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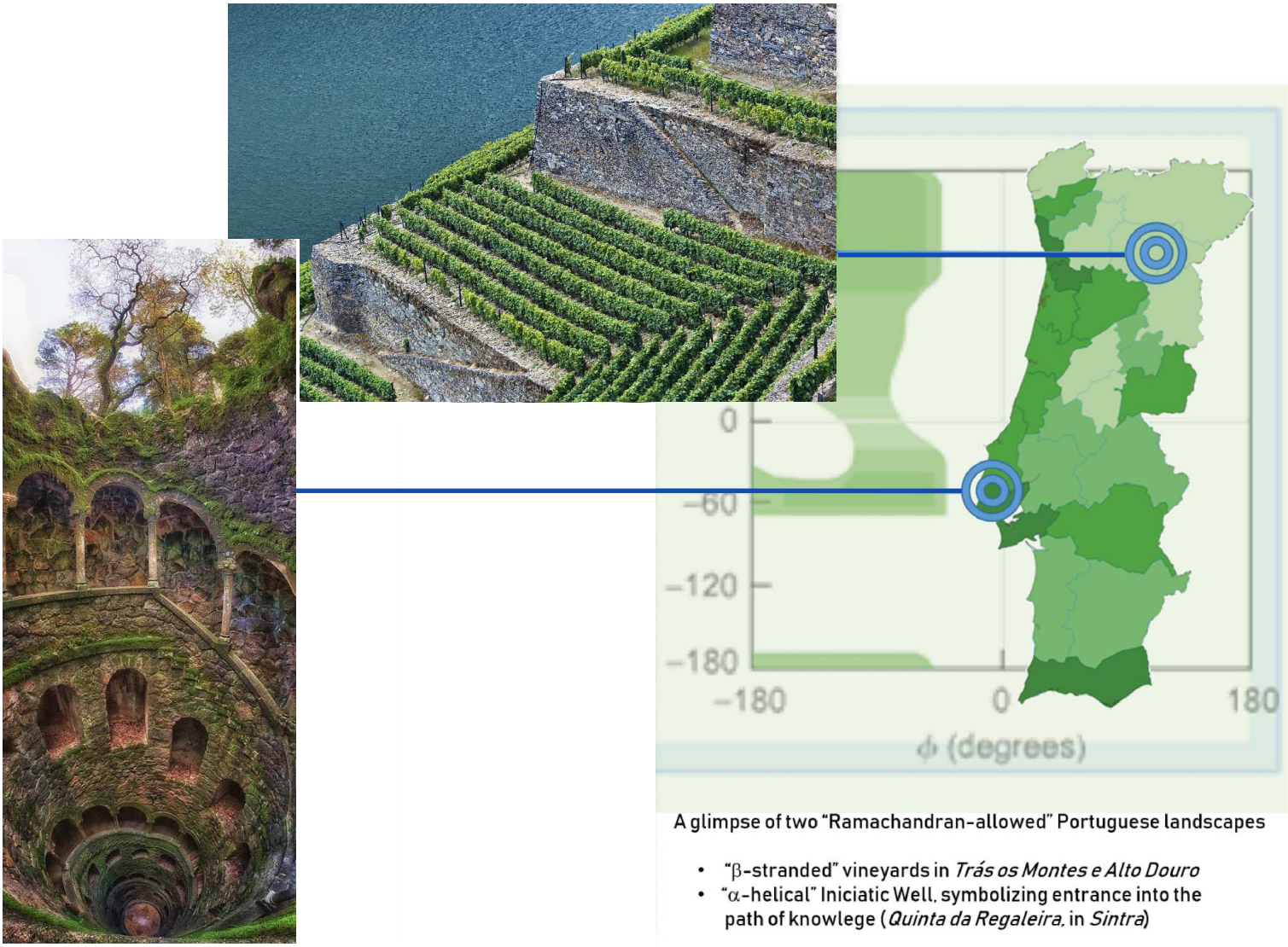

A glimpse of two "Ramachandran-allowed" Portuguese landscapes

- "β-stranded" vineyards in *Trás os Montes e Alto Douro*
- "α-helical" Iniciatic Well, symbolizing entrance into the path of knowlege (*Quinta da Regaleira*, in *Sintra*)

$(PT)^2$ – Peptide Therapeutics in Portugal
7th Austrian Peptide Symposium
16th Iberian Peptide Meeting
Jan Izdebski (1937–2018)
Society News

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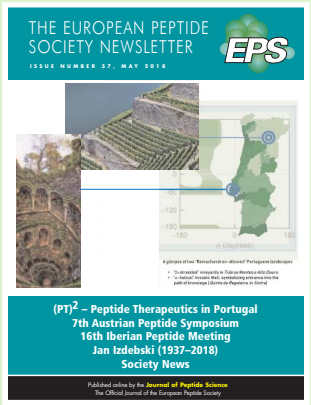

Cover photo: A glimpse of two "Ramachandran-allowed" Portuguese landscapes; designed by Paula Gomes

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SOCIETY NEWSLETTER

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(PT)^2 – Peptide Therapeutics in Portugal

Peptides are transversally relevant to many different fields of research and development, both in academic and industrial settings. They are ubiquitously found in diverse scientific, technological and biotechnological initiatives, spanning from Molecular Biology to Materials Science, from Synthetic Chemistry to Computational and Structural Biology, from Food Science to Biotechnology, from Early Drug Discovery to the Clinics ... still, Life and Health Sciences are undeniably the field of knowledge where peptides and proteins have been most widely and deeply studied and employed, aiming at development of novel peptide-based therapeutic molecules, devices and strategies. Moreover, the number of approved and marketed peptide and protein-based therapeutics has been steadily increasing, reflecting a paradigm shift at the Pharmaceutical Industry, while holding great promise for the future of Peptide Science.

On the ocasion of the EPS-sponsored XV Iberian Peptide Meeting, held in Porto, Portugal, in February 2016 (*photo below*), it was possible to witness the recent growth and diversification of peptide-based research led by Portuguese scientists, ultimately targeting development of innovative therapeutic approaches. This article is a snapshot of work conducted by those researchers.

Fuelling peptide drug discovery:

chemical synthesis of amino acids and peptides

Amongst the earliest established Portuguese research groups in Peptide Science, are those founded at the Universities of (**1**) Minho in Braga, and of (**2**) Porto, respectively by the Chemistry Professors Hernâni Maia and Maria Joaquina Amaral-Trigo. Today, both groups maintain their original focus on chemical synthesis of amino acids and peptides, in most cases aimed at therapeutic applications.

(1) Establishment of new methods for the synthesis of unnatural amino acids and peptidomimetics with possible biological activity, is the major focus of the Applied Biomolecular Chemistry group at the Chemistry Center of the University of Minho. There, researchers like Susana Costa, Sameiro Gonçalves and Sílvia Pereira-Lima develop non-proteinogenic amino acids, including α,α-dialkyl glycines or heterocyclic amino acids, by combination or modification of natural amino acids with oxygen, sulphur and nitrogen heterocycles, are valuable scaffolds for the assembly of new peptide analogues and mimetics with improved metabolic resistance and bioactivity (such as antimicrobial peptaibols) or photophysical properties. The introduction of unnatural fluorescent amino acids into peptide sequences can result in intrinsic labelling, which is of interest in order to further elucidate the mechanism of action of the resulting peptides, by fluorescence imaging techniques, acting as fluorescent imaging probes and chemosensors for biomedical analytes. Also, other heterocyclic UV and NIR fluorescent probes for biomolecule labeling, through covalent and non-covalent interactions to amino acids or DNA (intercalative and/or groove binding), and staining capability in gel electrophoresis were also developed based on new benzo[α]phenoxazinium derivatives. In addition to imaging applications, these benzo[α]phenoxazinium derivatives also display antiproliferative activity using the yeast *Saccharomyces cerevisiae* as a model organism, and function as photosensitizers in photodynamic therapy of *Candida albicans* biofilms.

Another branch of their research includes the development of new photocleavable protecting groups and photoactivable prodrugs that allow temporal and spatially controlled release of the drug. The design and synthesis of novel heterocyclic photocleavable protecting groups with one- and two-photon excitation for the caging of amino acids (including neurotransmitters), biogenic

amines and bioactive peptides is also being carried out.

(2) Peptide chemistry is a major toolbox in ORCHIDS (www.fc.up.pt/orchids/), the bioorganic and medicinal chemistry focused group settled at the Department of Chemistry and Biochemistry of the Faculty of Sciences of the University of Porto. There, the team led by Paula Gomes (www.fc.up.pt/pessoas/pgomes/) utilizes both solution- and solid-phase synthesis approaches to produce (i) bioactive peptides of diverse sizes and structural complexity, and (ii) amino acid or oligopeptide derivatives of active pharmaceutical ingredients.

