Evaluation of Departmental Research Projects – PRID 2016
External committee and Internal Committee

Project Title: Maternal obesity and high-fat diet in childhood: Study of the molecular mechanism underlying gastrointestinal and cardiovascular disorders
Applicant: Rocchina Colucci

General assessment of scientific quality and innovation

Reviewer 1
Comments: The proposal is well presented and it is related with the previous studies carried out by the PI. The proposal lacks innovation and novelty. It is not expected an improvement in the impact of the publications and in the ability of fundraising.
Reviewer 2
Comments: It is a very interesting and timely proposal on this high priority medical problem and the resulting and associated morbidities. It should generate data for future competitive grant proposal and further collaborations. It is built on the internal expertise but makes use of a strong collaborative network.
Reviewer 3
Comments: The topic is significant and the development of the specific mouse models is innovative and built on departmental know-how. The future development depends on the results of the preliminary study. If effects can be observed, future competitive funds are possible.
Reviewer 4
Comments: the project is scientifically significant, outcomes are very important, it clearly is built on indoor know-how and can have an impact on future collaborations, funding etc.

Assessment of scientific plan

Reviewer 1
Comments: The plan is feasible. The main objectives are reasonable presented. The project, which is supported by five senior scientists, lacks PhD students. This type of human resources is a fundamental part in any academic project and for the Department.
Reviewer 2
Comments: The experiments are well planned, with clear progression. The methodology is appropriate. However, lack of any information on the personnel to perform these experiments on the day to day basis (a post-doc, a research assistant or a PhD student) makes it impossible to evaluate the feasibility of the project and its deliverables. This problem is compounded by the lack of any buetary details.
Reviewer 3 Score: 5
Comments: Objectives and hypotheses clearly stated, plan seems feasible. However, I do not fully understand the time schedule of the work packages. When and how are mice bred, how many mice are bred and at which timing/intervals in order to accommodate all physiological experiments. Most importantly, it is not stated how many mice need to be bred in order to achieve statistical meaningful results. Research on live animals requires an a priori power analysis and N-number calculation. I am entirely missing any financial plans or a list of the requested funds. I am entirely missing the involvement of young scientists and PhD students.
Reviewer 4
Comments: objectives and hypothesis are quite clear, the plan although feasible seems somewhat very ambitious as to what can be reasonably carried out in 2 years. The time lags presented are very tight.
It is not mentioned which mouse strain will be used since they can either have low number of offspring, or have different vulnerability to obesity and display different cardiac and gastrointestinal physiological parameters. There is no mention about human resources and force-task.

Competence and expertise of the applicant

Reviewer 1
Comments: The merits and the scientific expertise of the applicant are adequate to carry out the proposal. The PI is coauthor of several publications in specific journals of medium and medium-low impact factor. She is not the corresponding author of the majority. The ability of the PI in achieving fundraising should be improved.
Reviewer 2
Comments: These are excellent and very appropriate for this proposal
Reviewer 3
Comments: Applicant (PI) seems is highly experienced in the relevant scientific field and methodology and

will be heading a highly qualified research team.
Reviewer 4
Comments: the PI's expertise is clearly evident and it is in very good agreement with the project. Also the applicant has been the recipient of 7 grants.

Competence and expertise of the research team

Reviewer 1
Comments: The team involves five senior scientists from the Department. No PhD students have been identified, which is more than desirable. The team has related backgrounds.
Reviewer 2
Comments: Apart from the lack of info about the dedicated researcher (see above), the team has all the expertise and experience to conduct this research and the collaborators bring the necessary complementarity into the project.
Reviewer 3
Comments: Team consist of well-established scientists, all experts in their respective fields. National research collaborations, but no international collaborations. The latter in my opinion is not required for the successful pursuit of the project.
In the course of this project, are Master or PhD students involved, is someone being trained?
Reviewer 4
Comments: the mentioned persons involved in the work bring each definitely a complementary expertise. However, there is no mention about the technicians or post-docs that will carry actually the job. All collaborators are professors and assistant professors, it seems somehow that each cannot be involved more than 20%. Therefore the workplan appears much heavier to achieve.

Overall assessment

Reviewer 1
Comments:
Strengths – The proposal is feasible. The research team has good skills to achieve the proposed aims.
Weaknesses – The project is not supported by young human resources as desirable. The proposal lacks novelty and innovation.
Reviewer 2
Comments: It is a very interesting and timely proposal
Reviewer 3
Comments: Idea is innovative, team is excellent, yet description of methods could be more complete. Statistics and animal numbers are missing. No trainees are involved, at least it is not mentioned.
Reviewer 4
Comments: Strength : clear and informative project
Weakness : how many persons will effectively do the job

Final comment
Overall, this is a fundable project, with the proviso that the work packages are in line with the project rationals.

Internal Committee:
Il progetto si basa su un buon razionale e un solido background dato da una serie di risultati precedentemente ottenuti relativamente ai meccanismi dei disturbi gastrointestinali basati su disturbi neuronali. Il work package è stato sviluppato in modo coerente e scientificamente valido, tale che la fattibilità del progetto è convincente. Risulta interessante l'acquisizione di nuove competenze per il Dipartimento e per la possibilità di instaurare collaborazioni internazionali. Il team è adeguato al progetto sia per numerosità che per background scientifico.
Punti di debolezza: Manca l'aspetto molecolare/in vitro per collegare l'osservazione sperimentale a un meccanismo cellulare. Non è stata effettuata una risk analysis
Punto da chiarire: "autorizzazione Ministeriale per la sperimentazione animale descritta".

Project title: Development of a metabolomics-based platform for the evaluation of nutraceutical role in ageing in mice
Applicant: Dall'Acqua Stefano

General assessment of scientific quality and innovation

Reviewer 1 ,3
Comments: The project is reasonably presented. The proposed research might find some pharmaceutical relevant effects of the compounds studied. However, it lacks innovation and novelty. It is not expected an improvement in the international visibility of the group, in the impact of publications and in the ability to fundraising.
Reviewer 2
Comments: It is an interesting project on the medically important subject of aging and aging prevention. It employs state-of-the-art methodology available locally to address research questions. It should lead to further grant applications and also new collaborations can be easily envisaged.
Reviewer 3
Comments: The topic is significant and the metabolomic characterization and classification of young/old mice is an important milestone. Builds on the PIs know-how and expertise. If successful, dataset of young/old mice are applicable for future comparison of a variety of substances. Thus, with this background future competitive funds are possible.
Reviewer 4
Comments: the project is clearly built on a departmental know-how. To some extent may present a certain impact for future development. As the project is presented, it is not possible to foresee any international collaborations or networking. The project can however be attractive for competitive and non-competitive funding.

