a great impact on the basic glycoscience research and, more generally speaking, on the whole society. Moreover, the active involvement and intense training of young investigators is an investment for future advances of glycoscience in the mainstream of biological sciences to bridge the gap with other life science disciplines.

3. IMPLEMENTATION

3.1. DESCRIPTION OF THE WORK PLAN

3.1.1. DESCRIPTION OF WORKING GROUPS

The INNOGLY scientific program is organized in Working Groups (WGs). The list of topics, objectives and tasks is not exhaustive and will be open to the inclusion of new ideas, developments and opportunities put forwards by the participants. Synergisms between the WGs will be promoted by WG Leaders in order to achieve the Action's objectives. For each WG, activities are described as Objectives (O), Tasks (T), Deliverables (D), and Milestones (M).

WG1 Glycan-based correlations in developmental and cancer biology. Discussion and exchange of knowledge and know-how between INNOGLY participants will be focused on the concept that cell behaviour and processes that are indispensable for embryonic development are also essential for cancer progression.

O 1.1 Investigate correlations between the glycosylation pattern changes in cancer and embryonic development.

O 1.2 Promote the development of novel and improved biosensors for detection and characterization of glycan biomarkers, and identification of new targets of protein glycosylation.

O 1.3 Promote the development of smart tools and innovative techniques for tracking glycosylation pathways.

T 1.1 Use molecular biological approaches and functional genomics in model organisms to assess changes and biologic functions of glycan epitopes in development and cancer states.

T 1.2 Employ advanced techniques to characterize protein-glycan interactions at atomic level.

T 1.3 Boost the development of saccharide-based biotools (nanometric and small molecules), for monitoring glycosylation pattern changes in proliferative-based events.

T 1.4 Boost the development of biosensors (nanomaterial- and polymer-based).

T 1.5 Promote the development of in vitro and in vivo models for functional analysis of glycans.

D 1 Report on the main advances in the field and developed activities related to WG1 (month 12, 24, 36, 48)

M 1.1 Workshops related to the topics of WG1.

M 1.2 Symposia of the Action.

WG2 Glycan dependent modulation of autophagy: cancer, lysosomal disorders and neurodegenerative diseases. Discussion and exchange of knowledge and know-how between INNOGLY participants will be focused on the role of glycans in the modulation of autophagy pathways.

O 2.1 Promote the investigation of the role of glycans in the modulation of autophagy in cancer.

O 2.2 Promote the investigation of the role of glycans in the modulation of autophagy in lysosomal disorders.

O 2.3 Promote the investigation of the role of glycans in the modulation of autophagy in neurodegenerative diseases.

T 2.1 Employ advanced techniques to track the glycosylation pattern of glycoconjugates associated to autophagy.

T 2.2 Promote the identification of relevant model systems to investigate the glycan dependent modulation of autophagy.

T 2.3 Boost the development of autophagy modulators (nanometric, small molecules and glycoconjugates).

D 2 Report on the main advances in the field and developed activities related to WG2 (month 12, 24, 36, 48)

M 2.1 Workshops related to the topics of WG2.

M 2.2 Symposia of the Action.

WG3 Glycan dependent fine tuning of immunity. Discussion and exchange of knowledge and know-how between INNOGLY participants will be focused on the role of glycan in the fine tuning of immunity

O 3.1 Promote the investigation of the modulatory role of glycans in innate and adaptive immune response.

O 3.2 Promote the investigation of the modulatory role of glycans in immune tolerance.

T 3.1 Employ advanced techniques to track the glycan-dependent modulation of immunity.

T 3.2 Boost the development of synthetic methodologies to achieve complex oligosaccharides involved in self/non-self recognition processes.

T 3.3 Promote the development of glycan-coated nanomaterials as mimicking systems

T 3.4 Promote the development of *in vitro* and *in vivo* models to enable the functional analysis of glycans in immunomodulation.

T 3.5 Promote the development of biosensors for detection of anti-carbohydrate antibodies.

