

Comparative genomics of giant viruses infecting marine protists (bioinformatics & evolution)

We invite applications for a 3-years PhD fellowship to characterize the structure, functioning and evolution of giant virus genomes through bioinformatics approaches.

The fellowship is funded by the “Infectiopôle Sud” foundation. The successful applicant will work at the interface between two collaborating research teams of the Institut Hospitalier Universitaire (IHU) Méditerranée Infection (Team 1: Prof Bernard La Scola) and the Mediterranean Institute of Oceanography (MIO) (Team 2: Dr Guillaume Blanc) in Marseille (South of France).

IMPORTANT NOTE: The fellowship is exclusively restricted to a non-French student who has not resided in France for more than 1 year (i.e. second-year master student accepted if they have not done their first year in France).

PROJECT DESCRIPTION: The Nucleo-Cytoplasmic DNA viruses (NCLDV [1]) are quite extraordinary in their size (capsid $\leq 1.5 \mu\text{m}$, genome $\leq 2.5\text{Mb}$), but also by the nature of the genes they code and their evolutionary trajectory [2]. Most of them infect unicellular eukaryotes (protist) living in soils or aquatic environments. In particular, they are major pathogens of phytoplankton, particularly involved in the extinction of episodes of massive proliferation of microalgae [3]. Some of these viruses could play a role in human pathologies [4,5] and coral bleaching [6].

The Faustoviruses belong to a new lineage of NCLDVs recently discovered by the team of Bernard La Scola [Team 1] [7]. These viruses, initially isolated by co-culture with the amoeba *Vermamoeba*, are also detected in hematophagous insects, as well as in blood / organs of rodents, bovines and human sera [8] [Team1]. Faustoviruses are related to African swine fever (Asfarvirus) viruses as well as Kaumobavirus, another large virus infecting *Vermamoeba* [9] [Team1]. Moreover, the host *Vermamoeba* is a common amoeba of the human body which is also found in abundance in the sewage ending their course in the seas. Thus the phylogenetic group formed by Faustovirus, Kaumobavirus and Asfarvirus (FKA group) represents an emerging interest in public and veterinary health. However, this viral lineage is still very poorly known and reveals surprising singularities within the NCLDVs. For example, Faustovirus are the first to possess a double protein envelope: a classic external viral capsid and an internal envelope unrivaled in other viruses [10] [Team1]. These viruses as well as Kaumobavirus possess a capsid protein gene containing many introns, a rare occurrence in viruses that are generally lacking. Recently, our work [Team2] identified fragments of viral genomes related to the FKAs integrated into the genomes of aquatic protists indicating that the spectrum of potential hosts is much larger [11]. Thus the FKA group could play a role in oceanic ecosystems by controlling certain planktonic populations.

In this project, we want to combine the expertise of our two teams in viral (meta)genomics and giant viruses isolation and culture [Team1] and viral and marine bioinformatics [Team2] to carry out a genomic study of the FKA group. Our goal is to better understand the ecology, biodiversity, metabolic capabilities and evolution of these viruses living in contrasting ecosystems. The PhD work will consist in characterizing essentially by bioinformatics [Team2] the metabolic potential, the infectious mechanisms and the evolution of these viruses through the analysis of the genomic sequences produced by [Team1]. We will measure the incidence of FKAs in marine ecosystems using existing metagenomic data [Team1 + 2] and elucidate their potential contribution in the control of planktonic populations [Team2]. If possible, we will attempt to isolate marine FKA specimens using the high-throughput virus isolation approach [Team1] and identify their natural host by co-occurrence methods [Team2].

1. Koonin, E. V.; Yutin, N. Nucleo-cytoplasmic Large DNA Viruses (NCLDV) of Eukaryotes. In eLS; John Wiley & Sons, Ltd, Ed.; John Wiley & Sons, Ltd: Chichester, UK, 2012. 2. Colson, P.; La Scola, B.; Levasseur, A.; Caetano-Anollés, G.; Raoult, D. Mimivirus: leading the way in the discovery of giant viruses of amoebae. Nat. Rev. Microbiol. 2017. 3. Short, S. M. The ecology of viruses that infect eukaryotic algae. Environ.

