Decree of the Rector n. 1037 of 20/10/2023
Competition for awarding 1 research grant at the University of Udine

DISCLAIMER:
The official and legally binding call for applications is in Italian only. This document cannot be used for legal purposes and is only meant to provide information in English on the call for applications (Decree of the Rector n. 1037 of 20/10/2023). Please refer to the official call published on: https://www.uniud.it/it/albo-ufficiale

Any change and integration will be made available on the above mentioned web page. Therefore, no personal written communication regarding the examination date and/or competition results shall be provided to applicants.

Annex 1

Competition Notice for the award of 1 research grant for carrying out research activities at the University of Udine on the following subject: “Synthesis of biologically active peptides and peptidomimetics: conformational study and their functionalization on nanomaterials” SSD: CHIM/06 (principal investigator, Rossella De Marco).

Research fellowship financed with the resources of the research project titled “Interconnected Nord-Est Innovation Ecosystem” (iNES). Public call No. 3277 of 30/12/2021, PNRR M4C2 Inv. 1.5, CUP G23C22001130006.

Art. 1

A selection procedure is hereby announced for the award of 1 research grant at the University of Udine, as identified in Attachment A which constitutes an integral and substantial part of this call. The research grant is linked to the research project and is subject and conditioned upon the relative funding.

Specifically, the project is placed within the context of the Italian National Recovery and Resilience Plan (i.e., PNRR) – Mission 4: Education and research, Component 2: From research to business, Investment 1.5: Creating and strengthening "innovation ecosystems", building "local R&D leaders", funded by the EU-Next GenerationEU; Project: "Interconnected Nord-Est Innovation Ecosystem" (iNES), ECS00000043; Thematic area: Digital, Industry, Aerospace. CUP: G23C22001130006.

The fellowship may be renewed, in compliance with Art. 22, Law No. 240 of 30 December 2010 (as in the text in force before the implementation of the Conversion Law of the D.L. 36/2022, L. 79/2022), Law No. 11 of 27 February 2015, and the current regulations of the University of Udine for awarding research grants, issued with the Rector’s Decrease No. 182 of 31 March 2021. The renewal is subject to the scientific coordinator’s positive assessment of the researcher’s activities, an adequate scientific rationale, and a corresponding financial covering.

The activities pertaining to this research fellowship will be monitored for compliance with the PNRR’s Do No Significant Harm principle (hereinafter DNSH), that is, they will not cause significant harm to the environment.

RESEARCH SERVICES AREA
Research Training Office
Department Head: Sandra Salvador
Procedure Supervisor: Sandra Salvador
Procedure Compiler: Francesca Mion
This call guarantees equal generational, gender and territorial opportunities.

The research findings resulting from the fellowship, as well as the related data, will be published in compliance with the Open Science and FAIR Data principles.

The research fellowship does not give rise to any right with regards to accessing University posts.

The signing of the contract is subject to the formalization of the agreement between the Hub and Spokes and between Spokes and Spokes’ Affiliates.

Any personal communication to candidates related to this selection will be sent exclusively to the email address indicated when registering for the selection, as mentioned in Art. 5.

Art. 2

The research grant described in this competition announcement and the required qualifications to apply for the position are identified in Attachment A. The lack of the admission requirements leads to the automatic exclusion from the competition procedure.

Possession of a PhD or equivalent degree obtained abroad or, only for the interested areas, of a medical specialization accompanied by an adequate scientific production, constitutes a preferential qualification for awarding the research fellowship of this selection, if it has not been provided as a mandatory requirement.

For the only purpose of the admission to the competition, the Examining Board (Art. 7) shall assess the equivalence of the qualification obtained abroad, except for the evaluation of the medical specialization qualification to which Article 38 of the Legislative Decree 165/2001 and subsequent modifications and additions, and EU regulations on the matter, shall be applied.

The Examining Board will proceed to the evaluation of the qualification obtained abroad according to the documentation attached to the application form. The Examining Board may exclude the candidate if the submitted documentation does not provide sufficient information for the assessment. Therefore, applicants must enclose all the documentation in their possession relating to their qualification in order to provide the Examining Board with sufficient information for assessment.

