DŠFS & PPSA Twinnet Poster presentation competition

Report with Abstracts

University of Ljubljana, Faculty of Pharmacy

9 March 2018

After a one-year break, Students' Section of Slovenian Pharmaceutical Society (ŠSSFD) has once again relaunched the Twinnet project for pharmacy students. Twinnet is a project under the patronage of the European Pharmacy Students' Association (EPSA), where two associations from around the Europe decide to establish a partnership and organize an exchange of the small group of students for the period of 5-7 days. It consists of two parts; each in every country and it aims to improve the mobility of students and ensures to provide extra-curricular education of students. It provides them with chance to enhance their communication skills and knowledge about different cultures. During the stay in partners' association country, students have a chance to experience the concepts of work, organisation and curricular programme in foreign country.

This year, ŠSSFD has stabilized a partnership with Polish association PPSA from Lublin. The first part of the mobility exchange project took place in Slovenia in Ljubljana from 5th to 11th March, where a group of 18 students (9 from each country) has gathered every day to participate in different sorts of activities organized by the group of three students from the Faculty of pharmacy in Ljubljana. With the help of our topic: "Implementing new approaches in patient therapy", we have earned a wider view on the clinical pharmacy and ideas on how to properly treat our patients in the future. Together, we have attended the presentation of the faculty and the way, how Slovenian students' association works. We had our own tour of the Faculty with each of the six Chairs presenting their activities. We've participated in various soft skills trainings delivered by our EPSA trainers, where we improved our skills in working as a group, communication and learning about the emotional intelligence. During the stay in Ljubljana we have also attended the science excursion organized by Krka, a generic pharmaceutical company from Novo mesto and sightseeing to the North-Western part of the Slovenia.

By the request of the Twinnet coordinator from PPSA Lublin, we have decided to organize the PPSA and ŠSSFD Twinnet Poster presentation competition, designed, according to the EPSA Science day. It is a competition where every pre- or postgraduate student, who has carried out a research in any field of pharmaceutical sciences can present his or her work to the group of experts. It is a great opportunity to gain experience on how to prepare a poster and a presentation and on how to present your own research work. From the comments from the jury and audience you can get some ideas on how to improve your work and also get additional motivation to continue with your scientific work.

The competition took place on 9th of March in 2018 at the Faculty of pharmacy, University of Ljubljana. 6 contestants; 3 from Slovenia and 3 from Poland participated. At first, the jury was presented to the participants and the audience around us. Afterwards, we have selected the presentation order and began with the competition. The jury, along with the audience, went around the room and listened to the presentations. Each of the contestants was given 7-10 minutes to present the work and then 5 minutes to answer all the question asked by

the jury. After the last presenter, the jury evaluated all the contestants and decided on the winner. Each of the contestants received a certificate from the Faculty of Pharmacy, University of Ljubljana.

The winner of this twinnet poster presentation competition was Emanuela Senjor with a poster entitled Cystatin F in tumor cells.

Nejc Ajlec

National Twinnet Coordinator of Slovenia

Figure 1. Winner of the Twinnet Poster competition award 2018 Emanuela Senjor.

Exploration of chemical space of InhA inhibitors by combining and modifying pharmacophores of existing classes

Andrej Šterman, Faculty of Pharmacy, Univeristy of Ljubljana

Tuberculosis represents one of the leading causes of death and in 2016 this disease outranked deaths caused by HIV/AIDS. The frontline drug isoniazid inhibits InhA, an enzyme crucial for cell wall synthesis, but resistance to it has emerged because of a mutation in the enzyme KatG which activates isoniazid. This problem can be overcome by designing a direct inhibitor of InhA.

Two distinct classes (thiadiazoles and tetrahydropirans) have already been developed so we designed and synthesised hybrids of both in order to further explore the chemical space by combining the pharmacophores (compounds 1 – 3). We also substituted the thiadiazole ring for pyridazine (compound 4) and enlarged the lipophilic part (compound 5), in both cases retaining all the other moieties. The hybrids have proven to be inactive, pyridazine compound had a marked decrease in potency while the more lipophilic compound had a good IC50 of 62 nM, yet not better than the leads. We can optimistically await the results of antibacterial assays on Mycobacterium tuberculosis as the compound's increased lipophilicity could improve the rate of passive diffusion into the cell. To establish the true importance of hydrophobic interactions, more compounds similar to 5 should be prepared in the future.

