

UMS
SERIES

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30 MARCH - 01 APRIL / MONA PLAZA Belgrade

EMERGING INFECTIOUS DISEASES:

Are we ready for new evolutionary challenges?

**CONGRESS
PROGRAM**

AND

**E-ABSTRACT
BOOK**

Esteemed colleagues, dear friends,

It is a great pleasure to greet you on the Congress

“EMERGING INFECTIOUS DISEASES: Are we ready for new evolutionary challenges?” of the Serbian Society of Microbiology UMS 2023 SERIES.

from 30th March to 1st April 2023 at the MONA PLAZA hotel in Belgrade.

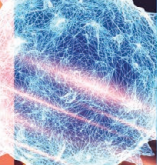
After the great success of the FEMS Microbiology Conference Belgrade 2022, the Serbian Society for Microbiology (UMS) is announcing the start of the UMS Series 2023 – a succession of congresses and symposia regarding current global topics and challenges in the field of microbiology for this year.

The COVID-19 pandemic has shed new light on the importance of advanced DNA technologies and the knowledge of pathogen evolution in the fight against emerging infectious diseases. Gaining the upper hand in this fight is achievable only with the continuous cooperation of microbiologists, clinicians, epidemiologists, biologists, bioinformaticians, representatives of public health and state policy makers.

These new global diagnostic and therapeutic challenges, extremely important in the third decade of the 21st century, will be addressed at the Congress from different sides. This will present an opportunity for microbiologists, epidemiologists and clinicians to recognize the importance of multidisciplinary approach to the prevention of epidemics, their timely detection and the prediction of potential epidemic events.

The Congress's main program sessions will present current topics at the global, regional and national level, while panel discussions will offer listeners the opportunity to exchange knowledge and experience with leading national and foreign experts in the fields of microbiology, molecular biology, infectology, epidemiology, pulmonology, gastroenterology and pediatrics.

We believe that this Congress will present an important next step in strengthening and expanding cooperation at the national and regional levels, thus improving the surveillance of emerging pathogens in Serbia through the implementation of new analytical strategies.



Over sixty international, regional and national experts are with us and will share their experience and expertise with all of us.. The Congress program has been accredited by the Health Council of Serbia as an international congress with the maximum number of CME points, yet another proof of its quality and appropriateness.

We are grateful to all of you who showed large interest and joined the Congress in such large numbers. We believe that attractive topics, high-quality program, dynamic presentation formats and excellent lecturers will prove your choice right. We are certain that you share our belief in the new opportunities ahead of us, aiming towards enhanced professional exchange & development in the SEE region and beyond.

Indeed, we are glad to host you in a pleasant atmosphere of Belgrade beginning April, to benefit from the attractive and dynamic program, exchange knowledge, and, equally important, to refresh existing and establish new contacts with colleagues and friends, while enjoying our hospitality and cherish the moment in one of the best partying cities of Europe.

You are most welcome!!!



Assistant Professor

Irena Arandelović

President of the
Organization Committee



Professor Lazar Ranin

President of the Serbian
Society for Microbiology



Professor

Aleksandra Knežević

President
of the Scientific Committee

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Dr. **Tijana Štajner** — *Serbia*

UMS
SERIES

23



30 MARCH

—
01 APRIL

**CONGRESS
PROGRAM**

DAN 1

ČETVRTAK 30. Mart 2023 / THURSDAY 30th March 2023

DAY 1

08:00-08:45

REGISTRACIJA UČESNIKA / PARTICIPANT REGISTRATION

08:45-09:00

POZDRAVNA REČ ORGANIZATORA I OTVARANJE KONGRESA
OPENING CEREMONY



SESIJA / SESSION

- Savremeni pristup u otkrivanju, praćenju i prevenciji bolesti izazvanih pretećim patogenima
- Cutting-edge approaches to detection, monitoring & prevention of emerging infectious diseases

Moderators: Maja Stanojević, Aleksandra Knežević

9:00
-
10:00

Maja Stanojević / Serbia

- Značaj primene molekularno-bioinformatičkih analiza u otkrivanju, praćenju i predviđanju bolesti izazvanih pretećim patogenima
- The importance of the application of molecular-bioinformatics analyses in the detection, monitoring and prediction of emerging infectious diseases