The team has a strong motivation towards development of new strategies against infectious diseases, both from the Medicinal Chemistry and the Biomedical Engineering perspectives, for which has established strong collaborations with colleagues having complementary skills while sharing this common interest. Amongst the major peptide-based synthetic targets in Gomes's lab, the following are included: prodrugs and peptidomimetic derivatives of classical antimalarial drugs, antimicrobial and cell penetrating peptides, and conjugates of the latter with anti-infective agents. Chemoselective approaches to graft antimicrobial peptides onto biomaterials with potential biomedical applications are also amongst the group's major research goals.

The "ORCHIDS" team, coordinated by Paula Gomes

In parallel, Gomes coordinates the University of Porto's Peptide Synthesis Facility (goo.gl/d5bRFi), the only of its kind in Portugal.

Tackling infectious diseases and beyond: understanding membrane-active peptides

Application of molecular biophysics tools to answer biological questions underpinning the putative mechanisms of action (MoA) of antimicrobial peptides (AMP), cell-penetrating peptides (CPP) and viral peptides (VP), has been the mainstay of Portuguese researchers who have brought together the worlds of biophysics and membrane-active peptides: Margarida Bastos (University of Porto, 3), Miguel A. R. B. Castanho (University of Lisbon, 4), and Nuno C. Santos (University of Lisbon, 5).

(3) Margarida Bastos has worked for more than a decade on AMP, as a potential new paradigm in antibiotic therapy.

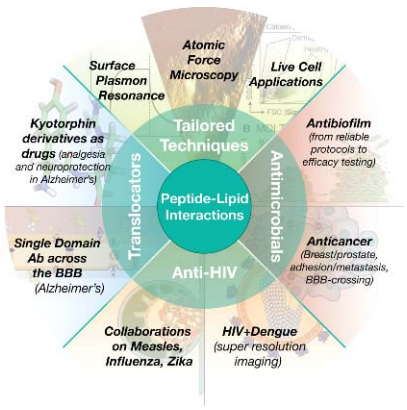
The work started in a collaboration that continues up to present with Paula Gomes (see 2) and David Andreu (Universitat Pompeu Fabra, Barcelona), initially testing peptides of the cecropin-melitttin family of known antimicrobial activity in lipid model membranes in order to unravel their MoA. In 2006, a collaboration was initiated with Jan G. Bolscher (Academic Center for Dentistry, Amsterdam), dealing with AMP from the lactoferrin family, known initially to be particularly active against *C. albicans*. The work conducted on model membranes used a wide variety of biophysical techniques, such as calorimetry (DSC and ITC), fluorescence microscopy (in collaboration with Manuel Prieto and Ana Coutinho, University of Lisbon), CD, DLS, SAXD and SANS. Bastos proposed DSC as a first line technique in these studies, to test for antimicrobial activity and toxicity, and showed that the biophysical studies involving model membranes can lead to mechanism unravelling, displaying a rewarding parallel with actual pathogen studies with the same peptide.

Aiming at bridging the model membrane work with the activity on actual pathogens, a collaboration was established with Luis Rivas (CSIC, Madrid), to study the activity of chimera peptides from the N1 domain of actoferrin against *Leishmania*. All the chimera peptides were leishmanicidal against *L. donovani* promastigotes, and more potent than their two parent peptides. The chimera induced plasma membrane permeabilization and bioenergetic collapse of the parasites.

In collaboration with Salomé Gomes (University of Porto) peptides derived from human and bovine lactoferrin were tested against *Mycobacteria*. This enabled

identification of key peptide features associated with improved antimicrobial activity, apparently associated to increased macrophage ability to kill infecting bacteria.

(4) Peptide-lipid biomembranes interactions are ubiquitous in the living world and a fertile ground for drug discovery and development. Enveloped viruses can be stopped at the entrance of cells, bacteria and cancer cells can be defeated almost without resistance using lytic peptides, and pain killing peptides can be modified to target the central nervous system across the blood brain barrier (BBB), among other applications. Miguel Castanho's group (https://imm.medicina.ulisboa.pt/en/investigacao/labs/castanho-lab/) is interested not only in drug targets and drug discovery itself, but also in developing innovative methodologies in search for tailored technical solutions to solve the most pertinent problems in the field of lipid membrane-active peptides (Figure 1, below). Their expertise is the development and application of tailored biophysical techniques to dissect the molecular mechanism of action of membrane-active peptides directly in viruses, bacteria or cells, so that innovative drugs and therapeutic tools can be devised. Using a judicious network of complementary collaborations, Castanho's team streamlines its activity from innovative molecules to effective applications. Castanho coordinates a H2020 project involving ten teams from five countries in three continents aimed at



Castanho's team core work is the study of peptide-lipid interactions in different domains using tailored biophysical techniques. Seminal work with translocator peptides ("cell-penetrating peptides"), anti-HIV peptides and antimicrobial peptides have evolved into recent applications in drug development against bacterial biofilms, cancer, viral infectivity, and neuroprotective drugs.

developing drug leads to fight bacteria and brain-targeted metastatic breast cancer.

Recent work of Castanho lab on viruses has been focused mainly on Dengue. They have shown that Dengue virus capsid protein is multifunctional, and proposed that this protein has a role in the transport of viral RNA across the virus envelope/endosome membrane interface. This is a disruptive working hypothesis in molecular virology that paved the way to unravel the biotechnological potential of Dengue virus capsid protein domains, whereby new antimicrobial and antivirals leads are being unveiled by combination of bioinformatics and experimental tools.

Castanho's team work that unraveled the mechanism of action of AMP bridged biophysics and microbiology, demonstrating that it is possible to correlate quantitatively physical chemistry data obtained in membrane model systems with the efficacy of killing of bacteria. The relationship is not universal but sets a general trend among peptides that target and disrupt bacterial membranes by direct physical action. This hypothesis has been confirmed by totally independent groups working with different techniques. Moreover, in Castanho's lab innovative methodologies were set using Atomic Force Microscopy (AFM), zeta potential spectroscopy (DLS), and flow cytometry (FACS) that are now being used by peers in the field. For instance, cellular applications of AFM have been used to unravel the impact of anticancer peptides in the biomechanical properties of both healthy and cancer live cells. Recently, a new methodology to calculate the affinity of peptides for lipid membranes using Surface Plasmon Resonance (SPR) was also developed.

Kyotorphin (KTP), a powerful endogenous analgesic molecule, has also been intensively studied by Castanho's team. After thoroughly balancing the charge and hydrophobicity of KTP derivatives they found that KTP-amide is effective after systemic administration in rats. Moreover, in a second stage they demonstrated that the covalent tandem drug ibuprofen-kyotorphin-amide, combining favorable charge and hydrophobicity, has synergistic advantage over ibuprofen, KTP-amide, and the co-administration of both. Recently, it was found clinical evidence of neuroprotective properties in KTP, which raise the potential to use KTP derivatives to fight Alzheimer's disease.

In recognition for his contributions to the advancement of peptide science, the European Peptide Society has awarded the prestigious Zervas Award to Miguel Castanho (*ex-aequo* with Phil Dawson, The Scripps Research Institute, USA), in 2014.

Nuno Santos Lab members

(5) The group led by Nuno Santos at iMM, in the University of Lisbon (https://imm.medicina.ulisboa.pt/pt/investigacao/laboratorios/santos-nuno-c-lab/) is mostly centered on the biochemical and biophysical processes occurring at the level of the membranes of human cells, as well as of their viral and bacterial pathogens. A special focus is given to the entrance of the virus or its content into the target cell and the assembly of new virions. Santos's team is interested in the molecular mechanisms involved in these interactions and on the development of effective molecules, mostly peptides and lipopeptides, to block these processes. They have shown that HIV fusion inhibitor peptides linked to cholesterol through a PEG spacer have enhanced membrane activity and efficiently block HIV entry. They further showed that these conjugates have high affinity for human peripheral blood mononuclear cell membranes, one of the HIV major targets. A similar strategy is being used on other enveloped viruses.

Dengue virus capsid protein binds specific proteins of host intracellular lipid droplets and very low-density lipoproteins, namely perilipin 3 and apolipoprotein E, respectively, in a potassium ion-dependent manner.

