



GOCE DELCEV UNIVERSITY - STIP  
FACULTY OF MEDICAL SCIENCES



International symposium at  
Faculty of medical sciences

# **CURRENT ACHIEVEMENTS AND FUTURE PERSPECTIVES IN MEDICAL AND BIOMEDICAL RESEARCH**



STIP, 24 NOVEMBER 2015  
MULTIMEDIA CENTRE – UGD, STIP

INTERNATIONAL SYMPOSIUM AT FACULTY OF MEDICAL SCIENCES  
“Current achievements and future perspectives in medical and biomedical research”

SCIENTIFIC PROGRAM

November 24, 2015 - Stip

8:30 – 9:00

**Registration**

9:00 – 9:15

Rector / Vice rector/Dean

**SESSION 1**

**Chair: Prof. Emilija Janevik Ivanovska**

**Co-chair: Ass. Prof. Elena Drakalska**

9:15 – 9:35

**Ass. Marija Darkovska Serafimovska**  
Macedonian agency of drug and medical  
devices, Director  
University Goce Delcev Stip  
Republic of Macedonia

*Step forward of Macedonian agency for medicines and medical devices, establishment and strategic plan for development*

9:35 – 9:55

**Assoc. Prof. Zorica Arsovska Sarafinovska**  
Institute of Public Health of the  
Republic of Macedonia, Skopje,  
University Goce Delcev Stip  
Republic of Macedonia

*Adherence to Therapy: A Modern Pharmacotherapeutic Approach*

9:55 – 10:15

**Prof. Biljana Gjorgjeska**  
University Goce Delcev Stip  
Republic of Macedonia

*Use of disinfectants and antiseptics in selected health institutions in Republic of Macedonia*

10:15 – 10:35

**Assoc. Prof. Bistra Angelovska**  
University Goce Delcev Stip  
President of Pharmaceutical Chamber  
of Macedonia. Republic of Macedonia

*Code of Ethics for Pharmacists – Pharmaceutical Chamber of Macedonia*

10:40 – 11:10

**Coffee break**

**Poster presentation**

**Chair: Prof. Milka Zdravkovska**  
**Co-chair: Ass. Prof. Darinka Gjorgieva Ackova**

10:10 – 11:50

**Prof. Neven Zarkovic**  
Rudjer Boskovic Institute, Croatia

*4-Hydroxynonenal – major bioactive marker of lipid peroxidation*

11:50 – 12:10

**Assoc. Prof. Tatjana Ruskovska** University  
Goce Delcev Stip Republic of Macedonia

*Nicotinamide adenine dinucleotide biosynthesis and consumption in dysfunctional white adipocytes*

12:10 – 12:30

**Prof. Rubin Gulaboski** University  
Goce Delcev Stip Republic of Macedonia

*New insights into the chemistry and functions of Coenzyme Q*

12:30 – 12:50

**Assoc. Prof. Darko Bosnakovski**  
University Goce Delcev Stip  
Republic of Macedonia

*Genetically modified systems to study muscular dystrophies*

12:50 – 14:00

**Coffee break**

**Poster presentation**

**Chair: Assoc. Prof. Cena Dimova**  
**Co-chair: Ass. Prof. Nevenka Velickova**

14:00 – 14:40	<b>Prof. Lia Rimondini</b> Università del Piemonte Orientale, Novara, Italy	<i>Counteracting microbial biofilm formation onto dental materials</i>
14:40 – 15:00	<b>Prof. Elizabeta Zisovska</b> Agency for Quality and Accreditation of Healthcare Institutions, Skopje, Republic of Macedonia	<i>The endless potential of the umbilical cord blood for investigation, research and treatment</i>
15:00 – 15:20	<b>Ass. Misko Milev</b> University Goce Delcev Stip Republic of Macedonia	<i>The cytokinesis-blocked micronucleus assay: Good choice for detection and evaluation of genotoxicity in human cells</i>
15:20 – 15:40	<b>Prof. Lence Miloseva</b> University Goce Delcev Stip Republic of Macedonia	<i>Multiple predictive model for clinical and subclinical depression in adolescence</i>
15:40 – 16:00	<b>Coffee break</b>	<b>Poster presentation</b>

