



LIETUVOS SVEIKATOS
MOKSLŲ UNIVERSITETAS



LIETUVOS SVEIKATOS MOKSLŲ
UNIVERSITETO LIGONINĖ
KAUNO
KLINIKOS



LSMU - CERN

Activities from Lithuanian University of Health Sciences

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About Lithuanian University of Health Sciences



- The largest institution of higher education for biomedical sciences in Lithuania;
- Integration of studies, research and clinical practice.
- Consists of two main academies: Medical Academy and Veterinary Academy.
- Includes 7 faculties, 6 research institutes, two animal clinics and the Hospital of LUHS.
- Has more than 7,000 students enrolled.



Hospital of Lithuanian University of Health Sciences Kauno Klinikos

The largest healthcare institution in Lithuania which aims to:

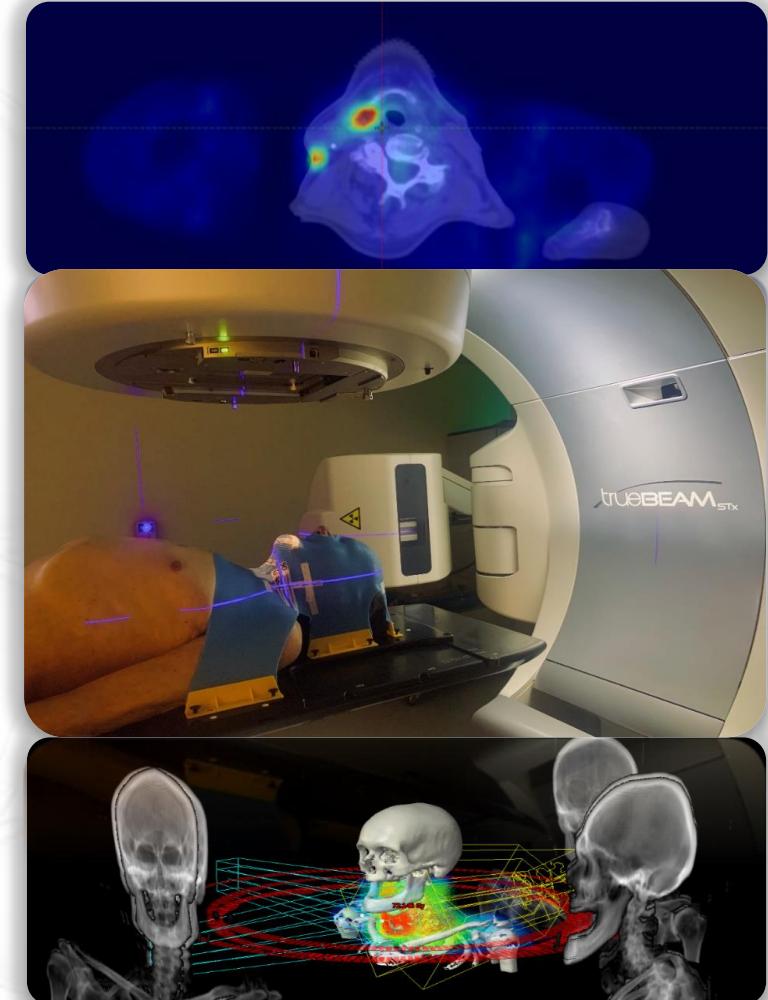
- improve the health and life quality of population
- develop ambitious and advanced health specialists
- create and implement innovations based on scientific research.
- uses state-of-the-art technologies in radiotherapy.





LSMU research areas in radiotherapy and radiobiology

- Prognostic and predictive molecular markers of solid tumors;
- Molecular mechanisms of sensitivity and resistance to radiotherapy in breast cancer or other cell lines;
- Association between common genetic variations with individual patient variability in normal tissue late radiation toxicities;
- Radiotherapy optimisation using ^{18}F -FDG-PET/CT images;
- Linac-based fractionated stereotactic radiotherapy vs. intensity modulated radiotherapy;
- New brachytherapy techniques.





LSMU-CERN collaboration

- During the last years training of medical physicists and radiation oncologists was organized in collaboration with CERN.
- Development of nuclear medicine is closely related to the deployment of cyclotron at LUHS University Hospital.
- Oncology institute: CERN- activities related to 4 projects in Radiobiology.





LSMU-CERN PROJECT No.1

2017.07.01 – 2017.12.31

“Molecular mechanisms determining breast cancer cells resistance to radiotherapy”

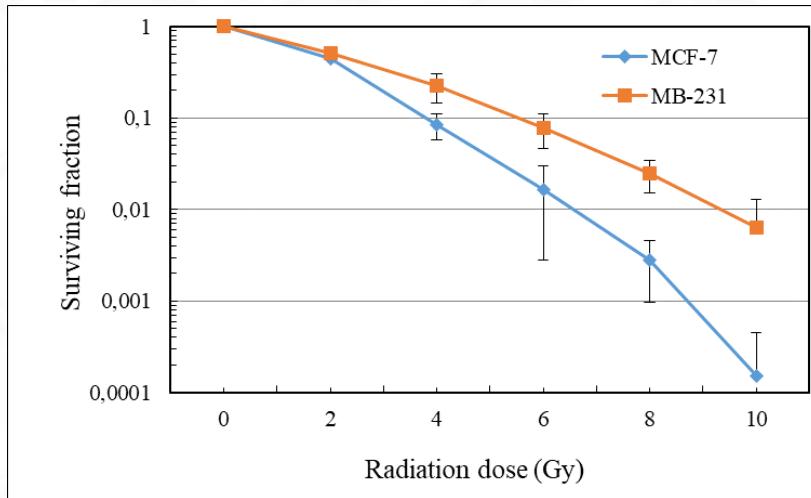
(lt. „Molekuliniai mechanizmai lemiantys krūties vėžio ląstelių atsparumą radioterapijai”)

The aim: to compare the response of breast cancer cells to radiotherapy.