Aleksandra Knežević / Serbia

- Kako odabrati DNK tehnologiju: direktno sekvenciranje vs. sekvenciranje nove generacije
- How to choose DNA technology: direct sequencing vs. next generation sequencing

Marina Šiljić / Serbia

- Upoznavanje evolucije patogena kroz filogenetske i filodinamičke analize
- Understanding the evolution of pathogens through phylogenetic and phylodynamic analyses

Valentina Ćirković / Serbia

- Putevi širenja patogena: filogeografske analize
- Routes of pathogens spread: phytogeographic analyses

10:00-10:10

LABENA / KOMPANIJSKO PREDAVANJE

Sensitivity and resistance of Gram negative pathogens, the view from green and red corner. / Gorkem Yaman


Labena

10:10-10:25



Pauza za kafu / Coffee break



SESIJA / SESSION

- Preteće mikobakterijske infekcije
- Emerging mycobacterial infections

Moderators: Lidija Ristić, Irena Arandelović

Paolo Miotto / Italy

- Genomika u dijagnostici antimikrobne rezistencije u tuberkulozi
- Genomics in the diagnosis of drug resistance in TB

Matthias Merker / Germany

- Transkontinentalno širenje i evolucija multirezistentnih sojeva *Mycobacterium tuberculosis* – implikacije za kliničku dijagnostiku i javno zdravlje
- Transcontinental spread and evolution of multidrug resistant *Mycobacterium tuberculosis* strains – implications for clinical diagnostics and public health

10:25

-

12:20

Lidija Ristić / Serbia

- Režimi lečenja MDR TB – izazovi sadašnjosti, nada budućnosti
- Regimens to treat MDR TB – today's challenge and hope for the future

Maja Stošić / Serbia

- Implementacija nacionalnog TB programa – izazovi u post-COVID eri
- National TB program implementation – challenges in post COVID era

Irena Arandelović / Serbia

- 15 godina molekularne dijagnostike TB i mikobakterioza u Srbiji
- 15 years of molecular diagnostics of TB and mycobacterioses in Serbia

Ljiljana Žmak / Croatia

- Mikobakterioze: zanemareni javno-zdravstveni problem
- Mycobacterioses: a neglected public health problem

Ivana Dakić / Serbia

- Netuberkulozne mikobakterije kao produktori biofilma
- Nontuberculous mycobacteria as biofilm producers



SESIJA / SESSION

- Virusne zoonoze
- Viral zoonoses

Moderators: Goran Stevanović, Marko Janković

12:20
-
13:55

Marko Janković / Serbia

- Virusne zoonoze – poznati patogeni i nove pretnje
- Viral zoonoses – known pathogens and new threats

Anna Papa-Konidari / Greece

- Primena sekvenciranja nove generacije u evolutivnim analizama virusa Zapadnog Nila
- Next generation sequencing for the evolutionary studies of West Nile virus

Valentina Ćirković / Serbia

- Endemska populaciona dinamika virusa Zapadnog Nila u komarcima sa teritorije Srbije
- Endemic population dynamics of West Nile virus in mosquitoes from the territory of Serbia

Jelena Protić / Serbia

- Hantavirusi na Balkanu: da li nas čekaju nove epidemije?
- Hantaviruses in the Balkans: can we expect new outbreaks?

Goran Stevanović / Serbia

- Epidemija majmunskih boginja: nova lica poznatog patogena
- The monkeypox outbreak: new faces of a known pathogen

Jasmina Poluga / Serbia

- Neuroinfektivni agensi: da li se nešto promenilo?
- Neuroinfectious agents: has anything changed?

14:00-15:00



Ručak / Lunch



SESIJA / SESSION

- *Helicobacter pylori* infekcija i infekcije koje se prenose hranom
- *Helicobacter pylori* infection and foodborne infections

Moderators: Marina Milenković, Dušan Kekić

Aleksandra Sokić-Milutinović / Serbia

- *Helicobacter pylori*: klinički značaj
- *Helicobacter pylori*: clinical importance

Tomica Milosavljević / Serbia

- Smernice za lečenje *Helicobacter pylori* infekcije
- Treatment guidelines for *Helicobacter pylori* infection

Vladimir Milivojević / Serbia

- Antimikrobna rezistencija *Helicobacter pylori*
- Antimicrobial resistance of *Helicobacter pylori*

Dušan Kekić / Serbia

- *Helicobacter pylori* infekcija u Srbiji: molekularna dijagnostika u rutinskoj praksi
- *Helicobacter pylori* infection in Serbia: molecular diagnostics in routine practice

