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ANTIRETROVIRAL RESISTANCE AND MOLECULAR EPIDEMIOLOGY OF HIV-1 IN BULGARIA: AN INTEGRATED ANALYSIS OF GENETIC DIVERSITY, PHYLODYNAMICS, AND DEMOGRAPHIC CORRELATIONS

ABSTRACT

of

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The extended version of the dissertation in English can be provided upon personal request to the author.

CONTENTS OF THE ENTIRE DISSERTATION

FREQUENTLY USED ABBREVIATIONS

STI – Sexually transmitted infection
HET – Heterosexuals
MSM - Men who have sex with men
IDU - Person who uses injection drugs
MSM+IDU - MSM with injection drug use
ART – Antiretroviral therapy
3TC – Lamivudine
ABC – Abacavir
AIDS - Acquired immune deficiency syndrome
ART - Antiretroviral therapy
ATV – Atazanavir
AZT/ZDV - Zidovudine/Azidothymidine
c, COBI – Cobicistat
CAB – Cabotegravir
CRF - Circulating Recombinant Forms
D4T – Stavudine
DDI – Didanosine
DOR – Doravirine
DRM – Drug Resistance Mutations
DRV – Darunavir
DTG – Dolutegravir
EFV – Efavirenz
ETR – Etravirine
FDA - Food and Drug Administration
FI - Fusion Inhibitors
FOS-APV, FPV – Fosamprenavir
FTC – Emtricitabine
HAART - Highly Active Antiretroviral Therapy
HIV - Human Immunodeficiency Virus
IDV – Indinavir
INSTI - Integrase Strand Transfer Inhibitors
LPV – Lopinavir
NFV – Nelfinavir
NNRTI - Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI - Nucleoside Reverse Transcriptase Inhibitor
NVP – Nevirapine
PI - Protease Inhibitors
PrEP - Pre-Exposure Prophylaxis
RAL – Raltegravir
RPV – Rilpivirine
RTV – Ritonavir
SDRM - Surveillance Drug Resistance Mutations (for transmitted resistance only) according to WHO 2009 list
SQV – Saquinavir
TAF - Tenofovir Alafenamide
TDF - Tenofovir Disoproxil Fumarate
TDR - Transmitted Drug Resistance
TFV – Tenofovir
TPV – Tipranavir
URF - Unique Recombinant Forms

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INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) was first documented in June 1981, when the US Centers for Disease Control and Prevention (CDC) published reports of rare pulmonary infection caused by Pneumocystis carinii and Kaposi's sarcoma in young homosexual men [MMWR Morb Mortal Wkly Rep. 1981]. By the end of 1981, 337 cases with severe immune deficiency had been registered, marking the beginning of one of the most serious epidemics of modern society. In September 1982, CDC officially introduced the term AIDS, and in 1983, Dr. Françoise Barré-Sinoussi and Prof. Luc Montagnier from the Pasteur Institute isolated the etiological agent - a retrovirus that received the universal designation human immunodeficiency virus (HIV) in 1986 [Barré-Sinoussi F, et al., Science, 1983].

The global HIV epidemic resulted from cross-species transmission of a retrovirus from primates to humans in Central and West Africa through transmission of simian immunodeficiency virus (SIV) [Faria NR, et al., 2014]. HIV-1 is characterized by extremely high genetic variability caused by the lack of corrective mechanisms in reverse transcription, leading to accumulation of multiple mutations and recombinations. As a result, HIV-1 is divided into four main phylogenetic groups: M (major), O (outlier), N (non-M/non-O) and P, each resulting from independent cross-species transmission [Sharp PM, et al., 2011].

Group M is epidemiologically most significant and is responsible for the current pandemic. It includes at least ten genetically distinguishable subtypes: A, B, C, D, F, G, H, J, K and L, as well as multiple circulating recombinant forms (CRFs) and unique recombinant forms (URFs) [Hemelaar J, et al., 2019]. The global distribution of subtypes is highly uneven and is influenced by a number of factors, including the founder effect, socio-economic determinants such as migration and urbanization, as well as circulation in specific risk groups. Subtype C represents 46.6% of all HIV-1 infections globally and predominates in Southern and Eastern Africa, subtype B dominates in North America and Western Europe, while subtype A is most common in Eastern Europe and Central Asia.

