

VALUTAZIONI PROGETTI DI RICERCA DI DIPARTIMENTO PRID – ANNO 2022

COMMISSIONE ESTERNA

<p>Project: Theranostic Copper Complexes in Prostate Cancer (THERACuPROST)</p> <p>Applicant: Marzano Cristina</p>
<p>General assessment of scientific quality and innovation - Assessment of scientific plan</p> <ul style="list-style-type: none"> - <i>Is the project scientifically significant, original and innovative?</i> - <i>Is the project built on a departmental know-how? Has the project a significant impact for future development? Is the plan realistically feasible?</i> - <i>Are the research methods, materials, work packages, tasks, milestones and timeline appropriate and in agreement with deliverables?</i> - <i>Are the risk assessment and the contingency plan properly considered?</i> - <i>This project has perspectives for international collaborations, applications, networking?</i> - <i>Has the project the character of start-up research that can attract in the future competitive and non-competitive funds?</i>
<p>Reviewer n. 1</p> <p>Well-planned project, with possibly an excess of activities (several lines, 2D and 3D cultures, patient-derived cultures), long in vivo experiments (pharmacokinetics, efficacy, etc). It seems difficult to accomplish everything in 2 y. It is not specified how 3D cultures will be assessed for toxicity, etc.</p> <p>Reviewer n. 2</p> <p>Scientific original and innovative, but the number of objectives are too elevated for a two years project. In addition, in the evaluation of toxicity, lack of copper-related iron homeostasis. Risk of low selectivity for cancer cells.</p> <p>Reviewer n. 3</p> <p>The project submitted by Dr. Marzano and all focuses on the synthesis of novel copper-based compounds against prostate cancer and their combination with tracers to increase the diagnostic efficacy by SPECT, ERT and SPECT. This is a real multidisciplinary project involving chemistry, in vitro, in vivo studies, pharmacokinetics. My personal opinion is that this program is too ambitious to be completed in two years. Although the team is very competitive, all facilities necessary for this work are already available and the study-plan is well designed many perplexities remain on the real possibility to get results to move to the next phase and so on.</p> <p>Reviewer n. 4</p> <p>The project rationale is solid, and objectives are well defined. While the originality of the proposal is moderate, the opportunity to bring multiple properties in a single molecule would represent an important and significant innovation. The background on which the proposal is based is very solid, while the risk may be underestimated due to some potential failure in terms of synthetic feasibility. One aspect has not been considered, that is the possibility that a compound is obtained with proper imaging properties while missing the therapeutic value; would it be considered a valuable result in the field? Clearly, a positive outcome of the project would open several opportunities for new collaboration and interest for clinical applications.</p>
<p>Competence and expertise of the applicant.</p> <ul style="list-style-type: none"> - <i>What are the merits and scientific expertise of the applicant?</i> - <i>Are they appropriate and sufficient for the proposed project?</i>
<p>Reviewer n. 1</p> <p>The proponent displays appropriate expertise as referred to the project aims, reporting a long dating work on Copper conjugates as antitumor agents; scientific production is declining in the last years and only in few articles she is as principal author.</p> <p>Reviewer n. 2</p> <p>Excellent merits and scientific expertise of the applicant.</p>

Reviewer n. 3

Dr Marzano has a great experience in the field of research and its documented knowledge can cover almost all areas of the project. Her publications and her bibliometric indexes well fit the role in the present project.

Reviewer n. 4

The applicant's CV clearly expresses the required level of experience and competence for the management of the proposed project

Competence and expertise of the research team.

- *Does the research team bring complementary expertise to the project?*
- *Is the project involved in international research collaborations that can significantly contribute to the success of the project?*

Reviewer n. 1

Well integrated units, involving external institutions.

Reviewer n. 2

Complementary expertise of the proposed team with no reported international collaborations.

Reviewer n. 3

The group is large, possessing a great experience and multidisciplinary. Interestingly, in the project the role of each "partner" for each task is well described. As previously reported it seems more appropriate to an international large project, but no doubts about the reliability and the robustness of the team.