Marina Milenković / Serbia

- Inovativne dijagnostičke metode za *Helicobacter pylori* infekciju
- Innovative diagnostic methods for *Helicobacter pylori* infection

Igor Kljujev / Serbia

- Patogeni koji se prenose hranom - načini širenja i njihova detekcija primenom molekularnih metoda
- Foodborne pathogens - ways of spreading and their detection by molecular methods

15:00

-

16:30

16:30-16:45



Pauza za kafu / Coffee break

16:45-17:45

Panel diskusija Panel discussion

- Implementacija molekularno-bioinformatičkog pristupa u rutinski rad mikrobiološke laboratorije
- Implementation of the molecular-bioinformatics approach to routine microbiological diagnostics

Učesnici / Participants: Paolo Miotto, Matthias Merker, Ljiljana Žmak, Anna Papa-Konidari, Maja Stanojević, Aleksandra Knežević



KRATKE ORALNE PREZENTACIJE SHORT ORAL PRESENTATIONS

Moderators: Ivana Dakić, Marko Janković

Margo Diricks / Germany

- Genomic surveillance of the emerging pathogen *Mycobacterium abscessus*

Ankica Vujović / Serbia

- Changing profile of intrahospital infections during the COVID-19 pandemic in Intensive Care Units - are we in danger of entering the pre-antibiotic era

Milica Šarčević / B&H

- Antimicrobial sensitivity and intrahospital transmission dynamics of *Klebsiella spp.* isolates during a one-year period

Anna Lyapina / Russia

- Immune response induced by the inactivated *C. psittaci* strain in mouse model

Artem Rozhin / Russia

- Synergistic effect of inhibiting bacterial growth when using an antibiotic and silver nanoparticles

Elena Krstevska-Kelepurovska / North Macedonia

- Change of antimicrobial resistance of *Streptococcus agalactiae* to erythromycin and clindamycin over a 10 years southwestern region of Republic of North Macedonia

Emel Mataraci Kala / Turkey

- *In vitro* activities of eugenol+ciprofloxacin combination against carbapenem-resistant Enterobacterales (CRE) strains Isolated from urinary tract infections

Mayram Hacıoğlu / Turkey

- Effects of CSA-44 and CSA-192 in combination with linezolid against *Enterococcus spp.*

Sanja Matić / Serbia

- The protective effect of IFNL3 and IFNL4 gene polymorphisms on development of COVID-19 pneumonia in female patients

Teodora Kukrić / Serbia

- *IN VITRO* ANTIFUNGAL ACTIVITY OF HYDROPHILIC CHOLINE CHLORIDE-BASED NATURAL DEEP EUTECTIC SOLVENTS

Damla Damar Celik / Turkey

- *In vitro* activities of ceftazidime/avibactam alone or in combination with antibiotics against multidrug-resistant *Stenotrophomonas maltophilia* isolates

Maria Pavlova / Bulgaria

- Epidemiological and clinical-laboratory characteristics of the covid 19 infection in Bulgaria during the spring-summer season of the 2022

18:00

19:00



SESIJA / SESSION

- Invazivne gljivične infekcije
- Invasive fungal infections

Moderators: *Ivana Čolović-Čalovski, Aleksandra Barać*

Paul Verweij / Netherlands

- Kako se suočiti sa rezistencijom na antimikotike kao pretnjom za javno zdravlje?
- Tackling the emerging threat of antifungal resistance to human health

Aleksandra Barać / Serbia

- Multidisciplinarni pristup u prevenciji, dijagnostici i lečenju invazivnih gljivičnih infekcija
- A multidisciplinary approach in the prevention, diagnosis and treatment of invasive fungal infections

Sanja Mitrović / Serbia

- Aktuelni pristup u ispitivanju osetljivosti gljiva na antimikotike: referentne metode i komercijalne tehnike
- Current approach in antifungal susceptibility testing: reference methods and commercial techniques

Ivana Čolović-Čalovski / Serbia

- Multirezistentne preteče kvasnice kao dijagnostički izazov: *Candida auris*
- Multidrug-resistant yeasts as a diagnostic challenge: *Candida auris*