According to UNAIDS data, more than 91.4 million people have been infected with HIV since the beginning of the epidemic, and approximately 44.1 million have died from AIDS-related diseases. In 2024, the number of people living with HIV amounts to 40.8 million, with 31.6 million having access to antiretroviral therapy (ART) [UNAIDS, 2025]. The implementation of ART led to a dramatic reduction in mortality and limitation of infection transmission.

Despite therapeutic successes, HIV drug resistance remains a serious risk to treatment sustainability and achieving global AIDS elimination. Resistance results from complex genetic and epidemiological mechanisms that impact both individual and population levels. Two main patterns are distinguished: transmitted drug resistance (TDR) in individuals infected with resistant strains before starting therapy, and acquired resistance developing during treatment with unsuccessful viral suppression [Clutter, D. S., et al., 2016].

Mutations associated with resistance to protease inhibitors (PI), nucleoside (NRTI) and non-nucleoside reverse transcriptase inhibitors (NNRTI) show different patterns of emergence and cross-resistance. Multiple resistance mutations can have cumulative impact on treatment efficacy, requiring precise virtual phenotypic interpretation of genotypic data. Genotypic testing for drug resistance is an established standard in clinical practice, allowing selection of appropriate therapeutic regimens, prevention of mutation accumulation and limitation of archived resistant variant formation [WHO, 2022].

The high genetic variability of HIV-1 and increasing prevalence of drug resistance pose serious challenges to the sustainability of therapeutic strategies. Molecular epidemiological analysis, including phylogenetic reconstruction, molecular clock dating and phylodynamic

modeling, allows tracking of evolutionary history and spatiotemporal dynamics of the epidemic. Identification of transmission clusters and networks through bioinformatics approaches such as ClusterPicker, MicrobeTrace and BEAST enables more precise epidemiological monitoring and targeting of preventive interventions.

Precise molecular and epidemiological monitoring is crucial for adapting clinical strategies and public health strategies at the national level. Integrated analysis of resistance mutations, subtype diversity, phylogenetic relationships and demographic correlations can contribute to treatment personalization and development of national resistance prevention strategies. In Bulgaria, systematic study of HIV-1 molecular epidemiology in the period 1989-2023 can provide valuable information for optimization of therapeutic strategies and improvement of public health policy. The present study is directed toward fulfilling this need through comprehensive molecular epidemiological analysis, including complex characterization of antiretroviral resistance, genetic diversity, phylogenetic relationships and transmission networks of HIV-1 infection in Bulgaria.

RELEVANCE AND SIGNIFICANCE OF THE DISSERTATION

Analysis of the current state of knowledge in the field of HIV-1 epidemiology and antiretroviral resistance reveals complex and multilayered scientific problems with critical importance for global public health. Despite significant achievements in developing effective therapeutic regimens and dramatic reduction in HIV/AIDS mortality, the emergence and spread of drug resistance represents a growing threat to the sustainability of achieved results.

The global picture of the HIV-1 epidemic is characterized by exceptional genetic diversity, including multiple subtypes, and continuously emerging new viral variants. This diversity, combined with regional differences in the distribution of specific genetic forms, creates significant challenges for HIV infection diagnosis, treatment and prevention. Particularly important is the influence of subtype affiliation on drug resistance development, which varies significantly between different geographic regions and population groups.

In the context of Eastern Europe, including Bulgaria, the epidemiological situation is characterized by specific features related to the predominance of certain subtypes, presence of complex recombinant forms and specific transmission patterns. Data from international studies show variability in transmitted drug resistance levels, highlighting the need for targeted national studies for accurate assessment of the local situation.

Molecular epidemiology as a scientific discipline provides unique opportunities for in-depth understanding of HIV-1 epidemic dynamics through integration of phylogenetic analysis, genomic characterization and epidemiological data. Modern bioinformatics approaches for transmission cluster analysis, evolutionary history reconstruction and epidemic event dating open new perspectives for understanding viral spread mechanisms and optimizing preventive strategies.

Despite significant progress in global efforts to control the HIV epidemic, substantial knowledge gaps still exist regarding specific features of the epidemic in Bulgaria. Comprehensive analyses of genetic diversity of circulating HIV-1 variants, detailed drug resistance studies, as well as in-depth phylogenetic studies of evolutionary dynamics and international connections of the local epidemic are needed.