Microbiol. 2012, 14, 2253–2271. **4.** Yolken, R. H.; Jones-Brando, L.; Dunigan, D. D.; Kannan, G.; Dickerson, F.; Severance, E.; Sabuncuyan, S.; Talbot, C. C.; Prandovszky, E.; Gurnon, J. R.; Agarkova, I. V.; Leister, F.; Gressitt, K. L.; Chen, O.; Deuber, B.; Ma, F.; Pletnikov, M. V.; Etten, J. L. V. Chlorovirus ATCV-1 is part of the human oropharyngeal virome and is associated with changes in cognitive functions in humans and mice. *Proc. Natl. Acad. Sci.* 2014, 111, 16106–16111. **5.** Campocasso, A.; Scola, B. L. Virus géants associés aux amibes. *Virologie* 2012, 16, 6–17. **6.** Correa, A. M. S.; Ainsworth, T. D.; Rosales, S. M.; Thurber, A. R.; Butler, C. R.; Vega Thurber, R. L. Viral Outbreak in Corals Associated with an In Situ Bleaching Event: Atypical Herpes-Like Viruses and a New Megavirus Infecting Symbiodinium. *Front. Microbiol.* 2016, 7, 127. **7.** Reteno, D. G.; Benamar, S.; Khalil, J. B.; Andreani, J.; Armstrong, N.; Klose, T.; Rossmann, M.; Colson, P.; Raoult, D.; La Scola, B. Faustovirus, an asfarvirus-related new lineage of giant viruses infecting amoebae. *J. Virol.* 2015, 89, 6585–6594. **8.** Temmam, S.; Monteil-Bouchard, S.; Sambou, M.; Aubadie-Ladrix, M.; Azza, S.; Decloquement, P.; Khalil, J. Y. B.; Baudoin, J.-P.; Jardot, P.; Robert, C.; La Scola, B.; Mediannikov, O. Y.; Raoult, D.; Desnues, C. Faustovirus-Like Asfarvirus in Hematophagous Biting Midges and Their Vertebrate Hosts. *Front. Microbiol.* 2015, 6, 1406. **9.** Bajrai, L. H.; Benamar, S.; Azhar, E. I.; Robert, C.; Levasseur, A.; Raoult, D.; La Scola, B. Kaumobavirus, a New Virus That Clusters with Faustoviruses and Asfarviridae. *Viruses* 2016, 8, 10. Klose, T.; Reteno, D. G.; Benamar, S.; Hollerbach, A.; Colson, P.; Scola, B. L.; Rossmann, M. G. Structure of faustovirus, a large dsDNA virus. *Proc. Natl. Acad. Sci.* 2016, 113, 6206–6211. **11.** Gallot-Lavallée, L.; Blanc, G. A Glimpse of Nucleo-Cytoplasmic Large DNA Virus Biodiversity through the Eukaryotic Genomics Window. *Viruses* 2017, 9, 17. **12.** Bou Khalil, J. Y.; Andreani, J.; Raoult, D.; La Scola, B. A Rapid Strategy for the Isolation of New Faustoviruses from Environmental Samples Using *Vermamoeba vermiformis*. *J. Vis. Exp. JoVE* 2016, 13. Maumus, F.; Blanc, G. Study of gene trafficking between *Acanthamoeba* and giant viruses suggests an undiscovered family of amoeba-infecting viruses. *Genome Biol. Evol.* 2016, 14. McLysaght, A.; Hurst, L. D. Open questions in the study of de novo genes: what, how and why. *Nat. Rev. Genet.* 2016, 17, 567–578. **15.** Domazet-Loso, T.; Brajković, J.; Tautz, D. A phylostratigraphy approach to uncover the genomic history of major adaptations in metazoan lineages. *Trends Genet. TIG* 2007, 23, 533–539.

FUNDING: The fully funded 3-year PhD scholarship pays a stipend of €1,100 (net) per month.

CANDIDATE: We are seeking excellent and highly motivated candidates 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). The fellowship is exclusively restricted to a non-French student who has not resided in France for more than 1 year (i.e. second-year master student accepted if they have not done their first year in France). The position will start at the earliest possible date, taking into account that drafting the work contract usually takes at least 4 weeks. The selected candidate will work with Guillaume Blanc, members of a group of seven bioinformaticians who are part of the MIO Environmental Microbiology and Biotechnology (MEB) team. The PhD work will be co-supervised by Prof B. La Scola through weekly meetings at IHU.

APPLICATION: Applications and informal queries should be addressed to Guillaume Blanc (guillaume.blanc@mio.osupytheas.fr). Interested candidates should send their CV and a cover letter describing their research interests and motivation. Candidates should also arrange for at least two referees to e-mail recommendation letters directly to <guillaume.blanc@mio.osupytheas.fr>. Review of applications will begin on June 1, 2017 and applications will continue to be accepted until the position is filled.

ENVIRONMENT: The 200+ staff of 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. Situated in Provence on the outskirts of Marseille close to the sea, in the middle of the Calanques National Parc, MIO is located on the Marseille Luminy scientific campus which hosts several world class research laboratories[5]. The MIO's new purposely built environmentally friendly 10000m² buildings provide a modern and attractive work environment.

IHU: The work of this team concentrates on the analysis of new giant viruses in the environment and in foodstuffs, from ecology to genetic study and their potential involvement in human pathologies. At the border of this work, we work on research and analyses of new viral agents in immune compromised individuals. The analysis will be done according to 4 research orientations' of the team to knowing research of the giant viruses and the small intracellular bacteria of protozoa in the environment, the genetics of these giant viruses and these bacteria, their potential role in human pathology and finally the search and the analysis for emergent viruses in human pathology for immunocompromised patients. See <http://en.mediterranee-infection.com> for more information.