After identifying these interactions, essential for viral replication, Santos's team developed a strategy for their inhibition, based on the peptide lead pep14-23. This lead acquires an α-helical structure in the presence of anionic phospholipids, previous to the interaction with their protein target.

The Unit also works on elucidation of membrane-binding mechanisms for peptides relevant in some of the most upsetting diseases today, as cardio-

vascular disease and, especially, antibiotic-resistant infections; namely, focus is on (i) binding of fibrinogen to erythrocyte membranes and its relevance as cardiovascular risk factor; (ii) membrane activity and mechanism of action of AMP and CPP; and, (iii) development of innovative biosensor systems, with improved selectivity and sensitivity.

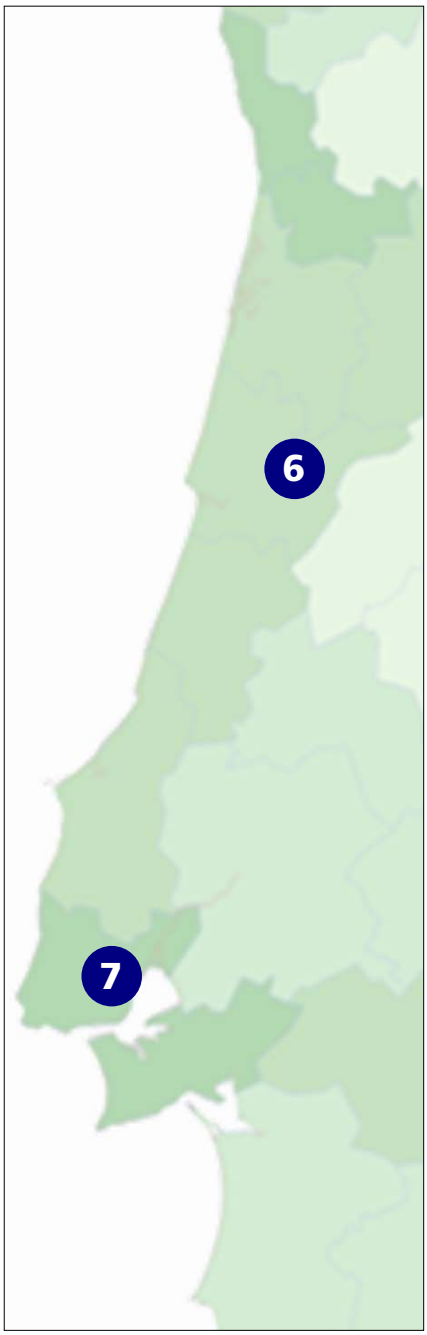
Fighting cancer with peptides:
from translocator to radiolabeled peptides

The huge health burden that cancer represents is well known, and underlies the intense efforts devoted by researchers worldwide in the search for novel anticancer drugs, including peptides. In Portugal, in parallel to research groups devoted to identification of peptides with anticancer properties *per se*, other researchers are using peptides to develop new tools to fight cancer. Examples are, e.g., use of (i) translocator peptides (CPP) for gene therapy, at the Centre for Neuroscience and Cell Biology (CNC, University of Coimbra, **6**), or (ii) radiolabeled peptides for radiotheranostics, at the Centre for Nuclear Science and Technology (C^2TN, University of Lisbon, **7**).

(6) The research activity in the Vectors and Gene Therapy Group at CNC (http://www.cnbc.pt/research/department_group_show.asp?iddep=1221&idgrp=1222), led by Maria Pedroso de Lima, has been focused on the design and development of non-viral vectors, including translocator peptides (CPP), for efficient nucleic acid delivery into target cells, both *in vitro* and *in vivo*, towards clinical application in gene therapy approaches. In this context, special emphasis has been placed on the karyophilic S413-PV peptide, a prototype translocator that results from combination of the 13-amino acid CPP sequence derived from Dermaseptin S4, with the SV40 large T antigen nuclear localization signal (NLS), which has been extensively investigated for its cellular uptake and potential for intracellular delivery of biologically active molecules. Biophysical and biochemical studies provided evidence that the S413-PV peptide is able to accumulate inside cells very efficiently, through a rapid, dose-dependent and non-toxic process.

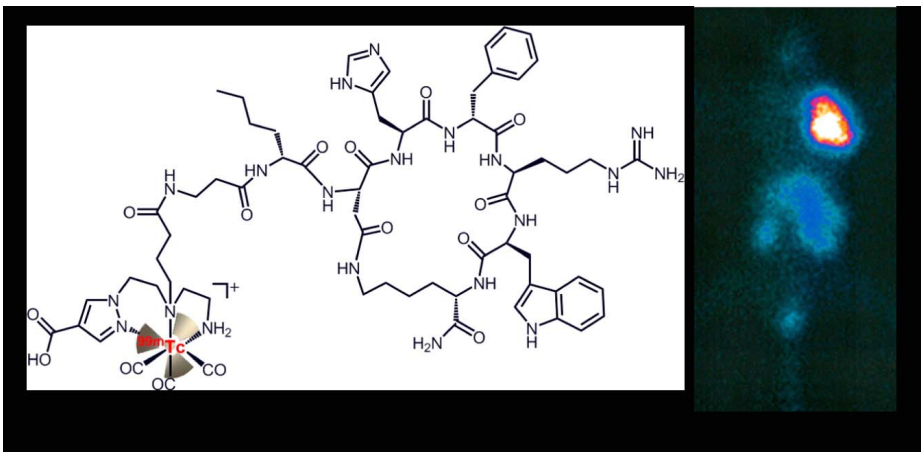
The above findings were enthusiastically considered of key interest to explore this peptide, for the safe and efficient delivery of different types of nucleic acids, including plasmid DNA, siRNAs and splice-switching oligonucleotides, into target cells.

More recently, a five-histidine tail was



added to the N-terminus of S413-PV, aiming at enhancing its biological activity. The histidine-enriched peptide was evaluated in terms of its efficiency to mediate gene expression and silencing of the oncogenic protein survivin in cancer cells, with overall promising results. Hence, both S413-PV and derivatives, either *per se* or in combination with cationic liposomes, are highly promising nucleic acid delivery systems with potential to be successfully applied in a therapeutic setting for cancer and other diseases.

(7) The Radiopharmaceutical Sciences group (RSG) at C^{2}TN (goo.gl/UovCWS), targets design and preclinical evaluation of molecular or nanosized radioactive tools for molecular imaging by positron emission tomography (PET) or single photon emission computed tomography (SPECT), and for targeted radionuclide therapy (TRT). Whereas PET and SPECT allow the visualization of interactions between physiological targets and ligands, TRT involves delivery of a cytotoxic radiation dose specifically to cancerous tissues. Radioactive tools must recognise specifically and bind with high affinity to surface or intracellular targets overexpressed in cancer cells. That is frequently attained upon attachment to specific peptides, as peptide receptors are often overexpressed in cancers. The RSG has been involved in the synthesis, radiolabeling and biological evaluation of



99mTc(CO)3-Labeled cyclic α-melanocyte stimulating hormone analog displaying favorable tumor-to-nontarget-organs uptake

Adapted with permission from Morais et al., J. Med. Chem. 2013, 56, 1961. Copyright 2013 American Chemical Society.

tumor-seeking peptides, namely, peptides containing the ArgGlyAsp (RGD) motif targeting the $\alpha_v\beta_3$ integrin receptor associated to tumor angiogenesis; Neuropeptide Y (NPY) agonists for targeting Y1 receptor and image breast cancer; and cyclic α-melanocyte-stimulating hormone analogs for targeting the Melanocortin-1 Receptor (MC1R) for melanoma imaging.

RSG researchers have also used bombesin (BBN) and derivatives to create (i) a novel ^{99m}Tc-bioconjugate further carrying a DNA intercalator, which revealed specific cell-targeting ability and pronounced nuclear internalization, and (ii) functionalise gold nanoparticles to get a better insight into the general transport mechanism of peptide-conjugated AuNP into tumors.

In order to deliver cytotoxic radiation doses and/or antitumor agents to nuclei and induce DNA damage in breast cancer cells, this group also used a multifunctional radiotheranostic agent with pendant LXXLL sequences that recognise the estrogen receptor. In collaboration with other groups, RSG has been further working in use of radiopeptides for image-guided drug design, and of small peptides as specific transport vectors for metal-based cytotoxic agents to tumor cells.

Biotechnology and human health:
from marine peptides to bioseparation matrices

(8) The Lisbon pole of the Research Unit on Applied Molecular Biosciences, UCIBIO (http://www.requimte.pt/ucibio), at the NOVA University of Lisbon in Caparica (**8**), has been focusing on (i) search and characterisation of new bioactive peptides from marine resources, (ii) molecular and structural characterisation of known bioactive peptides and proteins, (iii) use of peptides known as relevant for medical applications in the nanomedicine field, and (iv) peptide and protein engineering.

