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DECISION SUPPORT SYSTEM IN PSYCHIATRY: PAST AND FUTURE

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The review is devoted to one of the principal directions of the development of information technologies in the field of studies of mental illness-decision support systems (DSS). The relevance of this type of programming is due to a modern level of development technologies that fully realize the combination of clinical and neurobiological, including molecular genetic methods. Provides brief information about an independent development, namely the DSS "xGenCloud" capable of real-time selection of an optimal set of tests for genetic analysis based on clinical data with the subsequent automated formation of recommendations related to the therapy of mental diseases by identifying their genetic features susceptible to pharmacokinetics and pharmacodynamics. Refs 49.

Keywords: psychiatry, bioinformatics, decision support systems, professional systems, genetic testing.

СИСТЕМЫ ПОМОЩИ ПРИНЯТИЯ РЕШЕНИЯ В ПСИХИАТРИИ: ПРОШЛОЕ И БУДУЩЕЕ

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Обзор посвящен одному из приоритетных направлений развития информационных технологий в сфере изучения психических заболеваний — системам помощи принятия решений. Актуальность разработки программ такого типа обусловлена современным уровнем развития технологий, позволяющих полноценно реализовать сочетание клинических и нейробиологических, в том числе и молекулярно-генетических, методов обследования. Рассмотрены классификация систем поддержки принятия решения, история применения информационных технологий в психиатрии для диагностики и лечения заболеваний, сложности внедрения и использования. Приведена краткая информация о биоинформационных системах, применяемых в генетике для анализа последовательностей и клинико-генетических корреляций. Приводятся сведения о мировом опыте в области разработки и использования компьютерных программ в психиатрии и о собственной разработке — системе «xGenCloud», способной в режиме реального времени подбирать оптимальный набор тестов для генетического анализа в зависимости от клинических данных с последующим автоматизированным формированием рекомендаций по терапии психических заболеваний с учетом выявленных генетически обусловленных особенностей фармакокинетики и фармакодинамики. Библиогр. 49 назв.

Ключевые слова: психиатрия, биоинформатика, системы помощи принятия решений, экспертные системы.

Medicine of the 21st century is characterized by the rapid integration of computer applications and information systems research projects and clinical practice, while psychiatry like no other medical discipline, it seems alien to the digital processing of the results of specialized psychopathological examination of patients. Unlike most other areas of medi-

cine historically psychiatrists less rely on technology and application of computer software in practice was inappropriate-is it possible to mental illnesses, violation of consciousness, changes in inexhaustible range of emotional manifestations as measured by processing machine, as the main instrument for diagnosing mental disorders is acting psychiatrist, has, in addition to appropriate education, and specific set of personal qualities (logical thinking, and the inclination to reflection, empathy, etc.)[1]. Despite this interest some psychiatrists to being able to use computer programs in research and practical work sporadically became manifest since the mid 20th century [3–6], that is, from the very beginning of the introduction of computers in medicine. One of the first developers of computer programs for Psychiatry [7] enthusiastically assumed that eventually computers will also be in demand for the diagnosis and treatment of patients as a clinical and laboratory research.

Promising were developing decision support systems, widely applicable in other fields of medicine and themselves into several types according to their appointments [8]: a) advising or assisting (leaving a role as consultant for the man) used in clinical practice; b) test and criticizing or opponents have been widely disseminated in the course of training; in the decision of tasks of system analysis) and evaluation used in basic research.

Evolution of technological progress in the field of software reflects the four basic categories of DSS:

1. System of collating information, requiring the active work of the expert (EA) for a final decision. This category includes a searchable database of information (electronic directories, archives, etc.).

2. Clinical systems "trends" or ranges of states with the opportunity to develop a strategy for health care. DSS this category operate on the principle of generating recommendations based on generally accepted and official standards of practice.

3. A system of deductive retrieval on the principle of "logical" tree-selecting responses to consistently offered by questions from the imposed system, knowledge base, you can get automatically made diagnostic or therapeutic recommendations tailored to each patient.

