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agence d'évaluation de la recherche
et de l'enseignement supérieur

Section des Unités de recherche

AERES report on the research unit

EA 2106 : Biomolécules et Biotechnologies végétales

From the

Université de TOURS

December 2010



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et de l'enseignement supérieur

Section des Unités de recherche

AERES report on the research unit

EA 2106 : Biomolécules et Biotechnologies végétales

From the

Université de TOURS

Le Président de l'AERES

Didier Houssin

Section des unités
de recherche

Le Directeur

Pierre Glorieux

December 2010



Research Unit

Name of the research unit : EA 2106 « biomolécules et biotechnologies végétales »

Requested label : EA

N° in the case of renewal : 2106

Name of the director : Ms. Nathalie GUIVARC'H (ex director ; Benoit St PIERRE)

Members of the review committee

Committee chairman :

M. Serge DELROT (Université de Bordeaux)

Other committee members :

M. Guillaume BECARD (Université de Toulouse, France) member of CNU

M. Alain PUGIN (Université de Dijon)*

M. Hubert SCHALLER (Institut de Biologie Moléculaire des Plantes, Strasbourg)

M. Michael H. WALTER (Leibniz Institute of Plant Biochemistry, Halle (Saale), Allemagne)

* A. Pugin sent a report but could not attend on Dec 17 due to serious health problems

Observers

AERES scientific advisor

M. Steven BALL

University, School and Research Organization representatives

M. Michel ISINGRINI, vice-président du Conseil scientifique - Université de Tours



Report

1 • Introduction

- Date and execution of the visit

The visit took place in an amphitheater and in rooms close to EA 2106 on December 17 2010. It was conducted with a compact program and a tight schedule. Being well organized, it took the best advantage of the little time available and the program could be performed as planned. The members of the committee had received an extensive and well-written english assessment of the unit about six weeks before the visit, which facilitated the review process. During the visit, the former and the future directors of the lab, and the leaders of the axes, in 20-30 minutes presentations, have summarized and detailed some points of the written report, and prints of their presentations were handed-out to the committee members. Interviews were made with the scientific staff, the technical staff, the Ph.Ds and post-docs, the direction of the lab and with a representative of the University François Rabelais Tours (VP CS). The committee appreciated the strong commitment of all the members of the lab and the University of Tours in the organisation of this visit.

- History and geographical localization of the research unit, and brief presentation of its field and scientific activities

The EA 2106 was created in 1998, and its scientists, who gathered at the UFR Pharmaceutical Sciences in 2004, focus their work on the main topic "Therapeutical Plant Secondary Metabolites". The Unit has developed expertise in cell and molecular biology, biochemistry and analytical chemistry in order to study the biogenesis of monoterpene indole alkaloids (MIAs) in *Catharanthus roseus* (Madagascar periwinkle) plants and cell suspensions. Of major interest in this system are the cellular and tissue compartmentation of enzymes and metabolites as well as the regulation of the corresponding enzymes, which are involved in the production of two major antimitotics: vinblastin and vincristin. The Unit encompasses a single team dealing with two topics: (i) transduction of hormonal signals controlling the alkaloid metabolism, and (ii) architecture, regulation and compartmentation of alkaloid metabolism.

- Management team

The Unit has been led by Benoit St-Pierre with Joël Creche being Adjunct Director in the previous period but a major restructuring of the unit is currently going on, which also involves the nomination of a new Director, Nathalie Guivarc'h. The unit is organised as a single team, but has two major research axis led by B. St-Pierre and J. Creche and by N. Guivarc'h, respectively. Both axis are supported by technical staff dedicated to phytochemical analyses, molecular biology and in vitro culture. The research groups hold weekly lab meetings. Throughout the interviews with MCFs, postdocs and technical personnel, the good interaction in the laboratories was emphasized.



- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	14	15
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	4.15	3.55
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0.5	
N6: Number of Ph.D. students (Form 2.7 of the application file)	5	
N7: Number of staff members with a HDR or a similar grade	6	6



2 • Overall appreciation on the research unit

- Summary

The written report clearly explains the scientific evolution of the Unit. This is a small-sized Unit which does not host any full-time research scientist, has a strong teaching commitment and has a limited budget (around 80 keuros/year, of which half comes from contracts). The Unit has a long history and a strong expertise on the main topic announced, which covers the dissection and the metabolic regulation of the monoterpene indole alkaloid (MIA) pathway in periwinkle cell suspensions and leaves. The EA2106 as a whole has contributed over a period of almost ten years significantly and constantly to the elucidation of MIA biosynthesis. This highly complicated system, which is also investigated by two other groups in Canada and the Netherlands, has become a paradigm of cooperation of different metabolic pathways to specific secondary end-products of pharmaceutical value. It is also a model for both spatial separation of branch pathways and individual steps in cells and in subcellular compartments. Next to the two other competing groups mentioned, the Unit is an internationally recognized major contributor to this particular field of research. (Members of the Unit have also been involved in other activities such as the 40th anniversary of the University and in contributing to run the Botanical Garden of the City of Tours).

It is surprising and unfortunate that the industrial support to a research devoted to the identification of regulatory components that trigger the accumulation of anticancer MIAs is not stronger. Given the absence of full time research scientist and the low budget, the quality of publications is acceptable but the number of articles is low (0,52 article /year/staff scientist). Some of the data obtained are very original and should have been published in journals with higher ratings. The expertise of the EA is recognized by reviewing manuscripts for good international journals and proposals for funding agencies as well as by the participation to a good number of Ph.D. committees. The unit has acquired a reputation at the international level in the period 2002 - 2006 and earlier through a series of seminal original work and reviews in high-impact journals, but this has not been extended at a comparable level in the period 2006 - 2010. Doctoral training is good.

The proposal for the new 2012-2015 period involves a major restructuring of the Unit in terms both of new topics and of a new distribution of leaderships. The new projects are structured in three axes. The first one is a continuation of selected projects from the previous research on MIAs. The second is a whole new project area in the general context of functional plant biology, with a potential to expand, (see later comments). This second project will initiate experimental work on apple tree (*Malus domestica*), which is a fruit species with regional interest allowing interactions with other groups localized in Tours, Angers and Orléans. These interactions will not only better integrate the Unit into the regional scientific landscape and reinforce its position there. They will also provide access to important tools and resources of apple research such as a plant insect interaction system currently only approached from the animal side and to apple microarrays. The research program on apple has started with experiments on a glucosidase and a phytohormone project. Currently, it appears to be rather vague, since it includes too many different aspects of plant secondary metabolism. In the future it needs to be better focused on the competence areas of the unit (e.g. terpenoid metabolism). The currently proposed research project is oversized and seems not to make full use of the availability of the apple tree genome sequence and of genomic and genetic tools. Nevertheless, the Unit must be congratulated for the courageous moves into new research directions both on the fundamental and the applied sides. The third axis involves a new move into biotech partnership projects.

- Strengths and opportunities

The unit has recognized competence in molecular and particularly cellular aspect of plant secondary metabolic pathways. This includes important recent work on subcellular targeting of proteins to the nucleus. A broad spectrum of methodology is available ranging from in situ hybridization and cellular localization of GFP-labeled proteins to expression of proteins in heterologous systems, analysis of transcription factors and various other molecular methods. This competence in spatial architecture of pathways can now be applied to a new experimental (apple) system where these aspects are poorly developed. The switch towards the apple system may create new opportunities for conceptual and methodological interactions, and for a better integration in the Tours-Angers-(Orléans) context. Several young scientists have been recently recruited, thus providing new strengths and energy.



- Weaknesses and threats

Better integration and interactions into the local and national research landscape is desirable, and this has now been put on the agenda. In addition, international relations need to be developed for the new apple system. The previous publication record shows very few coauthors from abroad. Analysis of the publication record of the Unit also shows many journals of low impact factor and even the most impressive work (e.g. the recent « nuclear time bomb » paper) does not show up in truly high-impact journal. Therefore, the publication policy should focus on higher-impact journals. The basic competence for that exists as demonstrated in previous years by a series of papers in *Plant Journal* and *Plant Physiology*. In addition to the present biochemical and molecular expertise, group members should think of possible genetic/genomic approaches that are feasible with apple especially for aspects of plant metabolic biology. This may also be an attractive area for new funding, which was not sufficient in the previous project period.