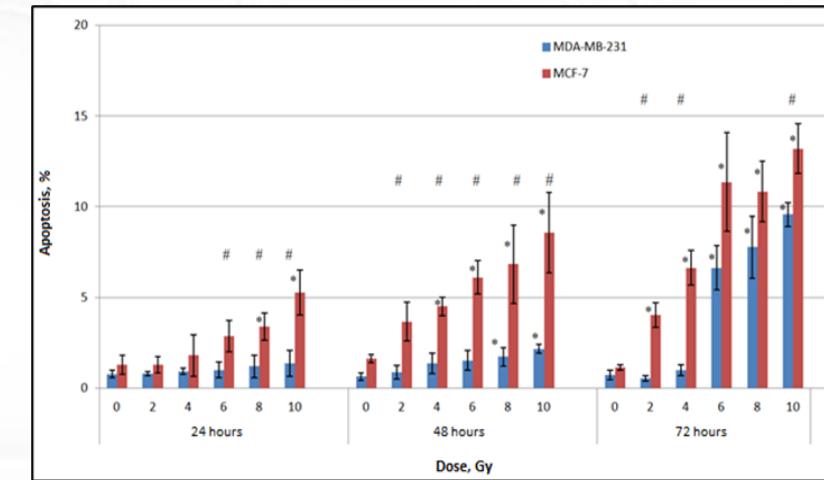
Cell survival, intensity of apoptosis, and cell cycle changes were analyzed on MCF-7 and MDA-MB-231 breast cancer cells.



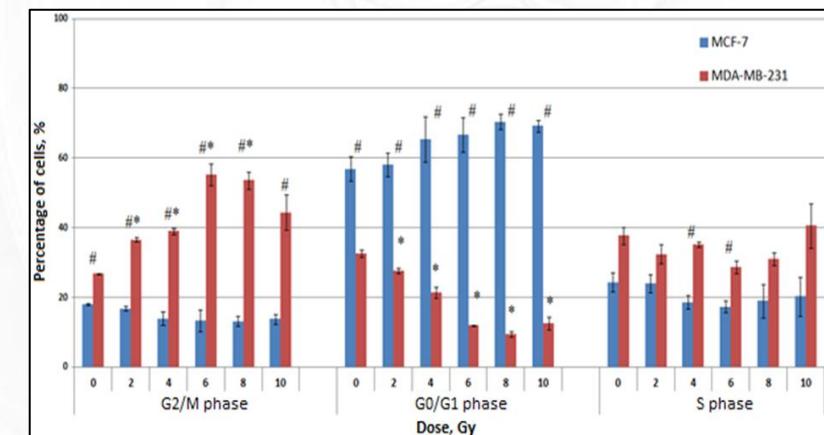
The effect of ionizing radiation (IR) on cell survival, apoptosis and cell cycle delay



Cell survival following the exposure to ionizing radiation (IR).



The apoptosis following the exposure to IR.



The cell-cycle phase distributions following IR.



LSMU-CERN PROJECTS No.2

2018.07.01 – 2018.12.31

“The identification of biomarkers responsible for head and neck cancer radioresistance”

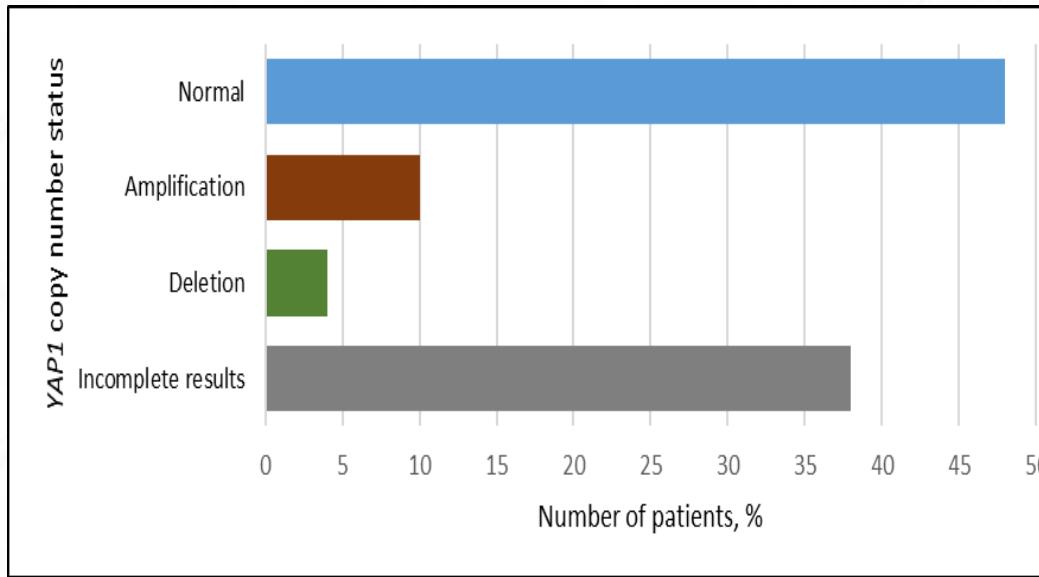
(lt. „Galvos ir kaklo navikų rezistentiškumą salygojančių biožymenų analizė“)

The aim: to determine *YAP1* gene copy number and several miRNA (miRNA-200a, miRNA-141, miRNA-375) expression in head-neck tumors relative to normal adjective tissue.

