ANNUAL REPORTING
2021

CALL:	**EEA grants Call for proposals 2018 - CRP**
Project code:	PROJECT: EEA-RO-NO-2018-0573
Project title:	Improving quality of life for Autism Spectrum Disorders patients by promoting strategies for early diagnosis and preventive measures
Project acronym:	IQUALASD
Duration (months):	48
Project signature date:	31.07.2019
Project eligibility end date:	30.07.2023
Total budget from the Programm (euro):	1,820,000
- Grant (85%):	1,275,000
- Co-financing (15%):	225,000
Own budget (euro):	320,000
Project Webpage:	http://www.eea-grant-autism.ro/ro/
Project Promoter organization:	Clinical Hospital of Psychiatry ”Prof. Dr. Alexandru Obregia” (OHP)
Principal Investigator:	Magdalena Budisteanu, MD, PhD, Senior Researcher
Project Partner organization (1):	University of Oslo (OU)
Project Partner organization (2):	“Victor Babes” National Institute of Pathology (IVB)

Iceland Liechtenstein Norway grants

UEFISCDI Executive Agency for Higher Education, Research, Development and Innovation Funding

TECHNICAL REPORT (Part 1)

Explanation of the work carried out by the participants (max 10.000 characters, including spaces)

The **project focuses on autism spectrum disorders** (ASDs), complex and severe neurodevelopmental conditions characterized by impaired social interaction and communication, and a restricted range of behaviors and interests. The comprehensive evaluation of a big cohort of patients with ASDs will contribute to the **establishment of the Romanian Registry for ASD**, and will offer data **for improving the early diagnosis and understanding of ASDs mechanisms**.

Phase III: Genomic characterization of patients and control groups; phenotype - genotype correlation

Activities

A 3.1. Completion of the patient and control groups

A 3.2. Genetic tests (Array-CGH studies, fragile X studies, WES) of patients and control groups included in the study

A 3.3. Phenotype-genotype correlations

A 3.4. Elaboration of scientific papers / communications

PP performed A.3.1 and participated in A 3.3 and A.3.4.

In this second phase we continued the enrollment of ASDs patients and started the enrollment of control individuals.

Inclusion criteria were represented by DSM 5 recommendations for ASD, and ADI-R / ADOS score positive for ASD. All children were evaluated as follows: general clinical examination with special attention for anthropometric parameters and dysmorphological features, neurological examination, psychiatric and psychological evaluation. Detailed data regarding pregnancy and birth, psychomotor development, association of other medical conditions, familial history positive for a neuropsychiatric condition (ASD, developmental delay, intellectual disability, speech delay, hyperkinesia etc.) were also recorded. Electroencephalographic studies – EEG - were performed routinely. The results of specific investigations, such as biological tests, neuroimaging studies, ultrasounds, ECG etc., were also analyzed and interpreted in the clinical context of each patient. The clinical data has been harmonized with the large Norwegian ASD database (P1) to enable comparisons across samples. Transfer of clinical data of both cases and controls will be done in Spring 2022 in accordance with GDPR. Analyses of the combined Norwegian and Romania dataset will be finished by the end of 2022.

65 children with ASD were included in the second year of project: 41 boys and 24 girls, with age ranging between 2 years and 16 years. This group included 2 pairs of ASDs siblings. Regarding the cognitive development, all children associated intellectual disability: 18 children mild intellectual disability, and 42 patients, moderate intellectual disability. All children had speech delay, especially in that concern the age of first syllables and first words, but also regarding the language development, dyslalia being a very common feature in our patients. 36 children had different dysmorphic features, especially at the level of the face and included epicanthus, long eyelashes, broad nasal bridge, malformed ears, micrognathia as the most common. Neurological features were represented by musclar hypotonia in 41 children, gross and fine motor skills. Frequent respiratory infections were noted in 39 patients; two children had heart malformation and another child, kidney malformation.

Blood samples were drawn from all these patients, from their parents and, eventually from their healthy siblings.