This work has proven that the chemical space of InhA inhibitors is very limited and that optimal spatial orientation of pharmacophores is essential to good activity as a small change in structure can diminish the potency even in compounds featuring all pharmacophores. We are certain our results will allow for further successful findings in this field as they suggest the key properties of an optimal InhA inhibitor.

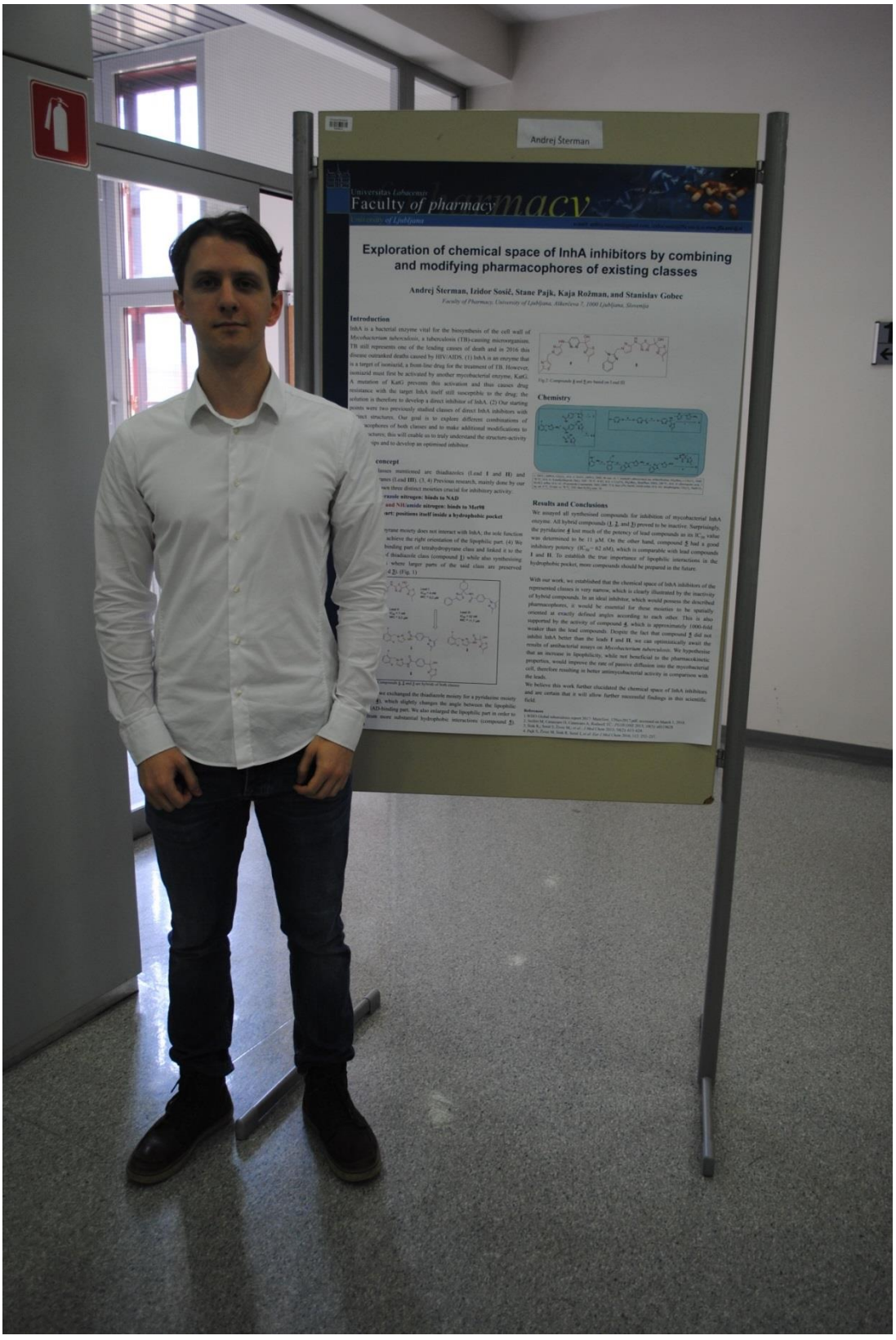

Figure 2. Andrej Šterman

Effect of active components cannabis, cannabionoids on the development of Schizophrenia