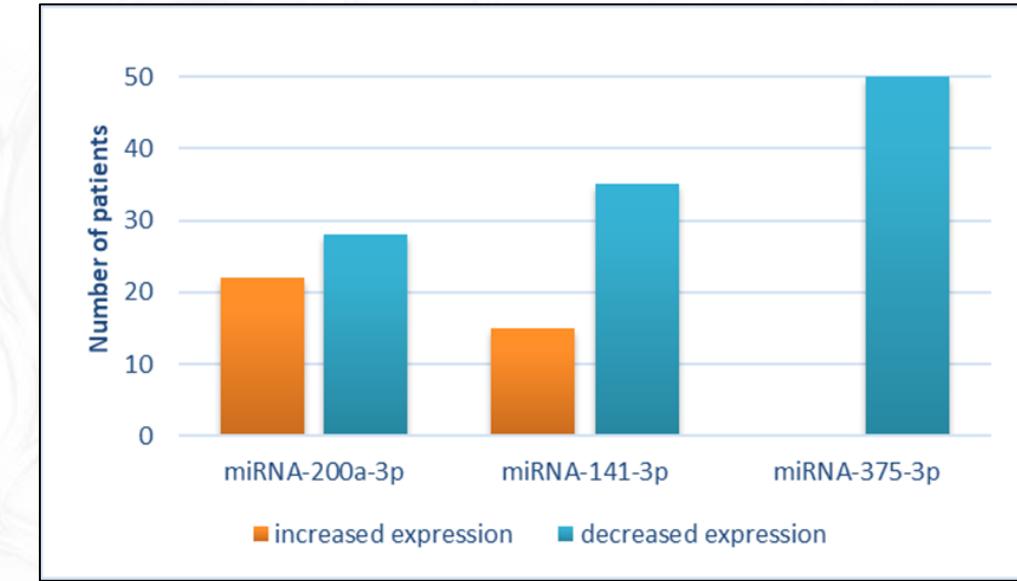
The cohort consisted of 50 head-neck cancer patients.



YAP1 copy number status and miRNA expression profiles



YAP1 gene copy number status in the studied head-neck cancer group (n=50)



Distribution of studied miRNA expression profiles among patients



CERN-LSMU PROJECT No.3

2019.07.01 – 2020.12.31

“Molecular mechanisms of resistance to radiotherapy in breast cancer cells and the effect of radio-sensitizing agents”

(lt. „Molekuliniai mechanizmai lemiantys krūties vėžio atsparumą radioterapijai ir radiojautrumą didinančių medžiagų poveikio analizė“)

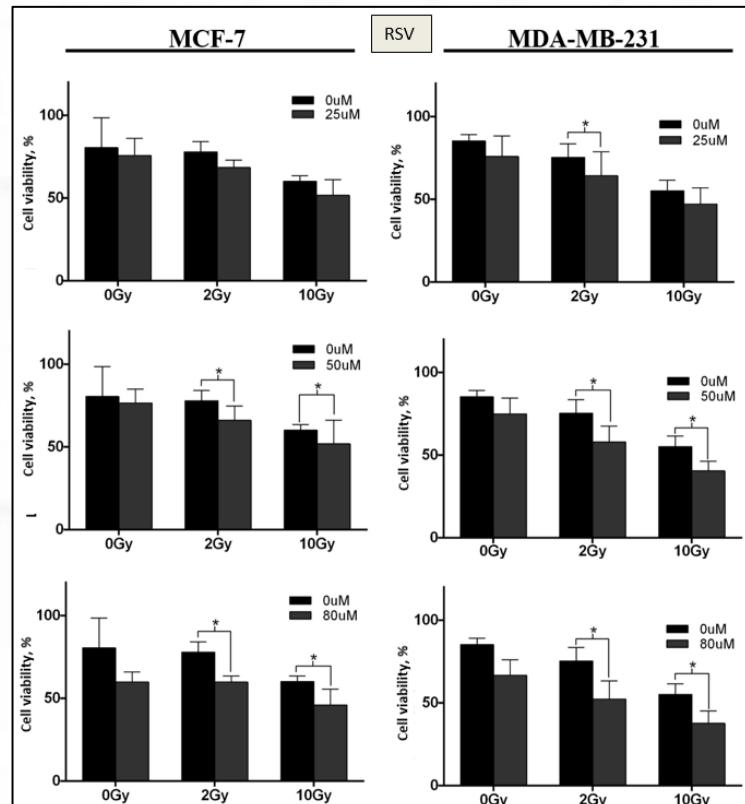
The aim: to analyze the substances which could decrease radioresistance in breast cancer cell lines (MDA-MB-231 and MCF-7).

Two phytochemicals were selected as potential radiosensitizing agents: resveratrol (RSV) and kaempferol (KMF).



