

**IAPETUS2 Project Submission Preparatory Template**

Please note, in order to submit a project to the IAPETUS2 2020-2021 Studentship Competition, supervisors must complete the Project Submission Form online. The Project Form will be opened for submissions on Tuesday 1st September 2020 and the web link will be circulated prior to this.

This document details the questions on the online form in the correct order. If you would prefer to complete all/some sections of the form in this Word document then simply copy and paste on to the online form, please feel free to do so. This is not essential though.

Please note, this Word version cannot be used instead of the online form, it is just meant as an aid for supervisors to use when completing the online form.

Please complete all sections (unless they are marked as Optional or If Applicable on the form). Approval for project submissions with missing fields will be delayed.

Please do not use any special characters, as the website will turn them into gobbledygook when publishing.

Please consult the *IAPETUS2 Studentships Competition 2021 Staff Guidance* for further details on the form and the process.

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| **General Information** |
| Project Title: |
| Dissecting the evolutionary ecology of a unique secondary endosymbiosis. |
| Lead Institution: | University of Glasgow |
| Department / School / Institute | Institute of Biodiversity Animal Health and Comparative Medicine.  |
| CASE Partner Organisations [OPTIONAL] Leave blank if not applicable |  |
| End-user Collaborations [OPTIONAL] Leave blank if not applicable | MSD Animal Health (Merck)Scottish Sea Farms Ltd |

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| **Project Team**The first supervisor should be from the lead institution. The Second Supervisor should be from a second IAPETUS2 organisation |
| Supervisor 1 |
| Name | Dr. Martin Llewellyn |
| Organisation | University of Glasgow |
| Email | Martin.llewellyn@glasgow.ac.uk  |
| Biography URL | <https://www.gla.ac.uk/researchinstitutes/bahcm/staff/martinllewellyn/> |
| Supervisor 2 |
| Name | Dr. Guillaume Chomicki |
| Organisation | Durham University |
| Email | guillaume.chomicki@durham.ac.uk |
| Biography URL | dur.ac.uk/research/directory/staff/?mode=staff&id=18524  |
| Supervisor 3 (if applicable) |
| Name | Dr. Mike Barrett |
| Organisation | University of Glasgow |
| Email | Michael.Barrett@glasgow.ac.uk |
| Biography URL | <https://www.gla.ac.uk/research/beacons/onehealth/professormikebarrett/> |
| Supervisor 4 (if applicable) |
| Name | In format: Dr Fred Blogs |
| Organisation | Choose an item. |
| Email |  |
| Biography URL |  |
| Supervisor 5 (if applicable) |
| Name | In format: Dr Fred Blogs |
| Organisation | Choose an item. |
| Email |  |
| Biography URL |  |
| CASE PartnersIf applicable, add any CASE Partners here |
| Name [optional] | In format: Dr Fred Blogs |
| Organisation |  |
| Email |  |
| Biography URL |  |
| End-user CollaborationsIf applicable, add any End-user Collaborations here |
| Name [optional] | Dr. Ralph Bickerdike |
| Organisation | Scottish Sea Farms |
| Email | ralph.bickerdike@scottishseafarms.com |
| Biography URL |  |
| End-user CollaborationsIf applicable, add any End-user Collaborations here |
| Name [optional] | Dr. Nikolaos Steiropoulos |
| Organisation | Scottish Sea Farms |
| Email | nikolaos.steiropoulos@merck.com |
| Biography URL |  |
| In Collaboration withAdd any non-IAPETUS University collaboration partners here.[OPTIONAL] Leave blank if not applicable |
| Name | Prof. Fiona Enriquez |
| Organisation | University of West of Scotland |
| Email | Fiona.Henriquez@uws.ac.uk |
| Biography URL | https://research-portal.uws.ac.uk/en/persons/fiona-henriquez-mui |
| In Collaboration withAdd any non-IAPETUS University collaboration partners here.[OPTIONAL] Leave blank if not applicable |
| Name | Dr. Neil Ruane |
| Organisation | Marine Institute Galway |
| Email |  |
| Biography URL |  |
| In Collaboration withAdd any non-IAPETUS University collaboration partners here.[OPTIONAL] Leave blank if not applicable |
| Name | Prof. John Archibald |
| Organisation | Dalhousie University |
| Email |  |
| Biography URL |  |

