MARIE SKLODOWSKA-CURIE ACTIONS

Co-funding of regional, national and international programmes (COFUND)

DOC2AMU THESIS PROJECT 2018 CALL FOR APPLICATIONS

Deciphering biodiversity and ecological role of viruses infecting microalgae

1. GENERAL INFORMATION

Call	2018-2
Topic	Climate change
Keywords	Virus; microalgae; plankton; biofuel; population dynamics; metagenomics; microfluidics; biodiversity; evolution

2. THESIS DIRECTOR(S), RESEARCH UNITS AND DOCTORAL SCHOOLS

Thesis director	Guillaume BLANC
Research Unit	Institut Méditerranéen d'Océanologie
Doctoral school	ED 251 - Sciences de l'Environnement
Thesis co-director	Christelle DESNUES
Research Unit	Unité de Recherche sur les maladies Infectieuses et Tropicales Emergentes
Doctoral school	ED 062 - Sciences de la Vie et de la Santé

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Deciphering biodiversity and ecological role of viruses infecting microalgae

1. DESCRIPTION OF THE PHD THESIS PROJECT (4 PAGES MAX.)

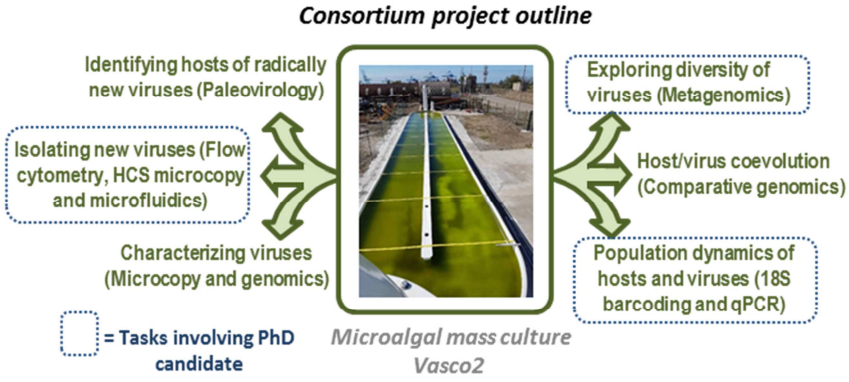
1.1 OBJECTIVES OF THE PROJECT BASED ON THE CURRENT STATE OF THE ART

Background: The photosynthetic microorganisms of the ocean form the basis of the marine food chain and are responsible for more than half of the primary production on Earth. The diversity of microalgae (eukaryotic unicellular algae) inhabiting phytoplankton, their abundance and dynamics are partly regulated by viruses. It is estimated that 20% of plankton is lysed daily due to viral infections (1), propelling viruses to the rank of major player in planetary biogeochemical cycles. The activities of microalgae and their viruses are highly relevant to climate change issues since the phytoplankton annually converts ~50 gigatons of climate-warming CO_2 into biomass through photosynthesis, a fraction of which eventually sink to the bottom of the ocean (biological pump). Viruses play a major control on this important carbon sink; potential large-scale changes in the interactions between viruses and phytoplankton triggered by a global warming may have significant impacts in biogeochemical cycling and ecosystem dynamics. To accurately predict the effects of climate change, a better understanding of the viral world and its interactions with their phytoplanktonic hosts is mandatory. In addition, these same viruses represent a potential threat to industrial processes based on microalgal mass cultures reaching critical densities favorable to the outbreak of viral epidemics. These systems are multiplying around the world for various biotechnological applications such as the production of biofuels or CO_2 sequestration, activities that aim to limit the greenhouse effect and to contribute to the energetic transition.

Viruses infecting microalgae usually show high levels of host specificity, infecting a single particular species if not particular strains within a species (1). In contrast, the same algal strain can often be parasitized by different DNA or RNA viruses, which can be totally unrelated. This observation, together with the abundance of algal viruses in the marine environment, suggests that every algal species is susceptible to at least one virus (1). Nonetheless, **diversity and environmental roles of algal virus remain in general poorly understood**. Almost all known algal viruses are lytic, but some algae may acquire resistance to cell lysis, resulting in “chronic” formation of viral particles without massive cell death (2). Most studies of marine virology over the past decades have focused on small DNA-containing viruses, which appear to be predominantly phages infecting bacteria. To date, about 50 eukaryotic-algae virus genomes have been fully sequenced (3). Most of those are large double-stranded DNA viruses, grouped in the *Phycodnaviridae* and *Mimiviridae* families (supergroups of the “nuclear-cytoplasmic large DNA viruses”, NCLDV), with genomes ranging from 160 to 560 kb and capsids ranging from 100 to 220 nm. Only a handful of very diverse, small DNA viruses infecting diatoms (genome size of 5.6 to 6 kb), green algae (31 Kb) or *Raphidophyceae* (38.5 kb) have been reported (3–5); their environmental prevalence is in general unknown but some may plays an integral role in the population dynamics of toxic bloom-forming alga (5). Our knowledge about the RNA viruses in the marine virioplankton is even more limited, but available data suggests that most of them likely infect protists, including diatoms, dinoflagellates, prasinophyte and raphidophytes. Furthermore recent studies provided evidence that these RNA viruses were