These knowledge gaps have direct impact on the possibilities for optimizing therapeutic strategies, developing effective preventive programs and formulating evidence-based national policy for HIV infection control. Understanding transmission networks and clusters is particularly important, as they can outline priorities in preventive interventions and provide guidance for targeted approaches to specific risk groups.

In light of these considerations, the need for comprehensive and systematic study of HIV-1 molecular epidemiology and antiretroviral resistance in Bulgaria emerges as a critically important scientific priority. Such a study should integrate modern methodological approaches for genetic characterization, phylogenetic analysis, resistance mutation research and epidemiological modeling, with the aim of creating a comprehensive picture of the local epidemic and its specific characteristics.

Results from such a complex study would have substantial application in clinical practice through optimization of therapeutic decisions, in public health - through informing preventive strategies, and in the scientific community - through contribution to global understanding of HIV-1 evolutionary dynamics. Furthermore, such a study would provide the necessary scientific basis for adapting international recommendations to the specific conditions of the Bulgarian epidemiological situation.

AIMS AND OBJECTIVES OF THE DISSERTATION

AIM

To conduct a comprehensive analysis of HIV-1 molecular epidemiology and antiretroviral resistance in Bulgaria through an integrated approach, including genotyping, phylogenetic analysis, characterization of resistance mutations, study of transmission networks and phylodynamic modeling, with the aim of optimizing therapeutic strategies and improving public health policies.

OBJECTIVES

I. ANTIRETROVIRAL RESISTANCE AND MUTATIONAL PROFILES

1. Characterization of antiretroviral resistance.
2. Identification and classification of mutations associated with resistance to PI, NRTI and NNRTI.
3. Analysis of multiple resistance mutations and their cumulative impact on treatment efficacy.
4. Study of cross-resistance within antiretroviral drug classes.
5. Phenotypic interpretation of resistance mutations and prediction of therapeutic response.

II. MOLECULAR CHARACTERIZATION AND GENETIC DIVERSITY

6. Comprehensive sequencing and phylogenetic analysis of the pol gene in HIV-1 isolates from individuals diagnosed in Bulgaria between 1989-2023.
7. Detailed definition and analysis of HIV-1 subtype distribution, circulating and unique recombinant forms in the Bulgarian population.
8. Identification and characterization of new or rare HIV-1 variants and recombinant forms that have been introduced and spread in the country.
9. Molecular characterization of evolutionary relationships between different HIV-1 isolates.
10. Analysis of distribution and evolutionary dynamics of major circulating subtypes.

III. EPIDEMIOLOGICAL DYNAMICS AND PHYLOGENETIC ANALYSIS

11. Reconstruction of phylogenetic trees through maximum likelihood and Bayesian methods for major subtypes.
12. Phylodynamic analysis and dating of introduction of major HIV-1 subtypes in Bulgaria through molecular clock.
13. Analysis of spatiotemporal evolution, geographic distribution and international origin of HIV-1 subtypes in Bulgaria through global phylogenetic approach.
14. Identification and characterization of phylogenetic transmission clusters.
15. Study of transmission networks and spread dynamics between different vulnerable groups.

IV. DEMOGRAPHIC AND EPIDEMIOLOGICAL CORRELATIONS

16. Study of the relationship between drug resistance-associated mutations and demographic characteristics of infected individuals.
17. Study of HIV-1 subtype distribution and drug resistance by transmission categories and vulnerable groups.
18. Analysis of geographic distribution of HIV-1 subtypes and drug resistance-associated mutations in different regions of Bulgaria.
19. Analysis of temporal trends in primary resistance spread in HIV-1 during the study period.

V. CLINICAL APPLICATIONS AND PREVENTIVE STRATEGIES

20. Assessment of clinical significance of identified resistance-associated mutations for antiretroviral therapy selection.
21. Assessment of national practices for monitoring HIV-1 drug resistance and formulation of strategic guidelines for limiting resistant strain spread among vulnerable populations.