Assessment of scientific plan

Reviewer 1 Comments: The plan is feasible. The main objectives are clearly presented. The project, which is supported by only two scientists, lacks PhD students or Postdocs. This type of human resources is a fundamental part in any academic project and for the Department.
Reviewer 2 Score:
Comments: This project plan is feasible providing that the aged (22 month old) mice are available at the onset of the project. Otherwise, the initial metabolomics comparisons and the subsequent treatment experiments would not be possible. It is not clear whether the n number of mice per group was established using power analysis or in previous experiments. It is not clear why these particular drug doses will be tested. These are important considerations. Furthermore, this Reviewer remains unconvinced that mixing the metabolomics analyses with preparation of drug derivatives would benefit the project. It seems to be a diversion.
Lack of any information on the personnel to perform these experiments on the day to day basis (a post-doc, a research assistant or a PhD student) makes it impossible to evaluate the feasibility of the project and its deliverables. This problem is compounded by the lack of any buReviewer 2etary details.
Reviewer 3
Comments: Objectives and hypotheses clearly stated. Mouse numbers are clearly mentioned and statistical know-how seems at hand. No description (milestone?) is provided on how to evaluate the chemically modified substances. How does the PI decide, which one is the most promising for future experiments?
Reviewer 4
Comments: The objectives and hypotheses of the project are clearly presented. The workplan seems realistically feasible, all in agreement with the deliverables.
Negative point : human resources are poor or not presented. The question that emerges is: who will technically do the job? Post-doc? PhD's? Engineers? Technicians?

Competence and expertise of the applicant.

Reviewer 1
Comments: The merits and the scientific expertise of the applicant are sufficient to carry out the proposal. The PI has diverse publications in specific journals of medium-low impact. The ability of the PI in fundraising seems to be low.
Reviewer 2
Comments: The applicant is an expert in the methodology to be used on this project and will be able to carry it out providing that adequate human resources for the day-to-day running are available.
Reviewer 3

Comments: Applicant (PI) seems highly qualified in the majority of topics involved in the proposal.
Reviewer 4
Comments: No doubts that the PI has all the expertise and know-how and records for leading such a project.

Competence and expertise of the research team.

Reviewer 1
Comments: The research team involves only two senior scientists. No PhD students have been identified, which is more than desirable. No international research collaborations have been identified. This type of collaborations would help to improve the visibility of the group and the Department.
Reviewer 2
Comments: The synthetic aspects of the project are fully covered by an expert support from Dr Ferlin.
Reviewer 3
Comments: Team consist of PI and one collaborating Professor in Padova, with expertise in chemistry (modifications). All other techniques seem to be relying on the PIs expertise.
Beyond that no national and international collaborations. The latter in my opinion is not required for the successful pursuit of the project.
In the course of this project, are Master or PhD students involved, is someone being trained?
Reviewer 4
Comments: Only one person in the team presented which actually, has a complementary expertise. The project is not part of an international research collaborations. It is therefore hard to evaluate whether the project can be achieved by only 2 persons.

Overall assessment

Reviewer 1
Comments: Strengths – The proposal is feasible. The PI experience in the proposed topic is good guarantee of its proper implementation.
Weaknesses – The project lacks innovation and novelty.
Reviewer 2
Comments: This is an interesting and innovative proposal , although the drug synthesis aspect makes it a little unfocussed.
Reviewer 3
Comments: Idea is innovative, team seems adequate. Description of one milestone (evaluation of compounds) is missing. Statistics and animal numbers are stated. Education and training of students is missing. The metabolomics platform could indeed be meaningful for research groups at the Department or at the University
Reviewer 4
Comments: Interesting, scientifically significant and feasible project but there is a lack of team staff.

Final comment: The project represents a combination of interesting approaches. However, we cannot recommend funding because there is no connection between the metabolomics aspect and the preparation of drug derivatives. The information on how and on what criteria the PI will decide on the most promising compound modifications is missing. Furthermore, the project is only achievable when the aged mice are already available and the access to the metabolomics platform is already secured.

Internal Committee:
Il progetto presenta come punto di forza la completezza dello studio ma manca di innovatività, sia per tematica che per approccio, e presenta alcuni limiti di carattere metodologico. Curcumina e resveratrolo sono già stati ampiamente studiati e nello stato dell'arte manca un analisi del bibliografia sull'argomento che sarebbe utile per dimostrare la reale innovatività del progetto proposto. Si evince una difficile trasferibilità degli eventuali risultati ottenuti all'uomo e una scarsa potenzialità di attivare collaborazioni internazionali e superare una collocazione prettamente locale del progetto.

Punti di debolezza: Scarsa innovatività e approccio scientifico da migliorare. Non è stata effettuata una risk analysis. Team ridotto.
Punto da chiarire: "autorizzazione Ministeriale per la sperimentazione animale descritta".

Project title: Bioactive and dual self-assembling compounds: novel strategies to fight breast cancer
Applicant: Lisa Dalla Via

General assessment of scientific quality and innovation

Reviewer 1
Comments:
The proposal, which deals with the search of alternative treatments of breast cancer, is scientifically relevant and it incorporates alternative technologies that are widely explored for diverse diseases. The project might have a significant impact for future development. The proposal is presented in quite general fashion.
Reviewer 2 Score: 5
Comments: This project addresses and important medical problem but it is unfocussed. It is based on drug derivatives and new compounds developed by another laboratory. It may lead to future grant applications but it is likely that these will benefit the drug developer not the applicant.
Reviewer 3
Comments: The topic is highly significant as it aims in exploiting the therapeutic potential of dual compounds for tamoxifen resistant cancer models. Builds strongly on the PIs know-how and expertise. Identification of active novel dual compounds (with all strategies used) could indeed attract future competitive funding. Further, on the long run this may be of interest to the pharmaceutical industry.
Reviewer 4
Comments: The project is built on a departmental know-how and is scientifically significant since it aims at developing new compounds and new drug-administration strategies to circumvent treatment-resistance in part of breast cancers. Therefore the outgrowth of this work may lead to a research start-up and funding.

