

Short-term visits - round 1

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Application No. STV00023Round1 From The University of Queensland

Form Submitted 5 Jun 2023, 12:18PM AEST

Eligibility criteria and grant conditions

* indicates a required field

Australian host eligibility criteria

The applying host must:

- be employed as a scientist/faculty member of an eligible research organisation, as listed below
 - Australian tertiary education institutions (as per the Higher Education Support Act 2003)
 - Australian cooperative research centres
 - Publicly funded research agencies
 - Australian state and territory funded research organisations
 - Australian public research companies
 - Australian private research companies
 - Australian not-for-profit research organisations
 - Other Australian incorporated entities.
- have appropriate delegation, or authority from the relevant delegate, to accept the terms of the award
- confirm, and be able to demonstrate upon request, that their mission, scope, and research serves civilian purposes. Military research is not eligible for funding.

Do you meet the above eligibility criteria? *

- Yes
 No

Visiting research eligibility criteria

The visiting Ukrainian researchers must:

- be either a:
 - **Ukrainian citizen** or **Ukrainian permanent resident** employed as a researcher, or enrolled in a higher degree by research*, at a research institute in Ukraine, or;
 - **Ukrainian citizen** or **permanent resident displaced by the war, and** be employed as a researcher, or enrolled in a higher degree by research*, at an internationally recognised research institute in another country.
- be undertaking, or have received, a higher degree by research*
- confirm, and be able to demonstrate upon request, that their mission, scope, and research serves civilian purposes. Military research is not eligible for funding.
- conduct research in one of the below fields:
 - Agricultural, veterinary and food sciences
 - Biological sciences
 - Biomedical and clinical sciences
 - Chemical sciences
 - Earth sciences
 - Engineering
 - Environmental sciences

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- Health sciences
- Information and computing sciences
- Mathematical sciences
- Physical sciences

**Master of Science/Philosophy or Doctor of Philosophy (PhD).*

Does the visiting researcher meet the above criteria? *

- Yes
 No

Terms and conditions of the grant

Grant funding may be used towards the cost of:

- a return economy international airfare from the closest major airport to where the Ukrainian researcher is based, to the location(s) of the Australian host.
- accommodation expenses, up to a limit of A\$300 per person, per night. Refer to the Australian Tax Office (ATO) taxation determination [TD2022/10](#) for a guide on reasonable accommodation rates in each major city in Australia.
- a per diem of \$140 for each day the visiting researcher is in Australia (including weekends), to cover food and incidental expenses. Funds must be paid to researchers by the Australian host institute immediately on arrival into Australia.
- Travel and medical insurance, and visa expenses, will be reimbursed up to a total limit of A\$1000 per visiting researcher. *Please note: all visiting researchers must have comprehensive travel insurance and full medical insurance for the entirety of their travel period under this program.*
- other direct support costs as agreed by the Academy.

The host's organisation is responsible for receiving the funding, making travel and logistical arrangements in conjunction with the visiting Ukrainian researchers, reporting on and acquitting the grant, and facilitating full payment of the daily allowance to the researcher on their arrival into Australia.

Grant funds cannot be paid to individuals. Host Australian organisations will invoice the Academy directly for the grant funding and any unspent funds must be returned to the Academy at the time of reporting.

The grant does not provide funds for research expenses, salaries, bench fees, managerial and administrative costs, or institute overheads. Funding can only be used for the direct travel and support expenses as outlined in the funding agreement.

Do you have the appropriate delegation or authority to accept the terms and conditions of the grant on behalf of the Australian host institute? *

- Yes
 No

Purpose of short-term visit

The short-term visit grants support Ukrainian researchers to travel to Australia to engage in project research at a host institution, or to participate in conference and site visit programs.

- Visits to engage in **research projects** are expected to be for a period of six to 12 weeks in duration for one person only.
- Visits to attend a **conference and site visit program** should be for a period of two to four weeks long for one or more people.

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The primary focus of all short-term visits to Australia should be the benefit of the activities to the visiting Ukrainian researcher.