CONCLUSIONS

Comprehensive Conclusions on the Epidemiology and Antiretroviral Resistance of HIV-1 in Bulgaria

The present dissertation provides an exhaustive and multifaceted analysis of the molecular epidemiology and antiretroviral drug resistance of HIV-1 in Bulgaria for the period 1989-2023. The integrated approach employed, encompassing genotyping, phylogenetic and phylodynamic analysis, as well as in-depth characterization of resistance mutations and transmission networks, reveals key epidemiological patterns and evolutionary trends. The obtained results have direct implications for optimizing therapeutic strategies and improving public health policies in the country.

I. ANTIRETROVIRAL RESISTANCE AND MUTATIONAL PROFILES

1. The detailed characterization of antiretroviral resistance in Bulgaria demonstrates a low frequency of primary resistance (5.7%) in treatment-naïve patients, corresponding to WHO criteria for a controlled epidemic, confirming the effectiveness of existing primary prevention strategies.
2. The systematic identification and classification of mutations associated with resistance to PI, NRTI, and NNRTI delineates a characteristic mutational profile. High heterogeneity in resistance patterns is observed, including combinations of multiple mutations, with acquired resistance in treated patients being associated with treatment duration and history of prior therapeutic regimens.
3. Analysis of multiple resistance mutations and their cumulative impact on treatment efficacy reveals complex interactions between individual mutations, necessitating a personalized approach to therapeutic regimen selection to achieve optimal clinical outcomes.
4. Investigation of cross-resistance within NRTI and NNRTI antiretroviral drugs demonstrates significant limitations in therapeutic options for certain mutational profiles, requiring adaptation of applied therapeutic algorithms.
5. Phenotypic interpretation of genotypic mutations through contemporary predictive algorithms, such as Stanford HIVDB, provides an evidence-based foundation for predicting therapeutic response and optimizing clinical decision-making in the context of antiretroviral resistance.

II. MOLECULAR CHARACTERIZATION AND GENETIC DIVERSITY

6. Comprehensive sequencing and phylogenetic analysis of 1,654 pol gene fragments collected over a thirty-five-year period creates an extensive molecular database representing a fundamental resource for understanding viral evolution and epidemic dynamics in Bulgaria.
7. The study established the presence of 26 different HIV-1 subtypes, circulating and unique recombinant forms in the Bulgarian population. The observed high genetic heterogeneity reflects complex epidemiological interactions and evidences multiple virus introductions from different geographic regions, underscoring the dynamic nature of the epidemic in the country.

8. Identification and characterization of novel or rare HIV-1 variants and recombinant forms introduced and disseminated in the country enriches knowledge of global molecular epidemiology and emphasizes Bulgaria's significance as an epidemiological crossroads in Southeastern Europe.
9. Application of bioinformatics methods for phylogenetic analysis reveals the presence of complex evolutionary relationships manifested through the formation of local clusters. Multiple international phylogenetic connections were also established, demonstrating the global connectivity of the HIV-1 epidemic.
10. Analysis of genetic variant distribution and evolutionary dynamics of major circulating subtypes reveals different patterns of population growth and temporal trends, reflecting specific epidemiological characteristics and contexts associated with each individual HIV-1 subtype.

III. EPIDEMIOLOGICAL DYNAMICS AND PHYLOGENETIC ANALYSIS

11. Reconstruction of phylogenetic trees through maximum likelihood and Bayesian statistical methods provides a reliable phylogenetic framework with high statistical confidence, validating the evolutionary relationships of Bulgarian isolates.
12. Phylodynamic analysis and dating of major HIV-1 subtype introductions (subtype B, CRF01_AE, CRF02_AG, and subtype C) in Bulgaria through molecular clock establishes the temporal framework of epidemiological events and their correlation with historical and social factors.
13. Combined analysis of spatiotemporal dynamics and global phylogenetic connections of major HIV-1 subtypes in Bulgaria reveals complex migration patterns, numerous independent introductions from different geographic regions, and phylogeographic dissemination routes. Uneven regional distribution was established, with concentration in major urban centers, as well as the presence of localized epidemic outbreaks, emphasizing the importance of this approach for strategic epidemiological planning and control.
14. Identification and characterization of phylogenetic transmission clusters through contemporary bioinformatics tools, such as ClusterPicker, MicrobeTrace, and BEAST, reveal active transmission chains, localized epidemic outbreaks, and provide valuable instrumentation for tracking epidemiological dynamics.
15. Investigation of transmission networks and dissemination dynamics between different vulnerable groups (MSM, HET, IDU) reveals complex interactions and virus spillover between populations, necessitating adapted preventive strategies for specific individual groups.