4. Systems multimodel knowledge management using sophisticated models logically display the answer, for example, on the basis of neural networks (mathematical models that mimic some of the biological properties of the nervous system) or analysis of statistical discrimination for accurate diagnosis or prognosis of the disease. Such systems have the ability to use the self-study and fuzzy logic (mathematical representation of uncertainties and ambiguities, which recalls the work of the human mind in decision-making during processing of approximate information).

The first two categories are widely used in practice, but not relevant to the intelligent decision support systems and help execute helper function.

Deductive systems deserve close examination search and multimodel knowledge management.

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[1] In the United States in the period from 1996 to 1997, the survey was 12528 practicing physicians of various specialties on the role of computer technology (registration and recording of clinical data and/or information search on treatment) in their daily work. According to the information received, psychiatrists are least relied on information systems compared with doctors in other specialties [1]. This trend to several factors-the lack of convenient and user-friendly interfaces for psychiatric practice, low levels of computer literacy among psychiatrists, compared with doctors in other specialties, issues of confidentiality and security of a specific number of patients [2].

One of the first DSS, according to available literature, can be considered diagnostic program DIAGNO [9–11], which is based on deductive built "logical trees. Basis of programme DIAGNO-a series of questions with two answers ("yes" or "no") by major diagnostic areas with the subsequent automated formulation of the most likely diagnosis is unique for each clinical case. Three versions of the programme, taking into account changes of clinical criteria and classifications of mental disorders (disease ontology, DSM-III and DSM-IV). DIAGNO developers hoped that this would reduce the time clinicians DSS primary consultation, however, the diagnostic computer program coherence and the private views of the independent expert was about 60 % [11], because an important drawback of the system is the lack of accuracy of data entered when correcting diagnosis due to carelessness and inattention users answers program.

Similarly ("logical tree, but with answer options "yes", "no" and "unknown") operates a modern AGRI-CB-SCID1 (Computer-based Structured Clinical Interview for DSM-IV Axis 1 Disorders) [12], based on clinical criteria for the DSM-IV. The system allows to correlate the survey identified symptoms and syndromes, and if the number of clinical criteria reaches the level required for the installation of the diagnosis, the program automatically generates a report. In the year 2015 was released on-line version of CB-SCID1 with the function of choices of medical appointments.

A fundamentally different method used the developers of Misssouri Standard System of Psychiatry (SSOP) [7; 13], found wide application to address clinical and legal issues in psychiatry. Formalized description of psychopathology, consistent with standard structured surveys or other, the authors compared with conventional texts, descriptions of mental status during the reception of patients. After the aggregation based on linear diskriminant analysis, highlighted eight "categories" of patients, accounting for 95 % of diagnoses. To work with DSS SSOP doctors must fill out two forms describing mental status-source and control. Impaired specified SSOD recognized the limited capacity for clinical practice, primarily to assess the forecast. It is worth mentioning the value of the program to identify patients with different risk groups-non compliance, with suicidal tendencies, aggression, etc., in addition, a large amount of clinical information has become useful in the formulation of similar programmes — such as CAPS (Community Adjustment Profile System) [14], focusing on the recommendations change treatment of individual patient data, comparing it with similar cases, available in the knowledge base of the programme.

A slightly different direction chosen developers SSOD SADDESQ (Slinical decision support system for the diagnosis of the band spectrum disorders) [15], functioning as a "trainer" training for students for the diagnosis of psychotic disorders. The system knowledge base contains clinical data, organized in several ways. Logical tree questions allow you to diagnose with accuracy of 66–82 %, and apparently that is why medical practice system is not implemented.

Several programs have been developed for monitoring the state of the DSS patients and the effectiveness of therapy. System Algorithms for Effective Reporting and Treatment (ALERT) [16] was created by analogy with the principles of work system SSOP, but has the ability to contribute along with the psychopathological variables and data to the subjective assessment of quality of life. In addition, the system provides two ways to enter information for doctors and patients at the specified intervals in time (daily, weekly, etc.). It is assumed that the function of feedback will help to change behavioural strategies (kouping models) in patients that would enhance the effectiveness of treatment and

rehabilitation activities. Since 1999 the ALERT system has been used successfully in the field of health insurance.