Assessment of scientific plan

Reviewer 1
Comments: The plan is feasible. The main objectives are reasonable presented. A more precise description of the type of compounds to be used to achieve the dual interaction with two targets will be desirable. The project, which is supported by three senior scientists, lacks PhD students. This type of human resources is a fundamental part in any academic project and for the Department.
Reviewer 2
Comments: There is a vast range of experiments looking into various potential modes of action and effects but without a focus. It is more like a service plan than a research application. Lack of clear info on the personnel to perform these experiments on the day to day basis makes it impossible to evaluate the feasibility of the project.
Reviewer 3
Comments: Objectives and hypotheses are clearly stated and well based on existing literature and evidence. All cell biological experiments are well described and indeed feasible. However, the planned in vivo mouse models are insufficiently described and a proposed mouse number is not mentioned. Allocation of a one year period seems not enough to accommodate different in vivo models. Having said that, I still believe that the in vivo models are important for the longterm perspectives of this project. However, the will clearly Reviewer 3beyond the 2-year frame of the proposed project. I am entirely missing the involvement of young scientists and PhD students.
Reviewer 4
Comments: Hypothesis and objectives are sound and the rationale is clear. The workplan appears feasible. The approaches and methodologies although very classical, are excessively and unnecessarily detailed.
It is not clear whether enough human resources are dedicated to the project.

Competence and expertise of the applicant.

Reviewer 1 Comments: The merits and the scientific expertise of the applicant are adequate to carry out the proposal. The PI has been active in achieving some fundraising from mainly national and Mexican sources. Although, the amounts achieved were low. The PI has a good publication record but mainly in medium-low impact journals.
Reviewer 2
Comments: This is appropriate
Reviewer 3
Comments: Applicant (PI) seems experienced and qualified for conducting the proposed project. In vivo experiments will be performed in collaboration with experienced scientists.
Reviewer 4

Comments: The PI is has a solid expertise in the antiproliferative action of synthetic or natural compounds on cell growth (normal or tumoral). She also has been PI and funding recipient in multiple national and international (Mexico) projects.

Competence and expertise of the research team

Reviewer 1 Comments: The team involves three senior scientists from the Department. No PhD students have been identified, which is more than desirable. The team has related backgrounds.
Reviewer 2
Comments: This is also good and there is complementarity in the team
Reviewer 3
Comments: The cell biological experiments will be carried out by the PI herself. Assessment of compounds on topoisomerase activities and in vivo experiments rely on collaborative team members. Both collaborators seem highly qualified for performing these tasks.
Beyond that no other national and international collaborations. The latter in my opinion is not required for the successful pursuit of the project.
Will students be trained in the course of the project? Description of such activities is entirely missing.
Reviewer 4
Comments: The two persons mentioned in the project clearly bring their specific and complementary expertise. The project is however not involved in an international research collaborations.

Overall assessment

Reviewer 1 ,7
Comments: *Strengths* – The proposal is feasible. The research team has good skills to achieve the proposed aims.
Weaknesses – The project is not supported by young human resources as desirable. The proposal is presented in quite general fashion whereas large details are provided in the experimental assays.
Reviewer 2 Score: 5
Comments: This project is unfocussed and fully reliant on the collaborator.

Reviewer 3
Comments: Proposal is innovative and of high significance, team seems adequate, yet in vivo experiments will demand more resources and Reviewer 3beyond the 2 year time of the project. Statistics and animal numbers should be stated. Education and training of students is missing.
Reviewer 4
Comments: Strength: the outcome of this research project if successfully achieved towards fruitful payback (start up and funding). Weakness: the human task force not visible in the proposal.

Final comment: The project is interesting but it relies entirely on the collaborator and would primarily benefit the collaborator and not the PI and the Department. Statistics and numbers of animals to be used should be clearly described.

Internal Committee:
Il progetto nel suo complesso è interessante ma la parte innovativa è svolta presso l'Università di Milano e non nel Dipartimento di Scienze del Farmaco. La fattibilità è buona ma questo rappresenta al contempo un limite in quanto non c'è una proposta di sviluppo di una nuova metodica ma si tratta di testare con saggi standard dei campioni preparati da un altro gruppo di ricerca. Tale progetto non porterebbe nuove competenze nel Dipartimento e non favorirebbe la visibilità internazionale. Il Team presenta competenze simili e non complementari.

Punti di debolezza: Scarsa innovatività, approccio scientifico standard, Team con competenze simili.

Project title: Enteric nervous system and dendritic cells: two players in tolerance failure in celiac disease?
Applicant: Rosa Di Liddo

General assessment of scientific quality and innovation

Reviewer 1
Comments: The proposal is continuation of recent studies by the PI on Wnt signaling. The results of the proposed studies might establish the basis of a spin-off. The proposal might attract some fundraising but at the level as it was achieved before.
Reviewer 2
Comments: It is a very innovative project combining the expertise of a cell biologist, a gastroenterologist and a tissue engineering expert. If successful, it has a potential to establish an ex vivo model for neuroendocrine interactions in the gut. This would lead to further grants and extensive collaborative activities.
Reviewer 3
Comments: The topic is highly significant. It aims at elucidating the interplay between dendritic cells and the enteric nervous system as well as the potential therapeutic potential of IL-10 for celiac disease.
The core of the project builds PIs expertise and utilizes the expertises of two other professors in Padova (for signalling and histochemistry). The project also involves a postdoc and a PhD student. It is planned that the development of the 3D in vitro model ultimately yields in a spin-off. However, the proposed 3D model was not introduced and the task allocation among the involved personnel is not fully clear to me.
Reviewer 4
Comments: A scientifically important translational research project. At the forefront in the field of the complex interactions between ENS and dendritic cells, the dysfunction of one of the elements of this finely tuned homeostasis. It is clearly built on indoor know-how and expertise. The project may fairly well lead, for some aspects, to the development of a research start-up.