IV. DEMOGRAPHIC AND EPIDEMIOLOGICAL CORRELATIONS

16. Statistical analysis established significant associations between the presence of resistance mutations and certain demographic variables. The obtained results emphasize the need for applying differentiated approaches in both epidemiological surveillance and personalized HIV infection therapy.
17. Analysis of HIV-1 subtype distribution and resistance mutations by transmission categories and vulnerable groups reveals clearly expressed epidemiological differences between populations, requiring targeted prevention and therapy strategies. The highest resistance frequency was established among MSM, significantly exceeding that in HET

and IDU. Subtype distribution also shows group specificity - subtype B predominates in MSM, while CRF01_AE and CRF02_AG are more common in IDU.

18. Analysis of geographic distribution of HIV-1 subtypes and resistance mutations in Bulgaria reveals pronounced regional differences relevant to epidemiological surveillance and intervention planning. Nearly half of all cases (47.9%) were registered in Sofia, where a higher resistance frequency (29.0%) is also recorded. Subtype CRF01_AE is primarily concentrated in Sofia, CRF02_AG dominates in Plovdiv, while subtype B is more evenly distributed throughout the country. These differences emphasize the need for applying regionally adapted prevention measures and epidemiological surveillance.
19. Analysis of temporal trends in drug resistance dissemination shows relative stability in primary resistance frequency during the analyzed period. This attests to the sustainability and effectiveness of applied antiretroviral therapeutic protocols and emphasizes the importance of continued monitoring for early detection of potential changes in resistance profiles.

V. CLINICAL APPLICATIONS AND PREVENTIVE STRATEGIES

20. Assessment of the clinical significance of identified drug resistance-associated mutations demonstrates direct impact on antiretroviral regimen selection, allowing avoidance of drugs with reduced efficacy. The results support the application of a personalized therapeutic approach based on genotypic analysis, aimed at increasing therapeutic success and limiting further resistance development in Bulgarian clinical practice.
21. Assessment of national practices for monitoring HIV-1 drug resistance confirms the implementation of an integrated epidemiological surveillance system based on routine genotyping of all newly diagnosed cases, aligned with European standards and international recommendations. Based on the analysis, key directions for improving prevention strategies through targeted interventions in at-risk populations were identified, aimed at limiting secondary transmission of resistant viral variants. These results provide a scientifically substantiated framework for developing sustainable, evidence-based policies for resistance control and prophylaxis at the national level.

CONTRIBUTIONS

The scientific contributions from the present research are classified into two main categories according to their originality and significance for the development of genotyping, resistance mutation analysis, and molecular epidemiology research of HIV-1 in Bulgaria.

CONTRIBUTIONS OF ORIGINAL SCIENTIFIC CHARACTER

I. MOLECULAR EPIDEMIOLOGY AND GENETIC DIVERSITY

1. The most comprehensive molecular epidemiological database for HIV-1 in Bulgaria was created with analysis of 1,654 pol sequences from a 35-year period (1989-2023), representing a fundamental resource for research both nationally and globally.
2. Exceptional genetic diversity of HIV-1 in Bulgaria was demonstrated with documentation of 26 different subtypes, CRFs, and URFs, significantly exceeding genetic heterogeneity in some European countries.
3. Seventy-four unique recombinant forms (URFs) were identified in the pol region, including 32 F1B URFs with identical recombinant profiles in the analyzed genetic region, suggesting origin from a common ancestor.
4. The complex molecular chronology and phylogeography of the HIV-1 epidemic in Bulgaria were reconstructed through phylodynamic analysis and molecular clock, establishing the temporal framework of major subtype introductions and revealing numerous independent introductions of individual subtypes - B, C, CRF01_AE, and CRF02_AG from different geographic regions worldwide.