D 3 Report on the main advances in the field and developed activities related to WG3 (month 12, 24, 36, 48)

M 3.1 Workshops related to the topics of WG3.

M 3.2 Symposia of the Action.

WG4 <u>Exploring the multifaceted roles of glycosaminoglycans (GAGs)</u>. Discussion and exchange of knowledge and know-how between INNOGLY participants will be focused on the role of GAGs in the activation of cancer and degenerative related pathways. Then, special attention will be devoted to the discussion on the development of GAGs-related biopolymers.

O 4.1 Promote the investigation of the role of GAGs in cancer development and progression.

O.4.2 Promote the investigation of the role of GAGs in the onset and progression of neurodegenerative diseases.

O 4.3 Develop GAGs-based fully biodegradable hydrogels which can be used as a patch for *in vivo* applications.

T 4.1 Combine theoretical analysis and advanced techniques to characterize GAGs structures and conformations.

T 4.2 Employ advanced techniques to study the protein binding properties of GAGs.

T 4.3 Foster the development of synthetic and chemo-enzymatic methodologies to achieve GAGs-related oligosaccharides to study their roles in cancer and neurodegenerative diseases.

T 4.4 Promote the development of model systems to investigate the interactions of GAGs with proteins involved in neurodegenerative diseases.

T 4.5: Develop GAGs-coated hydrogels as implant for rapid epithelialisation *in vivo*.

T 4.6 Develop GAGs-based hydrogel patch that can support *in vivo* vascularisation.

D 4 Report on the main advances in the field and developed activities related to WG4 (month 12, 24, 36, 48)

M 4.1 Workshops related to the topics of WG4.

M 4.2 Symposia of the Action.

3.1.2. GANTT DIAGRAM

Tasks		Year 1				Year 2				Year 3				Year 4			
		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
WG1	T 1.1																
	T 1.2																
	T 1.3																
	T 1.4																
	T 1.5																
WG2	T 2.1																
	T 2.2																
	T 2.3																
WG3	T 3.1																
	T 3.2																
	T 3.3																
	T 3.4																
	T 3.5																
WG4	T 4.1																
	T 4.2																
	T 4.3																
	T 4.4																
	T 4.5																
	T 4.6																

3.1.3. PERT CHART (OPTIONAL)

3.1.4. RISK AND CONTINGENCY PLANS

Risk	Likelihood	Involved structures	Impact	Proposed measures
Low or inexistent interactions between members	M	MC	H	Identification of topics of common interest
Partners leave the consortium	L	MC	M	Reorganize tasks, meetings and look for other members with similar skills
WG activities are not integrated	L	MC, WGs	H	Stimulate WG leaders to organize joined workshops and training courses
Delayed availability of glycan-based diagnostic tools and biosensors	M	WGs	H	Identification of the challenges and use of alternative strategies and techniques
Delayed availability of synthetic glycans and glycomimetics	M	WGs	H	Pro-active identification of the challenging steps and use of alternative synthetic strategies

3.2. MANAGEMENT STRUCTURES AND PROCEDURES

The Action will be managed by an Action Management Committee (MC), comprised of up to two members per each participating country. The MC members will be designated during the first weeks of the Action. The Memorandum of Understanding (MoU) will serve as the basis for participation in the MC by countries that might join the Action during the first three years. The Action is aimed for a total duration of four years. A key goal of the INNOGLY MC will be to implement COST rules and procedures, as reported in the COST Open Call – SESA Guidelines. In particular, the Action management will comply with the vision and mission of COST, being European, open and inclusive, involve researchers from different disciplines, gender equality, engage young researchers and develop easy networking tools within simple rules.

At the kick-off meeting, the MC will elect the Action Chair and Vice-Chair, the Working Group Leaders (and Vice-Leaders), and the Grant Holder. In addition, the MC will appoint amongst its members: i) Short-Term Scientific Missions (STSM) Committee/Coordinator; ii) Training School (TS) Committee/Coordinator; iii) Dissemination activities Committee/Coordinator.

The MC will reserve at least two of these key leadership positions to representatives of COST Inclusiveness Target Countries (ITC). All the Committees will hold teleconferences on an *ad hoc* basis.