Purpose of short-term visit *

- Research project
- Conference and site visit program

Australian host institute

* indicates a required field

Host institute name *

The University of Queensland

Organisation ABN *

63 942 912 684

Information from the Australian Business Register	
ABN	63 942 912 684
Entity name	THE UNIVERSITY OF QUEENSLAND
ABN status	Active
Entity type	Other Unincorporated Entity
Goods & Services Tax (GST)	Yes
DGR Endorsed	Yes (Item 1)
ATO Charity Type	Charity More information
ACNC Registration	Registered
Tax Concessions	GST Concession, Income Tax Exemption
Main business location	4067 QLD

Information retrieved at 4:48pm yesterday

Must be an ABN.

Institute address *

The University of Queensland
306 Carmody Road
St Lucia QLD 4072 Australia
Any, but at least one field is required.

Institute website *

<https://www.uq.edu.au/>

Must be a URL.

Host full name *

Prof Mary Fletcher

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Host preferred name

Mary

Position at institute *

Professor

Phone number *

0417 753 791

Must be an Australian phone number.

Email address *

mary.fletcher@uq.edu.au

Must be an email address.

Do you identify as Aboriginal or Torres Strait Islander? *

No

Host gender *

- Woman
- Man
- Non-binary
- Prefer not to say
- Other:

If you prefer to use a different term, please specify this in the 'other' text field

Australian host CV, including publication list *

Filename: Professor Mary Therese Fletcher CV 2023.pdf

File size: 520.8 kB

Research project visit

*** indicates a required field**

Proposed date of arrival into Australia *

01/08/2023

Must be a date.

Proposed departure date from Australia *

06/10/2023

Must be a date.

Total length of time in Australia. *

9 week and 4 days

Short-term visits for research project should be for a period of between six and 12 weeks long. List answer as weeks and days. For example, 5 weeks and 3 days.

Summary of proposed research project, including an outline of the contributions from the Australian and Ukrainian researchers. *

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"Indospicine from the Australian plant *Indigofera spicata* as potential anticancer agent"

The proposed research project builds on an existing interdisciplinary collaboration between Prof Fletcher (University of Queensland) and researchers in Ukraine. In the proposed project Dr Tupychak (an early career chemist from Ivan Franko National University of Lviv, Ukraine) will undertake research in the natural toxins chemistry laboratory of Prof Fletcher at UQ with further research to continue on his return to Lviv under the guidance of Dr Oleh Stasyk of the Department of Cell Signaling of the Institute of Cell Biology National Academy of Sciences of Ukraine (ICB NASU).

CURRENT STATE OF THE RESEARCH PROBLEM

Arginine is a functionally versatile semi-essential proteinogenic amino acid. It is a potent activator of mTOR signaling and is required for the synthesis of many important signaling molecules, such as nitric oxide, polyamines, proline, creatinine and agmatine. Paradoxically, genetic alterations during malignant transformation in humans often leads to the deficiency of cancer cells in arginine biosynthesis and to the profoundly elevated uptake of exogenous arginine. Such a dependency makes many malignant cells sensitive to arginine deprivation therapy (ADT) based on recombinant arginine-degrading enzymes [Stasyk et al., 2015 (PMID: 25231409) and references thereof].

Notably, the results of animal studies and stage I and II clinical trials suggested that ADT as the monotherapy, although inhibits tumor growth in many cases, is itself insufficient for elimination of cancer cells in vivo. Therefore, it was proposed that cancerocidal efficacy of ADT can be improved by rationally designing combinational approaches that involve a rginine-degrading enzymes and certain chemotherapeutic drugs. The Department of Cell Signaling (ICB NASU) headed by Dr. Oleh Stasyk has been exploring this approach since 2010. Dr Stasyk's group was the first to demonstrate selective anticancer effect of low doses of canavanine (Cav), a structural arginine analogue of plant origin, when arginine is concomitantly deprived by recombinant human arginase I. It has been established that Cav cytotoxic effect depends on its uptake by cultured cancer cells, misregulation of mTOR/eIF2a signaling, Cav misincorporation into nascent proteins instead of arginine, exacerbation of ER stress and progression of apoptosis. Such a combination was effective against various cancer cells grown in 2D or 3D cultures and against transplanted murine tumors [Vynnytska et al., 2011 (PMID: 20717004); Vynnytska-Myronovska et al., 2012 (PMID: 21647872); Kurlischuk et al., 2016 (PMID: 27689335); Karatsay et al., 2020 (PMID: 33008000)]. However, elucidation of Cav pharmacokinetics requires more detailed studies as Cav remains a weak substrate of arginase I.