A total of 300 healthy children were enrolled for the control group and blood samples were drawn from all these children.
The blood samples both from patients and from control group were sent to partner 2.
Due to the current COVID pandemic situation, the enrollment of control individuals was done, for the vast majority, towards the last semester of 2021.

Phenotype-genotype correlations

The pathogenic and likely pathogenic genomic imbalances detected by array-CGH were analyzed in correlation with the phenotype of the patients, allowing for phenotype-genotype correlations.
A deletion on 2q23.1 chromosome was identified in a boy with developmental delay, ASD, wide-based gait, and dysmorphic facial features; brain MRI showed a mega cisterna magna. This is a rare chromosomal anomaly characterized by developmental delay (DD) / intellectual disability (ID), severe speech delay, short stature, seizures, microcephaly and dysmorphic facial features. Other common features include stereotypic repetitive behavior or autistic behavior, a disturbed sleep pattern and a broad-based gait.
A duplication on 1q21.1-q21.2 chromosome was identified in a boy with ASD, moderate ID, speech delay, muscular hypotonia, macrosomia, macrocephaly, facial dysmorphic features, and congenital heart malformation. 1q21.1 duplication (MIM 612475) is characterized by macrocephaly, dysmorphic facial features, mild-moderate intellectual disability, learning problems, autism or schizophrenia.
7p22.2p22.1 duplication was identified in a girl with ASD, mild developmental delay, muscular hypotonia, and facial dysmorphic features. This chromosomal anomaly is very rare, and the common features include craniofacial anomalies, a large fontanelle, facial dysmorphism and psychomotor delay, with hypotonia; ASD was also reported in some patients (Udavakumar AM et al, 2015).
Duplications of 22q11.2 region were identified in two boys. The first patient, with Asperger syndrome and learning difficulties, had 22q11.2 duplication syndrome. This condition has a widely variable phenotype, even among affected members of the same family. Affected individuals may have ID, DD, behavioral problems (including ASD), slow growth leading to short stature, and hypotonia. The second patient, with ASD and a global DD had a distal 22q11.21q11.22 duplication. This is a recurrent CNV in ASD and ID and it was associated with phenotypic variability, including DD and facial dysmorphic features.
A duplication of 17p11.2 region was identified in a boy with severe ID, ASD, speech and motor delay, hypotonia, and dysmorphic features. This anomaly was associated with a well described syndrome, Potocki-Lupski syndrome, characterized by hypotonia, ID, ASD, congenital heart disease, and mild dysmorphic features.
16p13.11 duplication was identified in a girl with ASD, speech delay, and mild ID. This duplication was initially presented in the literature as benign; as emerging evidence supporting its role gathered, currently, this duplication is considered likely pathogenic in the context of neurodevelopmental phenotypes (El-Khattabi et al, 2018).
A deletion of 15q24.1q24.2 region was identified in a boy with ASD, mild ID, speech delay, hypotonia, and dysmorphic features. These features were noted in previously reported patients with this chromosomal anomaly. Recurrent microdeletion of chromosome 15q24 was described as a new genomic disorder after identification of patients with overlapping deletions, intellectual disability and similar clinical features (Mefford H et al, 2020)
A deletion on 2q24.3 chromosome was identified in a boy with ASD, developmental delay, hypotonia, and speech delay. Chromosome 2q24.3 microdeletion syndrome is a rare chromosome abnormality that can include as clinical features microcephaly, developmental delay (speech and motor delays), behavioral difficulties, distinctive facial features, eye