The MC is committed to recognize the crucial role of young researchers. They will participate in all INNOGLY symposia, and in workshops and TS more related to their specific field. All scientists involved in the network of proposers have been involved in the organization of conferences or meetings in which early stage researchers were deeply involved. In addition, INNOGLY aims at including Early Career Investigator (ECI) in each of the WGs as secondary responsible persons. In collaboration with the Dissemination Committee, the MC will appoint at least two ECI to actively promote INNOGLY in social media. The MC members will communicate through regular conference calls and email, but they will meet at least once per year. The tasks will be shared out among the committees as reported in the following table:

Tasks of the MC	
1.	Prepare a detailed Work and Budget Plan for each Grant Period.
2.	Monitor the progress of the whole Action, by writing a midterm report and annual reports, highlighting work made in collaboration among participants.
3.	Promote the participation of ECI in the Action.
4.	Monitor gender equilibrium within the program, analyse results and implement corrective measures to improve gender balance. INNOGLY aims at having gender equilibrium in the Chair-Vice Chair and in the WG leadership structures.
5.	Monitor the amount of publications made in collaboration among INNOGLY members, and foster collaboration to improve the ratio of collaborative publications with respect to all publications of the Action.
6.	Organize the Action symposia.
Tasks of the WG Leaders	
1.	Ensure the development of the objectives and tasks for reporting to the MC.
2.	Propose ECI for invited talks within INNOGLY meetings and in related conferences.
3.	Organize the workshops related to each WG.
Tasks of the STSM Committee	
1.	Organize and foster scientific exchanges through STSM, especially involving ECI.
2.	Monitor the STSM by preparing notes to outline the activities every three months and communicate the selection of STSM grantees to the MC in subsequent MC meetings.
Tasks of the TS Committee	
1.	Organize Training Schools to train ECI in the different themes of glycoscience.
2.	Invite prestigious scientists with different expertise to deliver lectures.
3.	Work in close cooperation with WG leaders in order to avoid possible redundancies.
Tasks of the Dissemination Committee	
1.	Establish and manage a INNOGLY website by the first six months of the Action.
2.	Advertise the INNOGLY website through emails, at glycoscience conferences and workshops, at societies, through personal websites of the proposers, and social media.
3.	Spread announcements on the web of schools, symposia and any other activity related to the INNOGLY scientific area.
4.	Foster dissemination of INNOGLY activities for great public and policy stakeholders through most popular social media (Linkedin, Twitter and Facebook).
5.	Work in close cooperation with the WG leaders and the TS Committee to support the transfer of knowledge between Action participants and the scientific community.
6.	Explore and inform participants about any kind of initiative for funding science or science dissemination activities related to INNOGLY topics.

3.3. NETWORK AS A WHOLE

The commitment of a large community of researchers to INNOGLY Action is made visible through the network of proposers. The INNOGLY network includes 34 proposers from 15 COST member countries (including a COST Cooperating Member and one SME), and one International Partner. In particular, the network consists of more than 30% of Inclusiveness Target Countries, 5 ECI and almost 23% of female participants. INNOGLY is:

Committed to support excellence. The network supports very active scientists in the fields of biochemistry, biophysics, (nano)material science, structural and cellular biology, medical biotechnology, immunology, analytical, medicinal, computational, and synthetic organic chemistry. However, despite their different backgrounds, the current research fields of the participants are related to glycoscience in one way or the other. The participants routinely use cutting-edge infrastructures, consisting of large or medium scale experimental facilities and computational facilities.

Engaged in fostering European leadership. The INNOGLY participants are prominent scientists in their own research area and they have high reputation both at national level and within the international context through connections with European and non-European colleagues.

Engaged in fostering networking activities. All networking activities of INNOGLY will aim at facilitating the formation of collaborative sub-groups of researchers, to favour applications for research grants from EU and other funding agencies. Particular attention will be also devoted to push scientific cooperation amongst INNOGLY members, in order to deliver a significant number of high-impact joined publications.

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