Assessment of scientific plan

Reviewer 1
Comments: The plan is feasible. The main objectives are clearly presented. The project has adequate human resources as combine senior scientists from diverse areas and PhD and Postdoc students.
Reviewer 2
Comments: This proposal is not focused. It will employ Coeliac disease (CD) biopsy material to establish whether ENS is involved in CD-correlated immune response by influencing dentritic cell activity. It also aims to identify new diagnostic targets of CD. These aims are clear but the multitude of readouts to be analysed is too great. Moreover, the second part of the proposal suggests analyses in isolated and co-cultured cells populations. While establishing an ex vivo model to study complex interactions of the nervous system and immune cells in the gut would be a great achievement, these interactions are so complex and dynamic that isolation and cell culture changes the temporal expression profiles and is of little relevance to the in situ processes. The strong point is the involvement of an experienced post-doc and a PhD student, who will (presumably) perform these experiments. There is also some financial support for this project already in place.
Reviewer 3
Comments: The aims of the study are clearly mentioned. Yet I think the methodological aspects could have been better described. The project is indeed supported by a young scientist and a PhD student. The plan seems feasible, yet I did not fully understand the individual contributions of the involved personnel. It is also not state how this study will affect the career of the postdoc and PhD student.
Reviewer 4
Comments: objectives and hypotheses are sound. Concerning feasibility: to my opinion somehow oversized. But, positive point: two young scientists are completely involved in the project.

Competence and expertise of the applicant.

Reviewer 1
Comments: The merits and the scientific expertise of the applicant are adequate to carry out the proposal. The PI has achieved some fundraising but of modest amount.
Reviewer 2
Comments: This is extensive and very appropriate for the cellular analyses.
Reviewer 3
Comments: Applicant (PI) is highly experienced and qualified for conducting the proposed project. **GV**

Reviewer 4
Comments: Project in complete adequation with the PI's expertise. Very nice track record and already has a moderate funding.

Competence and expertise of the research team

Reviewer 1
Comments: The team involves several senior scientists from diverse and complementary areas and young scientists. The group has collaborations with international research groups. These types of collaborations are important for the international visibility of the group and the Department.
Reviewer 2
Comments: The expertise of the PI is fully complemented by those of a gastroenterologist and a tissue engineering expert and two junior researchers.
Reviewer 3
Comments: Team selection was carefully performed and the team will contribute to the success of the research project.
Reviewer 4 -10
Comments: Coherent and well-sized team with complementary expertise and young scientists. No international collaboration in the frame of this proposal.

Overall assessment

Reviewer 1
Comments: Strengths – The proposal is feasible. The established protocols in the project might be the basis of a spin-off in the future. Weaknesses – The project is not very innovative
Reviewer 2
Comments: It is an interesting and innovative project but its feasibility might be affected by the methodological issues listed above, which make the project risky.
Reviewer 3
Comments: The idea is innovative and feasible. Yet, more insight should have provided on the cellular model system (e.g. what exactly is 3D?). A huge bonus is the involvement of young scientists and the plans to implement a spin-off. Nevertheless, the latter is not yet well defined and at present theoretical.
Reviewer 4
Comments: Positive point : Very promising in vitro 3D models of cell cultures

Final comment: We recommend funding this project. This was the only project that explicitly included a Postdoc and a PhD student in the research team. The 3D cell model may turn out to be more complex than it appears, this should be considered. Ethical evaluation and statistical analysis should be reported.

Internal Committee:
Il progetto, ben presentato, è importante e molto articolato. Forse i due anni di progetto non sono sufficienti per il raggiungimento di tutti gli obiettivi descritti ma l'orizzonte finale ambizioso risulta interessante. La prior art dovrebbe analizzare in modo più dettagliato quanto già riportato sull'argomento. L'interesse della tematica affrontata risulta rilevante per instaurare collaborazioni future in ambito internazionale oltre ad essere un tema che potrebbe generare dati preliminari per progetti da presentare a bandi internazionali. Buon Team in cui vengono presentate anche le persone che effettueranno il lavoro al banco.

Punti di debolezza: Complessità del progetto per l'arco temporale presentato, elevato rischio e assenza di risk analysis

Punto da chiarire: "autorizzazione per l'uso di biopsie umane".

Project title: Investigating the relationship between pcsk9 and chronic inflammation associated with obesity and insulin resistance
Applicant: Nicola Ferri

General assessment of scientific quality and innovation

Reviewer 1
Comments: The proposal is related to the recently published studies by the PI on Pcsk9 and supported by Fondazione Cariplo. The published results encourage further investigations in this area that might attract future funds as before. The proposed research would contribute to a better knowleReviewer 2e of the key role of this
protein in relevant diseases.
Reviewer 2
Comments: This project addresses the very important and growing medical problems that are intricately interlocked but not fully understood. Moreover, it investigates it from the perspective of the promising therapeutic target and in patients. Therefore, this project has strong developmental potential regarding future large grant applications and attracting collaborations.
Reviewer 3
Comments: Proposal to identify the relationship between PCSK9 and chronic inflammation observed in obese patients affected by insulin resistance status. Of high significance as PCSK9 represents a promising pharmacological target for the treatment of hypercholesterolemia. Project has start-up potential and may help recruiting future funds. Relies strongly on the recruitment of a patient cohort at the University Hospital of Verona. Ethics statement (approval) on experiments involving humans not mentioned.
Reviewer 4
Comments: The project is scientifically significant and innovative in that it tackles the issues by an original angle. The project is set-up according to solid indoor expertise and know-how. Important expected impact for future development as to public health. Potentially can participate in accelerating competitive and non-competitive funding.

Assessment of scientific plan

Reviewer 1
Comments: The plan is feasible. The main objectives are clearly presented. The project, which is supported by five senior scientists, lacks PhD students. This type of human resources is a fundamental part in any academic project and for the Department.
Reviewer 2
Comments:
The experimental part of the project and milestones are well defined but the scope of these protocols is rather limited given the 24 month duration of the project. It is hard to envisage that analyses described in Tasks 2 and 3 need to take 18 months. This, perhaps can be explained by the lack of a dedicated researcher to run these experiments, except for Dr Ruscica tasked with the determination of circulating levels of adipokines and cytokines and PCSK9 and interpretation of the results.
The liver biopsy during the bariatric surgery needs to be fully justified in the ethical approval application.
Reviewer 3
Comments: The aims of the study are clearly mentioned, however, description of milestones is somewhat confuse. Data from patients will be supplemented by in vitro experiments by exposing PCSK9 to cultured human macrophages. Statistical analysis is presented, yet a bit unclear (e.g. two-tailed analysis does not apply to general models). Project involves young scientists, yet no PhD students are involved in the study.
Reviewer 4
Comments: The rationale is sound and the project's objectives and aims are well-based. The workplan seems clearly feasible. All stages of the project, the tasks appear appropriate. Human resources may however be somehow limited, since 3 of the collaborators are from other institutions and towns (2 are in charge of patient recruitment).