just as abundant as DNA viruses in contrasted marine environments (6–8). Thus, eukaryotic RNA viruses may well be major players of marine plankton ecology, but their existence and role have been largely neglected until now. The NCLDV are relatively abundant in aquatic environments where they exclusively infect eukaryotes, including many protists, such as amoebae and microalgae. This viral group contains the so called giant viruses which are an order of magnitude greater in size than an average virus (e.g., the pithovirus particle length of 1.5 µm compared to 100 nm (9)). Their size is so large that they are even visible with an optical microscope, opening the door to real-time measurements in their natural state. Another surprising feature of giant viruses is the size and gene content of their genomes. One giant virus, the pandoravirus has a genome that is approximately 2.5 Mb in size, 50 times larger than the average viral genome and larger than the genomes of many bacteria (9). The genome contains genes with functions that have previously never been observed in a virus, including proteins involved in DNA repair, lipid metabolism and DNA translation.

Our understanding of the role of viruses in the environment, the diversity of their infectious cycles and their impact on the evolution of life is contingent upon the exploration of their biodiversity. However, the diversity of aquatic viruses and the identity of the hosts they infect remain poorly documented and require further exploration with innovative methods. There are only a small number of pathosystems developed around the world to study algae-virus interactions, and these are not sufficiently representative of viral diversity. Moreover, analyses of environmental metagenomic data suggest that the viruses that have been isolated represent a miniscule fraction of the total virus diversity in nature.



Project: To fill this gap, the PhD candidate will join a collaborative project between 4 research laboratories and a non-academic partner aiming at amplifying the discovery of radically new viruses (including small/giant; RNA/DNA) infecting marine microalgae (Fig. 1), using the most state-of-art high-throughput technical approaches. The consortium is also conducting research to characterize the diversity and ecological impact of these same viruses in experimental basins dedicated to intensive algal cultivation for biofuel production and industrial flue gas remediation. The PhD candidate will work at the interface between the 5 partners of this project. (S)he will lead the study of the dynamics of viral populations in the basins as well as the analysis of metagenomic data of DNA and RNA viromes. In addition, (s)he will contribute to the test and development of an innovative method for high-throughput isolation of microalgae viruses based on microfluidics, during which (s)he will travel to the laboratory of our partner in Quebec.

Literature: 1. Short SM (2012) The ecology of viruses that infect eukaryotic algae. *Environ Microbiol* 14(9):2253. **2**. Thomas R, et al. (2011) Acquisition and maintenance of resistance to viruses in eukaryotic phytoplankton populations. *Environ Microbiol* 13(6):1412. **3**. Grimsley NH, et al. (2012) Genomics of Algal Host–Virus Interactions. *Advances in Botanical Research* (Elsevier), pp 343. **4**. Pagarete A, Grébert T, Stepanova O, Sandaa R-A, Bratbak G (2015) Tsv-N1: A Novel DNA Algal Virus that Infects Tetraselmis striata. *Viruses* 7(7):3937. **5**. Lawrence JE, Chan AM, Suttle CA (2001) A novel virus (haniv) causes lysis of the toxic bloom-forming alga heterosigma akashiwo (raphidophyceae). *J Phycol* 37(2):216. **6**. Culley AI, et al. (2014) The characterization of RNA viruses in tropical seawater using targeted PCR and metagenomics. *mBio* 5(3):e01210. **7**. Steward GF, et al. (2013) Are we missing half of the viruses in the ocean? *ISME J* 7(3):672. **8**. Miranda JA, Culley AI, Schvarcz CR, Steward GF (2016) RNA viruses as major contributors to Antarctic virioplankton. *Environ Microbiol* 18(11):3714. **9**. Abergel C, Legendre M, Claverie J-M (2015) The rapidly expanding universe of giant viruses: Mimivirus, Pandoravirus, Pithovirus and Mollivirus. *FEMS Microbiol Rev* 39(6):779.