II. ANTIRETROVIRAL RESISTANCE

5. The first comprehensive national analysis of antiretroviral resistance was conducted on 1,654 HIV-1 sequences, establishing an overall frequency of 31.4% with differentiated profiles for PI (1.7%), NRTI (15.4%), and NNRTI (19.3%).
6. A controlled epidemic of transmitted resistance was documented with a frequency of 5.7% in 1,053 treatment-naïve patients, corresponding to WHO criteria for successful epidemiological control.
7. Statistically significant correlations between resistance mutations and demographic characteristics were demonstrated, with highest levels in MSM (35.7%) and lowest in IDU (13.6%).

III. TRANSMISSION CLUSTERS, NETWORK ANALYSES, GEOGRAPHIC AND DEMOGRAPHIC PATTERNS

8. A comprehensive methodology for phylogenetic transmission cluster analysis was applied using a broad range of bioinformatics tools, including ClusterPicker, MicrobeTrace, and BEAST, creating a new standard for molecular epidemiological surveillance.

9. Active HIV-1 transmission networks were mapped, revealing dominance of MSM-MSM connections and significant interpopulation MSM-HET connections, providing a valuable tool for understanding transmission structures and directing epidemiological surveillance.
10. Phylogenetic transmission clusters were analyzed for all major HIV-1 subtypes, revealing subtype-specific patterns of circulating resistance and epidemiological dynamics.
11. Subtype-specific geographic patterns (CRF01_AE concentration in Sofia, CRF02_AG dominance in Plovdiv), gender profiles, and transmission categories (MSM, IDU, heterosexual transmission) were documented, providing a valuable resource for understanding HIV-1 epidemiological dynamics in the country.

CONTRIBUTIONS OF APPLIED SCIENTIFIC CHARACTER

I. CLINICAL PRACTICE AND THERAPEUTIC STANDARDS

12. The national standard for personalized HIV therapy was improved through routine genotypic analysis, providing clinicians with current information on patients' resistance profiles, supporting individualization of first-line therapy, adaptation upon therapeutic failure, and planning of salvage therapeutic regimens.

II. EPIDEMIOLOGICAL SURVEILLANCE AND PREVENTION SYSTEMS

13. A scientific basis for improved epidemiological surveillance and targeted preventive strategies was provided through data on active transmission clusters and networks between risk groups to the Advisory Council on HIV/AIDS and sexually transmitted infections, facilitating informed decision-making for interrupting transmission chains.
14. The effectiveness of national preventive policies was confirmed by demonstrating stability of transmitted resistance and identifying key risk connections, providing an empirical basis for optimizing preventive programs and adapting interventions in different risk groups.

III. STRATEGIC PLANNING AND HEALTH POLICIES

15. A scientific foundation for regionally adapted health strategies was provided through documentation of geographic differences in subtype distribution and resistance, supporting targeted resource allocation and adaptation of therapeutic approaches according to regional characteristics.
16. Data on international phylogenetic connections and migration patterns were provided to the Advisory Council on HIV/AIDS and sexually transmitted infections to inform cross-border cooperation policies and coordinated preventive actions.
17. Comprehensive molecular epidemiological data were generated, providing an empirical basis for updating the national strategy for HIV/AIDS prevention and control and adapting interventions according to established epidemiological trends.

IV. SCIENTIFIC CAPACITY AND INTERNATIONAL COOPERATION

18. Methodological standards for HIV-1 molecular epidemiology were developed, establishing Bulgaria as a regional center through publication of unique data and documentation of rare epidemiological phenomena.
19. National expert competencies were built through specialist training, knowledge transfer, and creation of sustainable capacity for long-term epidemiological surveillance and research.

CONCLUSION:

The present scientific contributions represent the most extensive and in-depth virological research on HIV-1 in Bulgaria, creating a stable scientific foundation for clinical practice, public health, and national policies, while simultaneously enriching international understanding of HIV-1 molecular epidemiology in the Southeastern European region.