The next generation of DSS in addition to recommendations for the diagnosis and therapy includes alerting features based on analysing those or other indicators when making them. Modai et al. [17] and a Luchins et al. [18] describe two programmes, warning physicians about changes in laboratory parameters. Author Chen et al. [19] is a program that monitors the compliance of patients with schizophrenia based on analysis of pharmacy orders, which potentially allows you to change the psihocorrectional event.

On the unification of diagnostics, optimization of the treatment and prevention of recurrent unipolar depression using evidence-based medicine guidelines aims automated programs compTMAP [20], which is developed based on the results of a large-scale digitization was clinical approval project algorithms treat Texas Medication Algorithm (TMAP) [21] with the subsequent successful approbation and validization.

The complexity of implementing the programs listed above is linked to a greater extent from the fact that traditionally, information on psychopathology (clinical history and mental status) is an unstructured texts that are easy to store, but cannot process: natural language clinician does not translate into abstract information for machine analysis. To overcome such difficulties, Eiduson [22] offers store data on psychiatric examination in two ways: in the form of a structured, formalized questionnaire and unstructured text data included in the DSS PsyCHES (Psychiatric Case History Event System) which can perceive narrative history with his organization in units of information called "events". Each event consists of temporary and clinical characteristics as well as the circumstances of the state change. The main feature of the PsyCHES of the system lies in the ability of mathematical modeling of flow prediction of diseases.

Development of computer technologies with the introduction of functions of neural networks has enabled developers to create experimental multi-model DSS, which uses machine learning mathematical models 3: backpropagation neural networks (BPNN), radial basis function neural network (RBFNN) and support vector machine (SVM) [23]. Artificial neural network (ANN)-mathematical model built on the principles of the biological neural networks. ANN is a group of objects-"neurons", connected relationships through entrances and exits. Served at the entrance "neuron" data processed using the activation function and if it exceeds the threshold, the signal is transmitted with this value through the exit to "neuron" in the next layer. As a rule, ANN consists of several layers of "neurons": the first layer "neurons" receives input, following several layers handle activation signals the first layer and transmit their signals the last layer, which produces the result. ANN feature is that they require no programming, and learning. After training a neural network is able to carry out the synthesis and working with incomplete data and partially correct, restoring the missing signals. The multimodel DSS uses neural network with back propagation errors with hyperbolic tangent activation function. To describe the clinical picture used 44 variables collected based on a survey of 400 patients, randomly divided into 4 groups. According to calculations by authors, innovative method allows you to increase the accuracy of diagnosis of mental illness to 98.75 %.

High level diagnosis of endogenous mental illnesses in the long term ensure the widespread adoption of research results in the field of genetics, epigenetics, genomics, proteomics, metabolomics, lipidomics and other biological sciences. Selection and veri-

fication of specific biomarkers[2] of endogenous diseases may open new perspectives to clarify their ethiomechanisms [24; 25]. Multitasking a common algorithm for diagnosis and treatment of endogenous diseases makes them complex and ambiguous nosological boundaries[3] confirmed by numerous studies of molecular-genetic predictors [28–32]. For an account of the whole array of possible cross-interactions of various factors required for specialized DSS. The experience of the developers area of bioinformatics systems for solving the problems of molecular biology, which is conducted on hundreds and most of whom are already in a free on-line access[4], restricted to clinical medicine without involving data about mental disorders. Offered several DSS for differential diagnosis of monogenic diseases accompanied by mental retardation, which include information about optional symptomatology, accompanying basic pathology [45–48]. Basis of algorithm of automated search diagnosis DSS "NeuroGen" and "OftalmoGen" is a method of deterministic linear classification decisive function. The program automatically analyzes the user's input and produces symptoms differential-diagnostic range with a possibility of treatment in case of need to the virtual adviser tasked with analyzing captured data with subsequent narrowing of the differential-diagnostic series.