Candidates holding a qualification issued by a European Research Area country, if successful, must submit, if not already attached to the application form one of the following options:
- Supplement Diploma in English issued by the competent University.
- CIMEA Certificate of comparability of the foreign qualification, issued by CIMEA (Information Centre on Academic Mobility and Equivalence) via the "diplome" service at https://cimea.diplo-me.eu/udine/#/auth/login

Candidates holding a qualification issued by a non-European Research Area country, if successful, must submit, if not already attached to the application form one of the following options:
- Declaration of the on-site value of the qualification and the certificate relating to the degree with examinations and grades. A certificate in a language other than Italian or English must be accompanied by an official translation into one of these languages (certified by the competent diplomatic-consular authority or certified by a court in Italy).
- CIMEA Certificate of comparability of the foreign qualification, issued by CIMEA (Information Centre on Academic Mobility and Equivalence) via the "diplome" service at https://cimea.diplo-me.eu/udine/#/auth/login
If the Supplement Diploma or the statement/attestation of comparability are not available when signing the contract, the applicant must demonstrate that he/she has requested the documentation and submit it as soon as possible.

Any exclusion from the selection procedure due to lack of eligibility requirements, absence of required documents, failure to sign the selection application or submission of the selection application in a manner different from what is provided for in this call for applications will be communicated to applicants exclusively at the email address indicated in the application form.

Art. 3
The research grant referred to in this call for applications cannot be awarded:

a. to employees of Universities and the entities referred to in Article 22, section 1, of Italian Law no. 240 of 30 December 2010 (in the text prior to the reform introduced by Law no. 79 of 29 June 2022);

b. to those who have already been awarded research grants pursuant to Italian Law no. 240 of 30 December 2010 (prior to the reform introduced by Law no. 79 of 29 June 2022) for the maximum period provided by law, even if not continuously, excluding the period in which the grant was used in conjunction with the doctorate, up to the legal term of the relative course;

c. to those who have already benefited from research grants and fixed-term researcher contracts provided for, respectively, in Articles 22 and 24 of Italian Law no. 240 of 30 December 2010 (in the text prior to the reform introduced by Law no. 79 of 29 June 2022), for a total of 12 years, even if not consecutive;

d. to anyone who has a degree of kinship or affinity, up to and including the fourth degree, with:
   - the Rector, the Director General or a member of the Board of Directors of the University of Udine;
   - the scientific supervisor or a professor/researcher belonging to the department or organisation hosting the research grant in question.

The research grant provided for in this call for applications cannot be combined:

a) with scholarships of any kind, except for those granted by Italian or foreign institutions to supplement, by means of stays abroad, the fellow's training or research activities;

b) with other research grants;

c) with an employment relationship, even if part-time, without prejudice to the relevant provisions for employees of public administrations.

The grant awarded under this call for applications is also incompatible with simultaneous attendance at university degree courses, either Bachelors, specialist or Masters, research Doctorates with scholarships and medical specializations, in Italy or abroad.

Art. 4
Applicants must enclose with their application, under penalty of exclusion, the following documents:

a) their professional scientific CV, highlighting the candidate's aptitude for carrying out and implementing the research project (Attachment A);

b) their identity card, their passport or any other identification document1;

c) (for candidates with a foreign qualification only) certification or self-certification of both the academic qualification required for the admission to the selection, and of the exams (with

1 Please be aware that the residence permit is not an identification document.
evaluation) took during the period of study abroad, and of any other document that can be useful to the evaluation of the degree by the Examining Board.

Applicants can attach to the application, publications and any other certification considered useful to demonstrate the qualification based on the research program (Attachment A) and to certify any research activity accomplished at public or private institutes (indicating the starting and ending date and the duration).

The documents and qualifications mentioned above must be submitted in Italian or English. Those that are not as requested will not be evaluated. Documents originally written in a language other than Italian or English must come with a translation in Italian or English, that the candidate will do on its own responsibility. The translation can be an abstract concerning the thesis.

Italian and Community candidates wishing to submit qualifications referring to conditions and facts attested by Public Administrations must proceed exclusively with self-certification. Non-EU citizens legally residing in Italy may self-certify only data that can be verified or certified by Italian public bodies. They may also use declarations in lieu when provided for by an international convention between Italy and the declarant's country of origin. Non-EU citizens not residing in Italy cannot self-certify.