- Recommendations

The new apple system holds many promises and one should try to exploit these to the best possible extent on the local, regional, national and international level. Molecular research on apple will experience a boost with the genome sequence now available and this may also give new opportunities to join forces on an international level and enter into projects and contracts. The future of the new axis 1 should be monitored with a view to the development of the apple project and consider the option of shifting more resources to axis 2 and the new system (currently only 6 people in axis 2 versus 11 for axis 1). Moreover, axis 3 consisting of partnership projects and biotechnological approaches also has the potential to draw resources away from the unit to its topics. However, there is currently too little information available on the projects of the CoBaGen and Elixir projects to make any safe predictions on their future. In any case, it is quite unrealistic that each staff member is involved in axis 3 as proposed and for not more than 30% of its research time. Commitments must be more clearly distributed as axis 3 matures.

As a whole, the unit should develop a more ambitious policy for research contracts (ANR, Europe, national and international partnership), and high impact publications. It should also try to develop industrial partnerships more in relation with its research topics on the basic science side.

- Production results

(cf. http://www.aeres-evaluation.fr/IMG/pdf/Criteres_Identification_Ensgts-Chercheurs.pdf)

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	12 + 1
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	0
A3: Ratio of members who are active in research among staff members $[(A1 + A2)/(N1 + N2)]$	13/15 = 0.87
A4: Number of HDR granted during the past 4 years	4
A5: Number of PhD granted during the past 4 years	6



3 • Specific comments

- Appreciation on the results

The primary justification of the research topic of the team, which is to characterise the regulation of terpenoid and alkaloid metabolism in *Catharanthus roseus*, was the prospect to improve the plant production of the two anticancer alkaloids vinblastine and vincristine. It seems that the pharmaceutical companies have found other strategies and are no longer supporting this plant biology-based research. This was confirmed by the leaders of EA2106 during the discussion. Therefore, the topic is now mainly conducted for cognitive reasons. Unfortunately, *C. roseus* is not a plant easily amenable to classical genetics, genomic investigations, forward and reverse genetics. In this difficult context, the team has done a reasonably good research and its influence in the field is well recognized. Besides some review articles published in very good journals, most papers of the team have been published in journals of average ratings, several of them not directly linked to the main topic. The total number of articles falls into the required minimum standard, but a great deal of manuscripts is presently in preparation (related to MIA putative ABC transporters, or putative transcription factors involved in MIA metabolism).

It is worth noting that in addition to its research and heavy teaching activities, the team has been committed to the management of the Tours Botanical Garden and to the conservation of the valuable Tourlet herbarium (classified in the frame of the French "monuments historiques"). Among others, these activities demonstrate the interest of the team for knowledge diffusion to the public.

The team has had a fairly active PhD training and 4 HDR diplomas have been defended during the last contract. Several young faculty members and technical staff have been recently recruited, resulting in a significant rejuvenation of the Unit.

- Appreciation on the impact, the attractiveness of the research unit and of the quality of its links with international, national and local partners

A former member of the research unit (Vincent Burlat) was able to obtain a professorship in a renowned French laboratory, which can be taken as an indication for the appreciation of the previous work in the Unit. Another indication is the employment of an experienced foreign postdoc in the group for a period of two years. The Unit has good attractiveness to Master and PhD students as well as to highly competent assistant-professors (as shown by the recent recruitments).

Members of the Unit have been invited to give talks to four international conferences and to five national meetings. The team has organised the sixth congress of young researchers in plant biology and the national meeting of cell and molecular biology for francophone faculties of pharmacy.

The team has participated marginally to one ANR project, but has not been successful in setting up other ANR or EU projects. Overall, the Unit does not interact much with foreign laboratories. Existing interactions (i.e. ongoing experimental work) should be pursued whenever it is possible, with the aim of publishing the results and therefore increasing the international reputation (for instance, work currently done in axis 1 (prenyltransferases) for the preparation of an ANR proposal, as it was presented to the committee). People from axis 2 have published in collaboration with M. Rodriguez-Concepcion (leader of the prominent group in Barcelona) and collaboration with him is planned in the 2012-2015 project, as it was presented.