Rafał Poręba, Faculty of Pharmacy, Medical University of Lublin

Schizophrenia is a severe mental disorder characterized by a vast array of symptoms and diversified course that very often may be individual for each patient. The pathogenesis of schizofrenia remains unknown. However, it is believed that many biochemical systems are involved in its emergence such as: glutamatergic, GABAergic, dopaminergic, serotonergic and also the endocannaboininoid system (ECS) [1]. Available scientific literature indicates the relationship between taking cannaboinoids and development of mental disorders in humans including schizophrenia. Moreover, this relationship has been verified in animal testing. 2. Conducted preclinical tests show that administration of CB1 cannabinoid receptor agonists intensifiy psychotic symptoms and on the other hand, the CB1 receptor antagonists suppress these symptoms. One of the new, promising line of enquiry is the endocannabinoid system. It seems to be a very interesting treatment target in schizophrenia and it may constitute an anchor point for a completely new group of drugs acting through modification of the target towards agonism or antagoinism. In the future, this research may contribute to more effective control of the schizophrenic symptoms and to the greater understanding of its pathogenesis.

Figure 3. Rafał Poręba

Barnes maze test as a useful tool for assessing spatial memory

Kamil Bąk, Faculty of pharmacy, Mecial University of Lublin

Spatial memory is the part of memory responsible for recording information about one's environment and spatial orientation. For example, a person's spatial memory is required in order to navigate around a city, just as a animal's spatial memory is needed to learn the location of the shelter in unfavourable environment. Spatial memory in animals is obtained by exploration behaviour. This type of behaviour depends on natural curiosity and the need to acquire information about the new environment or stimulus. The Barnes Maze test was first developed by Dr. Carol Barnes in 1979. This noninvasive task is useful for evaluating drugs, psychostymulants and ethanol for their effects on cognition as well as identifying cognitive deficits caused by neurodrgenerative diseases such as Alzheimer's disease and addictions in rodents. The Barnes maze consists of a gray metal, circular platform, elevated above the floor, with 20 equally spaced holes located in the periphery, placed in a brightly lit room to provide inhospitable conditions and increase the motivation to escape. One of the holes is connected to an escape box of the same material and colour as the platform. The test consists of four phases: habituation phase, when rodent is introduced to an environment in order to reduce anxiety behaviour, acquisition phase, when animals learn to find the location of the shelter, probe trial, which allows an assessment of spatial memory retrieval and reversal learning to evaluate brain plasticity and cognitive flexibility. The Barnes maze test, besides being useful in evaluating spatial learning and memory deficits, can also be employed in assessing the potential neuroprotective or neurotoxic effects of new or used treatment of Alzheimer disease as well as to study the association between the administration of a drug and hippocampus function.