Only the qualifications possessed by the candidate on the date the application form is submitted and submitted in accordance with the procedures set out in Article 5 will be assessed.

Failure to submit mandatory documents provided for in this article will constitute grounds for exclusion from the selection.

Art. 5
The submission of the applications for the present call starts on October 26, 2023 at 2:00 pm (Italian time) and ends on November 14, 2023 at 2:00 pm (Italian time).

The application to take part in the selection must be completed, under penalty of exclusion, using the appropriate online procedure, available at the link https://pica.cineca.it/
The procedure involves an applicant registration step, for those who do not already have an account, and then an application completion step.

Once completed, the online application must be signed in the manner described in the online procedure (manual signature with attached identity document or digital signature), under penalty of exclusion from selection. The application does not have to be signed if you access the above-mentioned online procedure using your SPID ID.

The qualifications referred to in Article 4 must be attached to the application in .pdf format. Individual .pdf files may not exceed 30MB.

The application for participation in the selection is automatically sent to the University of Udine with the definitive closing of the online procedure.

The University Administration:
- is not responsible if it is impossible to read the submitted documentation in electronic format due to damaged files;
- shall not accept or take into consideration qualifications or documents received in paper form or by any means other than what is specified in this article.

Reference to documents or publications already submitted in connection with other competitions is not allowed.

The Administration is not responsible for any missing document or communication because of inaccurate indication of residence and/or address submitted by the candidate during the application. Also, the Administration is not responsible if the candidate has not communicated changes in this information, or has communicated them too late. The Administration is also not responsible for any postal or telegraphic problems not attributable to the Administration itself.

Applicants are advised not to wait until the last few days before the closing date to submit their application. The University accepts no responsibility for any malfunctions due to technical problems and/or overloading of the communication line and/or application systems.

**Art. 6**

The selection procedure is held in accordance with the modality indicated in Attachment A.

The test will aim to assess the general preparation, experience and aptitude for research of the candidate. It will consist in the evaluation of the professional scientific curriculum, of the publications and qualifications presented, and of the interview, where foreseen.

**Art. 7**

The Examining board for the competition is identified in Attachment A of the present competition announcement, of which it is an integral part.

At its first meeting, the Examining board shall appoint its President and Secretary, and establish the criteria and methods for evaluating the qualifications and the interview, where foreseen.

The results of the qualifications assessment must be disclosed to applicants during the interview, where foreseen.

The Examining board can award a maximum of 100 points (one hundred out of one hundred) to the selection.

At the end of the evaluation procedure, the Examining board shall formulate the general merit list based on the overall score of each candidate, and draw up the minutes of the whole competition procedure.

Based on the ranking list, the assignment is awarded to candidates who have obtained a minimum overall score of 70/100 (seventy out of one hundred).

The Examining board's judgement is final.

The ranking list will be made public exclusively through publication on the University's official website.

Applicants will not be notified of the outcome of the evaluation.
Those who do not declare their acceptance of the research grant and do not present themselves at the research centre within the deadline communicated by the latter, even if not formally, shall lose the right to receive it. Exceptions to this term will only be granted in cases of documented force majeure.

Art. 8
The research activity cannot be started before signing the contract defining the terms and conditions of the collaboration.

The activity covered by the research grant must have the following characteristics:

a) it must be carried out as part of the research programme covered by the grant and not be a merely technical support to it;
b) it must have a close connection with the realization of the research program for which the winner of the grant has been awarded the contract;
c) it must be continuous and, in any case, temporally defined, not merely occasional, and in coordination with the overall activity of the University;
d) it must be carried out autonomously, solely within the limits of the programme prepared by the programme supervisor, without predetermined working hours.

The researcher is required to submit a detailed written report on the work carried out and the results achieved, accompanied by the opinion of the scientific supervisor, to the reference organisation at the intervals set out in the contract. The researcher must also submit interim reports and timesheets, if requested by the reference organisation.

Either the fellow or the reference organisation may withdraw from the contract.

The reference organisation may terminate the contract not only in the cases referred to in Article 9, sections 2 and 3, of the "Internal rules for awarding research grants pursuant to law 240 of 30 December 2010" of the University of Udine, but also in the event the research project and therefore the financial coverage on which the research grant is based cease to exist.

The signing of the contract is subject to the formalization of the agreement between the Hub and Spokes and between Spokes and Spokes' Affiliates.