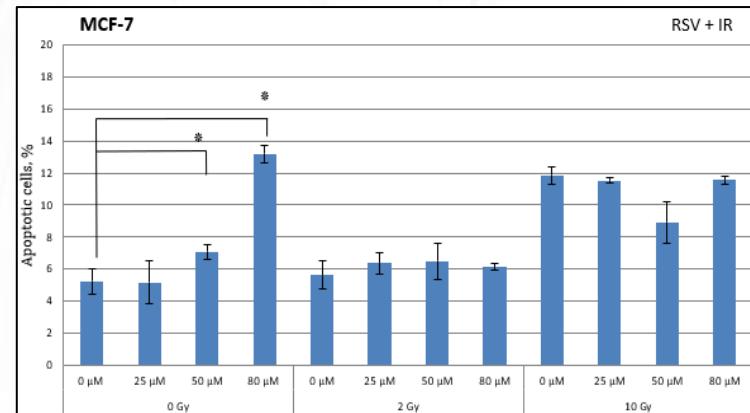
The effect of restveratrol (RSV) and RSV+IR on cell survival and apoptosis

RSV and **RSV+IR** significantly reduced the viability of cell lines.



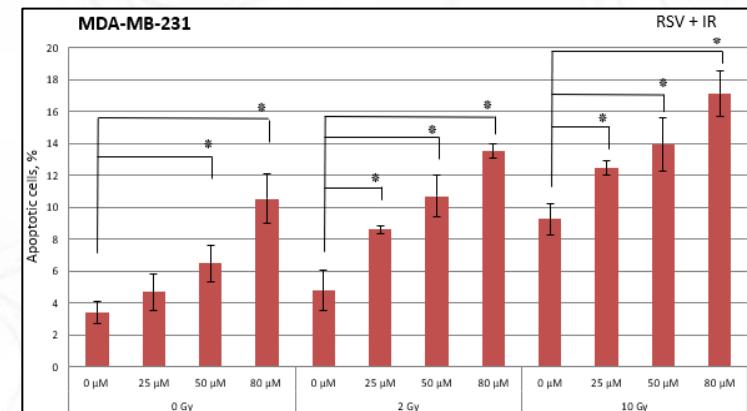
Cell viability following exposure to 25, 50, 80 μ M of RSV and IR (2 and 10 Gy)

In MCF-7 apoptosis was induced by **RSV**, but RSV + IR combination had no effect.



Effect of RSV and ionizing radiation on the apoptosis

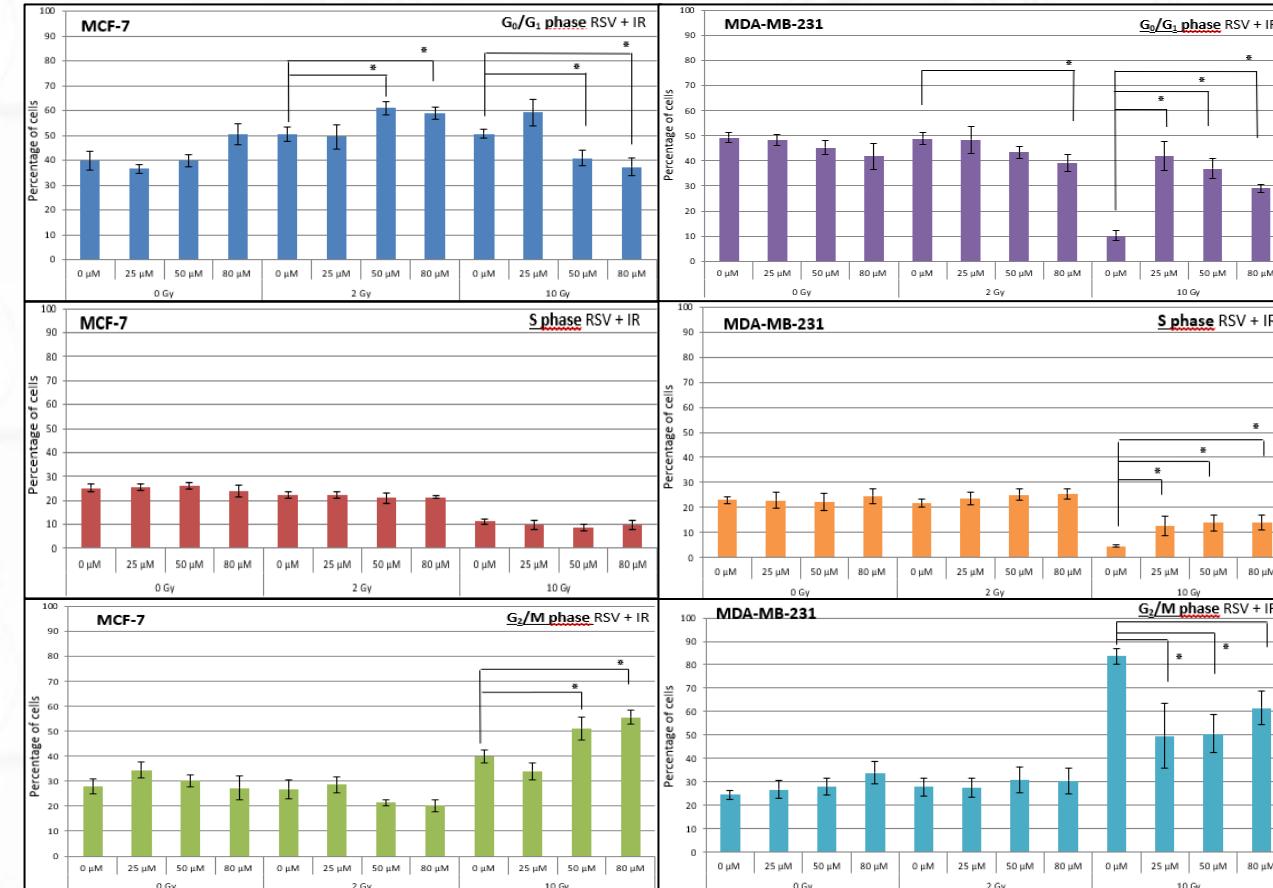
In MDA-MB-231 cells, both **RSV** and RSV+IR combination increased apoptosis.