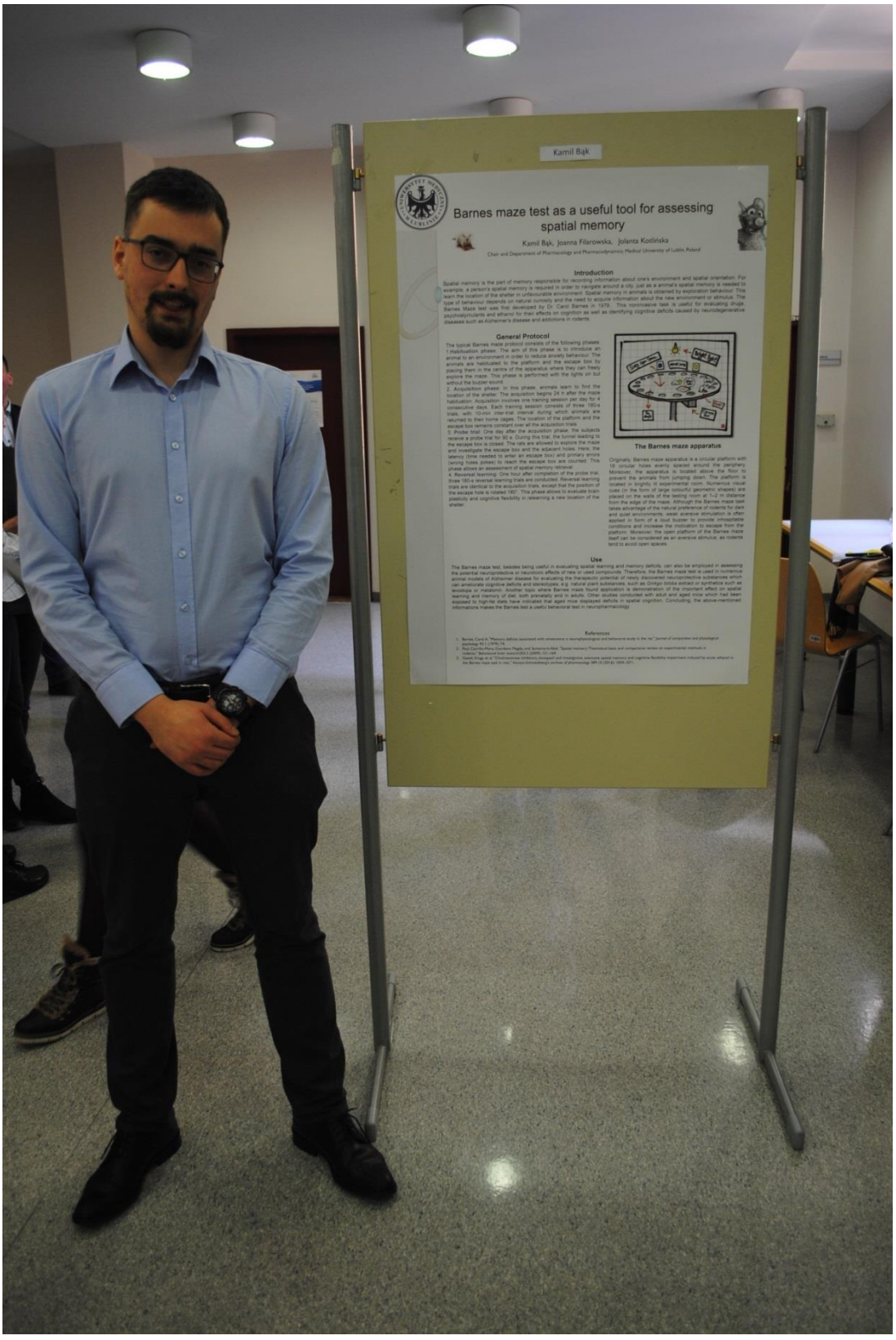

Figure 4. Kamil Bąk

Sialic acids, the pathophysiological processes they are involved in and possible diagnostics