defects, and seizures.
A deletion on Xp22.31 chromosome was identified in a boy with ASD, speech delay, moderate intellectual disability, microcephaly, mild dysmorphic features, dry skin, atopic dermatitis, and frequent respiratory infections. Submicroscopic deletions at Xp22.31 involving STS underlie X-linked ichthyosis. While patients with mutations involving solely the STS gene or the recurrent ~2 Mb deletion can present with attention-deficit hyperactivity disorder (ADHD), those with larger deletions including neighboring genes such as neuroligin 4 (NLGN4) may present with autism in addition to ADHD (Baek WS and Aypar U, 2017).
A deletion on 15q21.2q22.2 chromosome was identified in a girl with mild intellectual disability, speech problems, Asperger syndrome, facial dysmorphic features, and ataxia. This anomaly was prevously reported in association with intelectual disability, obesity and facial dysmorphisms (Velazquez-Wong A et al, 2015).
A deletion on 3q12.3q13.33 chromosome in a boy with severe global developmental delay, autistic behavior, musclar hypotonia, macrosomia with high stature, dysmorphic features, atrial septal defect, cryptorchidy, and frequent respiratory infections. 3q13 microdeletion syndrome is a rare syndrome with a highly variable phenotype, including significant developmental delay, postnatal growth above the mean, muscular hypotonia, and facial dysmorphic features, hypoplastic male genitalia, and skeletal abnormalities.
A deletion on 11q24.1q24.3 chromosome was identified in a boy with severe intellectual disability, autistic behavior, severe speech delay, focal epileptic seizures, facial dysmorphic features. This anomaly is associated with a well-described genetic syndrome – Jacobsen syndrome, with a variable phenotype in correlation with the size of the deletion. The most common features include growth delay, developmental delay or intellectual disability, characteristic facial dysmorphism, thrombocytopenia or pancytopenia (usually at birth), different malformations (heart, kidney, gastrointestinal tract, genitalia, central nervous system and skeleton). The severity of cognitive deficiency may vary from normal to severe. The psychiatric conditions are represented by attention deficit/hyperactivity disorder, schizophrenia, or bipolar affective disorder. Seizures have been, also, reported in some patients.
Four male patients presented an abnormal methylation pattern of *FMR1* promoter, consistent with a full mutation for Fragile X syndrome. Besides the autistic behavior, all patients had, also, the other characteristic features of fragile X syndrome: intellectual disability (severe, in two patients, moderate, in one child, and mild, in other boy), speech delay, hyperkinetic behavior with aggressivity (in three patients), macrocephaly, macrosomia (in three patients), specific dysmorphic facial features, One child had a familial history of intellectual disability and psychiatric diseases (the patient mother and maternal grandmother with severe intellectual disability and schizophrenia).

P1 performed A.3.2 and participated in A 3.3 and A 3.4.:
P1 received 281 biological samples, 219 from ASD patients and 62 control individuals. P1 will perform sequencing with state-of-the-art technology, such as Illumina HiSeqX-Ten. Due to restrictions imposed by government and limited laboratory logistics in relation to COVID-19 pandemic P1 are experiencing further delay. Once the situation will be improved, we P1 aim at completing these activities. P1 has in various projects across different brain-related disease groups whole genome sequenced 1497 samples. This experience is currently used to develop the data infrastructure and analytical pipeline to analyze the data. P1 will use the infrastructure thus created, for the whole genome sequence data from ASD participants.

P2 performed A.3.2 and participated in A 3.3. and A3.4

Sample processing and DNA isolation

One hundred and seventy-six biological samples were received in this phase, consisting of peripheral blood from 65 children with ASDs, 109 parent samples, and two samples from the siblings of ASDs patients. For the control group, 300 biological samples from healthy children were received.

The biological samples of patients and controls were processed for DNA isolation and long-term storage. Genomic DNA (gDNA) was further extracted using PureLink Genomic DNA Mini Kit (ThermoFisher Scientific) following the manufacturer protocol with minor changes; the quality parameters of gDNA were assessed using a Nanodrop 2000 spectrophotometer (ThermoFisher Scientific) and the quantification was performed by fluorometry with Qubit (ThermoFisher Scientific).