Competence and expertise of the applicant.

Reviewer 1
Comments: The merits and the scientific expertise of the applicant are adequate to carry out the proposal. The PI has achieved good fundraising for the initial results of the research proposal.
Reviewer 2
Comments: These are excellent and documented by relevant publications.
Reviewer 3

Comments: Applicant has a long history on research on atherosclerosis and lipid mediated disorders, thus serving as a PI on this project is fully feasible.
Reviewer 4
Comments: Project in complete adequation with the PI's expertise.

Competence and expertise of the research team.

Reviewer 1
Comments: The team involves several senior scientists from the Department and other Italian Departments. No PhD students have been identified, which is more than desirable
Reviewer 2
Comments: The collaborating team brings the necessary access to patients and samples and has all the required complementary expertise.
Reviewer 3
Comments: Collaboration with Verona hospital required for access to patients, thus a considerable national collaboration.
Reviewer 4
Comments: complementary expertise within the team. External (national) collaborations.

Overall assessment

Reviewer 1
Comments: Strengths – The proposal is feasible. The previous achievements by the group in the proposed topic encourage exploring further the role of this protein that can attract in future funds.
Weaknesses – The project is not supported by young human resources as desirable**.**
Reviewer 2 (9 - if funded for 12 to max. 18 months)
Comments: It is an innovative project but this referee would be inclined to shorten the duration of the funding on this project to make it more cost-effective.
Reviewer 3
Comments: The idea is highly significant and may provide novel insights in the disease mechanisms. Yet the outlook on a translational approach is not clearly mentioned. As with most of the project I am entirely missing a role of trainees in this project.
Reviewer 4
Comments: Expected for crucial outgrowth on the role of PCSK9 on macrophage switch.

Final comment: We recommend funding this project. Because liver biopsies are involved, information on the ethical evaluation and statistical analysis should be provided. The project makes a good use of available national collaborations.

Internal Committee:

Il progetto è interessante, ben scritto e propriamente organizzato nelle varie sessioni. Il grado di fattibilità della proposta pare elevato anche se questo è in parte dovuto ad non alta innovatività. Manca una menzione della significatività statistica necessaria per i campioni analizzati al fine di validare i risultati ottenuti e capire le reali dimensioni dei dati da processare. Il Team è composto in modo appropriato al progetto e alle attività di ogni membro, forse rimane complicata la gestione logistica di un Team suddiviso su tre sedi., soprattutto in relazione all'entità del progetto/finanziamento.

Punti di debolezza: Assenza di valutazione statistica. Quantità di lavoro effettivamente svolto nella sede di DSF. Non è stata effettuata una risk analysis

Punto da chiarire: "autorizzazione per l'uso delle biopsie umane".

Project title: New selective class III receptor tyrosine kinase inhibitors for cancer treatment
Applicant: Giovanni Marzaro

General assessment of scientific quality and innovation

Reviewer 1
Comments: The project is a continuation of the previous work of the PI on this enzyme in which the group like to improve the delivery of an identified hit by incorporation of temporary tags. A more detailed description of some sections of the project is recommended. The acquired skills on the use of these tags would use useful to establish collaborations with other research groups.
Reviewer 2
Comments: Tyrosine kinase inhibition is being exploited as a very promising strategy for cancer treatment and also has a therapeutic potential in other human diseases. This proposal is based on an important recent discovery of new selective inhibitors and by building on this departmental know-how has a potential to lead to further funding and collaborations.
Reviewer 3
Comments: The project aims at developing novel tyrosine kinase inhibitors building upon a recently discovered novel selective inhibitor. The project involves a wide variety of techniques (chemistry, drug modeling and design, cell culture model systems, drug delivery) cell involving the expertise of the project team. Most importantly, this proposal also aims at addressing, evaluation and developing novel modes of drug delivery for efficient cancer treatment. In my opinion, this proposal has a high chance for recruiting follow-up research grants and successfully characterized molecules or delivery technique may provide the basis of spin-offs.
Reviewer 4
Comments: The project is scientifically significant and sound. As a non-specialist in the field, it is however difficult to evaluate whether the project is innovative. Yet it is clear that the project is built on a departmental know-how and solid expertise. It is also clear that, if successful, it will attract in the future for competitive and non-competitive funding.

Assessment of scientific plan

Reviewer 1
Comments: The plan, which is supported by three scientists, is feasible. PhD students involved in the project, which are missing, would be more than recommended considering the large experimental work presented. The main objectives are clearly presented. However, a more rational and detail description of the purpose of the substituents in the other aromatic rings proposed in the project and how an improved binding affinity is expected to be obtained with them is omitted.
Reviewer 2
Comments:
The work-plan builds on previous synthetic achievements in lead compound development and is very well defined. Its goal is to functionalise compounds for liposomal delivery. It has to be stated that, while targeted liposomes are a very elegant drug targeting system experimentally, their complexity makes them unappealing to the pharmaceutical industry. The in vitro experiments are well designed and appropriately controlled and extend well beyond the standard cell culture toxicity assays. The proposed analyses of liposomal formulations are also extensive and technically high-end.
Reviewer 3
Comments: The aims and objectives are clearly state, the milestones are feasible and of significance. The project clearly builds upon the expertise of the entire team, yet as with most projects, no PhD students are involved.
Reviewer 4
Comments: Objectives and hypotheses are clear. The rationale is clearly developed. The workplan appears in complete coherence with the methodological approaches, although I am not able to estimate the timeline for such a project. Human resources and staff members support well the proposed project.