Borko Gobeljić / Serbia

- Invazivne gljivične infekcije kod dece sa transplantiranim matičnim ćelijama hematopoeze: klinička slika i terapijske mogućnosti
- Invasive fungal infections in children undergoing hematopoietic stem cell transplantation: clinical presentation and therapeutic options

Stefan Mijatović / Serbia

- Značaj primene multipleks PCR metode u dijagnostici invazivne kandidijaze
- The importance of applying the multiplex PCR method in the diagnosis of invasive candidiasis

9:00
-
10:35

10:35-10:50



Pauza za kafu / Coffee break



SESIJA / SESSION

- Bolničke infekcije
- Healthcare-associated infections

Moderators: Vesna Mijoljević, Ina Gajić

Arjana Tambić-Andrašević / Croatia

- Kako se nositi sa problemom rezistencije na antibiotike u 21. veku?
- How to overcome the problem of antimicrobial resistance in the 21st century?

Snežana Jovanović / Serbia

- Da li smo spremni za izazove antimikrobne rezistencije?
- Are we ready for the challenges of antimicrobial resistance?

Vesna Mijoljević / Serbia

- Značaj multidisciplinarnog pristupa u borbi protiv antimikrobne rezistencije
- The importance of a multidisciplinary approach in the fight against antimicrobial resistance

Ana Kaftandžieva / North Macedonia

- Karbapenem rezistentni sojevi *Klebsiella pneumoniae* – petogodišnja studija
- Carbapenem resistant *Klebsiella pneumoniae* – a five-year study

Ina Gajić / Serbia

- Molekularna epidemiologija infekcija izazvanih multirezistentnim sojevima *Pseudomonas aeruginosa* u Srbiji
- Molecular epidemiology of infections caused by multiresistant strains of *Pseudomonas aeruginosa* in Serbia

Zoran Todorović / Serbia

- Upravljanje antibioticima u bolnici u eri rastuće rezistencije: između kolektivne odgovornosti i istinske saradnje
- Hospital antibiotic stewardship in the era of increasing resistance: between collective responsibility and true collaboration

10:50
-
12:30

12:30-12:45

PFIZER / KOMPANIJSKO PREDAVANJE

Glijivične infekcije, koliko su retke i kako ih dijagnostifikujemo i lečimo?
/ Eleonora Dubljanin, Serbia



12:45-13:05

BIOMERIEUX / KOMPANIJSKO PREDAVANJE

Diagnostic stewardship: peer reviewed evidence to support the selection of the appropriate test for each patient / Barrios Abraham Florencia





SESIJA / SESSION

- Streptokokne infekcije
- Streptococcal infections

Moderator: **Nataša Opavski**

13:05

-

13:50

Nevena Jovičić / Serbia

- Izazovi u dijagnostici pneumokoknih pneumonija kod dece
- Challenges in the diagnosis of pneumococcal paediatric pneumonia

Uroš Karić / Serbia

- Različite kliničke prezentacije pneumokoknih meningitisa
- Different clinical presentations of pneumococcal meningitis

Nataša Opavski / Serbia

- Izmene u distribuciji invazivnih serotipova pneumokoka u Srbiji
- Changes in distribution of invasive pneumococcal disease serotypes in Serbia

13:50-14:05

PFIZER / INDUSTRY SESSION

Distribucija serotipova koji izazivaju pneumokoknu invazivnu bolest kod dece i značaj obuhvata serotipova konjugovanom vakcinom / **Nataša Opavski, Serbia**



14:00-15:00



Ručak / Lunch



SATELITSKI SIMPOZIJUM / SATELLITE SYMPOSIUM

- "Zajedno u borbi protiv antimikrobne rezistencije"
- "Fighting antimicrobial resistance: united we stand"

Moderator: **Irena Arandjelović**

Ana Kaftandžieva / Medicinski fakultet, Univerzitet u Skoplju

Snežana Jovanović / Služba za mikrobiologiju, UKCS

Janko Samardžić / Institut za farmakologiju, kliničku farmakologiju i toksikologiju, MFUB

15:00

-

17:00

Ana Stojanović / KBC "Bežanijska kosa"

Dragana Melentijević / Dom zdravlja "Dr Simo Milošević" Čukarica

Predrag Veljković / Specijalna bolnica "Dr Žutić"