Reviewer n. 4

The team expresses all the required complementary experiences required for the proposed project. The single RUs has international collaborations which could be involved in case of need, even though none are directly involved with the proposed project

COMMISSIONE INTERNA**Project: Theranostic Copper Complexes in Prostate Cancer (THERACuPROST)**

Applicant: Marzano Cristina

Punti di forza

Il tema dei complessi di Rame in ambito antitumorale è di notevole interesse industriale e non ancora completamente esplorato. Il PI ha già pubblicato molto sul tema. Questo sicuramente garantisce una buona prospettiva sul proseguimento dell'attività. Il team comprende componenti sia interne che esterne al DSF e appare essere già ben consolidato.

Criticità

Pur essendo stato presentato da un gruppo di esperti del settore il progetto non sembra essere caratterizzato da una forte componente innovativa. Inoltre progetto appare 'diffuso' su un numero troppo elevato di persone risultando quindi sovradimensionato rispetto alle risorse di tempo e denaro. La fattibilità del progetto è penalizzata dal numero troppo elevato di molecole e coniugati potenzialmente proposti.

VALUTAZIONI PROGETTI DI RICERCA DI DIPARTIMENTO PRID – ANNO 2022

COMMISSIONE ESTERNA

Project: Exploiting Mannose Receptor-blockers to treat metaflammation**Applicant:** Mastrotto Francesca**General assessment of scientific quality and innovation - Assessment of scientific plan**

- *Is the project scientifically significant, original and innovative?*
- *Is the project built on a departmental know-how? Has the project a significant impact for future development? Is the plan realistically feasible?*
- *Are the research methods, materials, work packages, tasks, milestones and timeline appropriate and in agreement with deliverables?*
- *Are the risk assessment and the contingency plan properly considered?*
- *This project has perspectives for international collaborations, applications, networking?*
- *Has the project the character of start-up research that can attract in the future competitive and non-competitive funds?*

Reviewer n. 1

The scientific background of the proposed project is validated by both preliminary data obtained by the Proponent Investigator and the literature data, and the proposed activities can bring to a strong innovation in the disease management. However, in my opinion there is a lack of mechanistic considerations which is a key factor to design the library to be synthesised as well as it may make data interpretation difficult. It should be clarified whether the effective target is or not an irreversible inhibitor of CD206/sCD206. On the other hand, the materials and methods are available, and timelines seems reasonable for all the proposed tasks.

Reviewer n. 2

The project submitted by Dr Mastrotto is mainly focused on the potential effect played by a new generation of mannose receptors blockers as pleiotropic anti-inflammatory agent. Although the state of the art seems to prove that this blockade may somehow prevent the amplification of a cascade of events associated with inflammation, some perplexities arises from both the specificity and the potency of this mechanism. First the mannose receptors are implicated in many other processes and its inhibition can be deleterious for the host, second because the model of obesity has already an altered regulation of glycans and their receptors. A further doubt emerges from the choice to move directly toward the development of new blockers when well standardized MR blockers or inhibitors have been described in literature. Although this part is a little bit weak, it is important to underline that the project is well described and well structured and balanced in terms of time and efforts. The risks is somehow underestimated and the contingency plan have should be better described.

Reviewer n. 3

Only one target for inflammation. Lack of international collaborations.

Reviewer n. 4

The study is relevant and its plan seems feasible; model non-ideal, the description is adequate and the interaction within units allows a full development of specific competence of collaborators.

Competence and expertise of the applicant.

- *What are the merits and scientific expertise of the applicant?*
- *Are they appropriate and sufficient for the proposed project?*

Reviewer n. 1

While the overall scientific expertise of the applicant is good, maybe some more competence from a mechanistic point of view would be useful.

Reviewer n. 2

Dr Mastrotto has an appropriate background and the research activity is well represented by the CV. However, the publications does not seem entirely fit the topic of project. Although she is an expert person in the field of pharmacological synthesis (covering the technological part of the study) the experience in

the field of inflammosome and role of MR seems to be limited.

Reviewer n. 3

Appropriate.

Reviewer n. 4

the PI fulfils the necessary competence to succeed in the project. Good scientific production reporting several recent publications

Competence and expertise of the research team.