1.2 METHODOLOGY

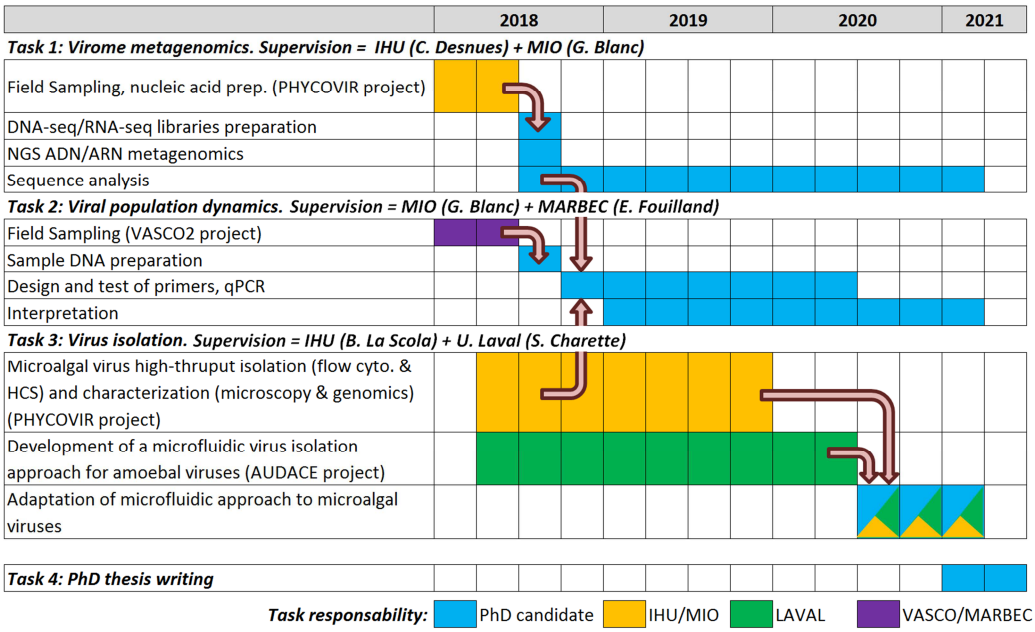
The doctoral research project will rely on a 160m^2 outdoor experimental basin located in the Fos-sur-Mer industrial area, dedicated to mass culture of marine microalgae and operated by the non-academic partner COLDEP in the framework of the VASCO2 project [see section 2.2 and https://goo.gl/XdBjaj for detailed description of the Vasco2 initiative (in French)]. This basin, adjusted in water to maintain constant volume and salinity, is colonized by natural populations of microalgal species, which are seeded by water supplies and aerosols. Microalgae grow freely and different algal populations follow one another during the year, mainly influenced by predators (including viruses), seasonality and weather conditions.

The **first task**, coordinated by C. Desnues (IHU), aims at drawing an inventory of biodiversity of RNA- and DNA-viruses present in the basin using a **metagenomic approach**. Four samples of culture will be harvested in spring and summer 2018 during algae population switches to maximize diversity. IHU will purify the ultra-viromes (0.2µm-100kDa; i.e., regular virus size) and mega-viromes (0.8µm-0.2µm; i.e., giant viruses); the encapsidated viral RNAs and DNAs of the 2 fractions will be extracted for analysis by DNA-seq (DNA genomes) and RNA-seq (RNA genomes and mRNA packaged in DNA viruses) high-throughput sequencing. On arrival, the PhD candidate will participate in the construction of the sequencing libraries and manipulation of the IHU Illumina sequencers. With the help of the IHU and MIO bioinformatician teams, (s)he will be in charge of the analysis of the generated sequences, including metagenome assembly and annotation. Using this data, (s)he will establish the global viral diversity of the basin, reconstruct the genome sequences of the most abundant viral species, and determine their metabolic capacities. In addition, (s)he will analyze the metatranscriptomes of encapsidated mRNA. These mRNA involved in the early stage of viral replication, will be instrumental to decipher the molecular mechanisms and diversity of viral replication processes.