Sofija Gičeva, Faculty of Pharmacy, University of Ljubljana

The sialic acid is involved in many biological processes, related to the non-reducing terminal end of glycolipides, glycoproteins and other glycoconjugates. Most frequently, in glycoconjugate complexes, the sialic acid is found in a monomeric form. Sialic monomers possess the ability to bond with one another and form dimers, oligomers and polysialic acids (Sato and Kijatima, 2013). Polysialic acids are mainly involved in changes of the many functions of the nervous system.The processes that polysialic acids are involved include neural cell migration, axonal guidance, myelination, fasciculation and plasticity of the nervous system. The mechanism of these actions is the anti-adhesive effect of polysialic acids in cell-cell and cell-matrix interactions. Schizophrenia is a psychiatric disorder with multiple factors contributing to its pathogenesis. Some reports suggest that polysialic acids are involved in schizophrenia and other related psychiatric disorders. Many cancer cells express polysialic acids on their cell surfaces. This results in attack to these cells by many molecules including anti-sialic antibodies (Sato and Kijatima, 2013). Furthermore, because of its anti-adhesive effect, polysialic acids stimulate metastasis of the disease. Many bacterial toxins such as toxins from cholera, tetanus and pertussis, as well as various virus types bind to sialylated glycoconjugates. An example of this is the binding of influenza virus with sialic acid containing glycans. The mechanism of action is based on the activity of influenza's most important glycoproteins: hemagglutinine and neuraminidase. Both glycoproteins recognize and bind to the the sialylated glycans of the cell membrane. (Gamblin and Skehel, 2010).