Oceans hold to most abundant and diversified lifeforms on our planet. Recent discoveries show that marine animals, especially invertebrates, secrete a vast array of peptides that take part in the complex cocktails of substances that form venoms, poisons and other secretions that altogether constitute their "chemical warfare". Researchers in UCIBIO are dedicated to the discovery of novel marine peptides and investigate their potential applications for Life and Health Sciences. Taking a series of common but hitherto inconspicuous marine invertebrates as case study, such as annelids and gastropods, those researchers are unravelling novel peptides of pharma-

cological interest through top-down research: from ecosystem to the molecular level. The findings show that marine peptides present in toxins and similar secretions are an extraordinary, albeit unexplored, contribution for the "biotechnology for blue growth" perspective that is setting the motto for the sustainable exploitation of the seas in the EU.

UCIBIO researchers also took inspiration from nature, in particular from small protein domains that can be produced biologically and chemically, to find new applications in bioprocessing. One of the applications is immobilization of native small protein domains produced chemically onto bioseparation matrices for purification of bioactive proline-rich peptides.

Biotechnology and human health:

from peptidomimetics to antigenic peptides presentation

UCIBIO is also actively enrolled in the rational design, preparation and screening of chemical combinatorial libraries of peptidomimetics that present several advantages over their natural counterparts. In particular, developed peptidomimetics have been designed to bind with moderate affinity and high selectivity for selected therapeutic targets. In addition, *in vitro* evolution and panning of phage display peptide libraries allowed the selection of peptides with high affinity and selectivity towards envelope proteins in retroviral particles, thus useful as affinity ligands for mild purification of viral particles.

Antigen activity and presentation by dendritic cells are dampened by high levels of sialic acids and sialylated glycans expressed by cancer cells. UCIBIO researchers found that removal of sialic acids from the surface of dendritic cells improves their antigen presentation and boosts stronger anti-tumoral T-cell responses. Presentation of specific peptides, such as gp100 or CMVpp65 is increased on desialylated dendritic cells, but also on other cells. Furthermore, *in vivo* studies, where dendritic cells were pulsed with ovalbumin-derived peptides, showed that desialylated cells have a greater ability to induce antigen-specific cytotoxic responses mediated by T-cells. Overall, it was demonstrated that peptide presentation by dendritic cells, mediated by MHC molecules, is influenced not only by peptide affinity for the presentation molecule, but also by the sialylation level of the cell membrane. The amount of sialic acid is correlated with lower expression of MHC molecules, and less antigenic peptide presentation by dendritic cells.

Biotechnology and human health:
peptide-modified gold nanoparticles as anti-angiogenic nanodevices and biomarkers for rheumatoid arthritis

(8) Angiogenesis results from an intricate network of pro- and anti-angiogenic molecules, endothelial cell receptors, and various modulators. UCIBIO researchers are managing active *in vivo* control of angiogenesis using gold nanoparticles (AuNPs) functionalised with peptides that selectively interact with cellular receptors involved in the regulation of angiogenesis by binding to the vascular endothelial growth factor receptor-1 and promoting signal cascade activation of angiogenic genes; or with specific peptides binding to neuropilin-1 receptor promoting internalization and suppression of angiogenesis.

Nanovectorisation of these peptides on AuNPs greatly enhances activity. Since tumour growth and progression require vascular supply, anti-angiogenic therapy is a highly effective strategy for treating cancer. By using a chorioallantoic membrane assay, these researchers have shown that combination of green laser irradiation with administration of a nanoformulation of 13nm spherical AuNPs functionalised with an anti-angiogenic peptide was able to achieve high localised temperatures and precisely cauterise blood vessels, blocking neovascularisation *in vivo*.

On a different line of research, UCIBIO researchers have been using specific antibody fragments and short peptides to develop a biomicrofluidics platform to assess biomarkers involved in rheumatoid arthritis within the framework of an EU-India project. This platform profits from the unique optical properties of small AuNPs immobilised on chip and their intrinsic ensemble localized surface plasmon resonance (eLSPR) profiles.

Modifying natural traits:
selective modification of bioactive peptides and proteins

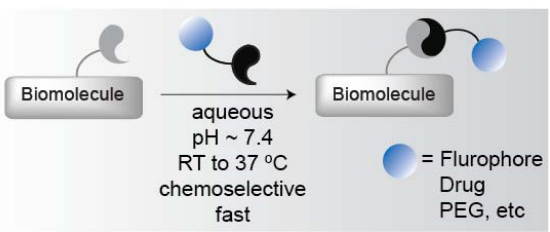
Modification of biomolecules to both study and control biological processes is seminal for chemical biology. Chemical tools to promote chemoselective, i.e., site-specific, conjugation of peptides and proteins to small synthetic molecules are, therefore, of chief importance in this field. In the University of Lisbon, two research groups have been working on such tools: Bernardes Lab (Institute for Molecular Medicine, 9) and Góis Lab (Faculty of Pharmacy, 10).

(9) Bernardes Lab (https://gbernardeslab.com/) is devoted to site-selective conjugation of synthetic molecules to peptides and proteins, to improve their functional and therapeutic traits. Chemo-

selectivity and mildness are fundamental to precisely install modifications at predetermined sites without disturbing structure, function and activity of the biomolecule. This group is engineering reactions that may be further utilised for structure and activity studies, and has disclosed methods that enable the stoichiometric and irreversible modification of native cysteine or disulfides within a peptide or protein of interest. The chemoselective cysteine labeling is achieved using stoichiometric amounts of carbonylacrylic reagents that can be easily prepared with any synthetic molecule of interest (e.g. drug, PEG or fluorescent probe). With this strategy, it is possible to form, e.g., homogenous antibody-drug conjugates (ADCs) that are stable in human plasma, unlike ADCs prepared using maleimide chemistry, and retain their targeting capacity. More recently, Bernardes Lab has demonstrated that oxetane can be readily grafted into native peptides and proteins through site-selective bis-alkylation of cysteine residues present as disulfides under mild biocompatible conditions. Using this stapling approach, they regioselectively introduced an oxetane graft in the more exposed disulfide of an immunogenic protein carrier, which led to higher antibody stability and titter in mice.

This group also developed an aza-Michael addition to dehydrolanine that enables construction of a chemically defined ADC. This ADC is unique, as the drug used, crizotinib – a known inhibitor of the MET, ALK and ROS1 kinases – was directly conjugated to the antibody without a linker. Upon successful internalisation of this stable ADC lead, a 10-fold improvement in crizotinib's cell killing efficiency was observed after lysosomal processing of the conjugate and consequent drug release.

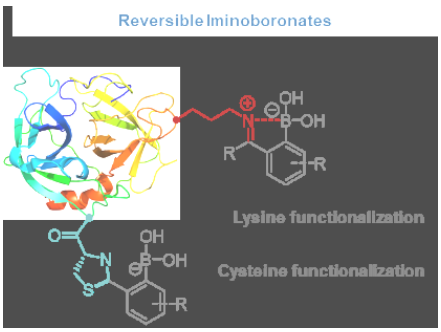
(10) Góis Lab (http://www.ff.ul.pt/~pedrogois/index.html) has been inspired



Fast site-selective conjugation of building blocks onto proteins in aqueous medium at physiological pH and temperature

by post-translational-modifications such as acylation, methylation, phosphorylation, ubiquitination or glycosylation, as part of Nature's "toolbox" used to extend the range of protein functions and to regulate central cellular processes like differentiation, trafficking or signaling. Appreciation for this strategy, has led chemical biologists to develop many different genetic and chemical methods to mimic Nature's ability to attach chemical handles onto peptides and proteins, though, the complex structure and stability of proteins, still constitute a formidable challenge for bioconjugation. A plethora of chemical methods has been developed to selectively modify specific residues without disturbing protein's architecture or function. This synthetic "toolbox" greatly expanded in recent years, benefiting from the nucleophilicity of the thiol and ε-amino groups of cysteine and lysine residues, respectively, though tyrosine, tryptophan or disulfide bridges have also become important bioconjugation hotspots. However, most of the scaffolds for protein modification are engineered to yield stable constructs that withstand complex conditions such as those in the biological milieu. In contrast, protein functionalisation based on reversible covalent bonds, has been rather overlooked despite the potential of this strategy to generate constructs that respond to a predetermined stimulus. This is where researchers from Góis Lab are focusing their efforts, being particularly interested in developing reversible bioconjugation strategies and their use in the synthesis of complex functional bioconjugates. In the course of these studies, they discovered that aromatic boronic acids *ortho*-substituted with aldehydes or ketones rapidly generate iminoboronates in aqueous media with biogenic amino groups of exposed lysines or *N*-terminal cysteines.