The **second task**, coordinated by G. Blanc (MIO) and E. Fouilland (MARBEC), aims at investigating the **dynamics of populations** of microalgae and viruses of the experimental basin. As part of the VASCO2 project, weekly samplings of the basin have been made by MARBEC over a 2-years period (till August 2018). For each sample, the microorganisms and large viruses have been harvested on filters (>0.2 µm) and their total DNA (metagenome) was purified and stored. At MIO, total nucleic acids (RNA and DNA) from small viruses (filtrate <0.2 µm) will also be purified from the same weekly samplings performed in spring and summer 2018 and be included for the downstream molecular analyses. The PhD candidate will then conduct a quantitative (RT-)PCR analysis on this long time series of (RNA and DNA) metagenomes to estimate the abundances of targeted viruses across seasons. PCR primers will be designed at MIO to specifically amplify potentially interesting virus sequences identified in the metagenomic data (task 1) or isolated by IHU (task 3). In parallel, the population of microalgae and other protists will be determined by 18SDNA barcoding on the same metagenomes by MARBEC, as part of the VASCO2 project. The comparison of both series of data (18SDNA and qPCR) will allow characterizing the reciprocal influence of viruses and microalgae on the dynamics of their respective populations. Importantly, this study will answer an important question addressed by the industrial partner: do viruses have a significant impact on the production of microalgae in his system?

The **third task**, coordinated by B. La Scola (IHU) and S. Charette (U. Laval), aims at developing **new strategies for virus isolation** (including small/giant; RNA/DNA). The PhD candidate will create an interface between two independent but complementary projects that will be running in 2018 and 2019. In the PHYCOVIR project (*PI* G. Blanc), the B. La Scola team will isolate viruses co-cultivated with selected microalgae living in the basin using a novel flow cytometry approach developed in his lab. During the same period, the S. Charette team will develop a microfluidic approach for isolating environmental viruses of amoebas within the framework of the AUDACE project, in which B. La Scola and G. Blanc are also involved. Toward the end of the doctoral project (2020), the PhD candidate will stay 2-3 months in the C. Charette lab in Laval (Canada) to adapt and extend the microfluidic approach to microalgal hosts (by substituting amoeba preys with microalgae), using viruses and algal strains isolated beforehand by B. La Scola (PHYCOVIR) to test the approach with known specimens.

1.3 WORK PLAN



1.4 SUPERVISORS AND RESEARCH GROUPS DESCRIPTION

Mediterranean Institute of Oceanography (MIO) at Aix-Marseille University (UMR7294). : The MIO oceanography research laboratory strives to better understand the oceanic system and its evolution in response to global changes. MIO constitutes a center of expertise in marine biology, ecology, biodiversity, genomics, microbiology, halieutics, physics, chemistry, biogeochemistry and sedimentology. MIO is located on the Marseille Luminy scientific campus which hosts several world class research laboratories. Within MIO, Guillaume Blanc (**Co-supervisor 1**) has 8 years of experience in studying the evolution, diversity and biology of DNA viruses infecting microalgae (13-18). This team has strong expertise in bioinformatics applied to sequence analysis and will take full advantage of the OSU Pythéas computer platform for intensive computing to process the sequence data generated by the project. The MIO also houses various dedicated technical platforms for experimental phytoplankton cultures, molecular biology and optical microcopy. Computers and bioinformatics activities associated to this doctoral project are already fully funded by CNRS (individual workstations), OCEANOMICS (1-BTBR-0008 ; To RAM computation node, web servers) and OSU Pytheas (FEDER 1166-39417; CPU cluster). In addition, G. Blanc is the coordinator of the project PHYCOVIR outlined in Fig. 1 which has been submitted to the CNRS X-life call and in which this doctoral project will be fully integrated.

Institut Hospitalo-Universitaire (IHU) of Marseille-La Timone (UMR7278). The team of Bernard La Scola and Christelle Desnues (**Co-supervisor 2**) is pioneer in the study of amoeba viruses and their virophages (19, 20), as well as environmental viral metagenomics or associated with a host (21, 22). This team has discovered and characterized several dozens of giant viruses (23) and has developed a new high throughput viral isolation approach based on flow cytometry and HCS microscopy (4, 5). The team has global expertise in virology and microbiology applied to infectious diseases. Within the Mediterranée Infection Institute, the team has all the technical platforms necessary for the success of this project including a morphological platform (2 electron microscopes, confocal microscope), cytometry, proteomics, transcriptomics and an IBISA platform for low- and high-throughput sequencing (3 Illumina MiSeq) as well as all of the staff and engineers dedicated to these platforms and trained in massive data processing. The routine team activities on virus isolation, viral metagenomics and Miseq sequencing included in this doctoral project are funded on recurrent budgets by the Méditerranée Infection foundation.