Art. 9
The following legal dispositions shall apply to the grant referred to in this call for applications:
- for tax matters, the provisions of Article 4 of Italian Law no. 476 of 13 August 1984, as subsequently amended and supplemented;
- for social security matters, the provisions of Article 2(26) et seq. of Italian Law no. 335 of 8 August 1995, as subsequently amended and supplemented;
- for mandatory maternity leave, the provisions of the Italian Ministerial Decree of 12 July 2007;
- with regard to sick leave, the provisions of Article 1(788) of Italian Law no. 296 of 27 December 2006 and subsequent amendments.

During the period of mandatory maternity leave, the allowance paid by INPS according to Art. 5 of the Italian Ministerial Decree of 12 July 2007 is supplemented by the University up to the full amount of the research grant.

The grant will be paid in monthly instalments.
Art. 10
The data collected as part of the procedure referred to in Art. 5 are necessary to properly manage the selection procedure, for any subsequent management of the research grant and for purposes related to managing services provided by the University. The University of Udine is the Data Controller. At any time, the data subject may request access, rectification and, depending on the University's institutional purposes, cancellation and restriction of processing or oppose the processing of their data. The data subject can always lodge a complaint with the Italian Data Protection Authority. The complete disclosure is available on the University of Udine website in the "Privacy" section, accessible from the home page www.uniud.it Direct Link: https://www.uniud.it/it/pagine-speciali/guida/privacy

Art. 11
For all matters not expressly mentioned in this call for applications, refer to the regulations in force on the subject cited in the introduction and to the "Internal rules for awarding research grants pursuant to Italian Law no. 240 of 30 December 2010" of the University of Udine, issued by Rector's Decree no. 182 of 31 March 2021.

Art. 12
The procedure supervisor is Dr Sandra Salvador, Head of the Research Services Area of the University of Udine.
The Responsible office at the University of Udine is "Area Servizi per la Ricerca - Ufficio Formazione per la Ricerca", via Mantica n. 31 - 33100 Udine, Italia.

To request information about the call for applications, please complete the following form available on the University of Udine website:
https://helpdesk.uniud.it/SubmitSR.jsp?type=req&accountId=universityofudine&populateSR_id=42105
Attachment A

Responsabile scientifico della ricerca / Principal investigator:

Nome e cognome / Name and surname: Rossella De Marco
Qualifica / Position: Professoressa Associata / Associate Professor
Dipartimento / Department: Scienze Agroalimentari, Ambientali e Animali (DI4A) / Agricultural, Food, Environmental and Animal Sciences
Area MUR / Research field: 03 - Scienze chimiche / Chemical sciences
Settore concorsuale e Settore scientifico disciplinare / Scientific sector: 03/C1; CHIM/06 - Chimica organica

Titolo dell'assegnò di ricerca / Topic of the research fellowship “assegno di ricerca”:
I bandi sono consultabili dal sito dell'Ateneo, del MUR e di Euraxess / The calls are available on the University, MUR and Euraxess websites

Testo in italiano:
Sintesi di peptidi e peptidomimetici biologicamente attivi: studi conformazionali e loro funzionalizzazione su nanomateriali.

Testo in English:
Synthesis of biologically active peptides and peptidomimetics: conformational study and their functionalization on nanomaterials.

Obiettivi previsti e risultati attesi del programma di ricerca in cui si colloca l'attività dell'assegnista di ricerca / Foreseen objectives and results of the research programme performed by the research fellow “assegno di ricerca”:
I bandi sono consultabili dal sito dell'Ateneo, del MUR e di Euraxess / The calls are available on the University, MUR and Euraxess websites

Testo in italiano:
Riferimenti al progetto: Il progetto è in linea con la “MISSIONE 4: istruzione e ricerca” del PNRR all'interno del quale si articola il progetto Ecosistemi per l'innovazione - iNEST: Interconnected North-East Innovation Ecosystem e si allinea alla componente C2: dalla ricerca all'impresa. Il progetto dell'assegnista rientra tra le attività previste per il gruppo di ricercatori di Udine affiliato allo Spoke 7 (Smart AgriFood). Il progetto Smart-Agrifood si caratterizza per una elevata multidisciplinarietà e l'assegnista oltre a svolgere prevalentemente l'attività di ricerca nell'ambito dei processi di sintesi di molecole collaborerà con i ricercatori del progetto fornendo un supporto analitico di alta qualifica (con analisi chimiche, chimico-fisiche funzionali, biofunzionali) per la caratterizzazione di matrici diverse (vegetali e animali e di derivati microbici) e dei relativi estratti di interesse per il progetto.