The effect of restveratrol (RSV) and RSV+IR effect on cell cycle delay

RSV in combination with IR caused cell cycle arrest depending on cell line, IR dose, and RSV concentration.

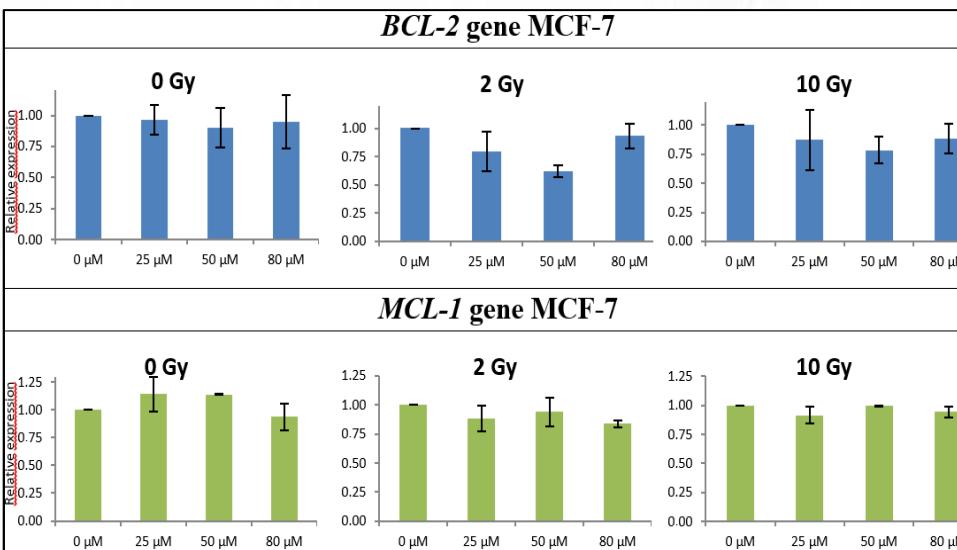


Effect of RSV and ionizing radiation on the cell cycle



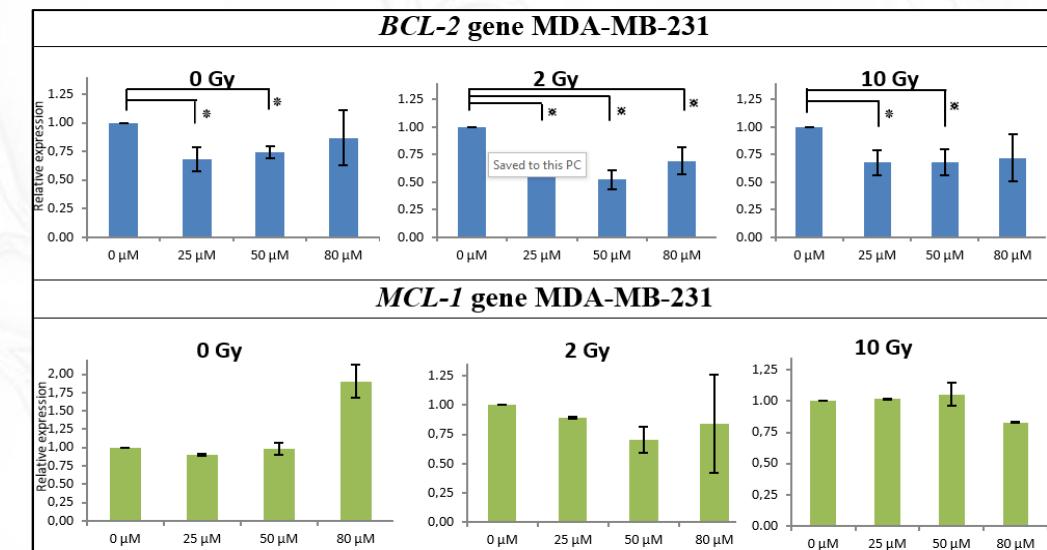
The effect of Restveratrol (RSV) and RSV+IR effect on gene expression

RSV did not cause changes in the expression of either *BCL-2* or *MCL-1* genes on MCF-7 cells.



Effect of RSV and ionizing radiation on *BCL-2* and *MCL-1* expression

RSV downregulated *BCL-2* gene expression on MDA-MB-231 cells.