MARine Biodiversity, Exploitation and Conservation lab (MARBEC) at Sète (UMR9190): Eric Fouilland (CR CNRS) is specialized in microbial ecology, and more specifically on the interactions between microorganisms (algae-bacteria-predators) in aquatic environments and systems for mass production of microalgae (24, 25). This team has the skills and tools needed to isolate and culture microalgae. It also has access to the infrastructures allowing the cultivation of microalgae in external basins, within the framework of the project VASCO2. The team activities on microalgal isolation, basin samplings and eukaryotic population dynamics studies are funded by ADEME as part of the VASCO2 project.

University of Laval (Canada). Steve Charette (FRQS Senior research scholar), is a health researcher working on the role of amoebae and other protozoa in the spread of human diseases. Together with Jesse Greener, a researcher specialized in the design and development of use of microfluidic devices for microbiological applications and Alexander Culley, a microbial ecologist, this group is developing a novel microfluidic approach to trap amoebal viruses from the environment (AUDACE project). Within this DOC2AMU proposal, Steve Charette is interested to know if his microfluidic approach can also be adapted to trap microalgal viruses.

2. 3I DIMENSIONS AND OTHER ASPECTS OF THE PROJECT

2.1 INTERDISCIPLINARY DIMENSION

The student will be hosted in the premises of MIO and will integrate a group of 10 bioinformaticians. Guillaume Blanc will provide daily supervision and bring his expertise in microalgae viruses, evolutionary analysis and genomics. In addition, the student will be trained to nucleic acids and qPCR manipulations and assisted by the lab's molecular biology team (PI Laurie Casalot). Within the IHU, Christelle Desnues' group will bring its expertise in the metagenomic study of viromes. She will train the student at the different stages of the analysis, from the environmental samples to the production of the data. Interpretation of the sequence data will be jointly supervised by C. Desnues and G. Blanc. Weekly meetings between both teams will be scheduled to monitor the work progress. In addition, B. La Scola's team (IHU) will bring its expertise on virus isolation and manipulation, to which the student will have to familiarize with prior to his stay in Laval. E. Fouilland from MARBEC will bring his expertise on the study of interactions between microorganisms and give access to the temporal series of DNA samples collected in the basin since November 2016.

2.2 INTERSECTORAL DIMENSION:

The start-up COLDEP will act as a non-academic partner of the doctoral project. COLDEP develops processes and equipment based on water/biomass separation techniques for several industrial applications including algal mass cultivation (http://www.coldep.com/). COLDEP is involved in the Vasco2 project, which brings together 12 partners (industrialists from the Fos-Sur-Mer area, research centers, start-ups and institutions) aiming at validating microalgae and biofuels production processes based on the biological recycling of industrial flue gases (CO_2). The Vasco2 project, co-financed by Ademe and labeled by the Pôle Mer Méditerranée and Trimatec, addresses the SRI-S3 objective « Développer la production d'énergie renouvelables marines" of the DAS "transition énergétique". In the framework of the Vasco2 project, COLDEP operates culture basins installed on various industrial sites of the port of Fos-Sur-Mer and Palavas, where marine microalgae are cultivated, harvested and then transformed into biofuel. **The impact of viruses on the production of microalgae is an unaddressed issue, to which COLDEP and the Vasco2 consortium wish to obtain answers through its collaboration in this doctoral project**. COLDEP will receive the PhD student on the sites of microalgal cultivation where (s)he will harvest his/her own samples for research. To help her/him in this task, (s)he will be given assistance and training by its technicians on the maintenance of microalgae mass cultures, culture sampling technics and isolation of microalgae strains. In return, the student will keep the intersectoral partner informed of the progress of his/her work through semi-annual seminars scheduled on the occasion of the Vasco2 consortium steering committee meeting. The Vasco2 consortium, coordinated by the port de Marseille-

Fos includes the following partners: port de Marseille-Fos, Codelp, Helio Pur Technologies, Ifremer, CEA, ArcelorMittal, Kem One, Solamat-Merex, LyondellBasell, Total, métropole d'Aix-Marseille-Provence, Inovertis.

2.3 INTERNATIONAL DIMENSION:

The international dimension of the doctoral project is twofold. First the PhD candidate will stay 2-3 months in the laboratory of Steve Charette (Laval U. Canada) where (s)he will participate to the development of a novel microfluidic approach to isolate microalgal viruses. In addition, the research group regularly participates in international conferences to which the PhD candidate will present his/her results, including the "aquatic virus workshop" which will gather (i.e., in spring 2020) the international scientific specialists of this research field.