Abstract: Molecole biologicamente attive a struttura peptidica presentano forti limitazioni per il loro impiego in ambito terapeutico dovuto agli effetti indesiderati, scarsa stabilità metabolica e ridotta biodisponibilità in vivo. L'approccio utilizzato per ovviare tali problematiche, è quello di sintetizzare peptidomimetici in grado di mantenere l’attività biologica o di aumentarla, maggiore stabilità metabolica e biodisponibilità. Questa strategia prevede l’inserzione, all’interno della sequenza peptidica, di D-amminoacidi, amino acidi non naturali, b-aminoacidi, eterocicli stabili a cinque o a sei termini, bioisosteri oppure la macrociclizzazione testa-coda, mantenendo i farmacofori responsabili dell’attività farmacologica. I peptidomimeticini avranno come target il recettore delle intregine ed i batteri. Le intregine sono over-espressive nelle cellule malate, sono eterodimeri costituiti da due subunità a e b, dalla loro combinazione si ha un totale di 24 intregine coinvolte in diverse funzioni quali l’angiogenesi o
formazione di nuovi vasi sanguigni che hanno lo scopo di portare nutrimento alle cellule cancerogene, l'adesione cellulare, l'apoptosi. Le intregine, sono recettori di membrana presenti sulla membrana cellulare ed interagiscono con ligandi cioè proteine della matrice extracellulare quali la fibronectina, vitronectina, fibrinogeno. Questa interazione porta alla loro internalizzazione nella cellula infetta con l'attivazione di pathway e signaling responsabili per esempio della crescita e invasione in altri tessuti delle cellule infettate. La fibronectina, interagisce con le intregine grazie alla presenza della sequenza RGD formata da tre amino acidi, nell'ordine Arginina, Glicina e Aspartato la quale lega in particolare le intregine αvβ3α5β1, coinvolte in patologie quali il cancro. La vitronectina, ma anche la fibronectina, riconosce la sequenza LDV formata dagli amino acidi, nell'ordine, Leucina, Aspartato e Valina. Questa sequenza è specifica per le intregine α4β1 e α4β7che sono coinvolte nei processi infiammatori quali l'asma, il morbo di Crohn, sclerosi multipia, la celiachia, fibrosi cicistica per citarne alcune.

La presenza, nelle sequenze di riconoscimento, di aminoacidi con stereochimica di tipo "L" le rende molto sensibili all'attività enzimatica. La sequenza RGD è stata introdotta in una sequenza pentapeptidica e successivamente ciclizzata andando ad ottenere la molecola RGD/NMeV anche nota come cilengitide. Il ciclo pentapeptico risulta essere formato dai farmacofori guanidino, presenti nella catena laterale dell'arginina, e l'acido presente nella catena laterale dell'acido aspartico, che funge da spaziatore, la fenilalanina presenta stereochimica di tipo "D" ed è situata adiacente all'aspartato e risulta fondamentale per la corretta disposizione spaziale ed interazione della molecola con il recettore. Mentre la N-MeVal, è stato osservato dagli studi di Ala scan, risulta essere l'amminoacido che può essere sostituito senza portare una riduzione dell'attività biologica. Il ciclo risulta essere stabile all'ione degli enzimi, mostra una elevata attività in vitro e in vivo sugli animali mentre perde di efficacia sull'uomo.

La sequenza LDV è stata usata per la sintesi del ligando semi sintetico BIO1211, il quale è costituito da una porzione di sintesi rappresentata dalla difenilurea, in grado di riconoscere la subunità α4 delle intregine, ed una parte naturale, la sequenza LDV, in grado di legare la subunità di tipo β. Il BIO1211 presenta una elevata attività in vitro mentre in vivo viene completamente degradato dagli enzimi.

Per quanto riguarda i batteri in questo caso il target è rappresentato dalla parete cellulare e verranno sintetizzati mimetici ricchi di gruppi amminic in grado di formare canali nella parete cellulare del batterio con lo scopo di provocare la morte.

