







# Research group 3.1.3. GROWTH (Group of Researchers for Opportunities in Writing who are Talented in Healthcare)

**APRIL 2023 – MARCH 2024** 

Assist. prof. Tsvetelina Velikova, MD, PhD, MPH

Medical Faculty, Sofia University St. Kliment Ohridski







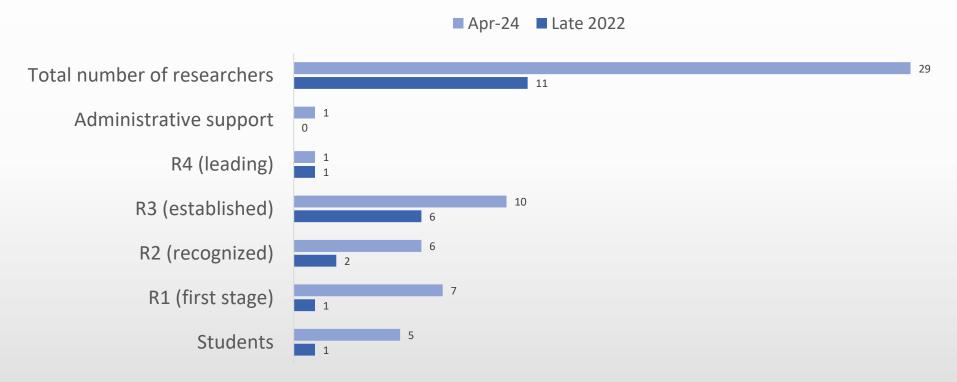
- RESEARCH UNIVERSITY: Sofia University
- Research group №: 3.1.3
- Research group name: GROWTH (group of researchers for opportunities in writing who are talented in healthcare)
- Members: 29 (10 on contract + 19 volunteers)
- Main research area of the group: Medicine, Biology and Public Health
- Budget: EUR 564,102.56
- Period: 2023-2026
- Leading researcher: Tsvetelina Velikova







### 1. Appointment of personnel



No equipment was purchased since it is not needed for the purposes of the research group.



# 3.1.3. GROWTH members



Issa El Kaouri, Medical student V grade

Georgi V. Vasilev, MD, Neurology

**FIRST-STAGE** 

R2 RECOGNIZED R3 ESTABLISHED R4 LEADING

Konstantina Bakopoulou, Medical student V grade

Yoanna Slabakova, MD Infectious diseases Niya Mileva, MD, PhD Cardiology Kremena Naydenova, MD, PhD. Allergology Dimitrina Miteva, PhD, Molecular biology and genetics Snezhina Lazova, MD, PhD, Pediatrics, Pediatric pulmology

Tsvetelina Velikova, MD, PhD, MPH Clinical immunology

Stavros Gerasoudis, Medical student VI grade

Vasilka Malinova, MD Pediatrics Hristo Valkov, MD, PhD. Gastroenterology Milena Peruhova, MD Gastroenterology Milena Gulinac, MD, PhD Clinical pathology Russka Shumnalieva, MD, PhD Rheumatology **TECH SECRETARY** 

Divna Shumanova

Vyara Pavlova, Medical student VI grade

Mariya Kokudeva, MPharm Mincho Vichev, Biochemistry Hristiana Batselova, MD, PhD Epidemiology Georgi H. Vasilev, MD, PhD, Clinical immunology Theodor Todorov, PhD, Molecular biology, genetics Emilia Naseva, PhD, Public health, medical statistics

Ralitsa Gesheva, Medical student VI grade

Dayana Abousaid, MD

Anita Nikolova, Molecular biology Antoaneta Mihova, Immunology, hematology Latchezar Tomov, PhD Mathematics, statistics, IT

Georgi Nikolaev, PhD Cell biology Lyubomir Chervenkov. MD, PhD Diagnostic imaging

10 researchers and 1 technical secretary have a contract at the project (in dark outlines)







### 2. Substantial research activities

- The research program is in the field of medical and biological sciences and public health, with four main areas:
  - (1) biomarkers in immune-mediated conditions;
  - (2) multisystem inflammatory syndrome in children (MIS-C);
  - (3) COVID-19 pandemic and COVID-19 vaccines;
  - (4) Reproductive health