The iminoboronate formation is selective and this function proved to be inherently reversible in the presence of endogenous molecules like glutathione (GSH), fructose or dopamine. The combination of stability and reversibility attributes made this bonding motif a useful, and increasingly popular strategy to perform the reversible functionalization of proteins and to assemble different functional bioconjugates.



Reversible iminoboronates for on/off labeling of lysine or cysteine residues in proteins

Innovating in biomedical engineering:
from tissue-regeneration to antifouling materials

Self-structuring peptides and peptide-tethered materials are rapidly gaining prominence in biomedical engineering, and represent one of the most promising fields of applied research in peptide science. Accordingly, the number of research groups and *spin-offs* working in this area has been steadily growing in Portugal. Examples can be found in, among others, the Universities of Minho (3B's, 11), Porto (INEB, 12), and Coimbra (CureMat, 13).

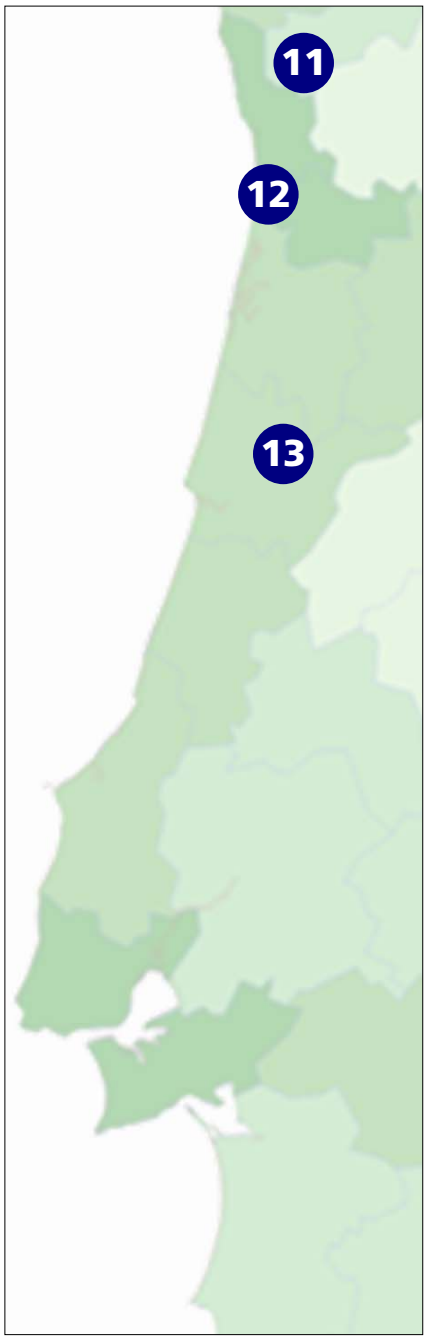
(11) Rui L. Reis, Ricardo A. Pires and Iva Pashkuleva, at the 3B's Research Group from the University of Minho, are developing different supramolecular systems for biomedical applications, using peptide and carbohydrate amphiphiles as well as their combinations.

The main aim of these studies is to mimic the structure and bioactivity of proteoglycans. In particular, mimics of extracellular matrix (ECM) are developed by self-assembly of short peptide amphiphiles alone or in combination with simple carbohydrate amphiphiles. The peptide amphiphile is used to guide the formation of nanofibers, while the carbohydrate amphiphile decorates the surface of the nanofibers rendering specific biofunctionality. Under physiological conditions, the generated nanofibers can further organise into highly hydrated nanofibrous meshes, i.e. supramolecular gel, which can host cells and guide their differentiation and/or protect growth factors retaining their bioactivity for timeframes much longer than the ones observed for isolated growth factors.

The 3B's Research Group is a pioneer in applying biocatalytic self-assembly to carbohydrate amphiphiles. Such approach was shown to be useful for selective cancer treatment, as enzymes overexpressed by cancer cells trigger transformation of micelles into nanonets, which trap the cells and kill them.

(12) The Institute of Biomedical Engineering (INEB), integrated in *Instituto de Investigação e Inovação da Universidade do Porto* – i3S (http://www.i3s.up.pt/), focuses on advanced research in biomedical engineering, aiming at development of combination products with clinical application in orthopedics, neurosurgery, obstetrics, cardiology, ophthalmology and oncology. Many of the investigational [bio]materials being developed at INEB comprise bioactive peptides for different purposes, as follows.

In the Bioengineered 3D Microenvironments group, led by Cristina Barrias, peptides are being used to create cell-



instructive hydrogels to advance the design of extracellular matrix-like 3D matrices for different therapeutic applications, such as regenerative medicine. In this connection, alginate hydrogels tethered with osteogenic growth promoting peptides (OGP) and their conjugates with metalloproteinase-sensitive sequences have been developed and found to induce osteogenic differentiation of mesenchymal stem cells.

At the NanoBiomaterials for Targeted Therapies group, led by Ana Paula Pêgo, researcher Isabel Amaral is using cell-adhesive peptides able to interact with $\alpha 6\beta 1$ integrin to enhance the biofunctionality of fibrin hydrogel matrices used in the 3D culture of embryonic stem cell-derived neural stem/progenitor cells (ES-NSPCs) and in matrix-assisted ES-NSPC transplantation. The peptide-tethered fibrin hydrogels were effective in promoting neurite outgrowth of ES-NSPCs, which hold promise for integrin-mediated regeneration of neurons following, e.g., spinal cord injuries.

Metastatic dissemination of prostatic cancer (Pca) cells to bone is the major research focus of Susana Sousa, from the Biocomposites group, led by Fernando Jorge Monteiro. The expression and activity of Osteonectin (SPARC protein) seems to be correlated with such dissemination, although SPARC's involvement in prostatic cancer metastasis is still a controversial issue. Sousa and co-workers are working in the unraveling of the specific function of SPARC and derived peptides, FS-E; 2.3 and 4.2, as their role in angiogenesis of PCa bone metastasis may allow development of anti-angiogenic therapies against metastatic bone tumors.

Cristina Martins, the leader of the Bioengineered Surfaces group, is focused on use of antimicrobial peptide-modified surfaces to create antibacterial [bio]-materials potentially useful to treat, among others, (i) gastric infections associated to *Helicobacter pylori*, and (ii) implant- or catheter-associated infections (IAI, CAI).

Martins and co-workers have been working, in collaboration with Gomes's lab (see **2**), on covalent chemoselective tethering of lactoferrin- and histatin-based AMP, such as hLF(1-11) and Dhvar-5, respectively, onto chitosan. This has produced antimicrobial surfaces with antifouling properties that hold great promise towards development of novel antimicrobial coatings for both prostethic implants and wound care patches.

Martins is also interested in magainin-inspired peptides, like MSI-78 and MSI-78A. Two MSI-78 segments, MSI-78(1-12) and MSI-78(4-20), were found as highly effective AMP. MSI-78(1-12) is an excellent candidate to fight *P. aeruginosa*

infections, as it displays potent and highly selective antimicrobial activity against this species. MSI-78(4-20) was found to be as effective as MSI-78 against several clinically relevant Gram-positive and Gram-negative bacteria, including MRSA; this shorter derivative is also more selective, as it was less hemotoxic than the lead AMP. These MSI-78 derivatives are being used for modification of materials employed in medical devices like, e.g., stents or catheters. In this connection, Martins's team is also working on immobilization of thrombin-inhibitor tetrapeptides onto nanostructured surfaces, for modification of blood-contact biomedical devices, whose clinical has thrombus formation as a downside.

(13) Peptide-based antibiofilm materials are also becoming a driving force for entrepreneurship in Portugal. One example of this is that of CUREMAT Technologies (https://www.curemat.com/), a spin-off company settled at *Parque Tecnológico de Cantanhede,* near Coimbra.