- *Does the research team bring complementary expertise to the project?*
- *Is the project involved in international research collaborations that can significantly contribute to the success of the project?*

Reviewer n. 1

The same comment as above applies in part for the team; also, the involvement of international setting is not evident.

Reviewer n. 2

The group of collaborators is of a good level in all components. The biomedical part appears to be a little more deficient than the chemistry. However, they can assure a covering of all tasks described in the experimental activity.

Reviewer n. 3

Complementary team without international collaborations.

Reviewer n. 4

Good level of participants, although all inside the PI Institution (collaboration with DSB 1 PA and 1 PhD student).

COMMISSIONE INTERNA

Project: Exploiting Mannose Receptor-blockers to treat metaflammation

Applicant: Mastrotto Francesca

Punti di forza

Il progetto è scritto in modo chiaro. Gli aspetti terapeutici affrontati sono innovativi con potenziali interessanti sviluppi.

Criticità

Il disegno dei sistemi si basa su reazioni che richiedono una chimica complessa con rischio di produzione di una popolazione eterogenea di prodotti. I limiti dei modelli sperimentali proposti non sono sufficientemente affrontati. Il progetto prevede per l'intera durata l'inserito a tempo pieno di una dottoranda.

VALUTAZIONI PROGETTI DI RICERCA DI DIPARTIMENTO PRID – ANNO 2022

COMMISSIONE INTERNA

Project: Therapeutic monoclonal antibodies: real-life stability and photostability

Applicant: Miolo Giorgia

Punti di forza

Il progetto affronta il tema di risk-assessment nella manipolazione dei farmaci biologici ed in quanto tale mostra carattere di innovatività. Infatti, lo stesso progetto, applicato a per prodotti biotecnologici in fase di sviluppo, è già finanziato. E' interessante l'integrazione di competenze tra il DSF e la farmacia ospedaliera.

Criticità

Per quanti riguarda gli studi di fotostabilità di prodotti biotecnologici approvati, la tematica dovrebbe essere di pertinenza dell'industria farmaceutica e i dati raccolti in fase di dossier. Non sono riportate indicazioni a riguardo.

La stesura del progetto mostra diffuse carenze. Non è riportato uno sviluppo temporale del lavoro proposto, non sono indicate le metodiche, non vi è un contingency plan e i criteri per la valutazione finale non sono esplicitati. Per quanto riguarda il personale, Il PI ha un CV molto solido per quanto riguarda lo studio e la caratterizzazione di piccole molecole ma più debole per quanto riguarda la proteine. I ruoli dei partecipanti non sono assegnati, il CV della dott.ssa Coppola e' in italiano e manca il CV di due partecipanti.

VALUTAZIONI PROGETTI DI RICERCA DI DIPARTIMENTO PRID – ANNO 2022

COMMISSIONE ESTERNA

Project: Interplay between alpha-synuclein, lipid membrane and an amyloid inhibitor: a tripartite system against the progression of Parkinson disease

Applicant: Polverino de Laureto Patrizia

General assessment of scientific quality and innovation - Assessment of scientific plan

- *Is the project scientifically significant, original and innovative?*
- *Is the project **built on a departmental know-how**? Has the project a significant **impact** for future development? Is the **plan realistically feasible**?*
- *Are the research **methods, materials, work packages, tasks, milestones and timeline appropriate and in agreement with deliverables**?*
- *Are the risk assessment and the contingency plan properly considered?*
- *This project has perspectives for **international collaborations, applications, networking**?*
- *Has the project the character of **start-up research that can attract in the future competitive and non-competitive funds**?*

Reviewer n. 1

Project developed on solid background nicely described and organized; the only concern regards the actual in vivo translation of the antiaggregating activity, that is nowadays somehow questioned by some research groups.

Reviewer n. 2

The project submitted by Dr. Polverino de Laureto focuses the attention on the potential role of polyphenols and catechols against α -synuclein amyloid fibril formation. In particular the project aims at providing results on the molecular interaction between these natural compounds and the α -synuclein fibrillogenic process. Overall the project is well balanced and feasible (I really appreciated the consistency of the project with the time allowed -2 years and with the budget). The project description is clear and tightly related to the state of the art. It is quite innovative, other similar studies about fibrillogenesis of other compounds have been already carried out. The impact could be relevant although this is a very preliminary study it seems to be clearly devoted to translational objectives.