DNA genomic profiling

Array-based comparative genomic hybridization (**array-CGH**) was performed for 248 ASD patients and 180 control individuals. Agilent SurePrint G3 Human CGH Microarray Kit 180K, with a median spacing of 11 kb (in Refseq genes), was used for array-CGH, following the manufacturer's protocol (Agilent Oligonucleotide Array-Based CGH for Genomic DNA Analysis Enzymatic Labeling for Blood, Cells, or Tissues Protocol, Version 8, December 2019). Commercial *Agilent Human Reference DNA* was used as sex-matched reference. The same protocol described in the previous phases was followed: input quantity of DNA 500-1000 ng gDNA; flipped labeling - Cy5-dUTP for reference DNA samples and Cy3-dUTP for patient DNA samples - using SureTag DNA Labeling Kit (Agilent Technologies). The hybridization at 67°C / 24 hours was followed by a two-step post-hybridization washing procedure. The slides were scanned at 3 microns resolution using Agilent SureScan Microarray Scanner System; data were extracted and analyzed using Agilent Cytogenomic Software v.5.1.2.1 with incorporated Feature Extraction software. The raw data from all the hybridized grids were extracted and quality metrics were evaluated. GC correction algorithm and diploid peak centralization were used for data normalization; ADM2 algorithm with an aberration threshold of 6 was used for CNVs calling. The aberration threshold was set at a log2 ratio value 0.30 for at least three consecutive probes. The genomic profiles were also manually evaluated for probes uniformity in the called intervals. CNVs classification was performed according to ACMG guidelines. CNVs annotation was performed using GRCh 37 (hg 19) build. Public resources / databases (UCSC genome browser, DGV, OMIM, DECIPHER, ClinVar, ClinGen Genome Dosage Map, GnomAD SV etc) and scientific papers were used for CNVs annotation and interpretation. Data analysis was performed for 124 patients in phase 3, totaling a number of 195 analyzed ASDs patients per project, by date. Furthermore, the genomic profiling data were correlated with the phenotypic data in order to assess the clinical significance of CNVs.

Ten pathogenic and likely pathogenic CNVs were detected in this stage: six deletions and four duplications. These CNVs involve four syndromic regions: deletion 11q24, deletion 15q13.3, duplication 17p11.2, and duplication 22q11.2. All these syndromes, Jacobsen Syndrome (MIM # 147791), Chromosome 15q13.3 Deletion Syndrome (MIM # 612001), Potocki-Lupski Syndrome (MIM # 610883) and Chromosome 22q11.2 Duplication Syndrome (MIM # 608363) show autism as part of their phenotypic spectrum. Several regions previously reported in neurodevelopmental disorders were involved in genomic imbalances: 2q24.3, 6q12, 15q24.1q24.2, 17p12, and 2q11.1q11.2. As some of these regions are rarely reported in neurodevelopmental or psychiatric disorders, autism included, these findings might bring new insights into rare genomic imbalances contribution to these conditions. A duplication of the entire chromosome Y, except for the pseudoautosomal region Yp, was detected in one patient;

this duplication may be generated by a chromosomal rearrangement (i.e. isodicentric) and needs further cytogenetic investigation for elucidating the chromosomal mechanism underlying the duplication.

All pathogenic/likely pathogenic CNVs were pure deletions or duplications. The pathogenic/likely pathogenic CNVs ranged from ~874 kb to 56 Mb, with a median of 3.2 Mb. The total number of genes altered by the pathogenic/likely pathogenic autosomal CNVs is 377. The genes included in our pathogenic/likely pathogenic CNVs list can be classified into the following molecular functions: binding, catalytic activity, molecular adaptor activity, molecular function regulator, molecular transducer activity, structural molecule activity, translation regulator activity, transporter activity (http://www.pantherdb.org/). Forty patients presented CNVs of uncertain significance (VOUS).

FMR1 gene investigation for trinucleotide repeats associated with Fragile X syndrome by triplet primed PCR (TP-PCR).

The methods chosen for the identification of CGG repeats in *FMR1* gene promotor have been based on the TP-PCR principle reported in the literature. The protocols described in three scientific papers have been taken into account when setting up our TP-PCR protocol (Teo et al., 2012, Rajan-Babu et al., 2015, Tan et al,. 2018).