#### SESSION 4

**Chair: Assoc. Prof. Darko Bosnakovski**  
**Co-chair: Ass. Prof. Katarina Smilkov**

16:00 – 16:40	<b>Prof. Adriano Duatti</b> University of Ferrara, Ferrara, Italy	<i>Molecular imaging and radionuclide therapy of prostate cancer</i>
16:40 – 17:00	<b>Assoc. Prof. Vaso Taleski</b> University Goce Delcev Stip Republic of Macedonia	<i>Where Nanotechnology and Nanomedicine meet – Applications and Potential Risks</i>
17:00 – 17:20	<b>Dr. Aleksandar Cvetkovski</b> University Goce Delcev Stip Republic of Macedonia	<i>The role of molecular cocrystals in drug development</i>
17:20 – 17:40	<b>Prof. Emilija Janevik Ivanovska</b> University Goce Delcev Stip Republic of Macedonia	<i>Drug development based on radiolabeled antibodies</i>
17:40 – 18:00	<b>Closing remarks</b>	

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***Gratitude is expressed to Alkaloid AD Skopje and Fitofarm for the financial support.***

# INTERNATIONAL SYMPOSIUM AT FACULTY OF MEDICAL SCIENCES

## “Current achievements and future perspectives in medical and biomedical research”

November 24, 2015 – Stip

ORAL PRESENTATIONS

- 1. Step forward of Macedonian Agency for medicines and medical devices. Establishment and strategic plan for development**  
*Author:* Marija Darkovska- Serafimovska
- 2. Adherence to Therapy: A Modern Pharmacotherapeutic Approach**  
*Author:* Zorica Arsovska Sarafinovska
- 3. Use of disinfectants and antiseptics in selected health institutions in Republic of Macedonia**  
*Author:* Biljana Gjorgjeska
- 4. Code of Ethics for Pharmacists – Pharmaceutical Chamber of Macedonia**  
*Author:* Bistra Angelovska
- 5. 4-Hydroxynonenal – major bioactive marker of lipid peroxidation**  
*Authors:* Neven Zarkovic, Kamelija Zarkovic
- 6. Nicotinamide adenine dinucleotide biosynthesis and consumption in dysfunctional white adipocytes**  
*Authors:* Prof. Tatjana Ruskovska, David Bernlohr
- 7. New insights into the chemistry and functions of Coenzyme Q**  
*Authors:* Rubin Gulaboski, Valentin Mirceski, Ivan Bogeski, Sasa Mitrev, Kokoskarova Pavlinka, Velo Markovski, Reinhard Kappl, Markus Hoth
- 8. Genetically modified systems to study muscular dystrophies**  
*Author:* Darko Bosnakovski
- 9. Counteracting microbial biofilm formation onto dental material**  
*Author:* Lia Rimondini
- 10. The endless potential of the umbilical cord blood for investigation, research and treatment**  
*Author:* Elizabeta Zisovska
- 11. The cytokinesis-blocked micronucleus assay: Good choice for detection and evaluation of genotoxicity in human cells**  
*Authors:* Misko Milev, Velickova N., Petrova B., Gorgieva P., Nedeljko B.,
- 12. Multiple predictive model for clinical and subclinical depression in adolescence**  
*Authors:* Lence Miloseva, Tatjana Vukosavljevic-Gvozden
- 13. Molecular Imaging and therapy with radionuclides of prostate cancer**  
*Author:* Adriano Duatti
- 14. Where Nanotechnology and Nanomedicine meet – Applications and Potential Risks**  
*Authors:* Vaso Taleski, Darko Bosnakovski, Milka Zdravkovska, Velo Markoski, Zdenka Stojanovska, Svetlana Jovevska
- 15. The role of molecular cocrystals in drug development**  
*Author:* Aleksandar Cvetkovski
- 16. Drug development based on radiolabeled antibodies**  
*Author:* Emilija Janevik-Ivanovska