#### WP1 - Biomarkers for WP2 - Multisystem Inflammatory syndrome in children (MISC) immune-mediated conditions 1. Gathering all kinds of data 1. mRNA, protein levels of on MIS-C in Bulgaria cytokines in IBD; 2. National Register of cases 2. Adipokines in rheumatic in the country diseases 3. Algorithm for diagnosis and mRNA of cytokines in asthma management and allergic rhinitis Immune-mediated conditions. COVID-19 WP3 – Epidemiological and WP4 - Reproductive health mathematical modelling studies of COVID-19 1. Establishing algorithms for pandemic in Bulgaria immunological diagnosing and Modeling the ongoing managing pandemic – age, excess 2. Biomarkers in uterine samples mortality, mitigations' effects 3. New protocols for the treatment 2. Assessing the hesitancy to of women with infertility and vaccination reproduction failure 3. Effectiveness of the vaccines









#### • WP 1 Biomarkers in immune-mediated diseases

We are interested in discovering new biomarkers but also in validating and implementing not so popular and established biomarkers into the practice and evaluating their usefulness and significance.

1.1. Patients recruitment; collecting of medical data; frozen biological samples (if	01.2023 -	Completion - 90% (slight delay
applicable);	08.2023	with the publication)
1.2. Performing investigations – assessment of mRNA and protein levels of a wide range of	09.2023 –	• Completion – 40% (on
cytokines in the mucosa and peripheral blood of patients with inflammatory bowel disease	12.2024	schedule)
(IBD); analyzing data; preparing publications		
1.3. Performing investigation - adipokines (i.e., Meteorin-like (Metrnl), Follistatin-like-1	01.2024 -	• Completion – 30% (on
protein (FSTL1), etc.) in samples of patients with rheumatic disease; analyzing data;	06.2024	schedule)
preparing publications		
1.4. Performing investigation of mRNA of a wide range of cytokines in peripheral blood and	06.2024 –	• Completion – 60% (ahead of
nasal lavage of patients with asthma and allergic rhinitis	12.2024	schedule)





World J Clin Cases. 2024 Feb 26; 12(6): 1050-1062.

Published online 2024 Feb 26. doi: 10.12998/wjcc.v12.i6.1050

PMCID: PMC10921308

PMID: 38464930

1s24065978.

#### s Metabolites Are

> Antibodies (Basel). 2023 Dec 8;12(4):81. doi: 10.3390/antib12040081

f Specific Autoantibodies in Neurodegenerative es: Pathogenic Antibodies or Promising rkers for Diagnosis

teva <sup>1 2</sup>, Georgi V Vasilev <sup>2 3</sup>, Tsvetelina Velikova <sup>2</sup>

ov 4 3, Aleksander Georgiev 1, Dimitrina Miteva 4 5,

390/antib13010016.

0303418

7388389

New strategies in the diagnosis and treatment of immune-checkpoint inhibitormediated colitis

<u>Tsvetelina Velikova, Boris Krastev, Milena Gulinac, Miroslav Zashev, Vasko Graklanov, and Milena Peruhova</u>

> Int J Mol Sci. 20 Immunogenicity and Loss of Effectiveness of Navigating the (Biologic Therapy for Inflammatory Bowel Disease Signaling Pathw Patients Due to Anti-Drug Antibody Development

Noyko Stanilov <sup>1</sup>, Tsvetelina Ve

allergi

Childhood Article Menu

Review

Genetic an

Tsvetelina Velikova <sup>1</sup>, Metodija Sekulovski <sup>1</sup> <sup>2</sup>, Monika Peshevska-Sekulovska <sup>1</sup> <sup>3</sup>

#### Diseases

by Dimitrina Miteva 1,2 \(\sigma \operatorname{0}\), Monika Peshevska-Sekulovska 2,3 \(\sigma \operatorname{0}\), Violeta Snegarova 4 \(\sigma\), Milena Peruhova <sup>5</sup> ☑, Georgi H. Vasilev <sup>2,6</sup> ☑ <sup>10</sup>, Georgi V. Vasilev <sup>2,7</sup> ☑, Metodija Sekulovski <sup>2,8</sup> ☑ <sup>10</sup>, Snezhina Lazova <sup>2,9,10</sup> ⊠ , Milena Gulinac <sup>2,11</sup> ⊠, Latchezar Tomov <sup>2,12</sup> ⊠ , Antoaneta Mihova 13 ☐ and Tsvetelina Velikova 2,\* ☐ [0]

gence in ging

Dimitrina Miteva <sup>1</sup>, Snezhina Lazova <sup>2,3</sup> and Tsvetelina Velikova <sup>4,\*</sup>