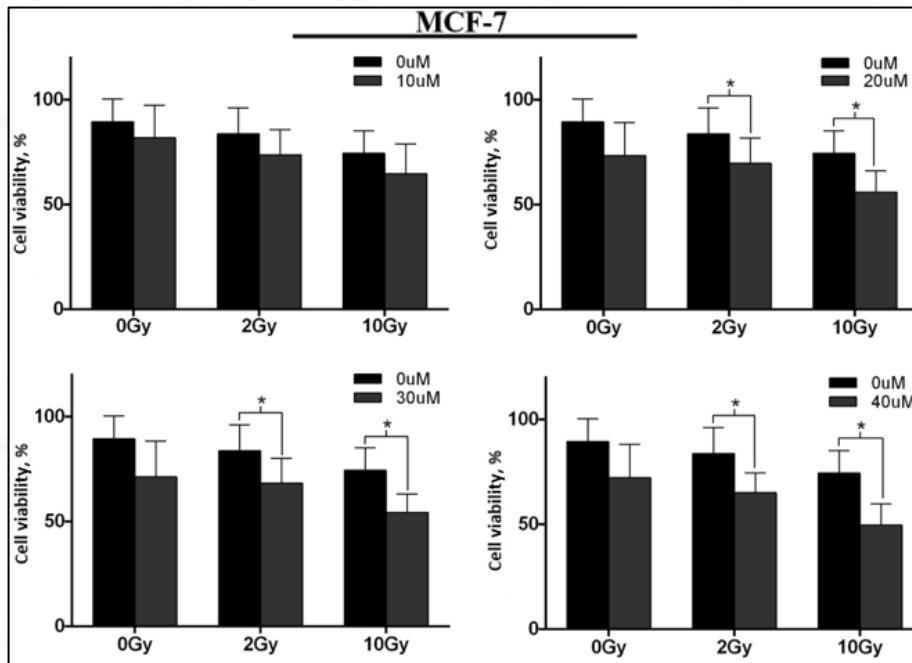
Effect of RSV and ionizing radiation on *BCL-2* and *MCL-1* expression



The effect of kaempferol (KMF) and KMF+IR effect on cell survival, apoptosis and cell cycle delay

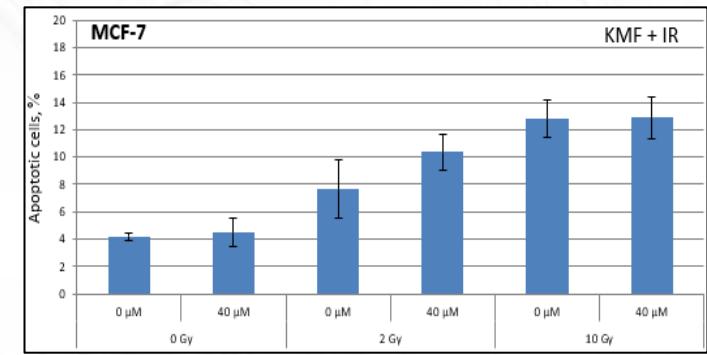
KMF was effective only on MCF-7 cells.

MDA-MB-231 cell line showed the resistance to KMF.



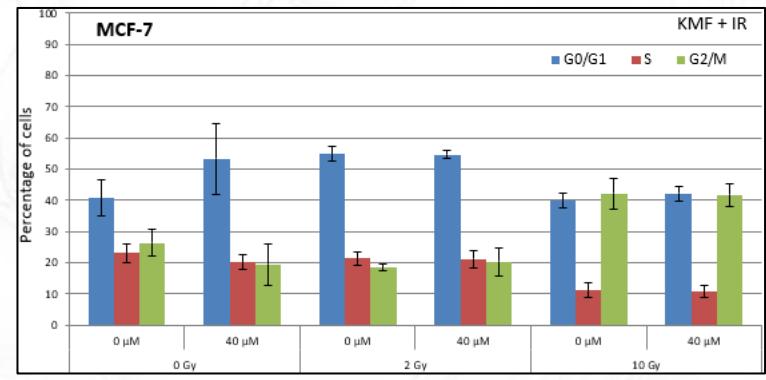
Cell viability following exposure to 10, 20, 30, 40 μM of KMF and IR (2 and 10 Gy)

KMF did not induce significant apoptosis of MCF-7 cells either alone or in combination with IR.



Effect of KMF and ionizing radiation on the apoptosis of MCF-7 cells

KMF did not induce cell cycle changes in MCF-7 either alone or in combination with IR.



Effect of KMF and ionizing radiation on the cell cycle



LSMU-CERN PROJECT No.4

2021.07.01 – 2022.12.31

“The search for radiosensitizing phytochemicals and the analysis of their effect on apoptosis mechanism in breast cancer cells *in vitro*”

(lt. „Radiojautrumą didinančių fitocheminių medžiagų paieška ir jų poveikio apoptozės mechanizmui analizė krūties vėžio ląstelėms *in vitro*”)

The purpose: to continue the search for radiosensitizing phytochemicals and their analysis on breast cancer cells.

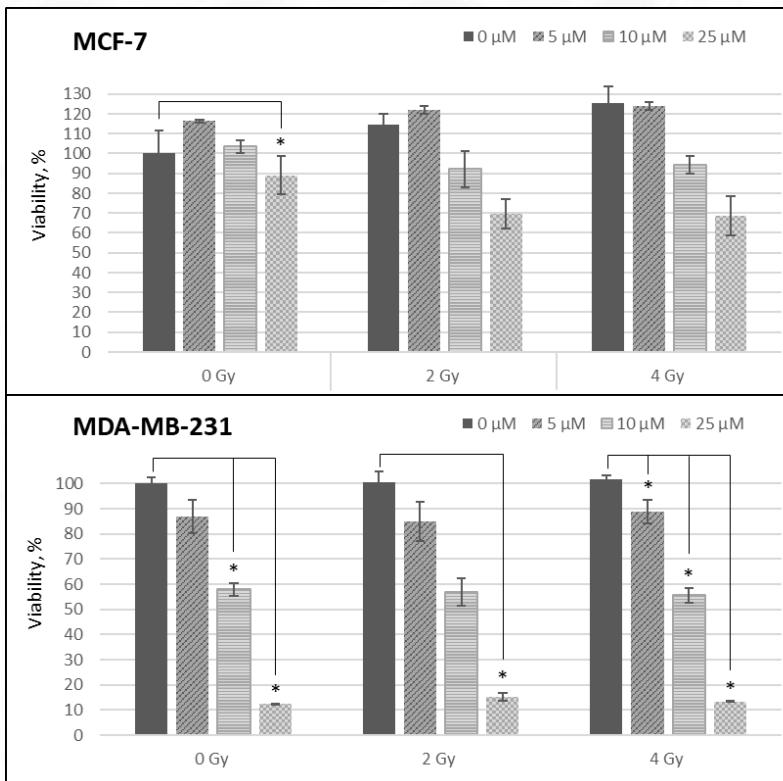
Sulforaphane (SFN), which is one of the strongest natural antioxidants, was chosen for this study.