# INTERNATIONAL SYMPOSIUM AT FACULTY OF MEDICAL SCIENCES

## “Current achievements and future perspectives in medical and biomedical research”

November 24, 2015 – Stip  
POSTER PRESENTATIONS

1. **Correlation between dynamic balance and gait parameters in patients with ischemic stroke in the chronic period**  
*Authors:* Danche Vasileva, Daniela Lubenova, Marija Mihova, Ivan Maznev, Lence Nikolovska, Zhu Jihe;
2. **Effect of kinesitherapy on physical activity in patient with Guillain-Barré syndrome**  
*Authors:* Antoaneta Dimitrova, Kristin Petrova Grigorova, Daniela Lubenova, Danche Vasileva, Milena Nikolova;
3. **Case Report :  
Oligoasthenoteratozoospermia, treatment with acupuncture**  
*Authors:* Jihe Zhu, Blagica Arsovska, Dance Vasileva, Andrijana Sterjovska-Aleksovska, Kristina Kozovska;
4. **Treatment of cervical spondylosis with acupuncture**  
*Authors:* Kristina Kozovska, Jihe Zhu, Blagica Arsovska, Andrijana Sterjovska-Aleksovska;
5. **Effect of kinesitherapy on static and dynamic balance in patient after vertebral basilar system stroke**  
*Authors:* Milena Nikolova, Antoaneta Dimitrova, Danche Vasileva, Daniela Lubenova, Kristin Petrova Grigorova;
6. **Malignant pleural effusions in lung cancer: the condition during the disease**  
*Authors:* Marija Karakolevska-Ilova, Elena Simeonovska Joveva, Aleksandar Serafimov, Lidija Petrovska;
7. **Systemic fungal infections in hematological malignancies**  
*Authors:* Petar Kuzmanovski, Velo Markoski;
8. **Morbidity and mortality of malignant neoplasms in Macedonia**  
*Authors:* Viktorija Vukovikj, Velo Markoski;
9. **Cognitive behavioral program in treating insomnia among elderly patients**  
*Authors:* Kneginja Richter, Lence Miloseva, Guenter Niklewski, Anja Piehl;
10. **Regulations and legal aspects in management of medical waste**  
*Authors:* Biljana Shikoska, Cena Dimova, Gjorgji Schumanov;
11. **Control of the psychiatric disorders in the Republic of Macedonia**  
*Authors:* Leonid Ramov, Velo Markoski;
12. **Monitoring of the renal function in Indometacin treated patients with rheumatoid arthritis**  
*Authors:* Drita Yzeiri Havziu, M.Hiljadnikova-Bajro, T. Kadifkova Panovska;
13. **Incidence of breast cancer in Macedonia**  
*Authors:* Dijana Stojanova, Velo Markoski;
14. **HPV virus as a cause of cancer of the cervix in R.Macedonia**  
*Authors:* Stefaniya Joveva, Velo Markoski, Vaso Taleski;
15. **Analysis of the Pap test results by age groups in the area of Kriva Palanka**  
*Authors:* Robert Nikolovski, Kristina Denchovska, Goran Mladenovski, Velo Markovski;
16. **Giant rhinophyma treated by excision and full thickness skin grafting**  
*Author:* Emilija Lozanovska Doneva;
17. **Incidence of patients with chronic renal failure in Skopje**  
*Authors:* Simona Kamceva, Velo Markoski;
18. **Calculation of effective dose to family members of patients with thyroid diseases**  
*Authors:* Marina Zdravevska Kochovska, Emilija Janjevik Ivanovska, Meri Angeleska, Sasho Nikolovski, Zlatko Filipovski;