Review for this Journal

Propose a Special Issue

, Nikolay Sirakov <sup>2</sup> <sup>3</sup>, Gancho Kostov <sup>4</sup>, Tsvetelina Velikova <sup>5</sup> <sup>6</sup>,

#### WP1 – Biomarkers for immune-mediated conditions

- mRNA, protein levels of cytokines in IBD;
- Adipokines in rheumatic diseases
- mRNA of cytokines in asthma and allergic rhinitis

Immune-mediated conditions.
COVID-19

#### WP2 - Multisystem Inflammatory syndrome in children (MISC)

- Gathering all kinds of data on MIS-C in Bulgaria
- 2. National Register of cases in the country
- Algorithm for diagnosis and management

#### WP4 - Reproductive health

- Establishing algorithms for immunological diagnosing and managing
- 2. Biomarkers in uterine samples
- New protocols for the treatment of women with infertility and reproduction failure

#### WP3 – Epidemiological and mathematical modelling studies of COVID-19 pandemic in Bulgaria

- Modeling the ongoing pandemic – age, excess mortality, mitigations` effects
- Assessing the hesitancy to vaccination
- 3. Effectiveness of the vaccines









### • WP 2 Multisystem inflammatory syndrome in children (MIS-C)

2.1. MIS-C patients recruitment, collecting medical data, frozen samples (when	01.2023 –	• Completion - 80%
applicable)	12.2024	(ahead of schedule)
2.2. Creating a register of MIS-C cases in Bulgaria	01.2023 –	• Completion - 50%
	12.2025	(ahead of schedule)
2.3. Immunological characterization of MIS-C patients; performing immunological	01.2023 –	• Completion - 50% (on
and other testing	12.2024	schedule)
2.4. Statistical analysis of the gathered data – focusing on different organs and	01.2023 –	• Completion: 50% (on
systems – i.e., neurological, cardiac, nephrological involvement, etc.	12.2025	schedule)
2.5. Proposing a generally accepted algorithm for the diagnosis and treatment of	06.2025 –	Not yet started.
children with MIS-C	12.2025	
2.6. Preparing informative materials – posts, brochures, key messages for media	01.2025 –	Not yet started.
	12.2025	

# WP2 Published papers





Article

# Clinical and Laboratory Manifestation of Gastrointestinal Involvement in MIS-C: A Single-Center Observational Study

Snezhina Lazova <sup>1,2,\*</sup>, Latchezar Tomov <sup>3</sup>, Dimitrina Miteva doi: 10.3390/medicina59122175.

Cardiovascular Manifestations of Multisystem Inflammatory Syndrome in Children: A Single-Center Bulgarian Study

Niya Mileva <sup>1</sup>, Georgi H Vasilev <sup>2</sup> <sup>3</sup>, Borislav Ganev <sup>4</sup>, Lyubomir Chervenkov <sup>5</sup> <sup>6</sup>, Hristiana Batselova <sup>7</sup>, Iren Tzotcheva <sup>8</sup>, Latchezar Tomov <sup>3</sup> <sup>9</sup>, Tsvetelina Velikova <sup>3</sup>, Snezhina Lazova <sup>3</sup> <sup>8</sup> <sup>10</sup>

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- mRNA, protein levels of cytokines in IBD;
- Adipokines in rheumatic diseases
- mRNA of cytokines in asthma and allergic rhinitis

Immune-mediated conditions. COVID-19

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### • WP 3 COVID-19 pandemic and COVID-19 vaccines

3.1. Analysis of the pandemic in Bulgaria based on the official epidemiological data for	01.2023 - 06.2023	Completion - 100%
morbidity, mortality and vaccinations rate in the country		
3.2. Modeling and predicting the ongoing pandemic with little or no information about	06.2023-12.2023	• Completion - 90% (a slight delay in the
different virus variants and their incubation periods		publications)
3.3. Modeling of the role of different age groups in COVID-19 transmission	06.2023-12.2023	<ul> <li>Completion – 60% (behind the schedule with the publications)</li> </ul>
3.4. Modeling the relationship between an ongoing pandemic and excess mortality	01.2024 – 06.2024	Completion - 50% (on schedule)
3.5. Modeling the influence of COVID-19 on other epidemics (i.e., flu, varicella, etc.)	01.2024 – 06.2024	<ul> <li>Completion - 30% (on schedule)</li> </ul>
3.6. Studying the effects of different mitigation efforts and measures	01.2024 – 12.2024	<ul> <li>Completion - 30% (on schedule)</li> </ul>
3.7. Assessing the hesitancy vs. willingness to vaccinate in different groups of people and patients. Determining and evaluating differences and factors that affect hesitancy	06.2023 – 06.2025	• Completion – 40% (on schedule)
3.8. Effectiveness of vaccines against SARS-CoV-2 in Bulgaria assessed by questionnaires and immunological studies (i.e., humoral and cellular immunity against COVID-19) in different populations	01.2023 – 06.2026	• Completion - 65% (ahead of schedule)



World J Clin Cases. 2023 Oct 16; 11(29): 6974-6983.