Cell viability, the intensity of apoptosis, apoptosis-related gene expression at RNA and protein levels following the combined effect of SFN and ionizing radiation are currently under investigation on MDA-MB-231 and MCF-7 breast cancer cells.



The effect of sulforaphane (SFN) and SFN + IR on cell survival and apoptosis

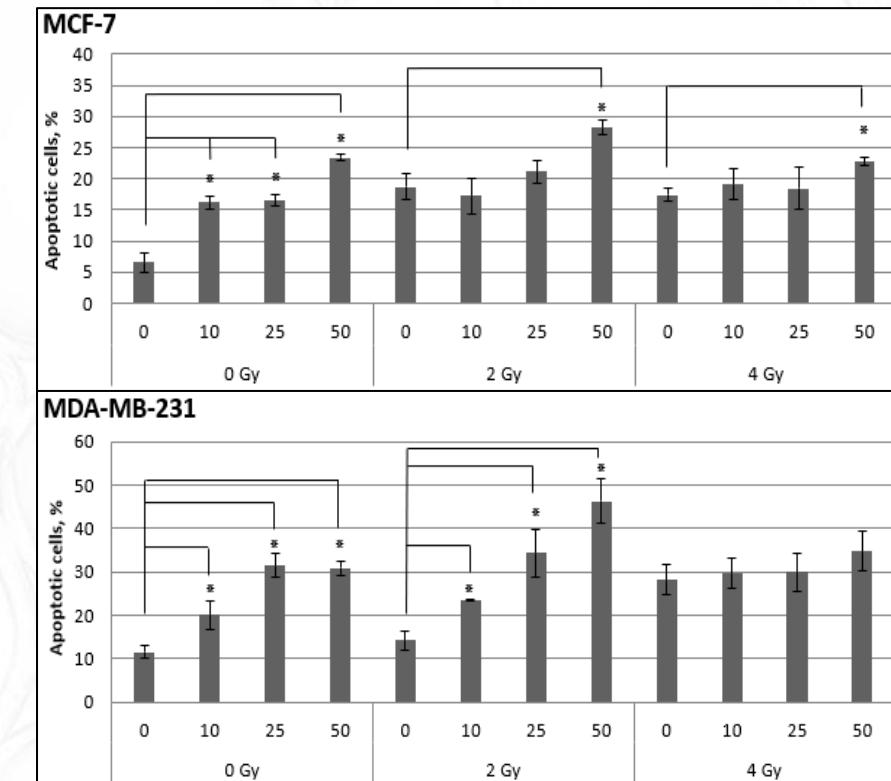
SNF and SNF + IR **decreased cell viability** in MDA-MB-231 cells



Cell viability following exposure to SFN and ionizing radiation

SNF and SNF + IR **increases apoptosis**.

The combination of 50 µM SFN and 2 Gy IR was the most effective.