3. RECENT PUBLICATIONS OF THE PROJECT TEAMS (MIO, IHU,MARBEC)

Khalil JYB, Andreani J, La Scola B (2016) Updating strategies for isolating and discovering giant viruses. *Curr Opin Microbiol* 31:80–87. **IHU**

Khalil JYB, et al. (2016) Flow Cytometry Sorting to Separate Viable Giant Viruses from Amoeba Co-culture Supernatants. *Front Cell Infect Microbiol* 6:202. **IHU**

Gallot-Lavallée L, Blanc G (2017) A Glimpse of Nucleo-Cytoplasmic Large DNA Virus Biodiversity through the Eukaryotic Genomics Window. *Viruses* 9(1):17. **MIO**

Blanc G, Gallot-Lavallée L, Maumus F (2015) Provirophages in the Bigelowiella genome bear testimony to past encounters with giant viruses. *Proc Natl Acad Sci U S A* 112(38):E5318-5326. **MIO**

Maumus F, Blanc G (2016) Study of Gene Trafficking between Acanthamoeba and Giant Viruses Suggests an Undiscovered Family of Amoeba-Infecting Viruses. *Genome Biol Evol* 8(11):3351–3363. **MIO**

Maumus F, Epert A, Nogué F, Blanc G (2014) Plant genomes enclose footprints of past infections by giant virus relatives. *Nat Commun* 5:4268. **MIO**

Blanc G, et al. (2010) The Chlorella variabilis NC64A genome reveals adaptation to photosymbiosis, coevolution with viruses, and cryptic sex. *Plant Cell* 22(9):2943–2955. **MIO**

Blanc G, et al. (2014) Deep RNA sequencing reveals hidden features and dynamics of early gene transcription in Paramecium bursaria chlorella virus 1. *PloS One* 9(3):e90989. **MIO**

Jeanniard A, et al. (2013) Towards defining the chloroviruses: a genomic journey through a genus of large DNA viruses. *BMC Genomics* 14:158. **MIO**

Rowe JM, et al. (2014) Global analysis of Chlorella variabilis NC64A mRNA profiles during the early phase of Paramecium bursaria chlorella virus-1 infection. *PloS One* 9(3):e90988. **MIO**

Dunigan DD, et al. (2012) Paramecium bursaria chlorella virus 1 proteome reveals novel architectural and regulatory features of a giant virus. *J Virol* 86(16):8821–8834. **MIO**

Rowe JM, et al. (2013) Evaluation of higher plant virus resistance genes in the green alga, Chlorella variabilis NC64A, during the early phase of infection with Paramecium bursaria chlorella virus-1. *Virology* 442(2):101–113. **MIO**

Raoult D, et al. (2004) The 1.2-Megabase Genome Sequence of Mimivirus. *Science* 306(5700):1344–1350. **IHU**

La Scola B, et al. (2008) The virophage as a unique parasite of the giant mimivirus. *Nature* 455(7209):100–104. **IHU**

Desnues C, et al. (2008) Biodiversity and biogeography of phages in modern stromatolites and thrombolites. *Nature* 452(7185):340–343. **IHU**

Halary S, Temmam S, Raoult D, Desnues C (2016) Viral metagenomics: are we missing the giants? *Curr Opin Microbiol* 31:34–43. **IHU**

Colson P, La Scola B, Levasseur A, Caetano-Anollés G, Raoult D (2017) Mimivirus: leading the way in the discovery of giant viruses of amoebae. *Nat Rev Microbiol*. doi:10.1038/nrmicro.2016.197. **IHU**

Galès A, et al. (2017) Efficiency of CO2 fixation in High Rates Algal Ponds under different pH using marine natural assemblages. Présentation Orale, Congress of International Applied Phycology, Nantes. **MARBEC**

Martinez C, Mairet F, Fouilland E, Galès A, Roques C, Jauzein V, Steyer J-P, and Bernard O (2017). The role played by predators in a high rate algal pond for wastewater treatment. Présentation orale, 1st IWA Conference on algal technologies for wastewater treatment and resource recovery , 16 & 17 Mars 2017, Delft, The Netherlands. **MARBEC**

4. EXPECTED PROFILE OF THE CANDIDATE

We are seeking an excellent and highly motivated candidate with a general background in biology, holding a Master's degree (MSc or equivalent) in one of the following areas: bioinformatics, genomics and/or molecular evolution. A first-hand experience in computational analysis of biological sequences will be highly appreciated, in as many as possible of the following areas: similarity searching, phylogeny, omics mining, proficiency in statistical methods using R, script programming in LINUX environments (Perl, python, bash etc.), familiarity with the use of compute farms.