Competence and expertise of the applicant

Reviewer 1
Comments: The merits and the scientific expertise of the applicant are adequate to carry out the proposal. A more detailed description on the ability of PI in raising funds
would be desirable.
Reviewer 2
Comments: The applicant has expertise and credentials in the subject area. The weakness of this project is

the lack of a clearly identified researcher for the day-to-day experimental support.
Reviewer 3
Comments: Applicant has a history on research on drug modelling, design and e.g. NMR analysis. I am convinced that he is highly qualified for serving as a PI on this project.
Reviewer 4
Comments: The applicant has a fairly good track record. He already was awarded research funding. He holds an international patent. He is definitely capable of conducting this proposal.

Competence and expertise of the research team

Reviewer 1
Comments: The team involves four senior scientists, the PI, an assistant and two associate professors, with close backgrounds. The participation of young research is more than recommended. No international research collaborations have been identified. The latter would help to increase the visibility of the group and the Department.
Reviewer 2
Comments: This project integrates the expertise of complementary and experienced research groups from within the institution.
Reviewer 3
Comments: The project strongly relies on the expertise of the team and this combined effort should increase the chance for successfully achieving the proposed milestones. Yet, as presented not international collaborations are involved.
Reviewer 4
Comments: The members of team all bring their expertise and are complementary. Some members already have some international connections which may help in the future open for fruitful collaborations.

Overall assessment
- ***Strengths and Weaknesses***

Score: The final score is not necessarily the algebraic sum of the above values

Reviewer 1 ,4
Comments: *Strengths* – The acquired skills on the use of these tags would be useful to stablish collaborations with other research groups. The proposal is feasible.
Weaknesses – The project is little innovative.
Reviewer 2
Comments: It is an interesting proposal form a PI with expertise and achievements in this area and supported by a very strong team of co-workers.
Reviewer 3
Comments: The proposal is significant, innovative, strongly relies on a team effort and likely results in future funding or novel treatment strategies. As with most of the project proposals in this call I am entirely missing a role of trainees in this project.
Reviewer 4
Comments: Despite not being in the field the project was appealing and solid enough to be scientifically sound and clear to so as to consider that it is achievable.

Final comment: We recommend funding this project. The project is supported by a strong team. However, this team would further benefit from establishing national/international collaborations.

Internal Committee:

Il progetto interessante che ha il suo punto di forza nella completezza dell'approccio e nella multidisciplinarietà scientifica e di composizione del Team. La fattibilità sembra buona e si possono prevedere importanti ricadute da un punto di vista dell'internazionalizzazione. Il progetto avrebbe giovato di una componente farmacologica per la selezione dei prodotti lead e la loro caratterizzazione in vivo. Team di composizione ottimale, forse i compiti del PI vengono parzialmente soprapposti a quelli di altri membri.
Punti di debolezza: Assenza di valutazione farmacologica in vivo.

Punto da chiarire: "autorizzazione Ministeriale per la sperimentazione animale descritta".

Project title: Development of biocompatible polymers for StereoLythogrAphy (SLA) bioprinting for controlled manufacturing of 3D cell spheroids dedicated to drug formulation testings.
Applicant: **Margherita Morpurgo**

General assessment of scientific quality and innovation

Reviewer 1
Comments: The project is an important change relative to the previous background of the PI, which has positive and negative issues. The project will open a new research line in the Department, which is positive. However, it is so generally presented that it is unclear to know the real challenges of the project relative to already published knowleReviewer 2e and beyond analyzing new compositions or new modified polymers of the existing ones. Therefore, it is unclear to know the real impact of the proposal considering that it is undefined the problems that the PI wants to solve. Those problems and issues have not been explained in enough detail.
Reviewer 2 Score: 4
Comments: This project is difficult to assess due to lack of important details regarding the competitive landscape. This technique has been in use for over a decade (Mironov et al., 2003). It has a potential to be innovative and can lead to the development of very useful drug testing systems, providing that it overcomes the SLA pitfalls. As described, it appears to be aimed at the technology import into the department but it is not stated if the SLA printer developer is supporting this project.
Reviewer 3
Comments: A highly innovative project aiming at implementing 3D cell culture models as a new departmental strength for drug screening and tumor model systems. The project has a high chance for future project fundings and spin off companies. The cell culture work depends on local collaborations, which, however, are not clearly mentioned.
Reviewer 4
Comments: The project as presented is scientifically significant and innovative. It is built on a declared will of the department's scientific policy to generate and bring new competences and technologies. However, if successful, it will have a strong impact for future development and applications in the field of drug screening in cancer research. The project has definitely a start-up research character.

Assessment of scientific plan

Reviewer 1
Comments: The plan is not realistically feasible and it is not well supported by an adequate human resources. The team is only composed by two scientists. No PhD students are involved in the project, which is highly recommended
Reviewer 2 Score: 4
Comments: As described, it is a plan to achieve a step-wise improvement but it is not a game changer. The reasons to use these particular polymers are not explained well. Are these materials of particular importance for the tumour cells to be tested? Would mimic any specific or known cell-ECM interactions? What is known about the effects of the energy to be used on live cells to be included in biopritning?
On the positive side, there is a dedicated researcher identified for this project.
Reviewer 3
Comments: The aims and objectives are clearly stated and well organized, the milestones are feasible and of high significance. The project clearly builds upon the expertise of the PI and a co-worker, yet no PhD students are involved and local collaborators are not further enclosed.
Reviewer 4
Comments: For a non-expert in the field, the objectives and hypotheses are very clearly presented. The rationale is sound and the outgrowth of this work is clearly comprehensible.
It is not possible for me to evaluate the realistic feasibility. As for human resources, only one young scientist may be a little short to achieve the project.

Competence and expertise of the applicant.

Reviewer 1 Comments: The merits of the applicant are adequate. Her scientific expertise in the specific topic of the proposal is more limited but it is good in related areas. Some fundraising has been achieved by the PI in recent years
Reviewer 2
Comments: This is a clearly accomplished PI with expertise in the subject area.
Reviewer 3
Comments: Applicant and the team member have a strong background on applied nanomedicine, the

required key expertise of the present proposal. I trust that local experts on the cell culture models are available, yet they should have been disclosed in the proposal.

Reviewer 4

Comments: From her track records, the applicant has the scientific expertise and is fully involved in the project, especially since she very recently has taken up new responsibilities as the Rector Delegate for Technology Transfer in the Life Sciences of the Padova University.

Competence and expertise of the research team.