Promising development of DSS xGenCloud [49] built a modular design with associative rules formed connection phenotypic (psychopathological) characteristics with known variations and polymorphisms involved in the etiopathogenesis of mental illness. Integration of internal services knowledge bases to refill the main open scientific resources ensures timely updating of data. xGenCloud system provides full private introduced information by assigning each clinical observation of complex identification number. Genetic testing panels are being developed taking into account the achievements of psychofarmakogenetics.

References

1. Kemper P., Blumenthal D., Corrigan J. M., Cunningham P. J., Felt S. M., Grossman J. M., Kohn L. T., Metcalf C. E., St. Peter R. F., Strouse R. C., Ginsburg P. B. The design of the Community Tracking Study: A longitudinal study of health system change and its effects in people. *Inquiry*, 1996, vol. 33 (2), pp. 195–206. PMID: 8675282.

2. Sturm R: Datapoints: The role of computer use in different medical specialties. *Psychiatric Services*, 2001, vol. 52, p. 443. PMID: 11274486, DOI: 10.1176/appi.ps.52.4.443.

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[2] Growing interest in biological factors in the etiology of mental disorders indirectly illustrates the fact that the number of publications, search for the keyword "genetics" and "Psychiatry" PUBMED portal on the genetics of mental disorders has steadily increased from 448 articles in 2011 to 3582 in 2015, and 2016 for an incomplete year number of publications exceeded 1690.

[3] Examples include the analysis of one molecular-genetic networks associated with the serotoninsystem. For 72 proteins-known molecular components serotonin system built by the earl of molecular-genetic interactions with other proteins and genes and their indirect interactions (through molecular partner), as well as associations with disease and biological processes. As a result, it was revealed that the associative network serotonin system of the first level contains protein, 1625 1021 gene, disease and 412 737 processes. Associative network of second level includes 7284 protein and gene 4534 [26; 27].

[4] Muscle [33; 34]-multiple comparison of nucleotide and amino acid sequence listings; PHYLIP [35]-package phylogenetic programs; Phylo_win [36]-phylogenetic analysis; Act (Artemis Comparison Tool) [37]-Genomic analysis; Bioconductor is [38]-scale project that provides many separate packages for bioinformatics research; BLAST [39]-search related sequences in the database of nucleotide and amino acid sequence listings; DnaSNP-analysis of DNA sequence polymorphism [40–42]; UGENE is a free Russian tool, multiple nucleotide and amino acid sequence alignment, phylogenetic analysis, annotation, database [43; 44].

3. Meehl P. E. *Clinical Versus Statistical Prediction*. Minneapolis, University of Minnesota, 1962, 149 p.

4. Lieff J. D. *Computer Applications in Psychiatry*. Washington, DC: American Psychiatric Press, 1987, 427 p.

5. Lim R. F. The Internet: Applications for mental health clinicians in clinical settings, training, and research. *Psychiatric Services*, 1996, vol. 47, pp. 597–599. PMID: 8726485, DOI: 10.1176/ps.47.6.597.

6. Huang M. P., Alessi N. E. The Internet and the future of psychiatry. *American Journal of Psychiatry*, 1996, vol. 153, pp. 861–869. PMID: 8659607, DOI: 10.1176/ajp.153.7.861.

7. Sletten I. W., Altman H., Ulett G. A. Routine diagnosis by computer. *American Journal of Psychiatry*, 1971, vol. 127, pp. 1147–1152. PMID: 4925300, DOI: 10.1176/ajp.127.9.1147.

8. Kobrinskii B. A. Sistemy podderzhki priniatiia reshenii v zdravookhranenii i obuchenii [Decision support systems in health and education]. *Vrach i informatsionnye tekhnologii*, 2010, no. 2, pp. 39–45. (In Russian)

9. Spitzer R. L., Gilford L. M. UPDATE: A computer program for converting diagnoses to the new nomenclature of the American Psychiatric Association. *American Journal of Psychiatry*, 1968, vol. 125, pp. 151–152.