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| **Project Details**The information provided here will be used to create the project advertisement online and in pdf format. The overall project description should not normally be longer than 1,200 words in total, including references. Please note that the boxes below are plain-text only, formatting & links will be stripped from the text. |
| KeywordsAdd up to 5 comma separated keywords that best describe the project. | symbiosis, genomics, parasites, evolution, trypanosomes |
| Overview |
| **Summary:** Endosymbiosis is recognised as a fundamental evolutionary innovation that underpins the origins of many unicellular and all multicellular lifeforms (Chomicki *et al*., 2019). Understanding the biology of such phenomena can shed light on key drivers of inter-species cooperation and provide an important window into early origins of cellular life on the planet. The PhD student will link to a recently funded project to deploy new tools: single cell genomics and transcriptomics, as well as metabolomics; to explore a unique and poorly understood endosymbiosis involving an emergent disease agent of major economic importance. Supported by a world class supervisory team (Prof. Mike Barrett, Dr. Martin Llewellyn, Wellcome Trust Centre for Integrative Parasitology, Glasgow; Dr. Guillame Chimocki, Life Sciences, Durham) and a range in international collaborators (Prof. John Archibald, Dalhousie University, Canada; Dr. Neil Ruane, Marine Institute, Ireland), the student will have the opportunity to develop skills at the cutting edge of genomics and molecular biology, undertake training at international centres of excellence in parasitology and evolutionary biology in the UK and North America, and engage in marine biological fieldwork on the west coast of Ireland and Scotland. Finally, this project has strong links with aquaculture industry via project partners Scottish Sea Farms (SSF, Dr. Ralph Bickerdike) and the student will also get valuable experience working alongside industry. **Secondary endosymbiosis:** The phenomenon in which eukaryotic organisms engulf other eukaryotes is termed ‘secondary endosymbiosis’. Secondary endosymbiosis underpins the evolution of many eukaryotic phototrophs and is thought to have involved the engulfment of an ancestral eukaryotic rhodophyte ([Oborník 2018](#_ENREF_5)). The number of times this has occurred in evolutionary history is a moot point. However, it is clear that rhodophyte-origin plastids play a key role in their host cell’s biology. In some cases, the symbiont has lost the ability to photosynthesize, which leaves them a relic non-photosynthetic plastid in a secondarily heterotrophic cell. This is the case for the apicomplexans, which include the causative agents of toxoplasmosis and malaria. The basis of ongoing metabolic dependency is not always clear, however some conserved functions across plastids belonging to different apicomplexan lineages include isoprenoid (IPP and DMAPP), tetrapyrrole, and fatty acid biosynthesis (Janouškovec *et al.* 2015).**The study system:** *Paramoeba perurans* causes amoebic gill disease (AGD) and is a major pathogen in salmonid aquaculture, causing > £400 million in losses per annum world-wide. There are currently no drugs available to treat AGD. *P. perurans* has a unique cellular biology that can be readily exploited given the right tools. Enclosed within its cytoplasm is a bizarre endosymbiont - *Perkinsela*. Genomic sequence data suggest that the basic physiology of this endosymbiont has many of the same biochemical features as found in kinetoplastid pathogens of man and domestic livestock (e.g. Sleeping sickness, Leishmaniasis and Chagas disease).**The endosymbiosis between *P. perurans* and *Perkinsela* is unique among eukaryotes because it does not involve an originally photosynthetic symbiont**. Prior investigations have established interdependence between the kinetoplasitid and amoeba based on predicted gene content and ontogeny in the related *Parameoba pemaquidensis* ([Tanifuji *et al.* 2017](#_ENREF_7)).