Reviewer n. 3

The project deals with the study of the effect of membranes and a novel catechol inhibitor on alfa-synuclein aggregation phenomena. The objectives are feasible and clearly presented.

Reviewer n. 4

The proposed project is scientifically significant and could shed light on to critical mechanistic feature concerning the amyloid aggregation, so providing elements of innovation in the way to PD management. All the required materials and method are available, while some concerns are due to the number of question marks to be answered from a mechanistic point of view and by using a mix of technological approaches for which proper protocols have to be implemented. This in some way is in contrast with a limited working time planned by different specialists along the project, while most of the work seems to be assigned to a fellow to be recruited on purpose and whose cost represents the main cost within the project. As well, from the risk analysis it appears that critical situations, eg unexpected experimental outputs, would be overcome simply applying the specialists' experience. Overall, an interesting project with potential for providing important results worth of further exploitation and practical clinical application, but with some important question marks regarding the project management and doubtful timelines in view of dedicated human resources.

Competence and expertise of the applicant.

- *What are the **merits and scientific expertise of the applicant**?*
- *Are they **appropriate and sufficient for the proposed project**?*

Reviewer n. 1

The proponent is active in the field of the proposal and displays a good quality publication record, demonstrating competence appropriate to carry on the proposed research.

Reviewer n. 2

The applicant has a consolidated experience and the publication list clearly highlights her relevant effort in biological, chemical and pharmacological areas. The expertise of Dr Polverino de Laureto perfectly fits the aims of the proposed project.

Reviewer n. 3

The applicant has the required expertise for reaching the goals of the project.

Reviewer n. 4

The applicant has a well-documented scientific expertise and competence concerning the proposed activities, but perhaps underestimates the risks concerning the probability of success of a number of experiments

Competence and expertise of the research team.

- *Does the research team bring complementary expertise to the project?*
- *Is the project involved in international research collaborations that can significantly contribute to the success of the project?*

Reviewer n. 1

The team is well integrated, including world-leading researcher on the topic of protein misfolding (UNIFI).

Reviewer n. 2

The collaborator and the internal group will be for granted an added value for the success of the project. They are well balanced (among chemist and biomedical research) covering all areas of the study.

Reviewer n. 3

The applicant and the involved team possess all the competences required to achieve the objective of the proposal; however, no international collaborations were reported in the project.

Reviewer n. 4

The working team does appear well integrated and with complementary expertise; as well each of the member has a good international network which could possibly bring some contribution to the project. However, most of the project activities will be apparently supported by a young researcher, whose limited experience could limit the probability of success.

COMMISSIONE INTERNA

Project: Interplay between alpha-synuclein, lipid membrane and an amyloid inhibitor: a tripartite system against the progression of Parkinson disease

Applicant: Polverino de Laureto Patrizia

Punti di forza

Il progetto presentato è ben scritto e facile da leggere. Il team comprende prevalentemente membri del DSF ma copre le expertises richieste per lo sviluppo previsto garantendo una buona fattibilità.

Criticità

L'innovatività risulta essere penalizzata in quanto la parte sperimentale si riferisce ampiamente ad un lavoro già pubblicato dal proponente. Manca un'analisi esplicita che aiuti a capire il potenziale dell'approccio proposto dal punto di vista dello sviluppo di nuovi trattamenti terapeutici. I ruoli dei partecipanti non sono descritti.