Contracts with private companies are few, sometimes only to provide technical services. Unfortunately, none of these contracts has been signed with pharmaceutical companies. The only external funds were obtained from the "ligue contre le cancer". However, two important translational projects in order to move basic science to application have been launched recently in collaboration with other partners including private companies. These efforts are supported by the "pole de compétitivité " Cosmetic Valley. The two projects will provide significant funding to the Unit much beyond the previous level. In addition, the unit has been instrumental for the start up of a company, which is now hosted in the Unit, but involved in a non-related biotechnological field (RNAgro).

The activities of the Unit with respect to the Botanical Garden of Tours and to the Tourlet Herbarium are relevant contributions to the development of an important local scientific heritage and to increasing the visibility of the François Rabelais University.



- **Appreciation on the management and life of the research unit**

The interviews with doctoral students, researchers and staff scientists as well as the conversations with technical staff (BIATOS), show that the atmosphere in the unit is very good as essentially few if any complaints were presented. Overall, people seem to be happy with the situation. The good interactions in the lab, including a lab meeting once a week are appreciated. On the negative side, it was only commented with regret that no permanent researchers at the postdoc level can be employed. The staff scientists have a heavy teaching load, which sometimes requires the help of technical personnel for preparations. A Master « Biotechnologies et droit » was created in 2005. The Unit also participated in the Master Biovigpa (Grand Ouest) as soon as it was created in 2007.

The preparation of the new project for the 2012-2015-period is a collective effort. It has allowed a good analysis of the context and of the situation of the unit, and all the staff seem to support the move to the apple system. The organization in one single team developing several research axes is relevant, as well as the attempts aiming at a better integration in the local and regional context.

The functioning rules of the lab are clearly stated.

- **Appreciation on the scientific strategy and the project**

The projects of the next contract are divided into three axes. In axis 1, the study of the regulation of the terpene and alkaloid metabolism in *Catharanthus* (regulation of gene expression involving prenylated proteins and hormonal signalling) will be continued, but the decision was made to give up some topics such as the studies of transcription factors and ABC transporters.

Some of the proposed work on Ca²⁺, ion channels and interactions of various phytohormones involves highly complicated systems, which will be difficult to analyze. Moreover, these topics are very competitive. One should think of further focusing the projects in this area. By contrast, analysis of the prenylation status of proteins remains an up-to-date and promising area to study. So far, the EA2106 is one of the few groups working on regulation of secondary metabolism by prenylated proteins. Prenylation can profoundly affect subcellular localization of proteins and this might well be relevant in the complicated compartmentalisation of MIA biosynthesis. It should thus be clear that this topic represents a main core of axis 1, on which the scientific efforts should be focussed. A potential move into additional approaches, such as for instance the interesting question of describing the prenylated proteomes should depend on the availability of sufficient funding and expertise for a complete coverage of such a complicated dataset.

In axis 2, the novelty is to move towards the study of the secondary metabolism (potentially including phenylpropanoids) of another plant model, *Malus domestica*. Some motivations of this important evolution are scientific. In contrast with *C. roseus*, *M. domestica* will be an adequate model for in-depth investigations of the secondary metabolism, because its genome has been sequenced, a large set of ESTs and a transformation system are available. Moreover, secondary metabolism studies of a plant like *M. domestica* can directly be translated into a context of plant defence and ecophysiology. Other motivations are to improve the local and regional positioning of the Unit. Production of apple is an important economic activity in the Loire Valley. *M. domestica* is of high interest to INRA Angers and to the IRBI UMR CNRS/University of Tours 6035 which studies an endophytic insect infecting apple trees. The Unit can also introduce its expertise in the localization of metabolic pathways at the cellular and subcellular levels into a new experimental system where these aspects are still poorly developed. This provides a good opportunity to make progress and make a distinct contribution to the field.

Secondary metabolites of *Malus domestica* are still poorly known for many aspects, in particular concerning their ecophysiological function. Terpenoids, phenylpropanoids or alkaloids have all been implicated in plant defence in various other plant systems. While alkaloids are not known to occur in apple to a relevant extent the two other classes of compounds are both candidates for potential roles in apple ecophysiology. It is therefore understandable that the research program on apple may appear as rather poorly defined at this time, but we suggest that the group finds some niche(s), related to its background knowledge and skills, and taking into account work done in other places (see for example ongoing work on *Malus*/Psyllid/terpenoids, Mayer CJ et al. 2008 J Chem Ecol 34, 1518).