CUREMAT has developed a coating that can be applied in several types of wound dressings that accelerate the wound healing while preventing bacterial colonization of the wound. This is possible due to the ingenious use of a natural occurring AMP that exhibits both properties. The strength of these two properties has been shown *in vivo* animal models. The reduction in wound healing time, the reduced incidence of complications due to infections of the wound and the reduce of number of dressing changes (nurse time) will altogether reduce the treatment time and therefore the healthcare costs significantly. This novel coating is formed by nanoparticles containing a peptide at high-density. It is the combination of high density of AMPs per nanoparticle surface area and nanoparticle size that makes CUREMAT formulation very effective in killing pathogens while showing low cytotoxicity against human cells. The antimicrobial and healing properties of CUREMAT formulation is multi-factorial: (i) increased stability of AMP immobilized on top of the nanoparticle against proteases and serum, (ii) synergistic effect of AMPs immobilized in the same nanoparticle that induce rapid pore formation in contact with bacterial membranes, and (iii) low

CUREMAT
TECHNOLOGIES

capacity to induce pore formation in mammalian cell membranes.

The expected impact of CUREMAT coating to tackle chronically-infected wounds is huge, considering that chronic wounds are affecting millions of people throughout the world and this number is steadily increasing due to the aging of the population in the developed countries and the effect of diseases such as diabetes and obesity. The current estimated average cost of a chronic wound patient in the US is approximately $4.000.

This article covers major lines of research under the topic "Peptide Therapeutics in Portugal" only at a glance. Other Portuguese initiatives and researcher groups exist that are intensively devoted to peptide-based therapeutics and to peptide science. Their scientific aims and endeavours will be timely reported as well.

Contributed by Paula Gomes

Bioengineered Surfaces Group, led by Cristina Martins at INEB.

CONFERENCE REPORT

7th Austrian Peptide Symposium

Vienna, Austria

7 December 2017

The 7th Austrian Peptide Symposium was held at the Van-Swieten Auditorium in Vienna on the 7th of December 2017 and was co-organized by Christian Gruber (Austrian representative to the EPS, Medical University of Vienna) and Christian Becker (University of Vienna). The event was held as a one-day symposium. It included invited lectures given by renowned national and international speakers, short oral presentations, which were selected from the submitted abstracts, and a poster session covering manifold aspects of peptide research. Overall, more than 70 participants from different European and overseas countries (Australia, Austria, Belgium, France, Germany, India, Israel and Serbia) attended the symposium. This mixture resulted in a truly international spirit of the meeting, which started-off with a speaker's dinner on the eve of the symposium.

The morning session focused on bioactive peptides: Roderich Süssmuth (Technical University of Berlin, Germany) held the opening lecture on ribosomal and non-ribosomal peptides from bacteria and fungi. Jan Tytgat (KU Leuven, Belgium)

Group photo of all participants of the 7th Austrian Peptide Symposium at the Van-Swieten Auditorium of the Medical University of Vienna.

continued on topic and described the pharmacology and bioactivity of novel peptides from marine worm. The first session closed with a presentation of Lachlan Rash (University of Queensland, Australia) on spider toxin peptides, their pharmacology and development as research tools and drugs.

The second morning session concentrated on chemical protein synthesis and included the lectures of Norman Metanis (Hebrew University of Jerusalem, Israel) on selenium chemistry for peptide research, followed by the lecture of Oleg Melnyk (CNRS Lille, France) on novel sulfur and selenium based chemistries for the total synthesis of proteins.

The poster session, which was held during the lunch break, featured 15 posters that were presented by PhD students and early-career researchers. There was also a poster award competition for the two best poster presentations.

The first afternoon session included six excellent short oral contributions selected from the submitted abstracts. Talks were given by Meder Kamalov (University of Vienna, Austria), Peter Keov (University of Queensland, Australia), Thomas Schlatzer (Graz University of Technology, Austria), Somnath Mukherjee (Indian Institute of Science), Vesna Stanojlovic (University of Salzburg, Austria) and Daniela Heilos (Medical University of Vienna, Austria).

Poster award ceremony. From left to right: Anne Conibear, Christian Gruber, Peter Keov, Philipp Schilling and Christian Becker.

The second and last afternoon session covered emerging technologies in peptide science with three lectures. The first speaker, Martina Marchetti-Deschmann (Technical University of Vienna, Austria) reported on the usefulness of MALDI mass spectrometry imaging. Then Monika Swiontek (European Life Science Technical Specialist, CEM GmbH) presented innovative techniques and tools for solid-phase peptide synthesis.

The scientific part of the symposium ended with the announcement of the two winners of the poster award competition: Peter Keov (University of Queensland, Australia) for his poster entitled "Identification of a cyclotide antagonist at the corticotropin-releasing factor type 1 receptor", and Philipp Schilling (University of Vienna, Austria) for her poster entitled "CuAAC-supported synthesis of mannosylated peptides for binding studies with cyanovirin-N".

A social get-together including a winetasting provided by Michaela Jöbstl

(Langenlois, Austria) followed the closing remarks. Overall, the meeting was successful and received a very positive feedback thanks to the comprehensive and high-level scientific program, the nice and friendly atmosphere among the participants and the stimulating place, the Van Swieten Auditorium of the Medical University of Vienna.

The seven Austrian Peptide Symposia hosted so far in Vienna, Graz and Salzburg have obtained very good resonance within the national and international scientific community, which strongly motivates the Austrian organizers to make of this event a consolidate tradition. Along this line, we are happy to announce that the 2018 meeting of the Austrian Peptide Society will be held in the beautiful city of Salzburg and co-organized by Chiara Cabrele (University of Salzburg), Christian Gruber (Medical University of Vienna) and Christian Becker (University of Vienna).

We are grateful to everyone who helped in the organization and realization of the 2017 Austrian Peptide Symposium, in particular all involved staff members from the organizing institutions. Finally, we very much thank the exhibitors and all sponsors of the symposium: Bachem, Bruker, CEM, Thermo Fisher Scientific, Intavis, peptides&elephants, Rieger-Industrievertretungen GmbH, and the European Peptide Society. Without their generous financial support, all this would not have been possible!

Contributed by Christian W. Gruber and Christian Becker

CONFERENCE REPORT

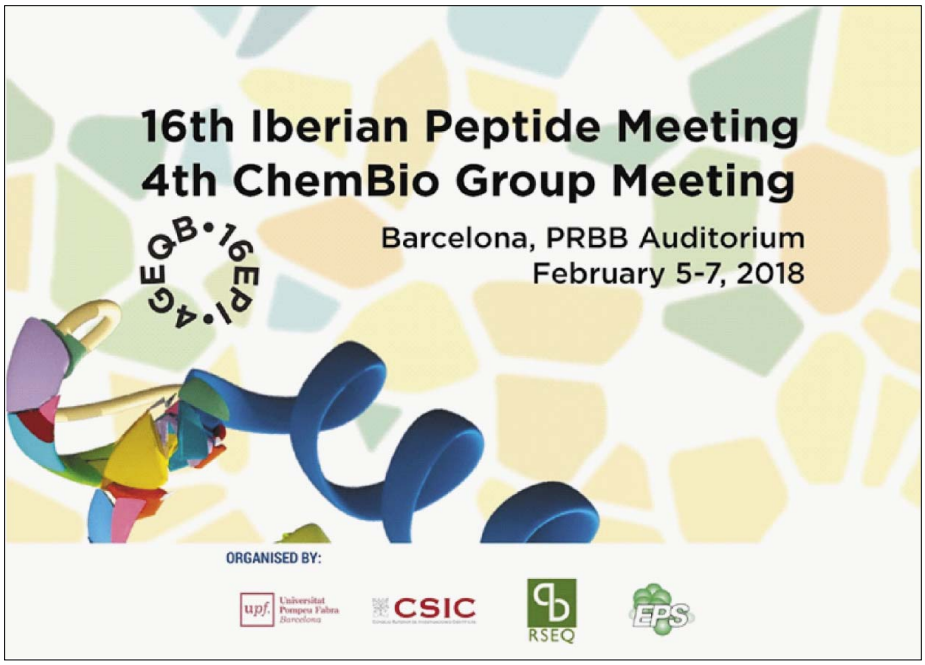
16th Iberian Peptide Symposium

Barcelona, Spain

7–9 February 2018

The 16th edition of the Iberian Peptide Meeting (16EPI), an EPS-sponsored reunion, was held at the auditorium of the Barcelona Biomedical Research Park on February 5–7, 2018, in conjunction with the 4th Meeting of the Chemical Biology Division of the Spanish Royal Society of Chemistry (RSEQ). Held for the first time in 1988, the EPI (Encuentro Peptídico Ibérico) is among the longest-running peptide events supported by the EPS. In this edition, jointly organized by Pompeu Fabra University and the Spanish National Research Council (CSIC), a close hyphenation between peptide and chemical biology talks resulted in a highly integrated, appealing program that retained a strong peptide flavor (roughly 70% of presentations), spiced with contributions from other fields, mostly glycobiology.