VALUTAZIONI PROGETTI DI RICERCA DI DIPARTIMENTO PRID – ANNO 2022

COMMISSIONE ESTERNA

Project: Smaller is Better: expanding the chemical space sampling in fragment screening by using ultra low molecular weight compounds and NMR

Applicant: Sturlese Mattia

General assessment of scientific quality and innovation - Assessment of scientific plan

- *Is the project scientifically significant, original and innovative?*
- *Is the project **built on a departmental know-how**? Has the project a significant **impact** for future development? Is the **plan realistically feasible**?*
- *Are the research **methods, materials, work packages, tasks, milestones and timeline appropriate and in agreement with deliverables**?*
- *Are the risk assessment and the contingency plan properly considered?*
- *This project has perspectives for **international collaborations, applications, networking**?*
- *Has the project the character of **start-up research that can attract in the future competitive and non-competitive funds**?*

Reviewer n. 1

High risk project proposal. Originality of the project is moderate considering what has already been developed for the classical FBDD by NMR. However, it could be considered a significant and innovative approach in view of the potential application to proteins not amenable for X-ray crystallography, as well as to a set of very soluble fragments, for which there are not examples by applying NMR technologies. All the required materials and methods are available and proposed timelines appear reasonable, while the risk analysis underestimate the risk of failure in view of the risky lower sensitivity of the method with respect to the XRC. On the other hands, should the project deliver good results the potential for important and wide applications could be high in view of the current relevance of the fragment-based approaches. This would in turn create great opportunities for extended collaborations.

As a final consideration, I must underly that the work could take advantage by the inclusion of more dedicated and specialised synthetic and drug discovery expertise at least at the consultancy level, particularly in the first part of the project.

Reviewer n. 2

The project is very innovative. The description is accurate and well described, despite the difficulties of the topic. The proponent clearly shows a great confidence with both theoretical part and the experimental procedures. Despite it is strongly challenging it has a great opportunity to create many other collaborations in different areas.

Reviewer n. 3

the project is innovative but probably too challenging. No international collaborations reported.

Reviewer n. 4

Ambitious project however based only on a PI and a PhD student.

Competence and expertise of the applicant.

- *What are the **merits and scientific expertise of the applicant**?*
- *Are they **appropriate and sufficient for the proposed project**?*

Reviewer n. 1

The applicant has a wide experience but seems a bit limited for the drug discovery part.

Reviewer n. 2

The candidate has a good CV, also considering the age and the academic level. Moreover, it completely fits the aim and the objectives of the project.

Reviewer n. 3

Good expertise of the applicant.

Reviewer n. 4

Expertise appropriate for the development of the proposed tasks; publication records is sufficient although few articles as principal author.

Competence and expertise of the research team.

- *Does the research team bring complementary expertise to the project?*
- *Is the project involved in international research collaborations that can significantly contribute to the success of the project?*

Reviewer n. 1

A very limited team, with some important missing experience (medicinal/synthetic chemistry).

Reviewer n. 2

The research team is quite restricted and with a limited experience but well focused on the topic.

Reviewer n. 3

The research team is rather limited.

Reviewer n. 4

Research unit composed by a single PhD student

COMMISSIONE INTERNA

Project: Smaller is Better: expanding the chemical space sampling in fragment screening by using ultra low molecular weight compounds and NMR

Applicant: Sturlese Mattia

Punti di forza

Il progetto si basa su solidi dati preliminari e presenta un buon livello di innovatività con interessanti potenziali sviluppi applicativi in futuro. Gli obiettivi dei singoli tasks e deliverables sono bene distribuiti temporalmente. Il lavoro proposto è adeguatamente bilanciato basandosi su infrastrutture e competenze già presenti.

Criticità

Il progetto è molto specifico risultando talvolta difficile da comprendere per i non addetti ai lavori. Il team è limitato cosa che potrebbe impattare sulla fattibilità.

VALUTAZIONI PROGETTI DI RICERCA DI DIPARTIMENTO PRID – ANNO 2022

COMMISSIONE ESTERNA

Project: Pharmacological characterization of Toll-like receptor 4 as a novel target for opioids in central and peripheral immune cells: implications for improving chronic pain management

Applicant: Zusso Morena

General assessment of scientific quality and innovation - Assessment of scientific plan

- *Is the project scientifically significant, original and innovative?*
- *Is the project **built on a departmental know-how**? Has the project a significant **impact** for future development? Is the **plan realistically feasible**?*
- *Are the research **methods, materials, work packages, tasks, milestones and timeline appropriate and in agreement with deliverables**?*
- *Are the risk assessment and the contingency plan properly considered?*
- *This project has perspectives for **international collaborations, applications, networking**?*
- *Has the project the character of **start-up research that can attract in the future competitive and non-competitive funds**?*