With the creation of axis 3, the Unit demonstrates its will to increase its partnership with industry. Three projects in partnership with several industrial partners, dealing with molecular code-baring of plants (CoBaGen), molecular diagnostic of plant pathogens (RNAgro) and biotechnological production of plant natural substances (ELIXIR), have recently been launched with the support of the Cosmetic Valley "pôle de compétitivité" or of OSEO.



This overall project is interesting and relevant in a French context where the number of laboratories working on plant secondary metabolism is extremely low. The decision to study secondary metabolism of a second plant model for the reasons given above is sound, scientifically and politically. The principle of reinforcing partnership with the industrial sector is also good, especially when facing the problem of insufficient public funding (here exclusively provided by the University), but care should be taken to select applied projects that may contribute to foster academic research on the core topics of the Unit.

However, considering the three research axis together, the committee also feels that the whole new project, as it is presented, entails several important risks and should be reduced in size. One risk is the thematic over-diversification of the Unit with three axes having too divergent objectives (not sufficiently synergistic). One way to reduce this risk is to make axis 2 more focused on particular aspects of secondary metabolism of *M. domestica*. Following an exploratory phase of this work encompassing several metabolic pathways as proposed and appreciated above (e.g. by unbiased metabolite analyses), the work should focus on a single pathway for mid-term and long-term work. Preferably, this focus should be on terpenoid metabolism in order to take advantage of a long established *C. roseus* expertise in this field and to maintain strong links with axis 1, unless important new findings point to a different direction. The Unit must take care to maintain its previous focus on secondary metabolism with a new system and not simply go for any parameters affecting apple insect resistance. Such side-aspects should be kept exploratory and/ or exploited in a collaborative context only.

Another risk is to consume too much time and energy in axis 3. The two projects CoBaGen and ELIXIR, considering their size, will occupy a significant amount of time and manpower. More bothering is the fact that, as far as can be made public, none of these projects, including RNAgro, is dealing with plant secondary metabolism, i.e. can synergistically boost the Unit core research. For maintaining its integrity and for improving the quality of its scientific production, the Unit should pay attention to these concerns and be more selective in their future industrial contracts.

The current project description also raises the question on the mid-term and long-term future of axis 1, which continues on selected projects of the previous Catharanthus work. The visit of the unit left the impression that the move into the new system *Malus domestica* is already more substantial than realized from the written report and is generally supported by the scientific staff. There are still some promising projects in axis 1, which need to be and will be finished. But on the long run, it needs to be discussed whether and how this axis will continue on Catharanthus with potentially more attractive axis 2 and axis 3 next to it. If the apple system proves successful one should consider to focuss efforts in the next contract on the new system as another way to avoid the overdiversification risk mentioned above

- **Conclusion :**

The Unit EA2106 has been reviewed by the committee at a difficult time in its history: a time of transition and restructuring from the previous MIA topic and the Catharanthus system to new (frontiers) plant model and to novel biological questions, both on the basic and on the applied side. This move can be considered as positive as long as some of the risks discussed above can be reduced. The Unit has the scientific and methodological competence to become successful in the new fields and improve its visibility as a secondary metabolism laboratory.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
BIOMOLÉCULES ET BIOTECHNOLOGIES VÉGÉTALES	B	B	A	B	B

- C1 Qualité scientifique et production
- C2 Rayonnement et attractivité, intégration dans l'environnement
- C3 Gouvernance et vie du laboratoire
- C4 Stratégie et projet scientifique



Statistiques de notes globales par domaines scientifiques (État au 06/05/2011)

Sciences du Vivant et Environnement

Note globale	SVE1_LS1_LS2	SVE1_LS3	SVE1_LS4	SVE1_LS5	SVE1_LS6	SVE1_LS7	SVE2_LS3 *	SVE2_LS8 *	SVE2_LS9 *	Total
A+	7	3	1	4	7	6		2		30
A	27	1	13	20	21	26	2	12	23	145
B	6	1	6	2	8	23	3	3	6	58
C	1					4				5
Non noté	1									1
Total	42	5	20	26	36	59	5	17	29	239
A+	16,7%	60,0%	5,0%	15,4%	19,4%	10,2%		11,8%		12,6%
A	64,3%	20,0%	65,0%	76,9%	58,3%	44,1%	40,0%	70,6%	79,3%	60,7%
B	14,3%	20,0%	30,0%	7,7%	22,2%	39,0%	60,0%	17,6%	20,7%	24,3%
C	2,4%					6,8%				2,1%
Non noté	2,4%									0,4%
Total	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

* les résultats SVE2 ne sont pas définitifs au 06/05/2011.