Therefore, we searched for and identified alternative an arginine analogue in plants that is not degraded by arginase, indospicine (Isp). Isp is found in leguminous plants of genera *Indigofera*, particularly those endemic to Australia, and was previously implicated as a cause of the wildlife meat toxicity for domestic dogs [Tan et al., 2014 (PMID: 24433171)]. As a result of collaboration between groups of Prof. Fletcher and Dr. Stasyk it was recently reported in a joint publication that Isp exerts selective antiproliferative effect on cultured cancer cells in combination with arginase I. Of note, the effective cytotoxic Isp concentrations were in the low micromolar range [Shuvayeva et al., 2021 (PMID: 32068315)].

RESEARCH PROJECT AIM FOR VISIT TO AUSTRALIA

In our previous studies, we studied chemically synthesized Isp (provided by Prof Fletcher), and Isp-containing crude extracts of *Indigofera spicata* plant material, from plants cultivated at greenhouse in Lviv, Ukraine. In the current project Dr Tupychak (an early career organic chemist from Lviv) will travel to Brisbane and undertake further collaborative research in the UQ laboratory of Prof Fletcher. Dr Tupychak will compare for the first-time Isp content of *I. spicata* plant material (leaves and seeds) either collected from a natural habitat in the Brisbane area or from plants grown in greenhouse conditions. Importantly, Cav content will

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also be determined as this amino acid is also possibly present in the corresponding extracts [Tan et al., 2016 (PMID: 27509381)]. Since chemically synthesized Isp is not commercially available and expensive to synthesize, we plan as a continuation of this project to purify Isp directly from collected plant material to compare the effects of *I. spicata* derived Isp on proliferation of model cancer cell lines and laboratory animals with transplanted tumors. Prof Fletcher has already collected ~10kg of *I. spicata* plant material which will be made available to Dr Tupyachak.

PROJECT TASKS:

1. Extraction of *I. spicata* plant material for isolation of amino acids, including arginine analogues
2. Analysis of Isp and Cav content in extracts of different origin using methods of chromatography and mass spectrometry

PROJECT EXPECTED RESULTS:

As a result of this project visit of Dr. Mykola Tupyachak to the Australian host laboratory at UQ, crude and derivative extracts of *I. spicata* will be analyzed for Isp content and conclusion will be made about their suitability as possible anticancer agents in combination with ADT. The analysis of corresponding extracts on cancer cell models will be further conducted in Dr Stasyk laboratory at ICB NASU in Ukraine (for which we aim to apply for a separate financial support).

This research visit provides a unique opportunity to work with endemic Australian plant and combine specialized expertise of the two scientific groups. It will strengthen the links between the respective Ukrainian and Australian research groups, lead to further joint publications and noteworthy research outcomes, and will lay the ground for further successful grant applications involving international collaboration.

INVOLVEMENT OF THE AUSTRALIAN HOST LABORATORY

Prof Fletcher's group will provide access to the already available bulk plant collection of *I. spicata* (~10kg) as source material for isolation of the amino acids of interest. Prof Fletcher will provide access to all equipment required for isolation and quantitation of Isp and Cav as outlined in tasks above.

INVOLVEMENT OF THE UKRANIAN LABORATORY

Dr Stasyk's group will provide *I. spicata* plant material grown under artificial greenhouse conditions in Ukraine for comparative analysis as indicated in Project tasks. Also, as indicated above, the Ukrainian laboratory will conduct cell culture and animal studies with *I. spicata* extracts resulting from the proposed research project visit.

Must be no more than 1000 words.

Outline the proposed research and how the visiting Ukrainian researcher will be involved in the project.

Describe the benefits of the short-term visit to the Ukrainian researcher. *

The main focus of Dr Mykola Tupyachak's research in organic chemistry has been the synthesis of low-molecular-weight compounds with antitumor activity, with significant success in the development of novel efficient reactions, molecular design and synthesis of a number of new functionalized heterocyclic compounds.