**This studentship has three major aims:****Aim 1**: **Understand the molecular basis of the obligate dependence between *P. perurans* and *Perkinsela***. The student will use genome sequencing (long read technologies jointly with illumina short reads for polishing), single-cell transcriptomics as well as metabolomics to dissect the molecular basis of the symbiosis. Specific drug knock outs jointly with transcriptomic analysis will allow to functionally test metabolic dependences.**Aim 2**: **Undertake rational Amoebic gill disease (AGD) drug discovery.** A detailed understanding of dependences in the between *P. perurans* and *Perkinsela* symbiosis will provide a window to test drugs efficient on AGD. In collaboration with the Wellcome Trust Centre for Intergrative Parasitology, the student will test drugs targeting metabolic dependences of *P. perurans*. Ultimately trials will be performed in fish farms with SSF.**Aim 3**: **Trace the evolution of this unique endosymbiosis**. Using a recent approach (Kwong et al., 2019), we will reconstruct the phylogenetic histories of both the host *P. perurans*  and the *Perkinsela* symbiont clades, relying on a range of archival environmental samples as well as new marine collections. Using targeted sequence enrichment, we will sequence the genomic regions of the host identified as driving the obligate dependence (Aim 1), and analyses of substitution rates (dn/ds) will inform of their functionality. When possible, close relatives will be cultured to assay the presence of the symbiont using microscopy and FISH. This will allow t evolutionary history of this unique endosymbiosis, specifically testing (i) the number of origins of this symbiosis across the clade encompassing *P. perurans*, (ii) whether the obligate dependence has been lost or is retained throughout the clade, and (iii) whether all *P. perurans* strains evolved the same or distinct dependences on *Perkinsela*. |
| Methodology |
| Via genome sequencing, standard and single-cell transcriptomics, as well as metabolomic analyses to validate predicted pathways, the student will establish the role of *Perkinsela* in *P. perurans* biology. At the University of Glasgow, the student will undergo training in genome sequencing and annotation (Aim 1 and 2). At Durham University, Biosciences, the student will receive training in key ecological and evolutionary theory around symbioses as well as in-depth phylogenetic comparative methods including phylogenetic inference, ancestral state estimation and gene substitution rate with the aim of reconstructing the origins of the symbiosis (Aim 3). At the University of Glasgow, Wellcome Trust Centre for Integrative Parasitology the student will learn how to exploit plastid-targeted drug knock-outs and single cell sequencing to unpick the metabolic interactions between host and symbiont. During a secondment to John Archibald’s laboratory at Dalhousie University, Canada, the student will receive further training in amoebozoan genome assembly and annotation with particular reference to secondary endosymbiosis.  |
| Timeline - Year 1 |
| Student, assisted by PIs and dedicated post-docs, sequences P. perurans genome and transcriptome. Visits Canada to undertake training in genome assembly  |
| Timeline - Year 2 |
| Student assists with targeted drug knock-outs of *P. perurans* organelles alongside metabolomics and transcriptomics to unpick ecological/biochemical basis of symbiosis.  |
| Timeline - Year 3 |
| Student will undertake sample collection and sequencing of *P. perurans* and symbiont clades to establish the evolution of the symbiosis |
| Timeline - Year 3.5 (6 months only) |
| Data analysis |
| Training & Skills |
| The student will receive training in genomics, transcriptomics (inc. single cell), phylogenetic, metabolomics, molecular biology, microscopy and more. The student will have access to world class supervision and benefit from links to international research networks as well as to industry. |
| References & Further Reading |
