Vol. 43 - No. 1 Special Edition 2021

Biologia Serbica

Department of Biology and Ecology,
Faculty of Sciences, University of Novi Sad, Serbia

BELBI 2021

Book of Abstracts
Belgrade BioInformatics Conference 2021
21-25 June 2021, Vinča, Serbia

http://ojs.pmf.uns.ac.rs/index.php/dbe_serbica/index

Biologia Serbica

JUNE 2021
Vol. 43 - No. 1 Special Edition

Biologia Serbica is formerly Review of Research, Faculty of Sciences, Biology Series (1971-2004), published by Department of Biology and Ecology, Faculty of Sciences, University of Novi Sad, Serbia

Aim and Scope

Biologia Serbica (BS) is an international scientific, peer-reviewed, open access journal that publishes original research articles, review articles, and short communications in all areas of biology.

Publisher

Department of Biology and Ecology
Faculty of Sciences
University of Novi Sad
Trg Dositeja Obradovića 2
21000 Novi Sad, Serbia
: +381 21 485 26 59
: +381 21 450 620
www.dbe.uns.ac.rs

Biologia Serbica is published biannually.

Printed by

"Sajnos"
Momčila Tapavice 2,
21000 Novi Sad
+381/21/499-461, +381/21/499-088
sajnosns@gmail.com

Date od publication: June 2018.

Subscription rates

Instructions available at
http://ojs.pmf.uns.ac.rs/index.php/dbe_serbica/index

ISSN 2334-6590

Biologia Serbica

Book of Abstracts
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Volume 43 - No. 1
(Special Edition)
2021

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Precision medicine and COVID-19: importance of host genome profiling and bioinformatics

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Abstract

Clinical picture and course of the disease in patients with COVID-19 vary from asymptomatic to lethal. Precision medicine could discover the cause of this phenomenon by analyzing the individual genomic profiles of the patients.

We aimed to understand a host genetic component of COVID-19 focusing on variants in genes encoding proteases and genes involved in innate immunity, important for susceptibility and resistance to SARS-CoV-2 infection. Also, we wanted to identify phamracogenes and pharmacogenomics markers associated with drugs used for COVID-19 treatment in different clinical protocols in Serbia, and to compare the results with various world populations.

Genotype information of 143 individuals of Serbian origin was extracted from database previously obtained using TruSight One Gene Panel (Illumina). Variants in genes encoding proteases and genes involved in innate immunity were identified and analysed *in silico* (PolyPhen-2, SIFT, MutPred2, Swiss-Pdb Viewer) to predict the impact of the variants to the structure and/or function of proteins. Genotype data from Serbian population was compared with European and 4 super-populations (total 2504 subjects). Data were extracted from VCF files of Phase 3 variant calls of the 1000 Genomes Project (1kGP) sample collection via Ensembl Data Slicer Tool. The level of population genetic variability at each selected loci was examined using the maximal global differences in minor allele frequencies (delta MAF) calculated by subtracting the maximum and the minimum MAF across analyzed population groups, and Fst statistics. Fisher exact test was used to measure differences in genotypes distributions between Serbian and 1kGP populations, applying Bonferoni correction. R software was utilized for genotype data manipulation and statistical calculations.

Based on high alternative allele frequencies in population and the functional effect of the variants, we identified variants in genes encoding proteases and involved in the innate immunity that might be relevant for the host response to SARS-CoV-2 infection. The potential pharmacogenomics markers in pharmacogenes relevant for COVID-19 treatment were also identified. Bioinformatics tools integrated into precision medicine could contribute to better understanding of inter-individual and population-specific genetic susceptibility and resistance to the SARS-CoV-2 infection, therapy response inconsistencies, and could be applied to improve the outcome of the COVID-19 patients.

Keywords:

COVID-19, precision medicine, bioinformatics, host genomics, population pharmacogenomics

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CIP – Каталогизација у публикацији
Библиотека Матице српске, Нови Сад 57
BIOLOGIA Serbica / editor-in chief Milica Matavulj. –
Vol. 34, no. ½ (dec. 2012) - . – Novi Sad : Faculty of Sciences, Department of Biology and Ecology, 2012-. –
Ilustr. ; 28 cm
Dva puta godišnje. – Je nastavak: Зборник радова Природно-математичког факултета. Серија за биологију = ISSN 0352 – 1788
ISSN 2334 – 6590 = Biologia Serbica
COBISS.SR – ID 275725831

ISSN 2334-6590

2021
Vol. 43 - No. 1 Special Edition

Biologia Serbica

ISSN 2334-6590