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APPENDICES

LIST OF PUBLICATIONS RELATED TO THE DISSERTATION

1.
Ivailo Alexiev, Anupama Shankar, Reneta Dimitrova, Anna Gancheva, Asia Kostadinova, Pavel Teoharov, Elitsa Golkocheva, Maria Nikolova, Mariya Muhtarova, Ivaylo Elenkov, Mariyana Stoycheva, Daniela Nikolova, Tonka Varleva, and William M. Switzer
Origin and spread of HIV-1 in persons who inject drugs in Bulgaria. Infection, Genetics and Evolution 2016, 46: 269-278.
Bioxbio Impact Factor: 2.885
Scimago Journal Rank: Q1
http://www.sciencedirect.com/science/article/pii/S1567134816302015?np=y

2.
Gkikas Magiorkinis, Konstantinos Angelis, Ioannis Mamais, Aris Katzourakis, Angelos Hatzakis, Jan Albert, Glenn Lawyer, Osamah Hamouda, Daniel Struck, Jurgen Vercauteren, Annemarie Wensing, Ivailo Alexiev, Birgitta Åsjö, Claudia Balotta, Ricardo J. Camacho, Suzie Coughlan, Algirdas Griskevicius, Zehava Grossman, Anders Horban, Leondios G. Kostrikis, Snjezana J. Lepej, Kirsi Liitsola, Marek Linka, Claus Nielsen, Dan Otelea, Roger Paredes, Mario Poljak, Elizabeth Puchhammer-Stöckl, Jean Claude Schmit, Anders Sönnerborg, Danica Staneková, Maja Stanojevic, Charles A.B. Boucher, Georgios Nikolopoulos, Tetyana Vasylyeva, Samuel R. Friedman, D.A.M.C. van de Vijver, G. Angarano, M-L. Chaix, A. de Luca, K. Korn, C. Loveday, V. Soriano, S. Yerly, M. Zazzi, Anne-Mieke Vandamme, Dimitrios Paraskevis
The global spread of HIV-1 subtype B epidemic.
Infection, Genetics and Evolution 2016, 46: 169-179.
Bioxbio Impact Factor: 2.885
Scimago Journal Rank: Q1
https://doi.org/10.1016/j.meegid.2016.05.041
https://www.ncbi.nlm.nih.gov/pubmed/27262355

3.
Ivailo Alexiev, Alessandra Lo Presti, Reneta Dimitrova, Brian Thomas Foley, Anna Gancheva, Asya Kostadinova, Lora Nikolova, Silvia Angeletti, Eleonora Cella, Ivaylo Elenkov, Mariana Stoycheva, Daniela Nikolova, Tsetsa Doychinova, Liliya Pekova, Massimo Ciccozzi.
Origin and Spread of HIV-1 Subtype B Among Heterosexual Individuals in Bulgaria
AIDS Res Hum Retroviruses, Vol. 34, No. 3 2017 Dec 19. Published Online:1 Mar 2018
Bioxbio Impact Factor: 1.935
Scimago Journal Rank: Q2
DOI: 10.1089/AID.2017.0167
http://online.liebertpub.com/doi/abs/10.1089/AID.2017.016

4.
Alexiev, I.; M. Campbell, E.; Knyazev, S.; Pan, Y.; Grigorova, L.; Dimitrova, R.; Partsuneva, A.; Gancheva, A.; Kostadinova, A.; Seguin-Devaux, C.; M. Switzer, W. Molecular Epidemiology of the HIV-1 Subtype B Sub-Epidemic in Bulgaria. Viruses 2020, 12, 441.
Bioxbio Impact Factor: 5.048
Scimago Journal Rank: Q1
https://doi.org/10.3390/v12040441
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5.
Alexiev I, Campbell EM, Knyazev S, Pan Y, Grigorova L, Dimitrova R, Partsuneva A, Gancheva A, Kostadinova A, Seguin-Devaux C, Elenkov I, Yancheva N, Switzer WM. Molecular Epidemiological Analysis of the Origin and Transmission Dynamics of the HIV-1 CRF01_AE Sub-Epidemic in Bulgaria. Viruses. 2021; 13(1):116.
Bioxbio Impact Factor: 5,818
Scimago Journal Rank: Q1
https://doi.org/10.3390/v13010116
https://www.mdpi.com/1999-4915/13/1/116#cite

6.
Alexiev I, Mavian C, Paisie T, Ciccozzi M, Dimitrova R, Gancheva A, Kostadinova A, Seguin-Devaux C and Salemi M. Analysis of the Origin and Dissemination of HIV-1 Subtype C in Bulgaria Viruses 2022, 14(2), 263;
https://doi.org/10.3390/v14020263
https://www.mdpi.com/1999-4915/14/2/263
Bioxbio Impact Factor: 3.8
Scimago Journal Rank: Q1