Reviewer n. 1

Nice study probably too ambitious for the time-frame of the project, although this concern is mitigated by a powerful research team. Some issues considered as contingency plan are expected (i.e. expression of KOR in microglia (see for ex. 10.1016/j.pbb.2021.173301) and can made very difficult the discrimination of the effects mediated by TLR4; similar consideration for the effects of metabolites (several studies attribute TLR4 activation to M3G 10.3389/fnmol.2022.882443).

Reviewer n. 2

The project presents complementary and interdisciplinary approaches with well-designed experimental plan, objectives, and international collaborations. However, too challenging many targets and pathways to be studied in two years.

Reviewer n. 3

The project submitted by Dr. Zusso starts from a good rationale and is supported by convincing preliminary data. The novelty is quite high and the impact is high. It combined basic and applied research in order to find a correlation between the paradoxical effect of opioids, the neuroinflammation and the key-role of Toll Like Receptor 4. Although well planned (in terms of exp. Plan and WP division) it remains highly challenging. However, the determination of milestones and contingency plan are correctly described and are convincing.

Reviewer n. 4

The proposed project is scientifically significant, while originality and innovation are moderate; it is feasible, materials and methods are available, while proposed timelines are probably underestimated. The project can produce significant results of potential interest for clinical application. There are however, in my opinion, some aspect which are not taken in due consideration, particularly in view of a more extended risk analysis. In this contest I wonder whether the selectivity of a putative TLR4/MD-2 complex antagonist vs the opioid receptors has been taken into consideration as well as the relevance of the opioid subtype receptors in triggering the proinflammatory effect.

Finally, the team composition expresses a complemented mix of competencies, also encompassing an international collaboration, with a possible extension to competitive funds. It appears however missing a medicinal chemistry component.

Competence and expertise of the applicant.

- *What are the **merits and scientific expertise of the applicant**?*
- *Are they **appropriate and sufficient for the proposed project**?*

Reviewer n. 1

PI displays a good activity in the field of neuroinflammation; the publication record is sufficient.

Reviewer n. 2

The scientific score of the applicant and her expertise are particularly appropriated for the proposed project.

Reviewer n. 3

The PI has a strong background. In particular She has a documented experience on the role of microglia and neuroinflammation in different applications. Her expertise covers almost all the fields related to this project and therefore guarantees a fine coordination and control of all studies.

Reviewer n. 4

The competence and expertise of the applicant are well documented.

Competence and expertise of the research team.

- *Does the research team bring complementary expertise to the project?*
- *Is the project involved in international research collaborations that can significantly contribute to the success of the project?*

Reviewer n. 1

well assorted RU including collaborations outside her institution (UNITO) and abroad (McGill University).

Reviewer n. 2

The involved team shows interdisciplinary and synergic expertise involving international clinical research collaboration.

Reviewer n. 3

The group does not seem so big, but the expertise of the components are somehow complementary to that of the PI.

Reviewer n. 4

As mentioned above, while the team member have a good and complemented set of competencies, I have the impression that the presence of a medicinal chemistry competence could add an important value to the team.

COMMISSIONE INTERNA

Project: Pharmacological characterization of Toll-like receptor 4 as a novel target for opioids in central and peripheral immune cells: implications for improving chronic pain management

Applicant: Zusso Morena

Punti di forza

Il progetto presentato è chiaro da leggere, affronta problema dolore cronico e uso oppioidi da prospettiva innovativa, I team è completo e include una collaborazione esterna di rilievo. I ruoli dei partecipanti sono ben definiti.

Criticità

Il tema dell'interazione oppioidi-TRL4 già documentato in letteratura.