In order to apply, candidates must not have resided or carried out their main activity (work, studies, etc.) in France for more than 12 months in the 3 years immediately prior to the start date of the thesis (Octobre 1st, 2018).

5. SUPERVISORS' PROFILES

Co-supervisor 1: Guillaume Blanc (44) of the Mediterranean Institute of Oceanography – Marseille, is CNRS researcher (HDR) since 2004, specialized in bioinformatics applied to the evolutionary and functional genomics of large DNA viruses and their microalgal hosts. He has supervised 3 theses, 5 masters and 2 engineers. Thesis: 2010-2013: Adrien Jeanniard – "Viruses of the small unicellular eukaryotic alga Chlorella" (3 articles)- now Post doc at UC Davis (USA); 2014-2017: Lucie Gallot – "Genetic exchanges between viruses and their hosts" (4 articles) - now Post doc at Dalhousie University (Canada); 2015-2018: Adrien Villain –PhD defence March 2018. – "Genomics of diatoms and associated microbiome" (4 articles);

Publications and awards: 41 articles including 12 as first author and 19 as last author and/or corresponding author, totalling > 8000 citations (Google Scholar). H index = 25. Nominated as external advisor of the NCBI RefSeq Virus group (https://www.ncbi.nlm.nih.gov/genome/viruses/advisors/).

Co-supervisor 2: Christelle Desnues of the URMITE laboratory of the Institut Hospitalo-Universitaire Méditerranée Infection – Marseille, is a CNRS researcher (HDR) since 2008, specialist in the study of the composition, the taxonomic / functional diversity and the spatio-temporal dynamics of the viral communities associated with human or animal hosts in physiological or pathological conditions. Since 2005, she has participated in the first developments of viral metagenomics in the marine environment and then transferred these skills as early as 2008 in the field of human and animal health. She has supervised 6 post-docs, 4 PhDs (2 in progress) and 18 undergraduate internships (master 1 and 2 students).

Publications and awards: about 50 articles in prestigious journals (Nature, PNAS ...) and received for her research work the CNRS Bronze Medal in 2010 and the International SANOFI-PASTEUR Prize for Biomedical Research in 2013.

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AVIS DES DIRECTEURS DES LABORATOIRES CONCERNES PAR LE PROJET DE THESE

Avis du directeur du laboratoire du directeur de thèse, M. SEMPERE Richard

☒ Favorable ☐ Défavorable

Commentaires :

Fait à Marseille, le 12 décembre 2017

Signature

Richard SEMPERE

Directeur de l'Institut
Méditerranéen d'Océanologie

Avis du directeur du laboratoire du co-directeur de thèse, M. RAOULT Didier

☒ Favorable ☐ Défavorable

Commentaires :

Fait à Marseille, le

Signature

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Objet : dossier DOC2AMU – lettre d'engagement

Je, soussigné Julien JACQUETY, président de la SAS Coldep Développement, dont le siège social se situe au 66 Bld Niels Bohr chez INSAVALOR - CS 52132 - 69603 VILLEURBANNE cedex, dont le n° de SIRET est le 535 051 486 000 20, certifie par la présente notre engagement à participer en tant que partenaire non-académique au projet doctoral portés par Dr Guillaume Blanc et Dr Christelle Desnues dans le cadre de l'appel à projet DOC2AMU 2018, pour travailler sur le sujet suivant :

Deciphering biodiversity and ecological role of viruses infecting microalgae

Je certifie en outre :

- avoir pris connaissance des règles d'attribution et de fonctionnement des bourses délivrées dans le cadre du programme doctoral DOC2AMU;
- que le sujet de recherche répond à une attente de la part de COLDEP de mieux comprendre l'incidence et le rôle des virus dans les systèmes de culture intensive de microalgues pour lesquels l'entreprise développe des procédés industriels.
- que *COLDEP* assurera le suivi du doctorant dans le cadre de son projet de recherche doctoral. Dans l'entreprise, le responsable du suivi du projet sera Bertrand BARRUT (Directeur R&D) ;
- que *COLDEP* facilitera l'accès du doctorant aux infrastructures de culture de microalgues sur les sites de Fos-sur-Mer et Palavas, mises en œuvre dans le cadre du projet Vasco 2, dans la perspective de lui permettre de réaliser son travail de recherche et d'accéder aux informations, méthodes, données, terrains, qui lui seront nécessaires ;
- que *COLDEP* participera à la formation et l'assistance technique du doctorant sous la forme d'un tutorat dans les domaines de la conduite de culture de microalgues, l'échantillonnage des cultures et l'isolement de souches d'algue, afin qu'il puisse mener à bien son projet de recherche.