Intitulés des domaines scientifiques

Sciences du Vivant et Environnement

- SVE1 Biologie, santé

- SVE1_LS1 Biologie moléculaire, Biologie structurale, Biochimie

- SVE1_LS2 Génétique, Génomique, Bioinformatique, Biologie des systèmes

- SVE1_LS3 Biologie cellulaire, Biologie du développement animal

- SVE1_LS4 Physiologie, Physiopathologie, Endocrinologie

- SVE1_LS5 Neurosciences

- SVE1_LS6 Immunologie, Infectiologie

- SVE1_LS7 Recherche clinique, Santé publique

- SVE2 Ecologie, environnement

- SVE2_LS8 Evolution, Ecologie, Biologie de l'environnement

- SVE2_LS9 Sciences et technologies du vivant, Biotechnologie

- SVE2_LS3 Biologie cellulaire, Biologie du développement végétal

SERVICE DE LA RECHERCHE ET
DES ETUDES DOCTORALES

REPONSE DE L'UNITE : BIOMOLÉCULES ET BIOTECHNOLOGIES VÉGÉTALES S2UR120001559

Nous avons pris connaissance du rapport du comité de visite de l'AERES et l'ensemble des membres de l'EA2106 « Biomolécules et Biotechnologie Végétale » souhaite remercier sincèrement les experts pour le travail d'évaluation réalisé sur leur activité de recherche ainsi que pour les conseils et les encouragements qu'ils ont émis quant à leur projet.

Après une lecture attentive du rapport, nous avons le sentiment que le comité de visite a bien perçu que le projet de l'EA2106 pour le prochain contrat est une transition vers une refonte des objectifs scientifiques de l'unité. Il a ainsi approuvé sous certaines conditions l'ouverture de l'EA vers une augmentation de projets collaboratifs avec l'industrie et la mise en place d'un nouvel axe de recherche sur le métabolisme secondaire du pommier, qui devrait, comme le soulignent les experts, permettre une meilleure intégration de l'équipe dans un réseau collaboratif et renforcer sa lisibilité dans le domaine du métabolisme secondaire des végétaux.

Le comité a souligné qu'un tel changement comporte certains risques. Il a notamment émis des réserves quant à une implication trop importante des enseignants-chercheurs dans les projets en partenariat avec l'industrie, parfois diversifiés et potentiellement chronophages. Il faut cependant souligner que l'un des projets transversaux de l'axe 3 porte effectivement sur le métabolisme secondaire et les biotechnologies, ce qui n'a pu être clairement précisé au comité en raison de clauses de confidentialité, et que deux personnels contractuels dédiés entièrement à ce projet sont en cours de recrutement. De même, le recrutement d'un étudiant en thèse est associé à un autre projet transversal.

Le comité a aussi relevé des contours du projet un peu trop ambitieux en regard du potentiel humain de l'unité. L'arrivée d'un nouvel enseignant-chercheur pour le prochain contrat devrait renforcer les récents recrutements déjà effectués dans l'unité. Bien que cette nouvelle organisation crée une dynamique, nous avons conscience qu'il sera nécessaire de redéfinir les contours du projet afin d'en assurer l'exécution ainsi que d'optimiser la valorisation des résultats. La proposition de re-concentrer nos efforts sur le métabolisme terpénique, thématique majeure de l'unité et pour lequel nous sommes reconnus, nous semble particulièrement opportune.

Enfin, nous apprécions pleinement les encouragements du comité dans la poursuite des changements que nous sommes en train d'opérer au sein de l'unité.



UNIVERSITÉ
FRANÇOIS - RABELAIS
TOURS

Les membres de l'EA2106 restent disponibles pour répondre à toutes les questions éventuelles. En leur nom, je vous prie, Monsieur le Président du comité, d'accepter l'expression de mes salutations respectueuses.

Pr Nathalie Guivarc'h

Le Vice-Président,
Chargé de la recherche

Michel ISINGRINI