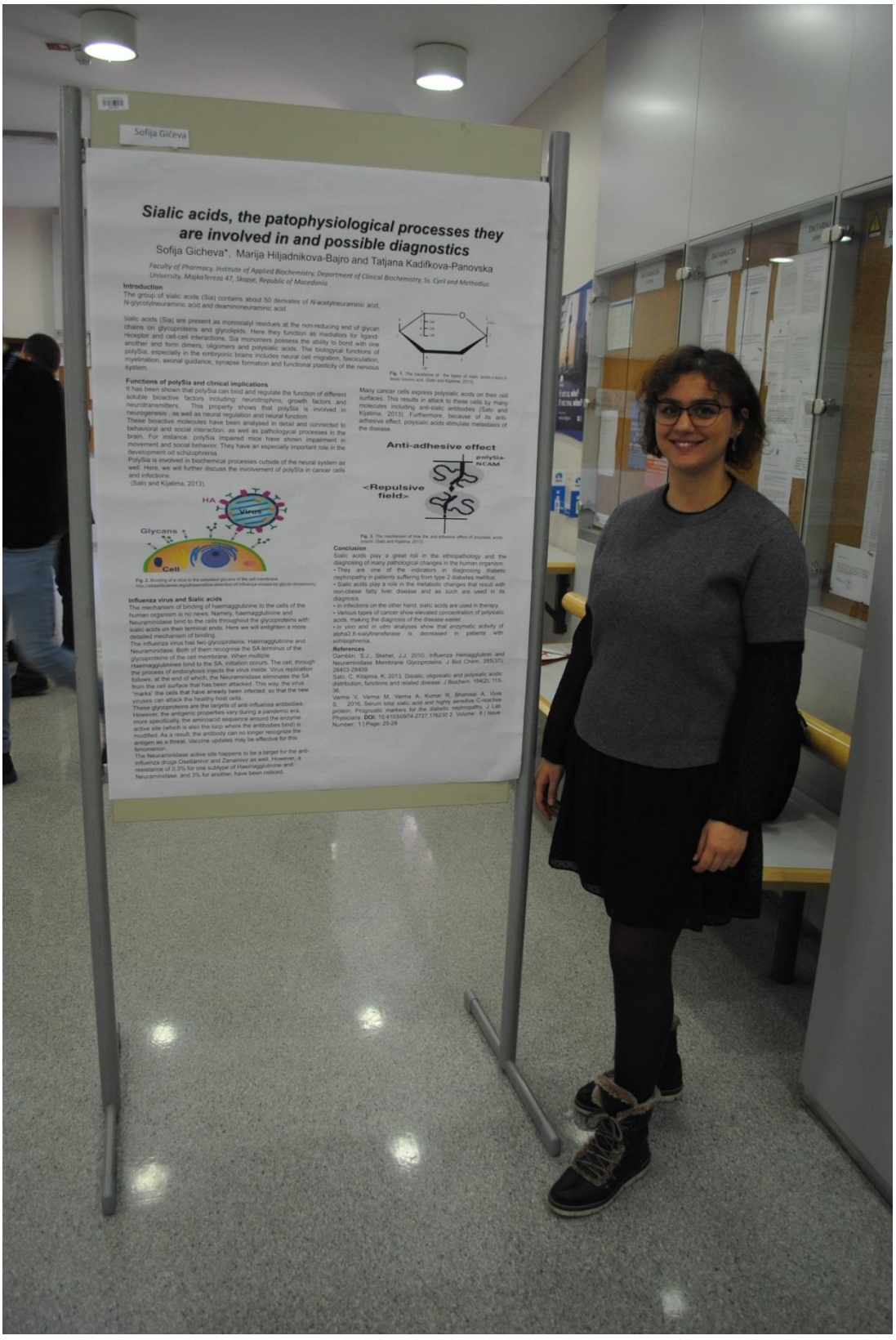

Figure 5. Sofija Gičeva

Cystatin F in tumor cells

Emanuela Senjor, Faculty of Pharmacy, University of Ljubljana

Cystatin F (CF) belongs to type II cystatins, inhibitors of cysteine peptidases. Unlike other type II cystatins, high proportion of CF is retained intracellularly and is targeted to endo/lysosomes. It is synthesized as inactive disulfide-linked dimer. N-terminal truncation makes it a strong inhibitor of cathepsin C (CatC). CF can be taken up from extracellular space enabling in trans regulation of intracellular proteolysis. Increased CF concentration surrounding NK cells may lead to decreased activity of intracellular CatC and to decreased NK cell cytotoxicity. Thus, CF secreted from tumor microenvironment can negatively impact antitumor immunity. CF is normally expressed only in immune cells (monocytes, cytotoxic T lymphocytes, NK cells). However, its expression was also shown in some primary tumors and cell lines. The aim of this study is to examine CF expression in cells of glioblastoma (GBM) and test if CF expression in tumor cells can be induced by immune cells, such as promonocyte line U937. Formalin-fixed paraffin-embedded tissue of GBM patients was used for immunohistochemical detection of CF. As in vitro GBM cell model we used U251 line. Impact of co-cultivation period and ratio between U251 and U937 on the CF expression was tested in whole cell lysates using non-reducing SDS PAGE and western blot. Localization of CF was analyzed in formalin-fixed single cell layers using fluorescently labelled CF antibodies and confocal microscopy. Effect of co-cultivation on CatC activity was also tested. Our results show that CF is present in GBM tissue. After co-cultivation, U251 cells contain CF mainly in active, monomeric form, localized in vesicular intracellular structures. CF quantity increases with the incubation length. Activity of CatC in U251 is decreased upon co-cultivation, presumably due to higher concentration of CF. Our future aim is to characterize the CF expressing cells in GBM tissue in more detail and to correlate its expression with patient prognosis.