**Obiettivi e risultati attesi, attività di ricerca proposta, metodologie e contenuti:** Il progetto si focalizzerà sulla sintesi di molecole biologicamente attive a struttura peptidica e loro funzionalizzazione con nanoparticelle. Le nanoparticelle sono sintetizzate partendo dal silicio estratto da scarti agroalimentari quali quelli della vendemmia del Nord-est risulta essere particolarmente ricco.

Verranno sintetizzati mimetici del BIO1211 e nuovi sistemi di drug-delivery. Lo scopo è quello di aumentare la biodisponibilità delle molecole all'interno delle cellule infettate andando a ridurre l’azione delle amino-peptidasi. Per raggiungere questo obiettivo, si andrà ad ottimizzare inizialmente la sintesi per l'ottenimento del ciclo a cinque termini idantoina. Verranno fatti studi sulla sua capacità di indurre ripiegamenti di tipo beta-turn tramite esperimenti di titolazione a 25°C con l’aggiunta di percentuali crescenti di DMSO6 su CDC13. Esperimenti di temperatura variabile a 25°, 35° e 45°C saranno fatti per misurare lo spostamento degli NH presenti all'interno delle sequenze modello sintetizzate per capire la presenza di eventuali turn, ed infine verranno fatti esperimenti di dicroismo circolare, utili per studiare la struttura secondaria della molecola tramite la misura di differenza di luce polarizzata in funzione della lunghezza d’onda. Solo dopo aver completato lo studio strutturale e conformazionale tramite esperimenti NMR mono e bi-dimensionali e l'utilizzo di programmi per predire la struttura 3D, quali Hyperchem e Gaussian, verranno sintetizzati mimetici della sequenza BIO1211 e nuovi citotossici/antibatterici contenenti l’eterociclo, che saranno sottoposti all’azione enzimatica per confermare la loro stabilità, ed infine verrà fatto il test biologico in vitro. I composti ottenuti verranno utilizzati per nuovi sistemi di drug-delivery. Dove si andranno ad utilizzare inizialmente molecole di riferimento per ottimizzare le condizioni, in un secondo tempo si useranno i mimetici che presentano la
maggior efficacia in vitro. Le molecole saranno legate su nanomateriali a struttura mesoporosa ottenute da fonti naturali, quali gli scarti del vino, con cavità vuote internamente, ma anche su superfici diverse. Le cavità dei materiali mesoporosi, avranno lo scopo di ospitare molecole citotossiche che verranno poi rilasciate tramite stimoli all’interno della cellula infettata.

Il lavoro sarà svolto presso i laboratori di chimica presenti nel Di4A in collaborazione con i componenti del progetto iNEST per l’ottenimento degli scarti agroalimentari e lo studio in vitro del sistema. Nello specifico, i risultati attesi e le metodologie impiegate sono di seguito riepilogati.

a. **Risultati attesi**
- Sintesi di composti biologicamente attivi;
- Sintesi di nuovi nanomateriali derivanti da scarti alimentari;
- Test biologico in vitro;
- Risultati attesi in termini di pubblicazioni: 3 articoli.

b. **Metodologie impiegate**
- Sintesi in fase solida e in soluzione e caratterizzazione tramite NMR di biomolecole;
- Sintesi di nuovi nanomateriali e caratterizzazione tramite DLS, IR, zeta potenziale e TEM;
- Studio della cinetica di rilascio;
- Analisi in vitro.

**Text in English:**

**Project references:** The project is in line with the "MISSION 4: education and research" of the PNRR within which the project Ecosistemi per l'innovazione - iNEST: Interconnected North-East Innovation Ecosystem is articulated and aligns with the C2: from research to business component. The research fellow's project is part of the activities planned for the group of researchers from Udine affiliated to Spoke 7 (Smart AgriFood). The Smart-AgriFood project is characterized by a high multidisciplinarity and the research fellow, in addition to mainly carrying out research activities in the field of molecular synthesis processes, will collaborate with the researchers of the project by providing a highly qualified analytical support (with chemical, chemical-physical, functional, biofunctional analyzes) for the characterization of different matrices (plant and animal and microbial derivatives) and related extracts of interest to the project.