Vesna Kovačević Jovanović / Zdravstveni sistem Medigroup

17:00-17:15



Pauza za kafu / Coffee break

17:15-18:15

Panel diskusija Panel discussion

- Značaj saradnje mikrobiologa i kliničara za uvođenje molekularno-bioinformatičkog pristupa u programe nadzora nad pretećim patogenima
- The importance of cooperation between microbiologist and clinician for the introduction of the molecular bioinformatics approach in surveillance programs for emerging pathogens

Učesnici / Participants: Paul Verweij, Arjana Tambić-Andrašević, Zoran Todorović, Aleksandra Barać, Borko Gobeljić, Nataša Opavski



KRATKE POSTER PREZENTACIJE SHORT POSTER PRESENTATIONS

Moderators: prof. dr Ivana Čolović-Čalovski, asist. dr Stefan Mijatović

Ljiljana Božić / B&H

- Immune response induced by different types of vaccines and SARS-CoV-2 infection in healthcare workers of the University Clinical Center, the Republic of Srpska

Ivan Pavlović / Serbia

- The role of dogs in the contamination of public surfaces in Belgrade with *Giardia intestinalis*

Mario Sviben / Croatia

- *Cryptosporidium spp.* and *Giardia spp.* in raw water used for water supply in Croatia

18:15

-

19:15

Radoslava Savić-Radovanović / Serbia

- The risk of *Listeria monocytogenes* occurrence in sushi

Elena Krstevska / North Macedonia

- Detection of respiratory viruses by Real-time polymerase chain reaction (PCR) in patients with acute respiratory infections in southwestern region of Republic of North Macedonia

Elvira Rozhina / Russia

- Biogenic silver nanoparticles: cytotoxic effect



KRATKE POSTER PREZENTACIJE SHORT POSTER PRESENTATIONS

Moderators: prof. dr Ivana Čolović-Čalovski, asist. dr Stefan Mijatović

Jasmina Nikolovska / North Macedonia

- Most common bacterial isolates from wound specimens

Sanja Jakovac / B&H

- *Klebsiella pneumoniae* resistant to carbapenems in the University Clinical Hospital Mostar

Vuk Marušić / Serbia

- Microbiological profile of surgical site infections after hip and knee arthroplasty in a tertiary surgical hospital

Nevena Milosavljević-Labus / Serbia

- Fluoroquinolone resistance rates of *Escherichia coli* isolates from outpatients urine samples in Medigroup system

Jasna Kureljušić / Serbia

- Listeriosis – zoonotic aspect

Amir Mešić / B&H

- *Helicobacter pylori* infection

Martina Jug / Serbia

- Monkeypox presenting as phimosis: a case report

Nataša Krtolina Banjac / B&H

- Effects of the COVID-19 pandemic on outpatient and in-hospital use of antibiotics and antimicrobial resistance rate

Dragica Đurđević-Milošević / Serbia

- Opportunistic Pathogen *Pseudomonas aeruginosa* – Determination of limit of Detection of PH, EUR.10th Method

Gordana Petrović / Serbia

- A Case Report of a Pediatric Patient with Atypical Form of Chickenpox

Gordana Petrović / Serbia

- Systemic form of cat scratch disease - differential diagnosis of prolonged fever in immunocompetent children

18:15

-

19:15



SESIJA / SESSION

- Preteće parazitoze i vektorske bolesti
- Emerging parasitic infections and vector-borne diseases

Moderators: Tijana Štajner, Snežana Tomanović

9:30
-
10:50

Barbara Šoba Šparl / Slovenia

- Kolaborativni pristup u detekciji autohtone *Dirofilaria repens* u Sloveniji
- The collaborative approach to detection of autochthonous *Dirofilaria repens* in Slovenia

Tijana Štajner / Serbia

- Rizik od infekcije parazitom *Toxoplasma gondii* nakon transplantacije: rezultati prospektivne kohortne studije Nacionalne referentne laboratorije
- Transplantation-related risk of *Toxoplasma gondii* infection: the National Reference Laboratory prospective cohort study results

Zorica Dakić / Serbia

- Importovana malarija u Srbiji: nekad i sad
- Imported malaria in Serbia: then and now

Snežana Tomanović / Serbia

- *Borrelia miyamotoi*, *Neoerlichia micurensis* i *Babesia microti* – retki zoonotski patogeni prenošeni krpeljima u Srbiji
- *Borrelia miyamotoi*, *Neoerlichia micurensis* and *Babesia microti* – emerging zoonotic tick-borne pathogens in Serbia