Twelve experiments were performed for TP-PCR optimization in order to accurately identify the CGG repeats expansion in *FMR1* gene promotor, based on the protocols reported by the above-mentioned papers. Several changes of the original protocols have been performed, including the DNA amount (100ng and 150ng per reaction instead of 50ng), amount of Q Solution (reduced to 75%), dNTPs ratio, primer concentration. As all the above-mentioned experiments led to suboptimal results, new primers with the sequences used by Rajan-Babu (Rajan-Babu et al., 2015) were obtained. These primers have been used in a reaction based on Tan et al., 2018 protocol, using the RotorGene 6000 qPCR equipment (Corbett, Qiagen). Using this new protocol, two experiments have been performed with optimal, expected results, allowing to discriminate de number of trinucleotide repeat expansions between samples. Subsequently, this optimized protocol, have been used for validation on 11 supplementary samples, with good experimental results. The final protocol, including the use of five DNA controls with a different number of trinucleotide repeats (CORIELL), has been performed for *FMR1* promotor investigation in 41 patient samples. For one patient, an expansion over 200 trinucleotide repeats consistent with the full Fragile X mutation, has been detected.

Methylation specific MLPA - MS-MLPA

The screening for abnormal methylation of FMR1 gene promotor was performed by MS-MLPA. One hundred and twenty-six male patient samples were tested in this phase. We used the same MS-MLPA protocol, optimized in the previous phases of the project, and maintained the concentration of the samples at 100ng peripheral blood gDNA in 5 ul volume for each MS-MLPA reaction. The PCR products volume added in reaction for fragment separation by capillary electrophoresis (ABI 3500 Genetic Analyzer) was 0.75 uL. The device parameters were the same as in the previous experiments. Data analysis was performed using the Coffalyser program, the analyzed samples being compared with three reference samples, a positive male control carrier of an abnormally methylated FMR1 promotor region, as well as a negative reaction control. Changes in the methylation status, as well as in the number of copies were determined by comparison with reference samples, as previously reported. Three patients were identified as presenting an abnormal methylation status of the *FMR1* gene indicative of a full mutation for Fragile X syndrome.

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Overview of the progress of work towards the objectives of the project, including milestones and deliverables identified in the project contract. The report must include explanations justifying the differences between the work expected to be carried out in accordance with the project contract and that actually carried out. (max 10.000 characters, including spaces)

Our project **aims** to: improve early recognition and clinical diagnosis of ASD; develop and implement a comprehensive protocol for genetic testing and biomedical imaging; devise recommendations for patient-centered intervention plan; provide research-based knowledge for development of social/school/professional integration programs, and ultimately initiate the establishment the Romanian National Registry for ASDs.

The project **key targets** are:

- optimized protocol for clinical evaluation of ASDs patients;
- imagistic protocol for brain MRI of ASDs patients;
- genetic testing algorithm for ASD patients;
- project database integrating patient clinical and genetic data for the initiation of the Romanian National Registry for ASDs;
- establishment of communication channels and dissemination of results towards patient associations and other suitable stakeholders, general public, healthcare authorities.

Due to the current COVID pandemic situation and to the interdependent nature of the project activities, there were some delays in the control group enrollment, which led to a decreased level of other activities during 2021. By the end of 2021 PP enrolled 300 control individuals, however, most of them in the last semester of 2021.

P1 is currently working to establish the data infrastructure and analytical pipeline to analyze data from whole genome sequencing data. The sequencing efforts have been delayed by the COVID-19 pandemic. This is due to both limited laboratory access (shut down of University labs, sequencing equipment and reagents used for COVID-19 testing), and lack of expert personnel. In 2022, sequencing will resume and less delay is expected.

P2 continued the screening of genomic imbalances by array-CGH and completed array-CGH experiments for the entire patient group; the genomic profiling has been started for the control group also, with 180 individuals tested. The screening for fragile X CGG repeats expansion continued with MS-MLPA being performed for the majority of male patients (187 out of 228). The optimization of fragile X testing by triplet primed PCR was completed and patient testing has started.