**Abstract:** Biologically active molecules with peptide structure have strong limitations for their use in the therapeutic field due to undesirable effects, poor metabolic stability and reduced bioavailability in vivo. The approach used to overcome these problems is to synthesize peptidomimetics able to maintain biological activity or increase it, greater metabolic stability and bioavailability. This strategy involves the insertion, within the peptide sequence, of D-amino acids, non-natural amino acids, ß-amino acids, stable heterocycles with five or six terms, bioisosteres or head-tail macrocyclization, keeping the pharmacophores responsible for the pharmacological activity. Peptidomimetics will target integrin receptor and bacteria. Integrins are over-expressed in diseased cells, they are heterodimers consisting of two subunits α and β, from their combination there is a total of 24 integrins involved in different functions such as angiogenesis or formation of new blood vessels that are intended to bring nourishment to cancer cells, cell adhesion, apoptosis. Integrins are membrane receptors present on the cell membrane and interact with ligands, i.e., extracellular matrix proteins such as fibronectin, vitronectin, fibrinogen. This interaction leads to their internalization in the infected cell with the activation of pathways and signaling responsible for example for the growth and invasion in other tissues of the infected cells. Fibronectin interacts with integrins thanks to the presence of the RGD sequence formed by three amino acids, in the order Arginine, Glycine and Aspartate which binds in particular the integrins αVβ3 / α5β1, involved in diseases such as cancer. Vitronectin, but also fibronectin, recognizes the LDV sequence formed by amino acids, in order, Leucine, Aspartate and Valine. This sequence is specific for the integrins α4β1 and α4β7 that are involved in inflammatory...
processes such as asthma, Crohn’s disease, multiple sclerosis, celiac disease, cystic fibrosis to name a few.

The presence, in the recognition sequences, of amino acids with stereochemistry type "L" makes them very sensitive to enzymatic activity. The RGD sequence was introduced into a pentapeptide sequence and subsequently cyclized to obtain the molecule RGDF-NMeV also known as cilenitide. The pentapeptic cycle is formed by the pharmacophores guanidinium, present in the side chain of arginine, and the acid present in the side chain of aspartic acid, glycine acts as a spacer, phenylalanine has stereochemistry type "D" and is located adjacent to aspartate and is fundamental for the correct spatial arrangement and interaction of the molecule with the receptor. While N-MeVal, it has been observed by Ala scan studies, turns out to be the amino acid that can be replaced without bringing a reduction in biological activity. The cycle is stable to the ion of enzymes, shows a high activity in vitro and in vivo on animals while losing efficacy in humans.

As far as bacteria are concerned, in this case the target is represented by the cell wall and mimetics rich in amino groups will be synthesized capable of forming channels in the cell wall of the bacterium with the aim of causing its death.

Objectives and expected results, proposed research activity, methodologies and contents: The project will focus on the synthesis of biologically active molecules with peptide structure and their functionalization with nanoparticles. The nanoparticles are synthesized starting from silicon extracted from agri-food waste such as those of the harvest of which the territory of the North-East is particularly rich.

BIO1211 mimetics and new drug-delivery systems will be synthesized. The aim is to increase the bioavailability of molecules within infected cells by reducing the action of amino-peptidases. To achieve this goal, the synthesis will initially be optimized to obtain the five-term hydantoin cycle. Studies will be done on its ability to induce beta-turn folding through titration experiments at 25°C with the addition of increasing percentages of DMSOd6 on CDCl3. Variable temperature experiments at 25°, 35° and 45°C will be performed to measure the displacement of the NH present within the synthesized model sequences to understand the presence of any turns, and finally circular dichroism experiments will be carried out, useful for studying the secondary structure of the molecule through the measurement of polarized light difference as a function of wavelength. Only after completing the structural and conformational study through mono and bi-dimensional NMR experiments and the use of programs to predict the 3D structure, such as Hyperchem and Gaussian, will be synthesized mimetics of the BIO1211 sequence and new cytotoxic / antibacterial containing the heterocycle, which will be subjected to enzymatic action to confirm their stability, and finally the in vitro biological test will be done. The compounds obtained will be used for new drug-delivery systems. Where reference molecules will initially be used to optimize conditions, in a second time the mimetics that have the greatest efficacy in vitro will be used. The molecules will be bonded on mesoporous nanomaterials obtained from natural sources, such as wine waste, with hollow cavities internally, but also on different surfaces. The cavities of the mesoporous materials will have the purpose of hosting cytotoxic molecules that will then be released through stimuli inside the infected cell. The work will be carried out at the chemistry laboratories present in the Di4A in collaboration with the components of the iNEST project for the obtaining of agri-food waste and the in vitro study of the system. Specifically, the expected results and the methodologies used are summarized below.