Published online 2023 Oct 16. doi: 10.12998/wjcc.v11.i29.6974

PMCID: PMC10631421

PMID: 37946767

Applications of time series analysis in epidemiology: Literature review and our experience during COVID-19 pandemic

Latchezar Tomov, Lyubomir Chervenkov, Dimitrina Georgieva Miteva, Hristiana Batselova, and Tsvetelina Velikova

Latchezar P. Tomov<sup>1</sup>(⋈), Hristina Batselova<sup>2,3</sup>, and Tsvetelina Velikova<sup>4</sup>(

Peer-Review Record

World Journal of Clini Open Access Review

DOI: 10.5306/wjco.v14.i9.343

Effectiveness and safety of COVID-19 va oncological diseases: State-of-the-art

Nedelcho Ivanov, Boris Krastev, Dimitrina Georgieva Miteva, Hri Tsvetelina Velikova

COVID

> World J Exp Med. 2023

Iren Tzocheva <sup>5</sup>, Tsvetelina Velikova

Endothelial Dysfunction aria i regulation control to Patients with Thrombophilia: A Narrative Review

Biomedicines 2023, 11(9), 2458; https://doi.org/10.3390/biomedicines11092458

by Metodija Sekulovski <sup>1,2,\*</sup> <sup>☑</sup> <sup>⑤</sup>, Niya Mileva <sup>3</sup> <sup>☑</sup>, Lyubomir Chervenkov <sup>4</sup> <sup>☑</sup> <sup>⑥</sup>. Monika Peshevska-Sekulovska <sup>2,5</sup> ☑ <sup>1</sup> Georgi Vasilev Vasilev <sup>2,6</sup> ☑. Georgi Hristov Vasilev <sup>2,7</sup> ⊠ <sup>(1)</sup>, Dimitrina Miteva <sup>2,8</sup> ⊠ <sup>(1)</sup>, Latchezar Tomov <sup>2,9</sup> ⊠, Snezhina Lazova <sup>2,10,11</sup> ☑ <sup>0</sup>. Milena Gulinac <sup>2,12</sup> ☑ and Tsvetelina Velikova <sup>2</sup> ☑ <sup>0</sup>

#### COVID 19-RELATED FACTORS THAT INFLUENCE THE DEVELOPMENT OF PNEUMOMEDIASTINUM

Apr 2023 · Anaesthesiology and ... ·

Lab: GROWTH study group

orld I Clin Cases 2023 Mar 6:11(7):1528-1548

Velikova

-2 Variant-Specific Gastrointestinal Symptoms of

Review > Biomedicines. 2023 Oct 17;11(10):2813. doi: 10.3390/biomedicines11102813.

**Blood Coagulation and Thrombotic Disorders** following SARS-CoV-2 Infection and COVID-19 **Vaccination** 

Role of children i Metodija Sekulovski 1 2, Niya Mileva 3, Georgi Vasilev Vasilev 2 4, Dimitrina Miteva 2 5, mathematical mc Milena Gulinac 2 6, Monika Peshevska-Sekulovska 2 7, Lyubomir Chervenkov 8, Hristiana Batselova <sup>9</sup>, Georgi Hristov Vasilev <sup>2</sup> <sup>10</sup>, Latchezar Tomov <sup>2</sup> <sup>11</sup>, Snezhina Lazova <sup>2</sup> <sup>12</sup> <sup>13</sup> Latchezar Tomov <sup>1</sup>, Hristi Dobrin Vassilev <sup>14</sup>, Tsvetelina Velikova <sup>2</sup>

> The End or a New Era of Development of SARS-CoV-2 Virus: Genetic Variants Responsible for Severe COVID-19 and Clinical Efficacy of the Most Commonly Used **Vaccines in Clinical Practice**