Gorana Veinović / Serbia

- *Borrelia lusitaniae* i *Borrelia valaisiana* – potencijal za uzrokovanje lajmske borelioze u Srbiji
- *Borrelia lusitaniae* and *Borrelia valaisiana* – potential for causing Lyme borreliosis in Serbia

10:50-11:05



Pauza za kafu / Coffee break



SESIJA / Vakcine SESSION / Vaccines

Moderators: Dragana Vuković, Eleonora Dubljanin

11:05
-
12:20

Miloš Marković / Serbia

- RNK vakcine - novo oružje za kontrolu pretećih infektivnih bolesti
- RNA vaccines - a novel weapon to control emerging infectious diseases

Olivera Lijeskić / Serbia

- Antitela specifična za SARS-CoV-2 nakon iRNK vakcine kao treće doze: homolog i heterologi pristup revakcinaciji
- SARS-CoV-2 specific antibody response after an mRNA vaccine as the third dose: homologous versus heterologous boost

11:05
-
12:20

Eleonora Dubljanin / Serbia

- Da li je vakcina ključni faktor u borbi protiv malarije?
- Is vaccine a game changer in the fight against malaria?

Dragana Vuković / Serbia

- Vakcine protiv tuberkuloze: zašto množina?
- Vaccines against TB: why plural?

Ljiljana Pavlović / Serbia

- Da li je difterija zaboravljena bolest?
- Diphtheria: forgotten disease



SESIJA / Antimikrobna terapija

SESSION / Antimicrobial therapy

Moderators: Aleksandra Šmitran, Jelena Srbljanović

12:20
-
13:35

Alexandra Nascutiu / Romania

- Antimikrobna rezistencija i etička pitanja
- Approach to the ethical issues raised by antimicrobial resistance

Nijaz Tihić / B&H

- Nadzor nad antimikrobnom rezistencijom u Bosni i Hercegovini
- Surveillance of antimicrobial resistance in Bosnia and Herzegovina

Jelena Srbljanović / Serbia

- Eksperimentalna terapija malarije – novi vidici
- Experimental treatment of malaria – newperspectives

Aleksandra Šmitran / RS, B&H

- Potencijal nanočestica i nanokompozita u terapiji infekcija izazvanih multirezistentnim bakterijama
- The potential of nanoparticles and nanocomposites in the therapy of infections caused by multidrug-resistant bacteria

13:35-13:50

PFIZER / KOMPANIJSKO PREDAVANJE

Antimikrobna rezistencija Gram negativnih bakterija, tiha pandemija
Ili oluja u najavi? / Snežana Jovanović, Serbia



14:00-15:00

Panel diskusija Panel discussion

Terapijske mogućnosti i prevencija pretećih infektivnih bolesti
Treatment options and prevention of emerging infectious diseases

Učesnici / Participants: Alexandra Nascutiu, Miloš Marković, Nijaz Tihić, Tijana Štajner

15.00-16.00

KOKTEL I CEREMONIJA ZATVARANJA

FAREWELL RECEPTION AND CLOSING CEREMONY

UMS
SERIES

23



30 MARCH

—
01 APRIL

CONGRESS
ABSTRACTS

Experimental treatment of malaria - new perspectives

Jelena Srbljanović¹, Tijana Štajner¹, Neda Bauman¹, Olivera Lijeskić¹, Igor Opsenica², Bogdan Šolaja³, Branko Bobić¹

-
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With an estimated 247 million cases annually and 619,000 deaths (in 2021) malaria remains a major disease of the developing world and globally the most important parasitic disease. Because of widespread resistance to available antimalarials including chloroquine (CQ) and its derivatives, new drugs are urgently needed. Here we report on the antimalarial efficacy of new 4-aminoquinoline derivatives, with modifications at the linker and at the quinoline nucleus.

In vitro screening was performed by the lactate dehydrogenase assay, based on measurement of the plasmodial lactate dehydrogenase activity in both a CQ-sensitive (3D7) and a CQ-resistant (Dd2) strain of *Plasmodium falciparum*, with a CQ as a control. In vivo antimalarial activity was investigated in C57BL/6 mice infected with *Plasmodium berghei* ANKA strain by the modified Thompson test.