The chilly, rainy, definitely non-Barcelona weather on the opening day, followed by similarly nippy – though gradually sunnier – days, discouraged any temptation of a seafront promenade-cum-beer and ensured a steady attendance of the 200 participants (more than 50% EPS members) during all sessions. In tune with its Iberian character, delegates came mostly from Spain (156) and Portugal (21), but also from elsewhere in Europe (UK, Italy, France, Germany, Denmark), North America, Australia and South Korea. The scientific sessions included four plenary (45 min) talks, 12 invited (30 min) talks, 20 oral (15 min) presentations plus an exciting session where 16 flash (5 min) talks, selected from 88 poster presentations, were given.



Meeting ad: peptides on a Gaudi-esque trencadís background

Among the highlights, and at risk of neglecting other worthy contributions, one would mention, on day one (February 5), a thorough overview of mechanistic and cellular aspects of medically relevant glycosidases, by Gideon Davies (U. York); a broad survey of native ligation techniques for the total synthesis of proteins, by Oleg Melnyk (CNRS-Pasteur Institute, Lille); an enticing talk by Marc Vendrell (a Barcelona native, now at Edinburgh U.) on the possibilities of activatable peptide fluorophores for live cell imaging, and last but not least an insightful talk on azapeptides and their therapeutic promise, delivered with the usual flair by Bill Lubell (U. Montreal). This was followed, on day two, by an absorbing lecture by Knud Jensen (U. Copenhagen) on DNA and carbohydrate-mediated building of artificial proteins and nano-

assemblies; an elegant update on peptide-conjugated nanomaterials by Lino Ferreira (U. Coimbra); an exciting account of how antibiotic resistance can be combated by disabling key enzymes in bacterial metabolism, by Concepción González-Bello (U. Santiago de Compostela), plus a detailed analysis of gomesin-membrane interactions and their antimicrobial and anticancer outcome, by Sónia Henriques (U. Queensland), and a very engaging lecture on CPPs as probes to study structure and function of GPCR oligomers, by Leonardo Pardo (Autonomous U. Barcelona). Finally, on day three, Marc Torrent (Autonomous U. Barcelona) gave a perspicuous talk on how new antibiotics – peptide or otherwise– can be unveiled by inhibiting host-pathogen protein interaction networks, and Salomé Veiga (U. Lisbon) discussed the antibiofilm activity and mechanism of Dengue virus-derived pepR.

In tune with EPI tradition, and in addition to the above leading contributions, a substantial part of the scientific program was dedicated to oral and flash communications by junior scientists from Portugal and Spain, covering a broad range of subjects, mostly peptide-related, with emphasis on therapeutic and nanomaterial opportunities, and again with fruitful dialogue with other areas of chemical biology. There was broad

Definitely non-Mediterranean weather on day one

Meeting session at the PRBB auditorium

consensus among participants that the meeting was a success. In the words of a seasoned participant: "Although a few more sunnier days could have added to the program [...] the science was impressive. My personal passions for medicinal chemistry and peptides were satisfied by a number of interesting talks, many from young investigators." Full details on the program can be found at the meeting website: http://eventum.upf.edu/go/16EPI-4GEQB, and a photo gallery at https://photos.app.goo.gl/4ZNsDsVcuWc0fUr82

Contributed by D. Andreu, Pompeu Fabra University

Oleg Melnyk hard at work

Group picture – sunshine at last

In Memoriam

Jan Izdebski
(1937–2018)

With profound regret and sadness we write to inform you of the sudden death of Jan Izdebski on March 5, 2018, a retired full professor at the Faculty of Chemistry at the University of Warsaw, deputy dean of the Faculty of Chemistry (1981–1990), and for years (1981–2008) a Head of the Peptides Laboratory.

Since the founding of the Peptides Laboratory at Chemistry Department of Warsaw University by Professor Stefania Drabarek in 1966, his scientific interests have been connected with peptide chemistry. Jan Izdebski took a post-doctoral internship in the laboratory of prof. Miklos Bodanszky (Case Western Reserve University, Cleveland, USA), and in later years he worked in the laboratory of prof. Choh Hao Li (University of California, USA) and as visiting professor in the laboratory of the Nobel laureate prof. Andrew Schally (University of New Orleans, USA).

His main interests concerned Structure Activity Relationship study of biologically active peptides and methodology of peptide synthesis. In particular, he worked on the modification of the Young test allowing to quantify the degree of racemization based on the composition of optical isomers. Thanks to the modified test, it was possible to point to a very efficient anti-racemic additive, 2-hydroxy-imino-2-cyanoacetic acid. Currently, it is a very frequently used reagent (trade name: OXYMA). In the following years, Professor Izdebski conducted research on mammalian hormones and the synthesis of active painkillers. A special achievement has been the research in the field of the synthesis of active analogs of growth hormone releasing factor (GH-RH) initiated during the stay of Professor Izdebski in the laboratory of Professor Andrew Schally.

He was a member of the Editorial Committee of the leading journal in peptide chemistry *Journal of Peptide Science*, he was the organizer of the IX Polish Peptide Symposium in Pulawy in 1987, and he was a representative of the Polish peptide group in the European Peptide Society (2006–2010).

Professor Izdebski will always be remembered by his students, colleagues and friends from the Faculty of Chemistry and the peptide community in Poland and around the world.

Contributed by
Aleksandra Misicka-Kesik

Society News

European Peptide Society
No Profit Scientific Society
VIA F. FERRUCCI 203/C – 59100 PRATO (PO)
Fiscal Code 92089560483 – VAT IT 02292750979

Extract from the Minutes of the Executive Committee Meeting, March 19, 2018, 10:00–12:30 h (part I), and on March 19, 2018, 14:00–19:00 h and March 20, 2018, 10:00–14:00 h (part II)

(Florence, Italy)

Part I (Studio Gori, Via Ferrucci 203/C, 59100 Prato)

Participants: D. Andreu, A.M. Papini, P. Gomes, P. Gori, P. Bottani

Chair: D. Andreu

1. Welcome

Both the president and Dr. Gori welcomed the participants and reminded them that the current Executive Committee (EC) is responsible for the approval of the financial statements of 2017 and the budget for 2018, both of which are to be presented to the General Assembly (GA) teleconference, which should take place by the end of May 2018. Also, it was reminded that this EC's mandate will cease in 2019, hence, the current EC will stay in function until March 2020.

2. Financial statement approval, audit for the fiscal year 2017 and budget for 2018

The following documents, were discussed:
a) Financial statements at 31/12/2017 (Accounts for the year of 2017);
b) Auditor's certification of the Financial Statement for the Fiscal year ended on 31/12/2017;
c) Budget of the European Peptide Society for the Fiscal year 2018.

3. General Assembly teleconference meeting 2018

The GA teleconference meeting was set for the 22nd of May, 2018, at 2 p.m. (CET time) – 1st call, and at 3 p.m. (CET time) – 2nd call.

4. Financial commitments for 2019–2024

The treasurer suggested to create a specific plan not based on a 1 year forecast, but on a 6-year timeframe, relying on continuation of the current Society's agreement with Wiley. This matter was further discussed in Part II of the Executive Committee Meeting.

Part II (University of Florence, Scientific Pole, via Ugo Schiff 6, Sesto Fiorentino)

- *March 19th 2018, 14:00–19:00 h*

Participants: D. Andreu, A.M. Papini, N. Sewald, K. Rolka, P. Gomes, C. Hewage

Chair: D. Andreu

1. **Welcome and special thanks to the Treasurer (DA)**
   The President welcomed all participants and, on behalf of the EC, and also of CH, expressed their gratitude to Prof. Anna Maria Papini for her excellent hosting of the present EC meeting in Florence.

2. **Organization of the forthcoming 35th European Peptide Symposium (CH)**
   EC members discussed extensively the organization details regarding the upcoming 35th European Peptide Symposium, with its chairman, CH.

- *March 20th 2018, 10:00–14:00 h*

Participants: D. Andreu, A.M. Papini, N. Sewald, K. Rolka, P. Gomes

Chair: D. Andreu

3. **Minutes of the Executive Committee meeting in March 2017 (PG)**
   The minutes of the EC Meeting held in Florence, March 27–28th, 2017 were read and, after one typo correction, were unanimously approved.