Expected results:
- Synthesis of biologically active compounds;
- Synthesis of new nanomaterials derived from food waste;
- In vitro biological test;
- Expected results in terms of publications: 3 articles.

Methodologies:
- Synthesis in solid phase and in solution and characterization by NMR of biomolecules;
- Synthesis of new nanomaterials and characterization by DLS, IR, potential zeta and TEM;
- Study of release kinetics;
- In vitro analysis.

### Struttura dell'Università di Udine presso la quale verrà sviluppata l'attività di ricerca / Department or other structure of the University of Udine where research activities will be carried out:

L'attività di ricerca sarà sviluppata presso il Dipartimento di Scienze Agroalimentari, Ambientali e Animali (DI4A) dell'Università degli Studi di Udine. / The research activity will be developed at the Department of Agricultural, Food, Environmental and Animal Sciences of the University of Udine.

**Nota / Note:** In base alle esigenze del progetto PNRR su cui grava il finanziamento, l'assegnista di ricerca potrà dover svolgere parte delle attività presso altre Università e Istituzioni coinvolte nel medesimo progetto. / Based on the needs of the PNRR project that finances the research grant, the research fellow may have to carry out part of the activities at other universities and institutions involved in the project.

### Importo dell'assegno di ricerca (al lordo oneri carico assegnista) / Total grant gross for the research fellowship:

€ 45,398,54

### Durata dell'assegno di ricerca / Duration of the research fellowship “assegno di ricerca”:

18 mesi / months

### Finanziamento / Financed by:


### Requisiti di ammissione / Minimum qualifications necessary:

- Possesso del titolo di Dottore di ricerca o titolo equivalente conseguito all’estero;
- Possesso di un curriculum scientifico professionale idoneo allo svolgimento dell’attività di ricerca contemplata.
- Research doctorate or equivalent qualification obtained abroad;
- Professional scientific curriculum suitable for the research activity above mentioned.

### Procedura selettiva / Competition procedure:

Valutazione per titoli e colloquio / Evaluation of titles and oral exam
I risultati della valutazione dei titoli saranno resi noti agli interessati nel corso del colloquio / The evaluation of the qualifications will be disclosed to candidates during the interview

<table>
<thead>
<tr>
<th>Calendario del colloquio / Calendar of the oral exam</th>
<th>Modalità / Modality</th>
<th>In presenza / On site</th>
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<tr>
<td>Data / Date</td>
<td>22 novembre / November 2023</td>
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<tr>
<td>Ora / Time</td>
<td>14:30 / 2:30 pm (Italian time)</td>
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<td>Luogo / Place</td>
<td>Studio della professoressa De Marco presso la sede di via Cotonificio del Dipartimento di Scienze Agroalimentari, Ambientali e Animali dell’Università di Udine / Professor De Marco’s office at the via Cotonificio site of the Department of Agricultural, Food, Environmental and Animal Sciences of the University of Udine</td>
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Per sostenere il colloquio i candidati devono esibire un valido documento di riconoscimento. / Candidates must come to the interview with a valid identity document.

Eventuali variazioni saranno rese note esclusivamente mediante pubblicazione all’albo ufficiale on line dell’Ateneo / Any change will be made public solely through publication on the University web site [http://web.uniud.it/ateneo/normativa/albo_ufficiale](http://web.uniud.it/ateneo/normativa/albo_ufficiale)

**Commissione giudicatrice / Examining Board:**

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<tr>
<th>Nome e Cognome</th>
<th>Qualifica</th>
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<td><strong>Membri Effettivi / Permanent members</strong></td>
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<td>Rossella De Marco</td>
<td>PA</td>
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<td>Daniele Zuccaccia</td>
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<td>Andrea Venerando</td>
<td>PA</td>
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<td>Rosanna Toniolo</td>
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