Compounds were first tested for toxicity. A total of 37 compounds were screened in vitro. Of the 22 that passed the first screening, 18 had IC₅₀ values lower than CQ in the Dd2 strain while only one was efficient in the 3D7 strain. However, even 15 compounds showed in vivo activity, significantly ($P < 0.05$) prolonging survival of treated vs. untreated mice. Among these, seven compounds afforded the survival of 20–100% of treated mice up to Day 31, with or without the detection of parasites in peripheral blood.

Most importantly, three of these, including CIAQ1, FCIAQ1 and CIAQ8, afforded survival of 100% of animals, the first two at 80 and 160 mg/kg/day and the last only at 160 mg/kg/day.

Experimental treatment of malaria - new perspectives

Survival was associated with complete parasite clearance, as shown by both microscopy and qPCR. Of note, continuous monitoring of parasitemia allowed the observation of a potentially important phenomenon, that a number of compounds were able to confer resistance to cerebral malaria and afford a switch to hyperparasitaemia to mice prone to the neurological syndrome.

By comparing the antimalarial activity of this group of novel compounds, we found that even minor structural modifications substantially affect activity. The results of this extensive study are important, as they may guide future work involving structural modifications of aminoquinolines, and as a contribution to the knowledge in the field of malarial chemotherapy.

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Eksperimentalna terapija malarije - novi vidici

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Malarija ostaje globalno najznačajnija parazitska infekcija sa procenjenih 247 miliona slučajeva i 619.000 smrtnih slučajeva godišnje (2021.). Zbog široko rasprostranjene rezistencije na dostupne antimalarike, uključujući hlorokvin (CQ) i njegove derivate, hitno su potrebni novi lekovi.

U ovom istraživanju ispitana je potencijalna antimalarijska aktivnost 37 novosintetisanih aminohinolina sa hemijskim modifikacijama na aminohinolinskom jezgru i bočnom lancu. In vitro skrining aktivnosti jedinjenja vršen je kolorimetrijskim esejom laktat dehidrogenaze na dva soja *Plasmodium falciparum*, osetljivim (3D7) i rezistentnim (Dd2) na CQ, uz CQ kao pozitivnu kontrolu. Aktivnost u in vivo sistemu je ispitana na ženjkama miševa soja C57Bl/6 inficiranim ANKA sojem *Plasmodium berghei* primenom modifikovanog Thompson-ovog testa. Ispitivanju aktivnosti jedinjenja prethodila je faza kliničkog praćenja zdravih životinja terapiranih eksperimentalnim jedinjenjima. Od 37 jedinjenja ispitanih u fazi in vitro skrininga, 22 koja su inhibirala $\geq 50\%$ rast bar jednog od dva soja *P. falciparum* odabrana su za titraciju do IC50 vrednosti.

Prema soju rezistentnom na CQ, 18 jedinjenja se pokazalo aktivnijim od CQ, dok je među njima samo jedno jedinjenje bilo aktivnije i prema osetljivom soju. Čak 15 jedinjenja ispitanih u in vivo sistemu značajno je produžilo život inficiranim životinjama u odnosu na kontrolnu grupu ($P < 0.05$).

Među njima, sedam jedinjenja je omogućilo preživljavanje 20–100% tretiranih miševa do dana 31, sa ili bez nalaza parazita u perifernoj krvi. Posebno treba istaći tri jedinjenja koja su dovela do izlečenja svih tretiranih životinja, CIAQ1 i FCIAQ1 (80 i 160 mg/kg/dan) i CIAQ8 (160 mg/kg/dan).



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Preživljavanje je bilo praćeno i kompletnim klirensom parazita što je dokazano mikroskopskim pregledom razmaza kao i qPCR analizom krvi i tkiva jetre preživelih životinja. Važno je pomenuti da je kontinuirano praćenje parazitacije svih tretiranih miševa omogućilo da se zapazi potencijalno znaćajan fenomen.

Naime, neka jedinjenja su omogućila da miševi postanu otporni na razvoj cerebralne malarije i uzrokovala da miševi skloni razvoju neurološkog sindroma tolerišu preživljavanje sa izuzetno velikim brojem parazita. Poređanjem antimalarijske aktivnosti novosintetisanih aminohinolina uoćeno je da i male strukturne promene u velikoj meri menjaju aktivnost. Rezultati ovog opsežnog istraćivanja su od znaćaja za buduća istraćivanja strukturne modifikacije aminohinolina i doprinose proširenju znanja u oblasti hemioterapije malarije.

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