Reviewer 1

Comments: The team involves only two people, the PI and a postdoc. The participation of young research is more than recommended. No international research collaborations have been identified. The latter would help to increase the visibility of the group and the Department

Reviewer 2

Comments: It is a small team, with competences in the subject area but it could benefit from a wider collaboration, especially from the involvement of the SLA printer developer and a cell biologist.

Reviewer 3

Comments: The project relies on the expertise of the PI and collaborations within the department. Yet, as presented no international collaborations are involved.

Reviewer 4

Comments: The project is set in collaboration with a young scientist expert in photolithography, 3D-bioprinting with complementary skills, located in another town. No other indoor staff members have been cited.

Overall assessment

Reviewer 1

Comments: *Strengths* – the project will open a new research line in the Department.
Weaknesses – it is unclear the real issues that the proposal want to solve

Reviewer 2 Score: 4

Comments: This project, as it is described, does not appear to be competitive.

Reviewer 3

Comments: The proposal is significant and highly innovative and will likely strengthen the methodological spectrum of the department. The project plan is excellently described, unfortunately the important collaborators on the cellular models systems are not clearly described. Despite this, in my opinion implementing this system will strongly strengthen the Department. As with most of the project proposals in this call, I am entirely missing a role of trainees in this project.

Reviewer 4

Comments: Ambitious and innovative project. Clearly defended and proposed. Maybe too few in number.

Final comment: Overall, this is a fundable project. However, there has to be a continuous access to the 3D printer and provision for an effective collaboration with a cell biologist overseeing the ongoing cell culture development and analysis.

Internal Committee:

Il progetto è sicuramente innovativo ed ambizioso, tanto da scostarsi in modo significativo dalle linee di sviluppo del DSF. Il progetto come presentato ha un elevato rischio di non fattibilità. Mancano delle competenze specifiche sia da parte del PI che da parte del Team che risulta composto da una sola persona con competenze non specifiche sull'argomento. Non è stato sufficientemente dettagliato l'aspetto organizzativo, l'accessibilità del Team alla stampante e il grado di coinvolgimento dell'azienda in questo progetto.

Punti di debolezza: Elevato rischio di insuccesso e assenza di una risk analysis. Team privo delle competenze necessarie descritte nel progetto.

Project title: Wild plants as pharmaceutical and food resources: the glucosinolate/myrosinase system in *crambe tataria* and its unexploited potential

Applicant: **Anna Piovan**

General assessment of scientific quality and innovation

Reviewer 1

Comments: The project is well presented and feasible. The proposed research might give pharmaceutical value to certain plants of the north of Italy. If the identified compounds have good pharmaceutical properties might provide patents or contribute to the future establishment of a spin-off company. However, it lacks innovation and novelty. It is not expected an improvement in the impact of the publications, in the international visibility of the research group and in the ability to fundrasing

Reviewer 2

Comments: The project is feasible and might lead to exploitation of a plant endemic to Italy but it should be addressed to industrial sponsors.

Reviewer 3

Comments: While the topix of this proposal is furthest away from my own research expertise, I particularly like this application for its holistic approach. The proposal combines a conservational biology of a plant with evaluation of its potential as a continuous food resource as well as its potential in serving as a source for novel and pharmacological active antioxidants. Like no other project in this call this proposal relies on the expertise of scientists with different background, thus, it brings together a diverse team and I am convinced that this combination may result in innovative approaches that may have longterm implications, both for the involved personnel as well as potential follow up projects.

Reviewer 4

Comments: The project is scientifically significant, yet I am not convinced whether original or innovative. The project is essentially important relative to conservation of endangered species and the characterization and identification of natural 'phyto-properties' of wild plants. An impact for a future development or spin-offs seems unlikely since the plant is a protected species and since the GLS/myrosinase system investigated is largely present in numerous other Brassicaceae plants that are extensively used in human food.

Assessment of scientific plan

Reviewer 1

Comments: The project is feasible and supported by an adequate team. The team involves scientists from diverse disciplines. More PhD students involved in the project would be desirable. International collaborations have not been identified

Reviewer 2 Score: 5

Comments: The same actives are present in common plants. Therefore, the basic premise is not clear to this reviewer. There is no PhD students involved.

Reviewer 3

Comments: The aims and objectives are clearly stated and well organized, the milestones are significant and clearly described. The project clearly builds upon the expertise of the PI and the entire research team, yet no PhD students are involved.

Reviewer 4

Comments: The objectives are clear, the workplan feasible and the project is fairly well supported by enough human resources.

Competence and expertise of the applicant.

Reviewer 1

Comments: The scientific expertise of the applicant is adequate to perform the proposed project. Raising funds by the PI in the last years have not been identified

Reviewer 2

Comments: These are very good

Reviewer 3

Comments: The applicant is experienced in the core techniques and background required for the successful pursuit of the project. She will be leading a diverse research team, which is an interesting and innovative challenge.

Reviewer 4

Comments: The applicant is an expert in the field of phytochemistry, plant biology and pharmaceutical biology. Her knowledge and know-how are completely appropriate for such a proposal.

Competence and expertise of the research team.

Reviewer 1
Comments: The research team have complementary expertise involving scientists from diverse disciplines. No international research collaborations have been identified and it would be difficult to reach them with such a specific project. More PhD students involved in the project would be desirable
Reviewer 2 Score: 5
Comments: It is a big team with partially overlapping expertises (several pharmaceutical biotechnologists) but also some skills complementarities (chemistry, molecular biology). No external partners.
Reviewer 3
Comments: As mentioned above, like no other proposal this project combines team members with various scientific background. This is likely resulting in a strong added value.
Reviewer 4
Comments: The research team is strong, complementary and with solid expertise in their field. There is no international research collaboration.

Overall assessment

- ***Strengths and Weaknesses***

Score: The final score is not necessarily the algebraic sum of the above values

Reviewer 1
Comments: *Strengths* – the project is feasible and might provide patents if interesting pharmaceutical properties are found in the plants studied. The potential intellectual property might also be the basis of a spin-off
Reviewer 2
Comments: This project has some interesting aspects but it is not competitive as it is.
Reviewer 3
Comments: In contrast to the majority of the proposal in this call, the focus of this project is not merely on the identification of novel drugs or applications. However, it presents a holistic approach combining an innovative pharmaceutical question with conservational aspects and evaluating novel and alternative food resources. As with most of the project proposals in this call, I am entirely missing a role of trainees in this project.
Reviewer 4
Comments: Important and necessary but a systematic project. Strength: all the in vitro culture techniques that have been developed.