VALUTAZIONI ASSEGNI DI RICERCA DI DIPARTIMENTO DI TIPO B ARD-B – ANNO 2022

COMMISSIONE ESTERNA

Project: Nano-in-macro delivery system for oral administration of biologics

Applicant: Arpaç Büşra

General assessment of scientific quality and innovation - Assessment of scientific plan

- *Is the project scientifically significant, original and innovative? yes*
- *Is the project built on a departmental know-how?*
- *Has the project a significant impact for future development?*
- *Are the objectives and hypotheses clearly presented?*
- *Is the plan realistically feasible?*
- *Are the research methods, materials, work packages and timeline appropriate and in agreement with deliverables?*
- *Has the project perspectives for international collaborations, applications, networking?*

Reviewer n. 1

The project is quite innovative and original. It has a scientific relevance, is clearly presented and has international collaborations.

Reviewer n. 2

The project is well designed and rationally divided in different tasks. This is quite original and the experimental plan, although a little bit ambitious for a young researcher, is reasonable. Interesting the approach by oral administration. The time-line is plausible even if the slot for the in vivo experiments is too short, maybe they can provide some preliminary proofs of concept but they can hardly define a real PK profile in a so narrowed range of time.

The state of the art is well described and allow to the reader to better appreciate the proposal. Overall it is an interesting project.

Reviewer n. 3

The project is well described, of limited innovation being based on well established technologies, but carrying some element of originality; on the other hand, it is of potential high impact. The objectives are clearly defined, and timelines are realistic; all the required materials are available, and a good international network is already in place.

The risk analysis is perhaps underestimating the overall risk also in view of the value of identified solutions.

Reviewer n. 4

Why test exanetide, when oral semaglutide is already in clinical use? The further development of the study can be hampered by this overlapping. It is also not clear how will be treated rats with EC.

Competence and expertise of the applicant.

- *What are the merits and scientific expertise of the applicant?*
- *Are they appropriate and sufficient for the proposed project?*

Reviewer n. 1

The applicant as 3d year PhD already work in the field of the project ad has a scientific expertise useful to achieve the objectives of the project.

Reviewer n. 2

The applicant has a good background and his previous experience is in line with the proposed project.

Reviewer n. 3

The applicant has a well documented scientific background and a solid experience concerning the requirements of the project from a technical point of view.

Reviewer n. 4

All the career of this young scientist was devoted to develop novel oral formulation for drug delivery

Competence and expertise of the supervisor and of the research team.

- *Does the research team bring complementary expertise to the project?*

Reviewer n. 1

The Supervisor and the team show an excellent and complementary expertise for the project.

Reviewer n. 2

The supervisor and the research team is strong and has a great and well documented experience in this field.

Reviewer n. 3

The competence of both the Supervisor and the team are well complemented and supportive with respect to the proposed activities.

Reviewer n. 4

Local team and international collaborations are of absolute scientific value and may provide all the know-how necessary to make the project successful

COMMISSIONE INTERNA

Applicant: Arpaç Büşra

Project: Nano-in-macro delivery system for oral administration of biologics

Il progetto presentato dalla Dott.ssa Arpac ha diversi spunti interessanti in termini di innovatività. Tuttavia il sistema è complesso prevedendo l'unione di micro e macro- e non prevede un'analisi preliminare dei modelli più promettenti rendendolo in parte debole in termini di fattibilità.

La candidata ha già esperienza nel settore oggetto di studio e ha presentato il progetto con buona sicurezza. Non ha presentato nessuna pubblicazione.

VALUTAZIONI ASSEGNI DI RICERCA DI DIPARTIMENTO DI TIPO B ARD-B – ANNO 2022

COMMISSIONE ESTERNA

Project: Innovative fluorescent chemical tools for real time calcium imaging in the Endoplasmic reticulum

Applicant: Andrea De Nadai

General assessment of scientific quality and innovation - Assessment of scientific plan

- *Is the project scientifically significant, original and innovative?*
- *Is the project built on a departmental know-how?*
- *Has the project a significant impact for future development?*
- *Are the objectives and hypotheses clearly presented?*
- *Is the plan realistically feasible?*
- *Are the research methods, materials, work packages and timeline appropriate and in agreement with deliverables?*
- *Has the project perspectives for international collaborations, applications, networking?*

Reviewer n. 1

The project deals with the production of novel fluorescent chemical tools for real time C2+ measurement in ER. The project is original, clearly presented with significant scientific impact.