- 19. Contemporary Microbiological Diagnostic Tests for Rapid Identification and Detection of Resistance of Mycobacterium tuberculosis**  
*Authors:* Oliver Taleski, Vaso Taleski;
- 20. Analysis of clinical features and complications in patients with  $\beta$ -thalassemia in the region of Strumica**  
*Authors:* Silvana Sinokapovska, Cena Dimova;
- 21. Lymphoepithelioma : A case report**  
*Authors:* Vase Stojcheska, Rade Filipovski, Dobri Stoimenov, Nikica Atanasova, Goran Karaivanov, Ana Doneva, Irena Shulevska, Silvana Kraveva;
- 22. F-ra Capitulum Radii L.Dex. – A Case report**  
*Authors:* Svetlana Jovevska, M.Idrizovikj;
- 23. Patient with intracranial hemorrhage and arteriovenous malformation detected with transcranial color duplex sonography – case report**  
*Authors:* Elena Simeonovska Joveva, Marija Karakolevska-Ilova, Aleksandar Serafimov, Lidija Petrovska, Anita Arsovska;
- 24. Hereditary supracondylar spur of the humerus: Case report**  
*Authors:* Strahil Todorov, Christian Lozanoski, George Zafirovski;
- 25. Prosthetic rehabilitation in patient with advanced degree of functional disorders (case report)**  
*Authors:* Natasa Denkova, Katerina Zlatanovska, Ana Radeska-Panovska, Sanja Nashkova, Ivona Kovacevska;
- 26. Marginal Implants Bone Loss – a Case Report**  
*Authors:* Kiro Papakoca, Ana Radeska-Panovska, Katerina Zlatanovska;
- 27. Ectodermal Dysplasia, a Case Report: Challenge for Prosthodontic Solution**  
*Authors:* Emilija Bajraktarova Valjakova, Bajevska Jagoda, Vesna Korunoska Stevkovska, Biljana Kapusevska, Nikola Gigovski, Aneta Mijoska, Katerina Zlatanovska, Cvetanka Bajraktarova Mishevska;
- 28. Alveolar socket preservation and shaping using temporary prosthetic construction – cases presentation**  
*Authors:* Nikola K. Gigovski, Vesna Korunovska- Stevkoska, Emilija Bajraktarova, Aneta Mijoska, Ana Radeska-Panovska, Ana Gigovska;
- 29. Porcelain veneers produced by refractory die method**  
*Authors:* Katerina Zlatanovska, Julija Zarkova-Atanasova, Ana Radeska, Natasa Denkova, Kiro Papakoca;
- 30. Correlation of Two Different Local Hemostatic Modalities in Oral Surgery Patients with Oral Anticoagulants**  
*Author:* Cena Dimova;
- 31. Assessment of orthodontic treatment need among school children by using iotn (index of orthodontic treatment need)**  
*Authors:* Ana Radeska-Panovska, Kiro Papakoca, Natasa Denkova, Ivona Kovacevska, Katerina Zlatanovska;
- 32. Oral Hygiene Level Maintenance among Dental Medicine Students**  
*Authors:* Darko Kochovski, Verica Toneva, Cena Dimova;
- 33. Poor oral hygiene and show of caries in 12 year old children**  
*Author:* Sanja Naskova;
- 34. Implant-prosthetic therapy failure in smoker and nonsmoker patients**  
*Authors:* Aneta Mijoska, Mirjana Popovska, Biljana Kapusevska, Nikola Gigovski, Vesna Korunovska- Stevkoska, Emilija Bajraktarova, Katerina Zlatanovska;
- 35. Oral surgery treatment in the patients with combination syndrome**  
*Authors:* Vesna Korunoska-Stevkovska, Katerina Zlatanovska, Nikola Gigovski, Žaklina Menceva, Julijana Nikolovska, Emilija Bajraktarova-Valjakova, Aneta Mijoska;
- 36. Iatrogenic mistakes, cause for a failure at surgical treatment of a chronic periapical processes**  
*Authors:* Sarita Kadrova, Cena Dimova;
- 37. Evaluation of Different Preparation of Artificial Teeth and Acrylate Prosthetic Base**  
*Authors:* Pavle Apostoloski, Cena Dimova, Katerina Zlatanovska, Julija Zarkova;