The deliverables of this phase are:

- the personal file for each patient – this file includes data about pregnancy, birth, psychomotor development, association of other medical conditions, familial history positive for a neuropsychiatric condition (ASD, developmental delay, intellectual disability, speech delay, hyperkinesia etc.), vaccinations, general clinical examination, anthropometric parameters, dysmorphological features, neurological examination, psychiatric and psychological evaluation, the results of specific investigations (neuroimaging studies – computed tomography, magnetic resonance imaging, electroencephalographic studies, blood tests, ultrasounds etc.);
- a database of the patients – with recorded patient data;
- biological samples collection with blood samples for genetic tests taken from the entire ASD and control groups;
- genomic profiles obtained by chromosomal microarray technique;
- methylation profiles of FMR1 and AFF2 by MLPA technique;
- high resolution melting curves for FMR1 triplet repeat expansion evaluation by TP-PCR;
- scientific papers

International publications in prep/submitted/in review:

1. Sigrun Hope, Aihua Lin, Shahram Bahrami, Linn Rodevand, Oleksandr Frei, Saira J. Hussain, Weiqiu Cheng, Guy Hindley, Heidi Nag, Line Beate Ulstein, Eva Malt, Magdalena Efrim-Budisteanu, Alexey A. Shadrin, Kevin O`Connell, Anders M. Dale, Srdjan Djurovic, Terje Nærland, Ole A. Andreassen, Bidirectional genetic overlap between autism spectrum disorder and cognitive traits", in prep.
2. Sigrun Hope, Aihua Lin, Shahram Bahrami, Oleksandr Frei , Magdalena Efrim-Budisteanu, Linn Rodevand, Eva Malt, Alexey A. Shadrin, Kevin O`Connell , Anders M. Dale , Srdjan Djurovic , Terje Nærland ,Ole A. Andreassen. Shared genetic architecture between autism spectrum disorder and Lonliness. In prep.
3. Shahram Bahrami, Kaja Nordengen, Alexey Shadrin, Oleksandr Frei, Dennis van der Meer, Lars T. Westlye, Ole A. Andreassen, Tobias Kaufmann. Multivariate genome-wide association analysis of the hippocampus formation identifies variants overlapping with major brain disorders" in review
4. Magdalena Budisteanu, Florentina Linca, Lucia Emanuela Andrei, Laura Mateescu, Adelina Glangher, Doina Ioana, Emilia Severin, Rad Florina. Recognition of early warning signs and symptoms by caregivers, general practitioners and paediatricians – the first steps on the road to autism spectrum disorder diagnosis. In review
5. Magdalena Budisteanu, Lucia Emanuela Andrei, Sorina Mihaela Papuc, Adelina Glangher, Rad Florina, Eugen Mihail Hinescu, Aurora Arghir. Neuroimaging studies in children with autism spectrum disorder. In prep.

Details on the exploitation and dissemination of the results and of the activities (max 3.000 characters, including spaces)

Dissemination activities were limited due to COVID-19 pandemic. The project team attended several on line scientific conferences, where scientific communications related to the project were presented (see list of indicators). Two scientific articles were published in 2021.

Indicators:

Indicator	***Unit of measurement***	***Type of scientific publication***[1]	***Description*** *Definition provided by Core indicators 2014-2021 Guideline (https://uefiscdi.gov.ro/eea-norway-grants)*[2]
Number of peer-reviewed scientific publications submitted	Number	Scientific article and conference communication papers (oral presentations and posters)	1.Budisteanu M, Papuc SM, Streata I, Cucu M, Pirvu A, Serban-Sosoi S, Erbescu A, Andrei E, Iliescu C, Ioana D, Severin E, Ioana M, Arghir A. The Phenotypic Spectrum of 15q13.3 Region Duplications: Report of 5 Patients. *Genes*. 2021; 12(7):1025. https://doi.org/10.3390/genes12071025 2. Phenotypic variability of 17q12 microdeletion syndrome – three cases and review of literature. Andreea Țuțulan-Cuniță, Anca Gabriela Pavel, Luiza Dimos,

[1]Gold Open Acces, pending Open Acces, other
[2]Definition provided by Core indicators 2014-2021 Guideline (https://uefiscdi.gov.ro/eea-norway-grants)