Final comment: The underlying idea of this project is interesting and the interdisciplinary composition of the research team is appreciated. However, in its present form, the project overstates the respective plant as a pharmaceutical and food resource. The project should be rewritten in the context of a conservational approach and resubmitted for a different funding stream.

Internal Committee:
Il progetto presenta un basso livello di innovazione e un ridotto impatto dal punto di vista dell'internazionalizzazione, sia in termini di visibilità che di collaborazioni. Nel suo complesso la proposta progettuale sembra ad uno stadio molto embrionale di conseguenza ci sono vari gradi di rischio su più livelli che possono limitare il proseguimento del lavoro.

Punti di debolezza: Bassa innovatività del progetto e dell'approccio scientifico. Non è stata effettuata una risk analysis

Project title: A natural compound from olive oil as potential inhibitor of α-synuclein aggregation
Applicant: **Patrizia Polverino de Laureto**

General assessment of scientific quality and innovation

Reviewer 1
Comments: The project is well presented and feasible. The proposed research might confirm the valuable pharmaceutical properties of Oleuropein oil for future applications. However, it lacks innovation and novelty. It is not expected an improvement in the international visibility of the group, the impact of publications and in the ability of fundraising

Reviewer 2
Comments: This project exploiting the involvement of synucleins in PD and the therapeutic potential of oleuropein aglycone is interesting and the results can be significant, leading to further grant applications and perhaps commercialisation. It builds on departmental know-how.

Reviewer 3 Score: 5
Comments: The proposed research project aims at testing the interaction between OleA and alpha Synuclein and exploiting whether OleA could slow down or alter pathological alpha-syn aggregation. If successful OleA or one of the derivatives could serve as a potential novel therapeutic tool targeting the Parkinson's disease progression. While the applicant is an expert on protein aggregation and plans to use a series of highly innovative biophysical techniques, I am not so positive about the overall concept of the study. First, after characterization of OleA variants, how is one variant selected or purified so that it can be utilized under comparable conditions in all experiments? Second, prior to the proposed experiments that actual interaction of OleA with alpha syn needs to be demonstrated. Third, I am not convinced that structural effects induced by the co-expression or co-incubation of equimolar amounts of alpha syn with OleA do have any physiological relevance unless an accumulation of OleA in Lewy bodies can be demonstrated.

Reviewer 4
Comments: the project is scientifically significant and should bring information on the interactions between a compound from olive oil (OleA) and alpha-synuclein in its diverse molecular forms, and the possible effect of OleA in preventing alpha-synuclein polymerization and cytotoxicity.

Assessment of scientific plan

Reviewer 1
Comments: The project is feasible. However, it is not supported by other human resources unless the PI that it limits the type and complexity of studies to be performed

Reviewer 2
Comments: The objectives are clearly presented, the methodology is described clearly and the work packages are well defined. However, there is no indication on the research personnel to perform these experiments. Is the work to be undertaken by the PI?

Reviewer 3 Score: 5
Comments: The aims and objectives are clearly stated yet the milestones not well defined. Instead, this part repeats the overall hypothesis already presented in the background and task sections.
No detailed information on human resources and PhD students is provided.

Reviewer 4
Comments: The project uses a very large panel of methodological approaches to analyse and determine molecular properties and conformational transitions: classical biochemistry and biophysics as well as the more recent ESI-MS, AFM and TEM. A large series of molecular and cellular biology assays. Yet no human resources are mentioned.

Competence and expertise of the applicant.

Reviewer 1
Comments: The scientific expertise of the applicant is adequate to perform the proposed project

Reviewer 2
Comments: The expertise of the applicant is extensive and very appropriate for most aspects of this project.

Reviewer 3
Comments: The applicant is highly experienced in the proposed biophysical methods, yet I am missing a strong collaborative partner with expertise in neuronal physiology and the in situ effects/aggregations of alpha synuclein.

Reviewer 4
Comments: No doubt that the applicant is a full expert in this field.

Competence and expertise of the research team

Reviewer 1 Score: 4
Comments: The research team includes only the PI. No international collaborations appear to be included in the proposal. A team involving PhD students or postdocs is highly recommended
Reviewer 2 Score: 2
Comments: There is none. It is a single person application and the project would benefit, or indeed require, collaborative arrangements that would support some of the important aspects of this project. This might be an unfortunate omission but it is a significant one.
Reviewer 3S core: 5
Comments: A collaboration concerning AFM expriments with a research group in Genova is proposed, yet no other team personnel is listed.
Reviewer 4 Score: /
Comments: No team presented. Just a national collaboration

Overall assessment

- ***Strengths and Weaknesses***

Score: The final score is not necessarily the algebraic sum of the above values

Reviewer 1 Score: 5.5
Comments: Strengths – the project is feasible and might find interesting pharmaceutical properties of the natural compound to be studied. ***Weaknesses*** – the project lacks innovation and novelty and the research team is too small for the training of young researchers.
Reviewer 2 Score: 4
Comments: This is a project with some developmental potential but it is not competitive under the arrangements presented in the application.
Reviewer 3 Score: 5
Comments: In this proposal, I am missing the preliminary proof of a potential physiological relevance of the proposed interaction. In vitro interactions at equimolar peptide/protein concentration will likely reveal some effects. No information on the composition of the research team is provided, also and in line with most of the other proposals, no PhD students seem to be involved
Reviewer 4
Comments: /

Final comment: While the expertise of the applicant was clearly appreciated the project in the present form is not competitive. This problem was compounded by the absence of any research team.

Internal Committee:
Progetto con bassa innovatività, migliorabile dal punto di vista del piano scientifico e dell'incisività. Non sono proposte nuove tematiche di ricerca. Ci sono limitate ricadute terapeutiche, le quali sebbene evidenziate non risultano sufficientemente giustificate. Il Team è completamente assente e la suddivisone temporale in termini di tempo necessario per le singole attività programmate non sembra adeguatamente motivata.

Punti di debolezza: Bassa innovatività del progetto e dell'approccio scientifico. Non è stata effettuata una risk analysis