- 38. Analysis of the dimensional stability of elastomeric silicone impression materials**  
*Authors:* Galaba Veresa, Cena Dimova, Julijana Miloseva;
- 39. Use of gypsum into working everyday in dental technician**  
*Authors:* Hadis Arslanov, Cena Dimova, Julija Vladikova, Pavle Apostoloski;
- 40. Mobile dental NOG-types used in working dental models**  
*Authors:* Julija Vladikova, Cena Dimova, Hadis Arslanov, Pavle Apostoloski;
- 41. Determining normal tissue toxicity of non-radioactively Lu/Y-labeled rituximab-conjugates in rat animal model**  
*Authors:* Darinka Gjorgieva Ackova, Katarina Smilkov, Icko Gjorgoski, Emilija Janevik-Ivanovska;
- 42. Genetically Engineered Mouse Models For Human Pancreatic Cancer: A Review Of The KC, KPC And iKRas\*P53\* Models**  
*Authors:* David Mwanza Wanjeh, Joel Munene Muchira, Aschalew Alemu Marie, Darko Bosnakovski;
- 43. Mouse Models For Human Prostate Cancer: Xenograft Vs Genetically Engineered Mouse Model**  
*Authors:* Aschalew Alemu Marie, Joel Munene Muchira, David Mwanza Wanjeh, Darko Bosnakovski;
- 44. HER2 Transgenic Mouse Models: A Way To HER2+ Breast Cancer Targeted Therapy**  
*Authors:* Joel Munene Muchira, David Mwanza Wanjeh, Aschalew Alemu Marie, Darko Bosnakovski;
- 45. Types of scaffolds and thier application in bone tissue engineering**  
*Authors:* Milena Volcheva, Darko Bosnakovski;
- 46. Significance of preparation of tissue samples for electron microscopy for observation and diagnosis**  
*Authors:* Jovanka Laskova, Gordana Petrusevska, Darko Bosnakovski;
- 47. Design and characterization of nanoparticles as platforms for delivery of curcumin**  
*Authors:* Elena Drakalaska, Denitsa Momekova, Stanislav Rangelov, Nikolay Lambov;
- 48. Freeze-drying approach to enhance antibody stability**  
*Authors:* Katarina Smilkov, Darinka Gjorgieva Ackova, Emilija Janevik-Ivanovska;
- 49. An overview of phytosomes as a novel herbal drug delivery system**  
*Authors:* Emilija Apostolova, Brankica Spaseska, Maja Simonoska Crcarevska, Maja Glavash Dodov, Renata Slaveska Raichki;
- 50. Determination of active pharmaceutical ingredient – chloropyramine in dragées**  
*Authors:* Vesna Kostik, Biljana Gjorgjeska, Sofija Petkovska;
- 51. Comparison of volatile aroma compounds between cultivated and spontaneous flowering stems of Sideritis scardica Griseb. from R. Macedonia**  
*Authors:* Bujar Qazimi, Gjoshe Stefkov, Marija Karapandzova, Ivana Cvetkovikj, Svetlana Kulevanova;
- 52. Bioactive compounds of cold-pressed oil from the seeds of Gojy Berry (Lycium barbarum)**  
*Author:* Sanja Kostadinovik Velickovska;
- 53. Development and validation of HPLC method for determination of flavonoids in herbal preparations**  
*Authors:* Tanja Janeva, Zorica Arsova-Sarafinovska;
- 54. Atomic emission spectrometry with inductively coupled plasma (ICP-AES) analysis of trace elements in Camellia sinensis teas**  
*Authors:* Dragica Doneva, Trajce Stafilov, Zorica Arsova-Sarafinovska, Katerina Starkoska, Maja Shishovska, Katerina Bačeva Andonovska;
- 55. Determination of trace elements analyzed by atomic emission spectrometry with inductively coupled plasma (ICP-AES) in Matricaria chamomilla L. teas present on macedonian market**  
*Authors:* Dragica Doneva, Trajce Stafilov;
- 56. Human health risks from heavy metals via consumption of contaminated food**  
*Authors:* Biljana Balabanova, Rubin Gulaboski;