4. **Guidelines for EPS Symposium organizers (Annex 9 of the EPS Bylaws) – revised version (DA, PG)**
   The revised version of Annex 9 of the EPS bylaws was thoroughly analyzed and, after some discussion and a few amendments accordingly, it was agreed to timely circulate an improved version amongst GA members, for approval in the forthcoming GA meeting to be held in Barcelona, on May 22nd, 2018.

5. **Treasurer's report and financial commitments to 2019–2024 (AMP)**
   Following what had been discussed and decided in Part I of the EC Meeting, the Treasurer informed about her next steps to prepare documents for approval by the forthcoming GA meeting, to be held in Barcelona on May 22nd 2018, which were consensually approved. A budget plan for 2019–2024 was discussed and it was agreed to include this plan along with the budget for 2018, in the document to be prepared by the Treasurer for approval by the GA. The treasurer further highlighted that, while Dr. Rao Makineni's sponsoring of the Zervas Award is ensured until 2032, PolyPeptide Laboratories sponsorship to the Rudinger Memorial Lecture, the Society's most prestigious award, remains an unwritten, non-binding agreement, typically enacted on dates rather close to the Symposium. This situation, which is seemingly happening once more for the forthcoming 34th European Peptide Symposium, was judged undesirable and the President will take further steps to secure time-reliable funding, from either PolyPeptide or other donors.

6. **Report of the Communication Officer (KR)**
   The Communication Officer gave a detailed explanation of

each of the items in his report. Most relevant issues in this report were (i) publication of two Newsletters in 2017 (May and November); (ii) EPS online archives project (Proceedings available online go back to 1998 now); (iii) statistics of e-mail bounces and confirmed message openings in consequence of four bulk e-mails sent to all registered EPS members through Public Marketing Communication, subcontracted by Wiley; (iv) seven contributions received in 2017 from the EPS "Pool of Writers"; and (v) EPS Website restructuration and update. Concerning item (iv), NS suggested that a DOI should be requested for each contributed paper, which was consensually agreed. In regard to item (v), it was agreed that "Meeting Reports" should be made available both through the EPS Newsletter and the EPS Website.

7. Report of the Scientific Affairs Officer (NS)

The Scientific Affairs Officer gave a detailed explanation of each of the items in his report, which were the following (i) EPS support to small meetings (support given to 2 events in 2017 and already requested for 7 events in 2018); (ii) EPS Mobility Fellowships (no applications in the 1st call, 1 application in the 2nd call, by Maya Georgieva, Roumen Tsanev Institute of Molecular Biology, Bulgarian Academy of Sciences, Sofia, Bulgaria, which was approved); and (iii) nominations for the EPS Awards (Bodanszky, Zervas and Rudinger). Concerning item (ii), it was consensual that a major reason for the low response to 2017 calls was likely the low number of PhD students who were members of the EPS for at least 12 months (a mandatory requisite to apply); considering that this situation may change in brief course (see point 9. Report of the Secretary), it was agreed that calls for Mobility Grant applications should be kept twice a year, on July 1st and December 1st. In regard to point (iii), NS explained the evaluation method applied by the Scientific Affairs Committee to rank and select the nominees to be taken forward for selection at the GA meeting, in Barcelona (May 22nd, 2018). The following candidates were proposed to the EC:

- for the Rudinger Award: Paul ALEWOOD; Maurice MANNING; James P. TAM
- ffor the Zervas Award: Ashraf BRIK; Christian HACKENBERGER; Richard PAYNE
- ffor the Bodanszky Award: Norman METANIS; Mukesh PASUPULETI

The EC accepted the proposal. The Secretary will organize a voting by all members of the GA and EC. The Secretary is in charge of sending in advance all relevant documents to GA members, so that Awardees are selected by May 22nd, 2018.

8. Report of the Secretary (PG)

The Secretary explained in detail the several items on her report, namely, (i) number of newly registered EPS members (110 from Jan. 2017 to Mar. 2018, most of which PhD students); (ii) nominations for new National Representatives, i.e., effective members belonging to the EPS General Assembly (15 countries) and Re-Appointments for the 2nd four-year term as National Representatives (7 countries); (iii) Members database pruning and digital archive. Point (i) above was consensually taken as symptomatic that more and more PhD students are becoming engaged with the EPS, which will likely be reflected onto, among other aspects, an increase in the number of applicants to Mobility Grants. In regard to point (ii), it was considered that its discussion should include analysis of the request presented by the

National Representative from Spain, Dr. Meritxell Teixidó, corresponding to point 11 in the Meeting Agenda. As such, it was agreed to change the Agenda accordingly, and it was decided to proceed with the normal nomination + election process for Spain, as per Society's Statutes and Bylaws, while reassuring Dr. Teixidó that she will receive all proper support from the EC, while organizing the 36th European Peptide Symposium, to be held in Sitges (Spain) in 2020. Still in regard with point (ii), the Secretary was entrusted with the tasks that usually follow the nomination process, namely, communication of results to voting members and organization of elections, when applicable. Finally, concerning point (iii), it was agreed that the Secretary should get in touch with National Representatives to ask for their feedback regarding the current status and contacts of EPS members from their countries whose contacts are apparently outdated.

9. **Hungarian, Portuguese and Polish Applications for the organization of a forthcoming European Peptide Symposium (DA)**

The President informed the Committee on the three formal requests to organize forthcoming European Peptide Symposia, received from Hungary, Portugal and Poland. Considering that (i) organizing countries have been already defined up to 2026 (Ireland 2018, Spain 2020, Italy 2022, Austria 2024, and France 2026), and (ii) last Symposia organized by the three applicant countries were in 1994 (Portugal), 1998 (Hungary), and 2006 (Poland), it was agreed to hold the Symposia in the three applicant countries according to the following chronological order: Portugal 2028, Hungary 2030, and Poland 2032. The President will communicate this decision to the applicants.

10. **Date, agenda and logistics for the upcoming GA Meeting**

The President reminded that the next ordinary GA meeting will take place in Barcelona, on May 22nd 2018, and commissioned the Secretary with timely organization of all documents and himself, together with NS, with arrangements for the teleconference. The preliminary agenda for this meeting will be given below.

1. Approval of financial documents (accounts for the fiscal year of 2017 and budget for the fiscal year of 2018)
2. Approval of new appointments and re-appointments of National Representatives
3. Approval of current European Peptide Symposia calendar
4. EPS Awards Winners

11. **Other business**

The date was set for the next EC meeting, to take place in Dublin, on 29th of August 2018, during the European Peptide Symposium lunch break. It was agreed that this meeting should be preceded by a meeting of EC members with JPS Editorial Board members, to whom invitations will be timely sent by the President and/or the Treasurer.

D. Andreu, P. Gomes March 20th, 2018

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CALENDAR of Forthcoming Events

PEPPERSCHOOL 2018
Carry-le-Rout, France
14–17 May 2018
URL: https://eventos.fct.unl.pt/pepper_school/

16TH NAPLES WORKSHOP ON BIOACTIVE PEPTIDES
Centro Congressi of University of Naples "Federico II", Naples, Italy
7–9 June 2018
URL: http://peptidesnaplesworkshop.org/

PEPTIDES AND CONJUGATES FOR TUMOR TARGETING, THERAPY AND DIAGNOSIS – RIMINIPEPTIDES2018
Campus of Rimini of the University of Bologna, Italy
16–18 June 2018
URL: https://events.unibo.it/international-chemistry-meeting-rimini-2018

5TH INTERNATIONAL CONFERENCE ON ORGANIC AND INORGANIC CHEMISTRY
Paris, France
12–13 July 2018
URL: https://organic-chemistry.chemistryconferences.org/

PEPMAT 2018
Birkbeck College Malet Street, London, UK
16–18 July 2018
URL: https://www.eventbrite.co.uk/e/pepmat-2018-tickets-37028785093?utm_term=eventurl_text

35TH EUROPEAN PEPTIDE SYMPOSIUM
The Helix Conference Centre, Dublin City University, Dublin, Ireland
26–31 August 2018
URL: http://www.eps2018.com/ehome/index.php?eventid=256357&

LATEST ADVANCES IN THE FORMULATION & STABILISATION OF PROTEIN AND PEPTIDE DRUGS
Holiday Inn Oxford Circus, London, UK
26–27 September 2018
URL: https://www.pharma-training-courses.com/latest-advances-in-the-stabilisation-and-formulation-of-protein-and-peptide-drugs_58.htm

10TH INTERNATIONAL PEPTIDE SYMPOSIUM AND 55TH JAPANESE PEPTIDE SYMPOSIUM
ROHM Theatre Kyoto, Kyoto, Japan
3–7 December, 2018
URL: http://aeplan.co.jp/10thips/