Reviewer n. 2

The proposal is a significant extension of previous work of the applicant and the research group. The study is feasible and the outcomes highly relevant. Alternative strategies are clearly defined, in case of being unsuccessful in obtaining some intermediate results.

Evaluation is extremely positive

Reviewer n. 3

Innovation concerns mainly the target, while lower innovation is represented by the described methods and technologies. Required materials are available, while foreseen timelines seem a bit overestimated. As far as the technical plan is concerned, it is not clear whether the new products will be tested in vitro also as free acid or only in the prodrug forms.

The working team has a well documented scientific expertise and competence, objectives are realistic and of potential interest for others, so that potential future new collaboration could be originated based on obtained results.

Reviewer n. 4

The present project is really interesting and impacting. It is well describing and, although similar studies are in progress, it conserves its originality and innovation. The description of work is clear and well balanced among the different tasks. The proposal can find many points of convergence with many other projects with a high perspective for collaborations. In particular the description of the section “potential for breakthroughs” deserves a special appreciation. It is not so common for a young students to have a so broad vision about his/her activity.

Competence and expertise of the applicant.

- *What are the merits and scientific expertise of the applicant?*
- *Are they appropriate and sufficient for the proposed project?*

Reviewer n. 1

The applicant has the merit and requested expertise because he already participated in the development of a similar fluorescence probe for mitochondria during the PhD.

Reviewer n. 2

The project is the development of the career of the proponent and he and his collaborators possess all the knowledge to carry on the project.

Reviewer n. 3

The applicant has a specific expertise with respect to both the target and to the targeted objectives, even though this experience is not so evident based on the very limited publication production

Reviewer n. 4

The skills of the candidate are pertinent to the project but his bibliometric index and his activity in terms of dissemination is a little bit lower than the excellence.

Competence and expertise of the supervisor and of the research team.

- *Does the research team bring complementary expertise to the project?*

Reviewer n. 1

The supervisor and the research team have an excellent expertise useful for the project.

Reviewer n. 2

Collaborators will provide all the know-how required for a successful project

Reviewer n. 3

Experience of both the supervisor and the rest of the team is proven by their published work.

Reviewer n. 4

The supervisor has the experience and the affinity to the project items to support the proponent during the whole duration of the project.

COMMISSIONE INTERNA

Applicant: De Nadai Andrea

Project: Innovative fluorescent chemical tools for real time calcium imaging in the Endoplasmic reticulum

Il Dott. De Nadai ha presentato un progetto che rappresenta un'evoluzione di uno studio preliminare. Da questo punto di vista l'innovatività è contenuta ma il disegno è interessante e il potenziale risultato utile in termini di futuri sviluppi.

Il candidato ha dimostrato un'ottima conoscenza della tematica.

COMMISSIONE INTERNA

Project: The clock is ticking on cannabidiol and hemp extract: a metabolomic and behavioral preclinical study investigating their effects on tryptophan to serotonin and kynurenine pathways

Applicant: Sut Stefania

Il progetto presentato dalla Dott.ssa Sut manca di innovatività in quanto ricalca fedelmente lo scopo e l'impianto sperimentale già riportati in una recente pubblicazione (Florensa-Zanuy E, Garro-Martínez E, Adell A, Castro E, Díaz Á, Pazos Á, Mac-Dowell KS, Martín-Hernández D, Pilar-Cuéllar F. Cannabidiol antidepressant-like effect in the lipopolysaccharide model in mice: Modulation of inflammatory pathways. *Biochem Pharmacol.* 2021;185:114433). Benché tale pubblicazione sia stata citata, nel progetto presentato questa sovrapposizione non emerge. Come si è potuto evincere durante la presentazione della Dott.ssa Sut, la differenza tra i due approcci, riguarda solo la via di somministrazione, intraperitoneale nel lavoro pubblicato, orale in quello presentato. Tuttavia, la candidata non è stata in grado di difendere in modo convincente le motivazioni scientifiche a supporto della sua proposta di ricerca. Queste condizioni pesano negativamente anche sulle potenzialità del progetto in termini di sviluppi futuri.