- 57. Development of an ultrasonic method for effective extraction of capsaicin as a potent bioactive compound**  
*Authors:* Viktorija Maksimova, Liljana Koleva Gudeva, Blaga Radovanovic, Rubin Gulaboski;
- 58. Electrochemical analysis of the properties of benzene-1,2,4-triol**  
*Authors:* Milkica Janeva, Rubin Gulaboski;
- 59. Comparison of the procedure for registration of medicines in the European Union and the Republic of Macedonia**  
*Authors:* Sofija Petkovska, Danica Zahkova, Biljana Gjorgjeska;
- 60. Pharmacoeconomic evaluation of the antibiotic prophylaxis in orthopedic surgeries**  
*Authors:* Dijana Atanasova, Bistra Angelovska, Biljana Lazarova;
- 61. Therapeutic approach in the treatment of benign prostatic hyperplasia**  
*Authors:* Rozeta Aceva, Zorica Arsova – Sarafinovska;
- 62. Oxidative stress, aging and antioxidants**  
*Authors:* Viktorija Trajkoska, Zorica Arsova Sarafinovska;
- 63. Oxidative stress, oxidative DNA damage and prostate cancer**  
*Authors:* Evgenija Nedelkoska, Zorica Arsova-Sarafinovska;
- 64. RNA interference (RNAi) mechanism as a basis for future successful treatment of chronic hepatitis B infection**  
*Authors:* Ana Nikolova, Darko Bosnakovski;
- 65. Anti-cancer target therapy based on drugs conjugated to hyaluronic acid**  
*Authors:* Marija Zafirova, Darko Bosnakovski;
- 66. Cancer specific conjugated monoclonal antibodies for anticancer therapy**  
*Authors:* Daniela Todosiova, Darko Bosnakovski, Emilija Janevik Ivanovska;
- 67. Accreditation of the Laboratory of Radiopharmacy – requested requirements or need of challenge**  
*Authors:* Apostolova Paulina, Delipetrev Katarina, Smilkov Katarina, Gjorgieva Ackova Darinka, Sterjova Marija, Janevik Ivanovska Emilija;
- 68. Quality control of PET radiopharmaceuticals, with reference to its specifics vs quality control of conventional pharmaceuticals**  
*Authors:* Filip Jolevski, Maja Velickovska, Maja Chochevska, Marija Atanasova, Katerina Kolevska, Emilija Janevik-Ivanovska;
- 69. Production of [11C] Choline in The University Institute for PET – new perspective in diagnostics of prostate malignancy in R. of Macedonia**  
*Authors:* Katerina Kolevska, Maja Chochevska, Marija Atanasova, Maja Velickovska, Filip Jolevski, Emilija Janevik-Ivanovska;
- 70. PET radiopharmaceuticals in the diagnosis of neurological diseases**  
*Authors:* Marija Pandeva, Emilija Janevik-Ivanovska;
- 71. Achievements and perspectives in formulation of stable immunoconjugate of the HER2-targeting trastuzumab – potential for rapid labelling with Gallium-68**  
*Authors:* Marija Sterjova, Predrag Dzodic, Katarina Smilkov, Darinka Gjorgieva-Ackova, Emilija Janevik-Ivanovska



*Faculty of Medical Sciences*

*University Goce Delcev – Stip, Macedonia*

**INTERNATIONAL SYMPOSIUM AT FACULTY OF MEDICAL SCIENCES**

**“Current achievements and future perspectives in  
medical and biomedical research”**

# **BOOK OF ABSTRACTS**

*November 24, 2015 – Stip*

## Contents

ORAL PRESENTATIONS .....	14
Step forward of Macedonian Agency for medicines and medical devices	
Establishment and strategic plan for development .....	15
Adherence to Therapy: A Modern Pharmacotherapeutic Approach .....	16
Use of disinfectants and antiseptics in selected health institutions in Republic of Macedonia.....	18
Code of Ethics for Pharmacists – Pharmaceutical Chamber of Macedonia .....	19
4-Hydroxynonenal – major bioactive marker of lipid peroxidation.....	20
Nicotinamide adenine dinucleotide biosynthesis and consumption in dysfunctional white adipocytes .....	21
New Insights into the Chemistry and Functions of Coenzyme Q .....	22
Genetically modified systems to study muscular dystrophies.....	23
Counteracting microbial biofilm formation onto dental materials .....	24
The endless potential of the umbilical cord blood for investigation, research and treatment .....	25
The cytokinesis-blocked micronucleus assay: Good choice for detection and evaluation of genotoxicity in human cells.....	27
Multiple predictive model for clinical and subclinical depression in adolescence .....	28
Molecular Imaging and therapy with radionuclides of prostate cancer.....	29
Where Nanotechnology and Nanomedicine meet – Applications and Potential Risks .....	31
The role of molecular cocrystals in drug development .....	33
Drug development based on radiolabeled antibodies .....	34
POSTER PRESENTATIONS .....	35
Correlation between dynamic balance and gait parameters in patients with ischemic stroke in the chronic period.....	36
Effect of kinesitherapy on physical activity in patient with Guillain-Barré syndrome .....	37
Case Report : Oligoasthenoteratozoospermia, treatment with acupuncture.....	38
Treatment of cervical spondylosis with acupuncture .....	40
Effect of kinesitherapy on static and dynamic balance in patient after vertebro-basilar system stroke .....	41
Malignant pleural effusions in lung cancer: the condition during the disease .....	42
Systemic fungal infections in hematological malignancies.....	44
Morbidity and mortality of malignant neoplasms in Macedonia .....	45
Cognitive behavioral program in treating insomnia among elderly patients.....	46
Regulations and legal aspects in management of medical waste .....	47
Control of the psychiatric disorders in the Republic of Macedonia .....	49
Monitoring of the renal function in Indometacin treated patients with rheumatoid arthritis .....	50
Incidence of breast cancer in Macedonia .....	51
HPV virus as a cause of cancer of the cervix in R.Macedonia.....	52
Analysis of the Pap test results by age groups in the area of Kriva Palanka.....	53
Giant rhinophyma treated by excision and full thickness skin grafting .....	55
Incidence of patients with chronic renal failure in Skopje .....	56
Calculation of effective dose to family members of patients with thyroid diseases .....	57
Contemporary Microbiological Diagnostic Tests for Rapid Identification and Detection of Resistance of Mycobacterium tuberculosis .....	59
Analysis of clinical features and complications in patients with $\beta$ -thalassemia in the region of Strumica...60	
Lymphoepithelioma: A case report .....	62
F-ra Capitulum Radium L.Dex. – A Case report .....	63
Patient with intracranial hemorrhage and arteriovenous malformation detected with transcranial color duplex sonography – case report .....	64
Hereditary supracondylar spur of the humerus: Case report .....	66
Prosthetic rehabilitation in patient with advanced degree of functional disorders (case report).....	67
Marginal Implants Bone Loss – a Case Report.....	68
Ectodermal Dysplasia, a Case Report: Challenge for Prosthodontic Solution.....	69