In addition, his research interests also include the isolation of low-molecular-weight antitumor compounds from natural sources. Under the Ukrainian domestic grant supervised by Dr. Oleh Stasyk (Institute of Cell Biology, National Academy of Sciences Ukraine ICB NASU) "Synthesis and analysis of new structural analogues of arginine and canavanine as components of metabolic antitumor therapy", Mykola developed original methods for the extraction of arginine analogue indospicine from the Australian leguminous plant *Indigofera spicata* (M.Tupyachak, O.Stasyk, M.Fletcher, unpublished data). The continuation of this

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research in collaboration with Prof. Mary Fletcher of the Queensland Alliance for Agriculture and Food Innovation/School of Chemistry and Molecular Biosciences at the University of Queensland (QAAFI/SCMB UQ) is the purpose of the Mykola's planned internship in the frame of this application.

The visit will allow him to enhance his professional skills in the identification and analysis of various natural toxins and bioactive substances, to learn new methods and master modern analytical techniques benefiting from the expertise of QAAFI/SCMB colleagues at UQ. This visit will also provide an opportunity to compare in one series of experiments the plant material of the endemic Australian plant *I. spicata* grown under natural conditions with the plants cultivated at a greenhouse in Ukraine under artificial conditions regarding the content of amino acid analogues and other important parameters. This data will be invaluable for the future cell culture work that is planned to be conducted at ICB NASU addressing anticancer activity of *I. spicata* extracts in comparison with the chemically synthesized arginine analogues.

It is necessary to emphasize that Mykola's research during the planned internship will involve state-of-the-art research equipment at QAAFI/SCMB UQ not available at his Ukrainian laboratory. The key aspects of the experimental work during the visit will involve the extraction, analysis and chromatographic purification of raw plant materials. The experience gained in chromatographic purification of plant extracts and working with different chromatography systems will be very valuable for Mykola as a young postdoc. This experience will be beneficial not only for his personal career growth but also for enhancing the scientific potential of the Department of Organic Chemistry of Lviv National University he represents. Importantly the University is about to establish a new scientific laboratory for chromatographic analysis, where Mykola's new experience will be in high demand.

Finally, the proposed internship will provide an opportunity to establish new connections between the Australian and Ukrainian scientific groups, facilitate the exchange of knowledge, research methods, advanced technologies, will result in new joint scientific publications, and foster new collaborations in the future. Working within a new group, interacting with scientists from different cultural backgrounds will definitely broaden Mykola's professional perspectives and increase his experience and competitiveness in applying for any further funding, which is extremely important in the current Ukraine's reality.

Must be no more than 500 words.

Outline the suitability of the applying host organisation in supporting the visiting researcher and providing access to appropriate facilities, equipment, and beneficial collaborative opportunities. *

The University of Queensland (UQ) is well-placed to provide support for the candidate and provide access to world-class facilities and equipment. UQ is ranked in the world's top 100 universities according to QS (50), ARWU (47) and THE (53), and worldwide is ranked #64 in Chemistry (QS) and #4 in Agriculture (NTU). It is envisaged that the visiting researcher will have ample opportunity during the research project visit to build collaborative networks that will be beneficial to his current and future career.

Professor Mary Fletcher is a natural product organic chemist and leads the Natural Toxin group within the Queensland Alliance for Agricultural and Food Innovation (QAAFI) at UQ. She is also an Affiliate Associate Professor in the UQ School of Chemistry and Molecular Biosciences (SCMB). Prof Fletcher is widely recognised as an applied organic chemist with specialist skills in the identification, separation, and analysis of natural toxins and other bioactives in a range of plants, fungi and agricultural products. She has a long-term interest in the atypical amino acid indospicine found only in Indigofera plants species. This toxin has been linked with multiple dog deaths in Australia through secondary consumption of meat derived from livestock grazing Indigofera species. It is thus somewhat ironic that the current

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research focuses on the use of the same atypical amino acid as an antitumor therapy.