Dimitrina Miteva <sup>1</sup>, Meglena Kitanova <sup>1</sup>, Hristiana Batselova <sup>2</sup>, Snezhina Lazova <sup>3</sup> <sup>4</sup>, Lyubomir Chervenkov <sup>5</sup>, Monika Peshevska-Sekulovska <sup>6 7</sup>, Metodija Sekulovski <sup>7 8</sup>, Milena Gulinac <sup>9</sup>, Georgi V Vasilev <sup>10</sup>, Luchesar Tomov <sup>11</sup>, Tsvetelina Velikova <sup>7</sup>

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### • WP 4 Reproductive health

Focus on improving the diagnosis of the immune-mediated factors for infertility, establishing uniform protocols for treatment and follow-up and increasing the results of assisted reproductive technologies (ART).

4.1 Analysis of the current concepts on diagnostics and therapy of reproductive diseases	01.2024 – 06.2024	• Completion - 50% (on schedule)
4.2 Assessing useful biomarkers and algorithms for diagnosis and management of immune-mediated reproductive failure (i.e., evaluating the current, improving and identifying new ones etc.)	06.2024 – 06.2025	Not yet started.
4.3. Assessing the significance of investigating immune biomarkers locally in uterine samples and comparing them with the peripheral blood markers	01.2025 – 12.2025	Not yet started.
4.4. Creating and evaluating new protocols for immunotherapy (i.e., IVIG, corticosteroids, etc.) in women with infertility	01.2025 – 06.2026	Not yet started.

# WP4 Published papers

Review

> Antibodies (Basel). 2023 Mar 2;12(1):20. doi: 10.3390/antib12010020.

## Intravenous Immunoglobulins as Immunomodulators in Autoimmune Diseases and Reproductive Medicine

Tsvetelina Velikova <sup>1</sup>, Meto Monika Peshevska-Sekulov

Review

> Antibodies (Basel). 2023 Dec 6;12(4):79. doi: 10.3390/antib12040079.

Navigating the Challenges of Gluten Enteropathy and Infertility: The Role of Celiac-Related Antibodies and Dietary Changes

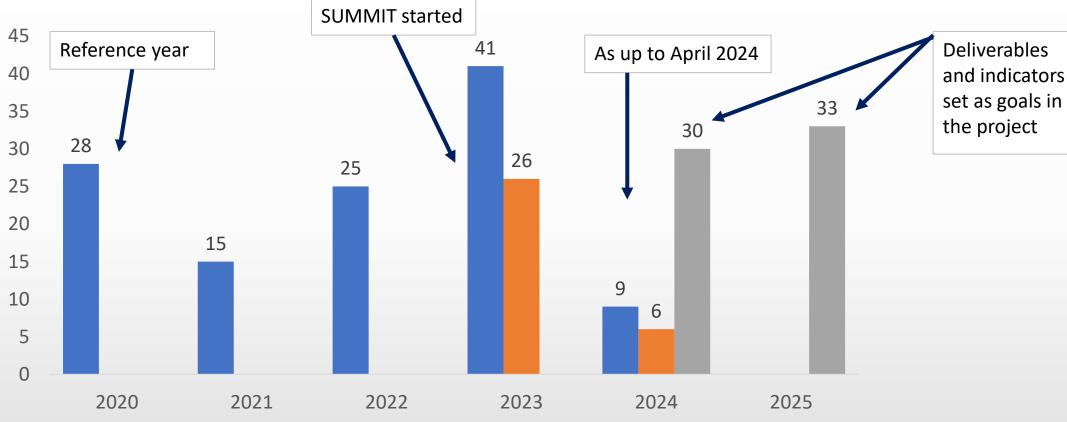
Monika Peshevska-Sekulovska <sup>1 2</sup>, Milena Gulinac <sup>3</sup>, Radoslav Rangelov <sup>4</sup>, Desislava Docheva <sup>4</sup>, Tsvetelina Velikova <sup>1</sup>, Metodija Sekulovski <sup>1 4 5</sup>





#### SOFIA UNIVERSITY -MARKING MOMENTUM FOR INNOVATION AND TECHNOLOGICAL TRANSFER





- Total number of publications in referenced databases (i.e., Scopus, WoS)
- Number of publications in journals indexed in WoS citing the project
- Number of planned publications in journals indexed in WoS citing the project





#### SOFIA UNIVERSITY -MARKING MOMENTUM FOR INNOVATION AND TECHNOLOGICAL TRANSFER



"Make having fun a top priority. Depriving yourself of fun leads to burn out, not success."

**Dave Crenshaw** 







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