10. Spitzer R. L., Endicott J. DIAGNO II: Further developments in a computer program for psychiatric diagnosis. *American Journal of Psychiatry*, 1969, vol. 125, pp. 12–21.

11. Spitzer R. L., Endicott J. Can the computer assist clinicians in psychiatric diagnosis? *American Journal of Psychiatry*, 1974, vol. 131, pp. 522–530. PMID: 4594558.

12. Bergman L. G., Fors U. G. Decision support in psychiatry — a comparison between the diagnostic outcomes using a computerized decision support system versus manual diagnosis. *BMC Med. Inform. Decis. Mak.*, 2008, no. 8, p. 9. DOI: 10.1186/1472-6947-8-9.

13. Sletten I. W., Altman H., Evenson R. C., Cho D. W. Computer assignment of psychotropic drugs. *American Journal of Psychiatry*, 1973, vol. 130, pp. 595–598. PMID: 4699932, DOI: 10.1176/ajp.130.5.595.

14. Evenson R. C., Sletten I. W., Hedlund J. L., Faintich D. M. CAPS: An automated evaluation system. *American Journal of Psychiatry*, 1974, vol. 131, pp. 531–534. PMID: 4819045.

15. Razzouk D., Mari J., Shirakawa I., Wainer J., Sigulem D. Decision support system for the diagnosis of schizophrenia disorders. *Brazilian journal of medical and biological research*, 2006, vol. 39 (1), pp. 119–128. PMID: 16400472, DOI: /S0100-879X2006000100014.

16. Brown G. S., Burlingame G. M., Lambert M. J., Jones E., Vaccaro J. Pushing the quality envelope: A new outcomes management system. *Psychiatric Services*, 2001, vol. 52, pp. 925–934. PMID: 11433110, DOI: 10.1176/appi.ps.52.7.925.

17. Modai I., Sigler M., Kurs R: The computerized labalert system for patient management in clinical care. *Psychiatric Services*, 1999, vol. 50, pp. 869–870, 885. PMID: 10402605, DOI: 10.1176/ps.50.7.869.

18. Luchins D. J., Klass D., Hanrahan P., Qayyum M., Malan R., Raskin-Davis V., Fichtner C. G. Computerized monitoring of valproate and physician responsiveness to laboratory studies as a quality indicator. *Psychiatric Services*, 2000, vol. 51, pp. 1179–1181. PMID: 10970925, DOI: 10.1176/appi.ps.51.9.1179.

19. Chen R. S., Nadkarni P. M., Levin F. L., Miller P. L., Erdos J., Rosenheck R. A. Using a computer database to monitor compliance with pharmacotherapeutic guidelines for schizophrenia. *Psychiatric Services*, 2000, vol. 51, pp. 791–794. PMID: 10828112, DOI: 10.1176/appi.ps.51.6.791.

20. Trivedi M. H., Kern J. K., Grannemann B. D., Altshuler K. Z., Sunderajan P. A Computerized clinical decision support system as a mean of implementing depression guide lines, *Psychaitric Services*, 2004, vol. 55(8), pp. 879–885.

21. Moore T. A., Buchanan R. W., Buckley P. F., Chiles J. A., Conley R. R., Crismon M. L., Essock S. M., Finnerty M., Marder S. R., Miller D. D., McEvoy J. P., Robinson D. G., Schooler N. R., Shon S. P., Stroup T. S., Miller A. L. The Texas Medication Algorithm Project antipsychotic algorithm for schizophrenia: 2006 update. *J. Clin. Psychiatry*, 2007, vol. 68(11), pp. 1751–1762. PMID: 18052569.

22. Eiduson B. T. An approach to retrieval of narrative textin case records. The psychiatric case history event system (PsyCHES). *Methods of Information in Medicine*, 1970, no. 9, pp. 201–210. PMID: 5534332.

23. Suhasini A., Palanivel S., Ramalingam V. Multimodel decision support system for psychiatry problem. *Expert Systems with Applications*, 2011, vol. 38, pp. 4990–4997.

