



Detailed curriculum for the course:

Laboratory apprenticeship – Mental illness and protein aggregation

Academic year:	2020/2021
Program:	Biotechnology for the Life Sciences (1 st year)
Course code:	EBS102
ECTS points:	12
Language of the course:	English
Teaching hours:	280 hours (all practical work)
Pre-requisites:	Successful completion of BLS103 “Introduction to Laboratory Work and Safety”

Course leader and contact information:

Title and name: Doc. dr. sc. Nicholas J. Bradshaw
Address: Odjel za biotehnologiju, O-226
E-mail: nicholas.b@biotech.uniri.hr

Time period: 1st March - 16th April 2021
or
19th April – 4th June 2021

Teaching staff: Course leader:
Doc. dr. sc. Nicholas J. Bradshaw

Associates:
Beti Zaharija, mag.med.chem.
Bobana Samardžija, mag.pharm.inv.



Required reading:

Bradshaw & Korth, "Protein misassembly and aggregation as potential convergence points for non-genetic causes of chronic mental illness", *Molecular Psychiatry* (2019) 24:936-951

Additional articles, specific to each student's research, may be assigned by the course leader.

Optional reading:

- 1 Leliveld et al, "Insolubility of Disrupted-in-Schizophrenia 1 disrupts oligomer-dependent interactions with Nuclear Distribution Element 1 and is associated with sporadic mental disease", *Journal of Neuroscience* (2008), 28:3839-3845
- 2 Ottis et al, "Convergence of two independent mental disease genes on the protein level: Recruitment of dysbindin to cell-invasive Disrupted-In Schizophrenia 1 aggresomes", *Biological Psychiatry* (2011), 70:604-610
- 3 Bader et al, "Proteomic, genomic and translational approaches identify CRMP1 for a role in schizophrenia and its underlying traits" *Human Molecular Genetics* (2012) 21:4406-4418
- 4 Bradshaw et al, "Aggregation of the protein TRIOBP-1 and its potential relevance to schizophrenia" *PLoS One* (2014) 9:e0111196
- 5 Zhu, Shen & Xu "Propagation of dysbindin-1B aggregates: exosome-mediated transmission of neurotoxic deposits" *Neuroscience* (2015) 291:301-316
- 6 Trossbach et al, "Misassembly of full-length Disrupted-in-Schizophrenia 1 protein is linked to altered dopamine homeostasis and behavioral deficits", *Molecular Psychiatry* (2016) 21, 1561-1572
- 7 Nucifora et al, "A mutation in NPAS3 that segregates with schizophrenia in a small family leads to protein aggregation" *Molecular Neuropsychiatry* 2:133-144
- 8 Bradshaw et al, "An unpredicted aggregation-critical region of the actin-polymerizing protein TRIOBP-1/Tara, determined by elucidation of its domain structure" *Journal of Biological Chemistry* (2017) 292:9582-9895
- 8 Nucifora et al, "Increased protein insolubility in brains from a subset of patients with schizophrenia" *American Journal of Psychiatry* (2019) 176:730-743
- 9 Trossbach et al, "Dysregulation of a specific immune-related network of genes biologically defines a subset of schizophrenia" *Translational Psychiatry* (2019) 9:156

Course description:

Chronic mental illnesses such as schizophrenia and major depressive disorder are devastating conditions which impact greatly both on patients themselves and wider society. Progress in improving the diagnosis and treatment of these conditions, however, has been greatly limited by a lack of understanding regarding their underlying biology, and in particular their very complicated genetic background. Alternative approaches to studying these conditions are therefore required.

Dr. Nicholas Bradshaw and his research group have therefore been pursuing an alternative approach, with funding from the Croatian Science Foundation (HRZZ). Specifically, they have been investigating the potential role of insoluble protein aggregates in the development of these conditions, in analogy to similar biological events in conditions such as Alzheimer's or Parkinson's disease.



During this course, students will spend 8 weeks conducting laboratory work in Dr. Bradshaw's research group. This will begin with basic training in the various cell and molecular biology techniques required. This teaching will occur in a "mentorship" situation, with two students being taught at a time. As the skills of the students develop, they will then begin to perform research experiments, using these techniques, to gain novel insight into the research field of protein aggregation in mental illness.

After completion of the course, students will then have the option of continuing their research as a Research Project under the mentorship of Dr. Bradshaw, or of instead performing their project in a different research group.

Learning outcomes:

Students will gain an in depth theoretical knowledge of the study of mental illnesses through cell and molecular biology and protein biochemistry techniques. This will come through reading on the subject, discussion with the course leader/mentor and other members of the research group, as well as first-hand experience in the laboratory.

Practically, students will gain significant practical experience at culturing mammalian cells, performing Western blots, and immunofluorescent microscopy. Options for performing bacterial culture, DNA cloning and biochemical fractionation experiments will also be available. This will be obtained through guided training, and reinforced through using the techniques to perform genuine research experiments. In this way, the skills learned should become relevant to the students in a research context.

Through work in a research environment, students will also have an opportunity to hone their soft research skills, including searching the academic literature, critical review of papers, experimental design and analysis, and writing of scientific reports.

Requirements, methods of assessment and evaluation:

Students are required to perform work in the laboratory for the duration of the course, as indicated in "Schedule of Classes" below. They will engage fully in the day-to-day activities of the work group, including observing the work of others, engaging in research work of their own, and performing other tasks required for running of the laboratory. They are required to keep a laboratory book/journal of their work, written in English, in a manner that is understandable to their supervisor. They will also engage in scientific discussions, lab meetings and/or presentations of their work to the same degree as other members of the research group. They will work at all times in a safe manner, as defined in the course "Introduction to Laboratory Work & Safety" plus any additional safety measures that apply to members of this laboratory.

Students will receive continuous assessment from the mentor/course leader who will meet with and teach the students on a regular basis. In this way, the student will both be assessed, and received continuous feedback concerning their work. At the end of the course, the mentor will submit a report on their work and progress at the end of the course. The mentor's report, and accompanying grade, will account for 50% of the student's grade for the course.

Additionally, at the end of the course, the student will submit a short report (approximately 3 pages), detailing the area that they worked in, the experiments they performed, any results they obtained, and skills that they learned and used.



This report will then be assessed by the mentor and one other member of faculty, who will together agree on a grade for the remaining 50% of the course.

Qualification and grades (according to the *University of Rijeka Study Regulations*):

The following grades will be awarded based on the final score:

Percentage score	ECTS grade	Numerical grade
90% to 100%	A	Excellent (5)
75% to 89.9%	B	Very good (4)
60% to 74.9%	C	Good (3)
50% to 59.9%	D	Satisfactory (2)
0% to 49.9%	F	Unsatisfactory (1)

The final grade is based on the sum of percentage points accumulated during the course. Passing grades are excellent (5), very good (4), good (3) and satisfactory (2).

Schedule of classes:

Daily, from 9:00-12:00 and 13:00-17:00, every weekday, either from 01.03.2021 to 16.04.2021, or from 19.04.2021 to 04.06.2021 (excluding national and University holidays). All work will be performed in laboratories O-136 and O-137, unless otherwise indicated by the course leader/supervisor. Variations in exactly which hours are worked can be made with the agreement of the course leader/supervisor. Some laboratory time may be replaced with private study and background reading, subject to the requirements of the research performed, and with the agreement of the course leader/supervisor.

Additional information:

Academic integrity

Students are required to respect the principles of academic integrity, and refer to the documents: *Ethics Guidelines of the University of Rijeka* and the *Ethics Guidelines for Students*.