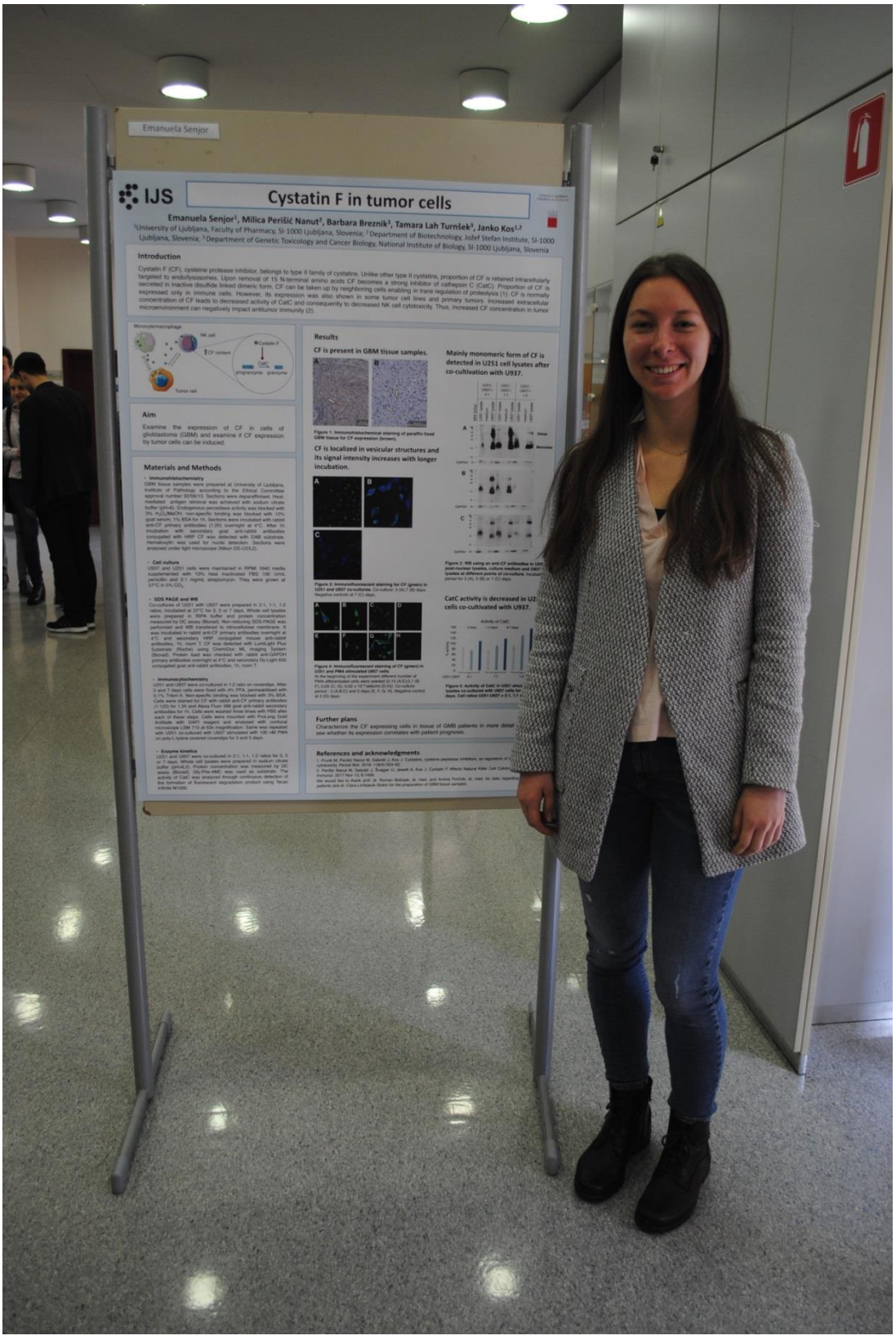

Figure 6. Emanuela Senjor

Serotonin stimulators and modulators (SMS) – a new group of drugs – comparison with other classes of antidepressants

Joanna Bąk, Faculty of pharmacy, Mecial University of Lublin

Depression is one of the most common mental disorders. All over the world, more than 300 million people suffer from this disease.There are people of all ages, more often women than men. The main symptoms of depression are: persistent sadness, feeling guilty, anxiety, loss of interest and enjoyment. Many people also suffer from disturbed sleep, poor concentration and decreasing cognitive functions. It is a serious illness, which is a reason of difficulties at work, school and in relations with family and society; it can also lead to suicide. Studies have suggested that the depression is caused by low levels of three key neurotransmitters – serotonin (5-HT), norepinephrine (NA) and/or dopamine (DA); this theory is called monoamine hypothesis. Different theories do not agree with this hypothesis, but now, treatment of depression is based on use of antidepressant drugs which work by increasing the level of these neurotransmitters in the brain. Older drugs are divided into several groups according to the mechanisms of action: a) TCAs – tricyclic antidepressants b) SSRIs – selective serotonin reuptake inhibitors c) SNRIs – serotonin/norepinephrine reuptake Inhibitors d) MAOIs – monoamine oxidase inhibitors e) Atypic drugs Recently, the new group of antidepressants have become available. These antidepressants, abbreviated as SMS (serotonin modulators and stimulators) have multimodal action, which is specific to the 5-HT neurotransmitter system. Apart from inhibiting the reuptake of 5-HT, they act on more than one type of 5-HT receptor. The group includes: nefazodone, trazodone, vilazodone, vortioxetine. The work presents characteristics of the SMS group in comparison with other classes of antidepressants and it is based on a literature review using the PubMed, Scopus, Web of Science and Google Scholar reference databases.