24. Kobeissy F., Alawieh A., Mondello S., Boustany R.-M., Gold N. Biomarkers in psychiatry: how close are we? *Frontiers in Psychiatry*, 2013, vol. 3, pp. 114–115. PMID: 23316174, PMCID: PMC3539768, DOI: 10.3389/fpsyt.2012.00114.

25. Uzbekov M. G., Gurovich I. Ia., Ivanova S. A. Potentsial"nye biomarkery psikhicheskikh zabolevanii v aspekte sistemnogo podkhoda [Potential biomarkers of mental disorders from the standpoint of systems biology]. *Sotsial'naia i klinicheskaia psikhiatriia* [*Social and clinical psychiatry*], 2016, vol. 26, no. 1, pp. 77–94. (In Russian)

26. Ananko E. A., Podkolodny N. L., Stepanenko I. L., Ignatieva E. V., Podkolodnaya O. A., Kolchanov N. A. GeneNet: a database on structure and functional organisation of gene networks. *Nucleic Acids Res.*, 2002, vol. 30, no. 1, pp. 398–401. PMID: 11752348, PMCID: PMC99151.

27. Kolpakov F. A., Ananko E. A., Kolesov G. B., Kolchanov N. A. GeneNet: a database for gene networks and its automated visualization. *Bioinformatics*, 1998, vol. 14, pp. 529–537. PMID: 9694992.

28. Biological insights from 108 schizophrenia-associated genetic loci. *Nature*, 2014, no. 51. 421 p. PMID: 25056061, PMCID: PMC4112379, DOI: 10.1038/nature13595.

29. Costa e Silva J. A. Personalized medicine in psychiatry: new technologies and approaches. *Metabolism*, 2013, vol. 62, suppl. 1, pp. 40–44. PMID: 23018148, DOI: 10.1016/j.metabol.2012.08.017.

30. Hong L. S., Ripke S., Neale B. M., Faraone S. V., Purcell S. M., Perlis R. H., Mowry B. J., Thapar A., Goodard M. E., Witte J. S., Absher D., Agartz I., Akil H., Amin F., Andreasssen, O. A., Anjoriin A., Anney R., Anttila V., Arking D. E., Asherson P. Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. *Nature Genetics*, 2013, vol. 45 (9), pp. 984–994. PMID: 23933821, PMCID: PMC3800159, DOI: 10.1038/ng.2711.

31. Mathers C. D., Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med.*, 2006, vol. 3 (11). 442 p.

32. Moller H. J., Rujescu D. Pharmacogenetics — genomics and personalized psychiatry. *Eur. Psychiatry*, 2010, vol. 25 (5), pp. 291–293. PMID: 17132052, PMCID: PMC1664601, DOI: 10.1371/journal.pmed.0030442.

33. Edgar R. C. MUSCLE: multiple sequence alignment with high accuracy and high throughput. *Nucleic Acids Res.*, 2004, vol. 32 (5), pp. 1792–1797. PMID: 15034147, PMCID: PMC390337, DOI: 10.1093/nar/gkh340.

34. Edgar R. C. MUSCLE: a multiple sequence alignment method with reduced time and space complexity. *BMC Bioinformatics*, 2004, no. 5, 113 p. PMID: 15318951, PMCID: PMC517706, DOI: 10.1186/1471-2105-5-113

35. Felsenstein J. Evolutionary trees from DNA sequences: a maximum likelihood approach. *J. Mol. Evol.*, 1981, vol. 17 (6), pp. 368–376. PMID: 7288891.

36. Gouy M., Guindon S., Gascuel O. SeaView version 4: a multiplatform graphical user interface for sequence alignment and phylogenetic tree building. *Molecular Biology and Evolution*, 2010, vol. 27 (2), pp. 221–224. PMID: 19854763, DOI: 10.1093/molbev/msp259.

37. Carver T. J., Rutherford K. M., Berriman M., Rajandream M. A., Barrell B. G., Parkhill J. ACT: the Artemis Comparison Tool. *Bioinformatics*, 2005, vol. 21 (16), pp. 3422–3423. PMID: 15976072, DOI: 10.1093/bioinformatics/bti553.