Fait pour valoir ce que de droit,

Julein JACQUETY

Le Président

Le 11 décembre 2017

Description du partenaire non académique dans la section 2.2 du projet doctoral :

The start-up COLDEP will act as a non-academic partner of the doctoral project. COLDEP develops processes and equipment based on water/biomass separation techniques for several industrial applications including algal mass cultures (http://www.coldep.com/). COLDEP is involved in the Vasco2 project, which brings together 12 partners (industrialists from the Fos-Sur-Mer area, research centers, start-ups and institutions) aiming at validating microalgae and biofuels production processes based on the biological recycling of industrial flue gases (CO_2). The Vasco2 project, co-financed by Ademe and labeled by the Pôle Mer Méditerranée and Trimatec, addresses the SRI-S3 objective « Développer la production d'énergie renouvelables marines" of the DAS "transition énergétique". In the framework of the Vasco2 project, COLDEP operates culture basins installed on various industrial sites of the port of Fos-Sur-Mer and Palavas, where marine microalgae are cultivated, harvested and then transformed into biofuel. The impact of viruses on the production of microalgae is an unaddressed issue, to which COLDEP and the Vasco2 consortium wish to obtain answers through its collaboration in this doctoral project. COLDEP will receive the PhD student on the sites of microalgal cultivation where (s)he will harvest his/her own samples for research. To help her/him in this task, (s)he will be given assistance and training by its technicians on the maintenance of microalgae mass cultures, culture sampling technics and isolation of microalgae strains. In return, the student will keep the intersectoral partner informed of the progress of his/her work through semi-annual seminars scheduled on the occasion of the Vasco2 consortium steering committee meeting. The Vasco2 consortium, coordinated by the port de Marseille-Fos includes the following partners: port de Marseille-Fos, Codelp, Helio Pur Technologies, Ifremer, CEA, ArcelorMittal, Kem One, Solamat-Merex, LyondellBasell, Total, métropole d'Aix-Marseille-Provence, Inovertis.

Marseille Fos

A l'attention de **Guillaume Blanc**

Mediterranean Institute of Oceanography
Aix-Marseille Université

163 avenue de Luminy
13288 Marseille

Marseille, le 12 décembre 2017

Objet : Soutien au projet doctoral « Déchiffrer la biodiversité et le rôle écologique des virus infectant les microalgues »

Monsieur Blanc,

Vasco2 est un projet de recherche appliquée fédérant 12 acteurs industriels et publics majeurs de la région marseillaise et nationaux, pour mettre en œuvre le recyclage des fumées industrielles produites dans la zone industrialo-portuaire de Fos-sur-Mer par des cultures de microalgues marines destinées à la production de biocarburant. Dans le cadre de ce projet, nous faisons une démonstration couvrant toute la filière des biocarburants de 3ème génération, et la phase culture, pierre angulaire du projet, est essentielle.

Le projet Vasco2 ambitionne de lever plusieurs interrogations et notamment sur la compétitivité du mode production et sur les conséquences de l'usage de fumées industrielles sans préfiltre. Vasco2 a reçu le soutien financier l'agence de l'environnement et de la maîtrise de l'énergie (ADEME) et les labélisations des pôles de compétitivité Pole Mer Méditerranée et TRIMATEC.

En plus des différentes recherches et démonstrations que nous avons mises en œuvre, le projet a pu être enrichi par des études complémentaires comme une étude écotoxicologique.

Ainsi, la proposition de projet doctoral visant à déchiffrer la biodiversité et le rôle écologique des virus infectant les microalgues a reçu un fort intérêt de la part des membres du consortium.

Par la présence, et tant que coordonnateur du projet Vasco2, je vous informe que le comité de pilotage du projet a voté à l'unanimité son soutien au projet doctoral que vous portez. La société Coldep, membre du consortium Vasco2, se portera partenaire non-académique du projet doctoral.

Dans l'attente de vos nouvelles concernant l'aboutissement de vos démarches, je vous prie d'agréer, Monsieur Blanc, l'assurance de ma considération distinguée.

Michaël PARRA
Coordonnateur du projet Vasco2

Vasco2

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