Alveolar socket preservation and shaping using temporary prosthetic construction – cases presentation...	71
Porcelain veneers produced by refractory die method .....	72
Correlation of Two Different Local Hemostatic Modalities in Oral Surgery Patients with Oral Anticoagulants.....	73
Assessment of orthodontic treatment need among school children by using iotn (index of orthodontic treatment need) .....	75
Oral Hygiene Level Maintenance among Dental Medicine Students .....	76
Poor oral hygiene and show of caries in 12 year old children.....	77
Implant-prosthetic therapy failure in smoker and nonsmoker patients .....	78
Oral surgery treatment in the patients with combination syndrome.....	79
Iatrogenic mistakes, cause for a failure at surgical treatment of a chronic periapical processes.....	80
Evaluation of Different Preparation of Artificial Teeth and Acrylate Prosthetic Base .....	81
Analysis of the dimensional stability of elastomeric silicone impression materials .....	82
Use of Gypsum Into Working Everyday in Dental Technician.....	84
Mobile dental NOG types used in working dental models.....	85
Determining normal tissue toxicity of non-radioactively Lu/Y-labeled rituximab-conjugates in rat animal model.....	86
Genetically Engineered Mouse Models For Human Pancreatic Cancer: A Review Of The KC, KPC And iKRas*P53* Models.....	87
Mouse Models For Human Prostate Cancer: Xenograft Vs Genetically Engineered Mouse Model .....	88
HER2 Transgenic Mouse Models: A Way To HER2+ Breast Cancer Targeted Therapy .....	89
Types of scaffolds and their application in bone tissue engineering .....	90
Significance of preparation of tissue samples for electron microscopy for observation and diagnosis .....	91
Design and characterization of nanoparticles as platforms for delivery of curcumin .....	93
Freeze-drying approach to enhance antibody stability.....	94
An overview of phytosomes as a novel herbal drug delivery system .....	95
Determination of active pharmaceutical ingredient – chloropyramine in <i>dragées</i> .....	97
Comparison of volatile aroma compounds between cultivated and spontaneous flowering stems of <i>Sideritis scardica</i> Griseb. from R. Macedonia.....	98
Bioactive compounds of cold-pressed oil from the seeds of Goji Berry ( <i>Lycium barbarum</i> ) .....	99
Development and validation of HPLC method for determination of flavonoids in herbal preparations.....	100
Atomic emission spectrometry with inductively coupled plasma (ICP-AES) analysis of trace elements in <i>Camellia sinensis</i> teas .....	101
Determination of trace elements analyzed by atomic emission spectrometry with inductively coupled plasma (ICP-AES) in <i>Matricaria chamomilla</i> L. teas present on macedonian market.....	102
Human health risks from heavy metals via consumption of contaminated food.....	103
Development of an ultrasonic method for effective extraction of capsaicin as a potent bioactive compound.....	104
Electrochemical analysis of the properties of benzene-1,2,4-triol .....	105
Comparison of the procedure for registration of medicines in the European Union and the Republic of Macedonia .....	106
Pharmacoeconomic evaluation of the antibiotic prophylaxis in orthopedic surgeries .....	107
Therapeutic approach in the treatment of benign prostatic hyperplasia.....	108
Oxidative stress, aging and antioxidants .....	109
Oxidative stress, oxidative DNA damage and prostate cancer.....	111
RNA interference (RNAi) mechanism as a basis for future successful treatment of chronic hepatitis B infection.....	112
Anti-cancer target therapy based on drugs conjugated to hyaluronic acid.....	114
Cancer-specific conjugated monoclonal antibodies for anticancer therapy .....	115
Accreditation of the Laboratory of Radiopharmacy – requested requirements or need of challenge .....	117
Quality control of PET radiopharmaceuticals, with reference to its specifics vs quality control of conventional pharmaceuticals .....	119