			Florina Mihaela Nedelea, Alina Ursuleanu, Anca Teodora Neacșu, Magdalena Budișteanu, Danai Stambouli. Balkan Journal of Medical Genetics. In press 3. Speech problems in children with autism spectrum disorders. Florentina Linca, Doina Ioana, Cristina Anghelescu, Emanuela Andrei, Magdalena Budișteanu. National Conference of Psychiatry, 14-17.07.2021, virtual. 4. Microduplications associated with autism spectrum disorders. M. Budisteanu, S.M. Papuc, A. Erbescu, L. Albulescu , Laura Mateescu, Florentina Linca, Doina Ioana, Cristina Nedelcu, I. Dobrescu, F. Rad, A.Arghir. National Conference of Mental Health of Child and Adolescent. 24-26.11.2021, virtual. 5. Microdeletion associated with autism spectrum disorders. A.Arghir, S.M. Papuc, A. Erbescu, L. Albulescu , Laura Mateescu, Florentina Linca, Doina Ioana, Cristina Nedelcu, I. Dobrescu, F. Rad, M. Budisteanu. National Conference of Mental Health of Child and Adolescent. 24-26.11.2021, virtual. 6. Sindrom de deletie 3q13.31 la un pacient cu autism si tulburare globala de dezvoltare. M. Budisteanu, S. M. Papuc, A. Erbescu, G. Gaina, C Burloiu, A. Arghir. Congresul National de Pediatrie, Craiova, 14-16.09.2021. 7. Genomic profiling in a group of romanian patients with autism spectrum disorders. S. M. Papuc, A. Erbescu, F. Rad, G. Gaina, L. Mateescu, R. Grozavescu, M. Dobre, L. Albulescu, E. Andrei, B. Budisteanu, C. Anghelescu, F. Linca, D. Ioana, I. Dobrescu, M. Budisteanu, A. Arghir. 13th European Cytogenomics Conference, 3-5.07.2021, virtual. 8. Motor development disorders in children with autism spectrum disorders. Magdalena Budișteanu, Florentina Linca, Emanuela Andrei, Doina Ioana, Laura Mateescu, Iuliana Dobrescu, Florina Rad. Excellence in Pediatrics Conference, 2-4.12.2021, virtual.

			9. The psychiatric phenotype of 15q11.2-q13.3 duplications. Magdalena Budisteanu, Sorina Mihaela Papuc, Alina Erbescu, Ioana Streata, Mihai Cucu, Andrei Pirvu, Simona Serban-Sosoi, Iliescu Catrinel, Cristina Anghelescu, Doina Ioana, Mihai Ioana, Aurora Arghir. European Conference of Psychiatry. 10-13.04.2021, virtual. 10. Evaluarea genomica prin microarray a pacientilor cu tulburare de spectru autist. A.Arghir , S.M. Papuc, A. Erbescu, M. Dobre, G. Gaina, L. Albulescu , Emanuela Andrei, Cristina Anghelescu, Doina Ioana, Florentina Linca, Laura Mateescu, Iuliana Dobrescu, Florina Rad, Magdalena Budisteanu. Workshop organizat cu ocazia Zilei autismului, 1.04.2021, virtual. 11. Tulburarile de dezvoltare motorie la copiii cu tulburare de spectru autist. Magdalena Budisteanu, Emanuela Andrei, Cristina Anghelescu, Doina Ioana, Florentina Linca, Laura Mateescu, Iuliana Dobrescu, Florina Rad. Workshop organizat cu ocazia Zilei autismului, 1.04.2021, virtual.
Number of joint, peer-reviewed, scientific publications submitted	Number		Submission confirmation from editorial board
Number of jointly registered applications for Intellectual Property Protection	Number	N/A	Proof of submission and register number from IP office
Number of joint applications for further funding	Number	N/A	Proof of applications submission from the funding body
Number of jobs created	Number	N/A	Project records
Number of (pro) Roma organisations involved in projects	Number	N/A	Semi-annual

Signature
Principal Investigator