7.
Luka Jovanovic, Marina Siljic, Valentina Cirkovic, Dubravka Salemovic, Djordje Jevtovic, Ivailo Alexiev, Snjezana Zidovec-Lepej, Maja Oroz, Josip Begovac, Dimitrios Paraskevis, Lemonia Skoura, Dimitrios Chaztidimitriou, Evangelia G Kostaki, Snezana Dragas, Brankica Dupanovic, Dan Otelea, Simona Paraschiv, Mario Poljak, Maja M Lunar, Maja Stanojevic
(2022). HIV-1 subtype B spread through cross-border clusters in the Balkans: a molecular analysis in view of incidence trends. AIDS (London, England).
DOI: 10.1097/QAD.0000000000003394
https://journals.lww.com/aidsonline/Abstract/9900/HIV_1_subtype_B_spread_through_cross_border.115.aspx
Bioxbio Impact Factor: 3.8
Scimago Journal Rank: Q1

8.
Alexiev, I., Shankar, A., Pan, Y., Grigorova, L., Partsuneva, A., Dimitrova, R., Gancheva A., Kostadinova A., Elenkov I., Yancheva N., Grozdeva R., Strashimirov D., Stoycheva M., Baltadzhiev I., Doichinova T., Pekova L., Kosmidis M., Emilova R., Nikolova M. and Switzer, W. M. (2023). Transmitted HIV Drug Resistance in Bulgaria Occurs in Clusters of Individuals from Different Transmission Groups and Various Subtypes (2012–2020). Viruses, 15(4), 941.
https://doi.org/10.3390/v15040941
https://www.mdpi.com/1999-4915/15/4/941
Bioxbio Impact Factor: 3.8
Scimago Journal Rank: Q1

Monograph
A monograph related to the dissertation thesis for the award of the Doctor of Sciences degree has been published.
Author: Ivaylo Alexiev Ivanov. Title: "HIV, ANTIRETROVIRAL DRUGS AND RESISTANCE MUTATIONS" Sofia, 2024, ISBN 978-619-04-0323-4

INTERNATIONAL TRAINING AND SPECIALIZATIONS

- 2018: Fulbright Scholarship – Visiting Researcher, University of Florida, Gainesville, USA (5 months)
- 2016: Training in HIV Sequencing and Resistance Mutation Analysis, Luxembourg Institute of Health (2 weeks)
- 2014: International Workshop on Bioinformatics, Virus Evolution and Molecular Epidemiology (VEME), Rome, Italy (1 week)
- 2013: Training in Phylogenetics and NextGen Sequencing (MiSeq, PacBio), CDC, Atlanta, USA (2 months)
- 2009: Sequencing of Viral and Zoonotic Agents, NAMRU-3, Cairo, Egypt (1 week)
- 2006: International Workshop on Bioinformatics, Virus Evolution and Molecular Epidemiology (VEME), Athens, Greece (1 week)

INTERNATIONAL COLLABORATION

- CDC – Atlanta, USA
- University of Florida, USA
- Bio-Medico University, Rome, Italy
- Luxembourg Institute of Health
- UMC Utrecht the Netherlands

AWARDS

- 2017 FULBRIGHT SCHOLARSHIP USA Fulbright Scholarships for Teaching and Research 2018 Topic: Fulbright Scholarships for Teaching and Research Project Leader: Ivaylo Alexiev Period: January-May 2018
- 2017 SCHOLARSHIP from Virology Education Netherlands Topic: Scholarships for participation in the 15th European Meeting on HIV and Hepatitis - Treatment Strategies and Antiviral Drug Resistance, June 7-9, 2017, Rome, Italy Period: June 7-9, 2017
- Best Poster Award from the 12th European Meeting on HIV and Hepatitis, March 26-28, 2014, Barcelona, Spain. The award included funding for the following meeting in 2015.

MEMBERSHIP IN SCIENTIFIC ORGANIZATIONS

- Union of Scientists in Bulgaria
- Bulgarian Society of Virology
- European Society for Translational Antiviral Research (ESAR)
- Euroguidelines in Central and Eastern Europe Network Group (ECEE)

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Ivaylo Aleksiev Ivanov
(Ivailo Alexiev)

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