Production of [ <sup>11</sup> C]Choline in The University Institute for PET – new perspective in diagnostics of prostate malignancy in R. of Macedonia .....	120
PET radiopharmaceuticals in the diagnosis of neurological diseases .....	122
Achievements and perspectives in formulation of stable immunoconjugate of the HER2-targeting trastuzumab – potential for rapid labelling with Gallium-68 .....	123

# HER2 Transgenic Mouse Models: A Way to HER2+ Breast Cancer Targeted Therapy

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## **Abstract**

Breast cancer remains the second leading cause of cancer mortality in women worldwide despite major advances made in the recent years. About 20-30% of breast cancer cases show HER2 over expression and amplification which predicts poor prognosis. Though HER2 has been successfully targeted with anti-HER2 therapies including mAbs such as trastuzumab and tyrosine kinase inhibitors, resistance to trastuzumab is a major setback. Resistance is proposed to occur by steric hindrance of antibody binding to HER2, expression of mutant HER2 as well as increased PI3K/Akt pathway activation. Since there is need to develop better therapies, HER2 transgenic mouse models will contribute greatly to the search for these therapies.

The aim of this review is to analyse HER2 transgenic mouse models and demonstrate their potential towards development of new targeted therapy. The first model evaluated was generated in 2003 using wild-type HER2 and the whey acidic promoter (WAP) under the C57BL/6 background. The mouse was injected with ID8/E2, ovarian tumor cells and there was no tumor rejection in the transgenic mice which indicated tolerance to HER2. On vaccination with five cycles of a robust HER2 DNA based vaccine, there was induction of the immune system in the transgenic mice which was shown by anti-HER2 antibodies and 33% of the transgenic mice were protected from tumor growth. Consistent findings were obtained using the FVB-huHER2 mouse model which uses the MMTV promoter. In both models tolerance was broken by DNA vaccination hence offering protection.

A newer HER2+/PIK3CA mutant transgenic mouse using a Tet-inducible system for gene expression was described in 2013. It was shown that HER2+/PIK3CA expressing mice developed tumors with shorter latency compared to mice expressing HER2 or PIK3CA mutant oncogene alone. Cells from HER2+/PIK3CA tumors showed more lung metastases in the nude mice and the tumors were resistant to trastuzumab alone or in combination with lapatinib. Resistance was reversed by a PI3K inhibitor. This shows that increased PI3K activation has a role in trastuzumab resistance.

The transgenic mouse models expressing human wild-type HER2 oncogene only is suitable for testing of vaccines while the HER2+/PIK3CA mutant transgenic mouse model is suitable for studying trastuzumab resistance and testing of PI3K inhibitors. HER2 transgenic mouse models therefore have great potential towards development of better targeted therapy. If new drug targets are to be identified, new HER2 transgenic mouse models will need to be developed.

**Keywords:** HER2, HER2 transgenic mouse, PI3K, targeted therapy, trastuzumab.