38. Gentleman R. *2002 Annual Report for the Bioconductor project, DFCI*. Available at: http://www.bioconductor.org/about/annual-reports/AnnRep2002.pdf (accessed: 16.12.2016).

39. Altschul S., Gish W., Miller W., Myers E., Lipman D. Basic local alignment search tool. *Journal of Molecular Biology*, 1990, vol. 215 (3), pp. 403–410. PMID: 2231712, DOI: 10.1016/S0022-2836(05)80360-2.

40. Rozas J., Rozas R. DnaSP, DNA sequence polymorphism: an interactive program for estimating Population Genetics parameters from DNA sequence data. *Comput. Applic. Biosci.*, 1995, no. 11, pp. 621–625. PMID: 8808578.

41. Librado P., Rozas J. DnaSP v5: A software for comprehensive analysis of DNA polymorphism data. *Bioinformatics*, 2009, no. 25, pp. 1451–1452. PMID: 19346325, DOI: 10.1093/bioinformatics/btp187.

42. Rozas J. DNA Sequence Polymorphism Analysis using DnaSP. *Methods Mol. Biol.*, 2009, vol. 537, pp. 337–350. PMID: 19378153, DOI: 10.1007/978-1-59745-251-9_17.

43. Okonechnikov K., Golosova O., Fursov M. Unipro UGENE: a unified bioinformatics toolkit. *Bioinformatics*, 2012, no. 28, pp. 1166–1167. PMID: 22368248, DOI: 10.1093/bioinformatics/bts091.

44. Golosova O., Henderson R., Vaskin Y., Gabrielian A., Grekhov G., Nagarajan V., Oler A. J., Quiñones M., Hurt D., Fursov M., Huyen Y. Unipro UGENE NGS pipelines and components for variant calling, RNA-seq and ChIP-seq data analyses. *PeerJ*, 2014, no. 2. PMID: 25392756, PMCID: PMC4226638, DOI: 10.7717/peerj.644.

45. Pelz J., Arendt V., Kunze J. Computer assisted diagnosis of malformation syndromes: an evaluation of three databases (LDDB, POSSUM, and SYNDROC). *Am. J. Med. Genet.*, 1996, vol. 63 (1), pp. 257–267. PMID: 8723119, DOI: 10.1002/(SICI)1096-8628(19960503)63:1<257::AID-AJMG44>3.0.CO;2-K.

46. Strømme P. The diagnosis of syndromes by use of a dysmorphology database. *Acta Paediatr Scand.*, 1991, vol. 80 (1), pp. 106–109. PMID: 2028781.

47. Ugarov I. V., Dadali E. L., Evdokimenkov V. A. Informatsionnopoiskovaia diagnosticheskaia sistema dlia nasledstvennykh nervno-myshechnykh zabolevanii [Information and detection diagnostic system for

hereditary neuromuscular disorders]. *Meditsinskaia genetika* [*Medical genetics*], 2004, no. 9, pp. 428–432. (In Russian)

48. Beklemisheva N. A., Khlebnikova O. V., Dadali E. L., Ugarov I. V. Avtomatizirovannaia informatsi-onno-poiskovaia sistema dlia nasledstvennykh boleznei organa zreniia [Automated information and search diagnostic system for hereditary diseases of the vision]. *Meditsinskaia genetika* [*Medical genetics*], 2005, vol. 4, no. 9, pp. 420–424. (In Russian)

49. Ugarov I. V. *Ekspertnaia sistema «xGenCloud» dlia avtomaticheskogo naznacheniia i interpretatsii rezul'tatov geneticheskogo testirovaaniia.* Svidetel'stvo ob ofitsial'noi registratsii programmy dlia EVM № 2013615830, 20 iiunia 2013 g [*Expert system xGenCloud to automatically assign and interpret the results of genetic testing*]. Certificate of official registration of the computer programme N 2013615830, 20 June 2013. (In Russian)

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