The proposal builds on preliminary studies conducted in Ukraine by Dr Tupyckak under the guidance of Dr Stayk (ICB NASU) and utilising plant material provided by Prof Fletcher. The proposed research visit will enable Dr Tupyckak to further this research utilising the breadth of chemistry facilities and expertise available at UQ. Whilst at UQ, Dr Tupyckak will have access to complementary research environments in QAAFI and in SCMB. The Fletcher research group provides access to high-level HRMS-UPLC, UPLC-MS/MS, GC-MS/MS instrumentation, with co-location with government (Queensland Health and Department of Agriculture and Fisheries) scientists providing a wide depth of industry exposure. Linkages with SCMB enable collaboration with world-class synthetic organic chemists within a state-of-the-art synthetic space and access to high field NMR and advanced mass spectrometric facilities for compound characterisation and structure elucidation. Dr Tupyckak will also have access to UQ library facilities and associated on-line journal access to facilitate the preparation of scientific manuscripts based on the research visit.

Both QAAFI and SCMB maintain a regular seminar programme which Dr Tupyckak will be welcome to attend to widen his professional networks. Prof Fletcher is a Fellow of the Royal Australian Chemistry Institute (RACI), and very involved within this organisation. She will provide opportunities for the visiting researcher to engage with the RACI Early Career Chemists group. This group is very active both professionally and socially and will enable Dr Tupyckak to establish beneficial links across the wider RACI chemistry community.

Must be no more than 500 words.

Visiting researcher information

Visiting researcher full name *

Dr Mykola Tupyckak

Preferred name

Mykola

Visiting researcher gender *

Man

If you prefer to use a different term, please specify this in the 'other' text field

Visiting researcher home institute name *

Ivan Franko National University of Lviv

Position at home institute *

Lecturer

Home institute address *

Universytetska str., 1,
Lviv Lviv 79000 Ukraine

Address Line 1, Suburb/Town, State/Province, Postcode, and Country are required.

Phone number *

+380 50 287 8356

Email address *

tupyckakmykola@gmail.com

Must be an email address.

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Visiting researcher degree status

- I have a Master of Science/Philosophy degree
- I am a Master of Science/Philosophy student
- I have a PhD
- I am a PhD student

Date degree received, or date degree studies commenced *

09/09/2022

Must be a date.

Visiting researcher CV including publications list *

Filename: CV Tupychak-1.pdf

File size: 675.6 kB

Maximum of six pages in total

Proof of Ukrainian citizenship or permanent residency *

Filename: Passport Tupychak M..pdf

File size: 1.2 MB

Attach a copy of the visiting researchers passport and, if relevant, their Ukrainian permanent residency visa.

Budget outline

Outline the requested funding in the below table. Attach any supporting documentation, such as quotes for flights, accommodation, insurance or visa costs.

Refer to the [Activity 1 website](#) for information on eligible expenses.

Expense type	Total for expense	Additional information about expense
Flights *	\$4,500.00	Warsaw to Brisbane and return
Accommodation	\$3,600.00	10 * \$300 per week plus bond (University Park Accommodation, Robertson)
Per diem	\$9,380.00	67 days * \$140 per day
Visa and insurance costs	\$1,000.00	Travel and medical insurance, and visa expenses

Total funding requested

\$18,480.00

This number/amount is calculated.

Supporting documentation

* indicates a required field

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Information on the supporting documentation requirements

Applications must include the below attachments.

- The letter of support from the Australian host organisation should confirm the support that will be provided to the visiting Ukrainian researchers as outlined in the proposal. See letter template here.
- The letter of support from the visiting researchers' home institute should confirm the support for the proposed research project. If the researcher is based outside of Ukraine, due to being displaced by the war with Russia, the current home institute is asked to confirm this in the letter. See the letter template here.

See the [Activity 1 website](#) for additional information on the supporting documentation required for each application.

Letter of support from the Australian host organisation. *

Filename: UQ support letter STV00023 230602_signed.pdf

File size: 240.8 kB

Letter of support from the Ukrainian researchers' home institute. *

Filename: Letter of Support Lviv National University.pdf

File size: 173.2 kB

Filename: Letter_of_Support_ICB_NASU.pdf

File size: 1.0 MB

A minimum of 1 file must be attached.