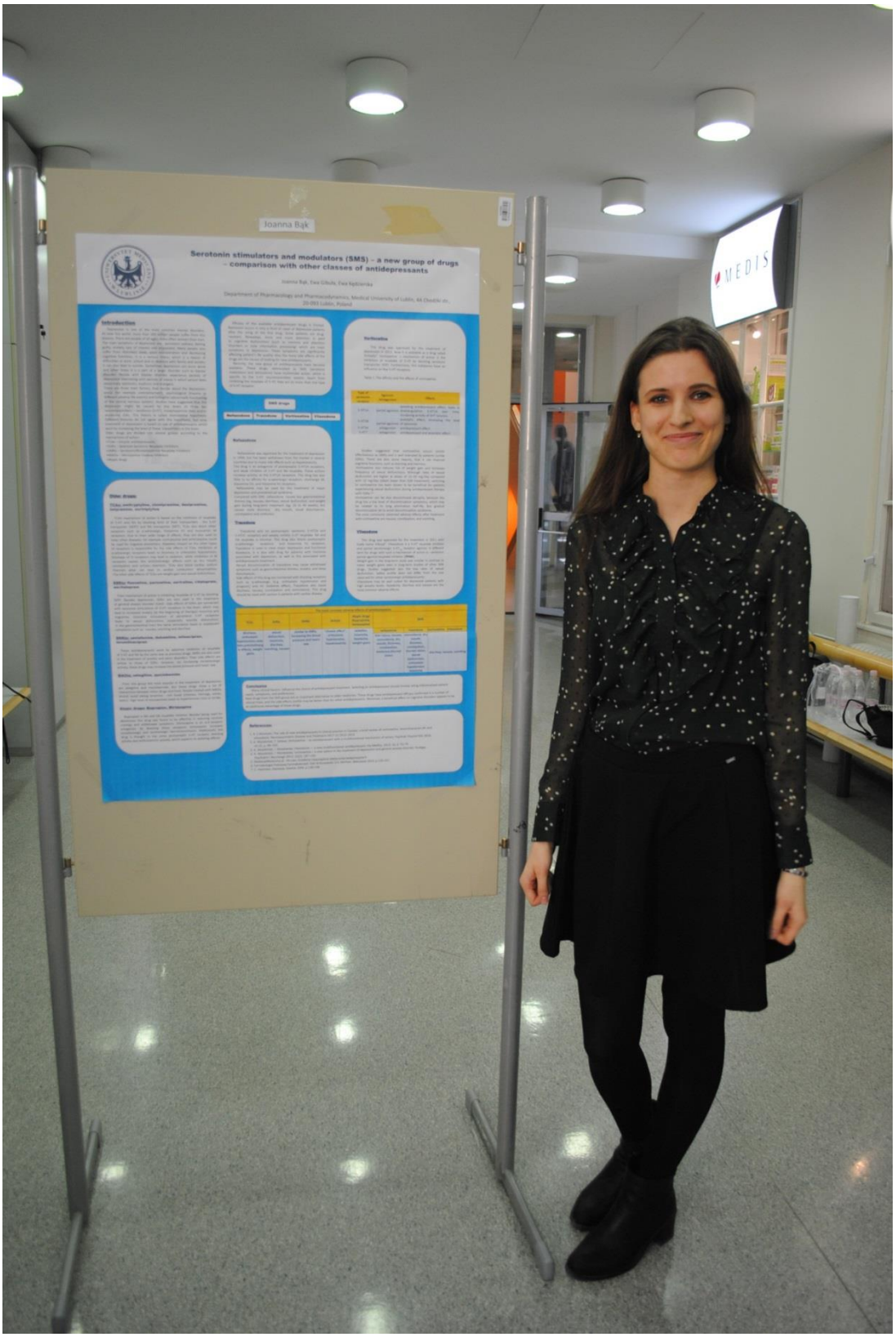

Figure 7 Joanna Bąk