| Rodger HD (2013.) Amoebic gill disease (AGD) in farmed salmon (*Salmo salar*) in Europe. . Fish Veterinary Journal 16.Harmer J, Yurchenko V, Nenarokova A, Lukeš J, and Ginger ML 2018 Farming, slaving and enslavement: histories of endosymbioses during kinetoplastid evolution Parasitolgy 145, pp. 1311-1323Creek DJ, Barrett MP (2013) Determination of antiprotozoal drug mechanisms by metabolomics approaches. Parasitology 141: 83-92.Schwabl, P., Imamura, H., Van den Broeck, F. … & Llewellyn, MS Meiotic sex in Chagas disease parasite *Trypanosoma cruzi.* Nat Commun 10, 3972 (2019)Räz B, Iten M, Grether-Bühler Y, Kaminsky R, Brun R (1997) The Alamar Blue® assay to determine drug sensitivity of African trypanosomes (T.b. rhodesiense and T.b. gambiense) in vitro. Acta Tropica 68: 139-147.Chomicki, G., Weber, M., Antonelli, A., Bascompte, J. and Kiers, E.T., 2019. The impact of mutualisms on species richness. Trends in ecology & evolution, 34(8), pp.698-711.Chomicki, G., Kiers, E.T. and Renner, S.S., 2020. The evolution of mutualistic dependence. Annual Review of Ecology, Evolution, and Systematics, 51. (in press)Kwong, W.K., Del Campo, J., Mathur, V., Vermeij, M.J. and Keeling, P.J., 2019. A widespread coral-infecting apicomplexan with chlorophyll biosynthesis genes. Nature, 568(7750), pp.103-107. |
| Further Information |
| All enquiries please email martin.llewellyn@glasgow.ac.uk |
| At this point in the form, you will be able to upload any project related images or photographs that you wish to be used online with your submission. Please upload either jpeg or png filesMaximum upload size: 52.43MBAll images must be owned/copyright by the uploader or suitable licensing arrangements must be in place prior to upload. IAPETUS may request proof of licensing for any commercial / copyrighted content uploaded. |
| Image annotations and attributions. If required, please add any image titles/ attributions etc. |
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| **Administrative Information** |
| Principal Disciplinary ThemePlease select one of the following |
| Evolution-Biodiversity-Ecosystems |
| Additional Disciplinary Theme |
| Global Environmental Change  |
| Supervisors who are Early-Career researchers (if applicable) |
| Dr. Guillame Chimocki |
| Amount of RTSG Requested |
| Total of Amount of RTSG Requested (must not exceed £10,000) | £7000 |
| Of which amount of Training Component is | £3000 |
| Of which amount of Research Component is | £4000 |
| Justification for RTSG RequestPlease provide sufficient detail (a) to ensure that the training and research needs are appropriately supported so that the student will be able to complete the thesis within a timely fashion in the 3.5 years of funding; and (b) to ensure the proposal can be audited as following the [UKRI Harmonized Guidelines for training grants](https://www.ukri.org/funding/information-for-award-holders/grant-terms-and-conditions/). |
| Training Component |
|  Funds are requested to support two training visits to collaborators:1) Training visit to Dalhousie University, Canada to develop skills in genomics and evolution.2) Training visit to Ireland to undertake training in sample collection, microscopy and parasite culture.  |
| Research Component |
| Costs associated with phylogenetics and sequencing in Aim 3 of the proposal. |
| Is this a Case Partner Project | Yes  |
| CASE Partner Contributions & Other Relevant Information (if applicable) |
| TBC |
| At this point in the form, you will be able to upload a letter of support from the CASE partner. If you do not yet have one, please email it to contact.iapetus@durham.ac.uk once you receive it. |
| End-user Collaboration Contributions & Other Relevant Information |
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| Any other relevant information? |
| Please apply at these sites:[www.iapetus2.ac.uk](http://www.iapetus2.ac.uk)[www.gla.ac.uk/SchoalrshipApp](http://www.gla.ac.uk/SchoalrshipApp)  |

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| **NERC Research Areas** |
| NERC require information about advertised and funded projects to see how they align to the breadth of NERC topics, as well as to evaluate whether there is any bias in topics supported. This form is based on the NERC Research Areas (see <https://nerc.ukri.org/funding/application/howtoapply/topics/> for further details).Please select all the categories that most align with this project. The first category you select will be recorded as the Primary Classification. The total category weight for all categories must be 100%.For a full list of categories, please see Appendix 7 of the *IAPETUS2 Studentships Competition 2021 Staff Guidance* |