



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

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

#### SESSION 4

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

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

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# 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 vertebro-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: Stefanija 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 Korunoska- 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 Korunoska- 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**  
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- 37. Evaluation of Different Preparation of Artificial Teeth and Acrylate Prosthetic Base**  
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- 38. Analysis of the dimensional stability of elastomeric silicone impression materials**  
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- 39. Use of gypsum into working everyday in dental technician**  
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- 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 Gorgieva-Ackova, Emilija Janevik-Ivanovska



*Faculty of Medical Sciences*

*University Goce Delcev – Stip, Macedonia*

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# **BOOK OF ABSTRACTS**

*November 24, 2015 – Stip*

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# Genetically Engineered Mouse Models For Human Pancreatic Cancer: A Review of The KC, KPC and iKras\*P53\* Models

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## **Abstract**

Pancreatic cancer is almost always a ductal adenocarcinoma of the exocrine pancreas, called pancreatic ductal adenocarcinoma (PDAC). Over 80% of PDAC cases show oncogenic Kras activation, mostly co-occurring with p53 gene mutation. Pancreatic intraepithelial neoplasms (PanIN) are the precancerous lesions that usually precede PDAC. Desirable mouse models for PDAC must be able to reliably and predictably recapitulate the human disease. The choice of a mouse model for a particular research study requires careful evaluation of all the available models with respect to their characteristics and the research question.

The aim of this paper is to review and compare the characteristics of the conditional **KC** (Pdx1 Cre; LSL-Kras<sup>G12D</sup>), **KPC** (Pdx1 Cre; LSL-Kras<sup>G12D</sup>; LSL-P53<sup>R172H</sup>) mouse models and the newer inducible **iKras\*p53\*** (Ptf1a Cre; LSL-rtTa; LSL-P53<sup>R172H</sup>; tetO-Kras<sup>G12D</sup>) mouse model and to make an opinion about their suitability to use in oncogenic Kras-targeting translational research for PDAC.

The KC mouse model, developed in 2003, was the proof of principle. It shows a PanIN penetrance of 100% starting prenatally, PDAC penetrance of less than 10% in its first year of life and a transgene expression that is targeted to its usual Kras genomic locus. However, it lacks pancreas-specificity in its transgene expression. The KPC mouse model, developed in 2005, demonstrates 100% PanIN penetrance starting prenatally, 100% PDAC penetrance, a transgene that is targeted to its usual genomic locus and 5months mean survival. Like the KC mouse model, it lacks pancreas-specificity in its transgene expression. The iKras\*p53\* mouse model was developed in 2012. Unlike the other models above, its oncogenic KRas transgene expression is inducible and more pancreas-specific. It has about 7months mean survival, more rapid formation of PDAC and metastases with larger tumor masses than the KPC model. Its oncogenic Kras transgene expression, is however targeted to a different locus than the usual Ras locus of the mouse genome.

Our current opinion is that each of the above models has a unique place in pancreatic cancer research. The KC model (especially its Ptf1a-Cre analog) is more suited for preclinical evaluation of diagnostic agents and the others are useful for evaluating therapies. The iKras\*p53\* mouse is more suitable for studying oncogenic Kras pathway inhibitors but generally, the KPC mouse is still a reasonable choice since it has been studied for longer and researchers have had more years experience with it.

**Keywords:** GEMMs, oncogenic Kras, pancreatic cancer.