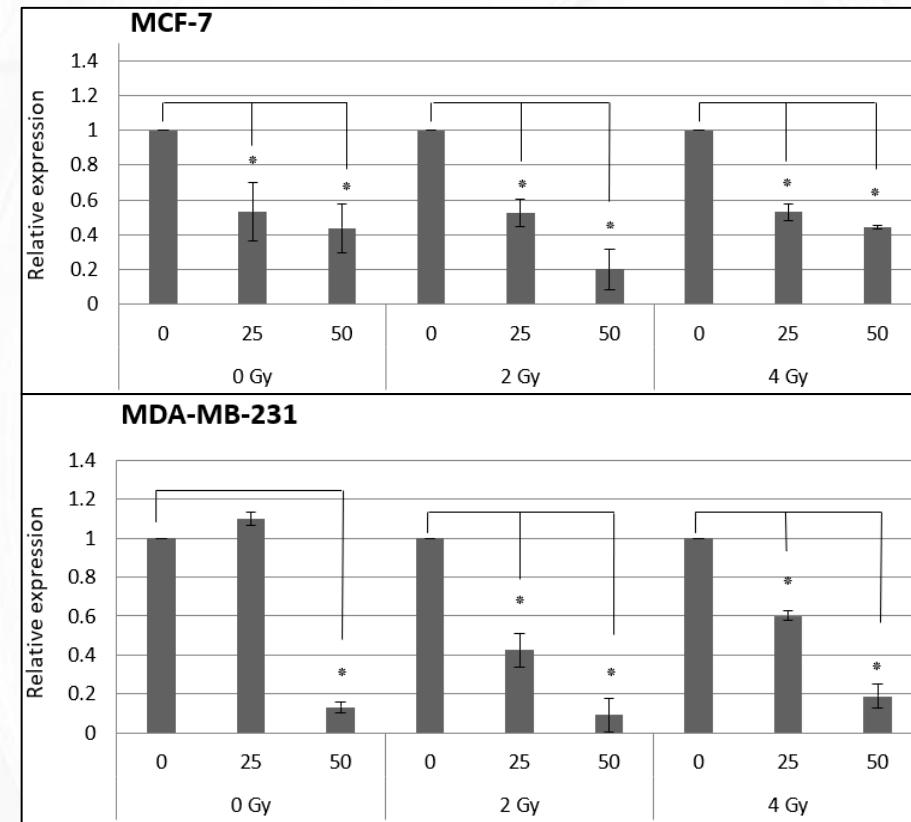


Effect of SFN and ionizing radiation on apoptosis



The effect of sulforaphane (SFN) and SFN+IR on *BCL-2* gene expression

SFN and SFN+IR decreased the expression of *BCL-2* gene in both cell lines.



Effect of SFN and IR on *BCL-2* gene expression



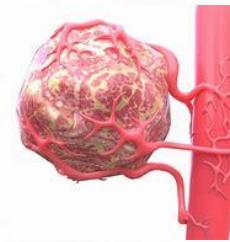
FUTURE DIRECTIONS

- Combined radiosensitizing agent effect analyses

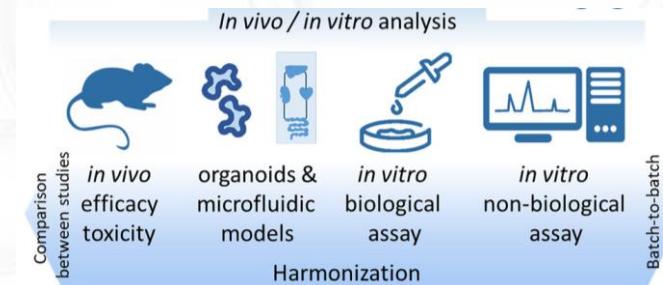


- Multiple gene expression analysis at RNA and protein level

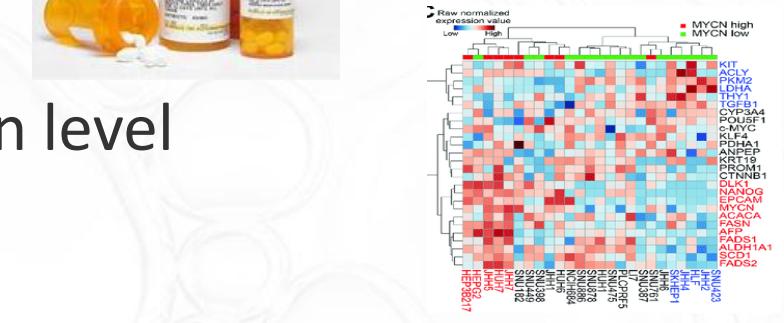
- 3D cell models



- Additional functional cell assays



- Precision radiotherapy biomarkers analyses





PUBLICATIONS

- Laukaitienė, Danguolė; Ugenškienė, Rasa; Inčiūra, Arturas; Juozaitytė, Elona. **The Radiosensitizer Potential of Sulforaphane on Breast Cancer Cells** // 7th Kaunas / Lithuania International Hematology / Oncology Colloquium : 26 May **2022**, Kaunas, Lithuania : Online Poster Abstract Book / Editor Elona Juozaitytė ; Abstracts' Reviewers Rolandas Gerbutavičius, Arturas Inčiūra, Dietger Niederwieser, Domas Vaitiekus ; Kaunas Region Society of Oncologists, Hematologists and Transfusiologists. Kaunas : Eventas, 2022. ISBN 9786099616759, p. 9-9.
- Laukaitienė, Danguolė; Vaitkus, Antanas; Savukaitytė, Aistė; Vadeikienė, Roberta; Inčiūra, Arturas; Ugenškienė, Rasa; Juozaitytė, Elona. **Skirtingų krūties vėžio ląstelių linijų atsparumo radioterapijai tyrimas** // Sveikatos mokslai = Health sciences in Eastern Europe. Vilnius : Sveikatos mokslai. ISSN 1392-6373, **2021**, t. 31, Nr. 3, p. 81-87. doi:10.35988/sm-hs.2021.085. Prieiga per internetą: <<https://doi.org/10.35988/sm-hs.2021.085>>.
- Laukaitienė, Danguolė; Bartnykaitė, Agnė; Ugenškienė, Rasa; Inčiūra, Arturas; Juozaitytė, Elona. **Radiosensitization Effect of Resveratrol on Breast Cancer Cell** // 6th Kaunas / Lithuania International Hematology / Oncology Colloquium : 28 May **2021**, Kaunas / Lithuania : Online Poster Abstract Book / Editor Elona Juozaitytė ; Abstracts' Reviewers Arturas Inčiūra, Viktoras Rudžianskas, Milda Rudžianskiénė, Aistė Savukaitytė ; Kaunas Region Society of Oncologists, Hematologists and Transfusiologists. Kaunas : Eventas, 2021. ISBN 9786099616728, p. 10-11.
- Gudoitytė, Greta; Ugenškienė, Rasa; Savukaitytė, Aistė; Bartnykaitė, Agnė; Vaitkus, Antanas; Juozaitytė, Elona. **The Effect of Kaempferol on the Change in Vitality of Breast Cancer Cells in Combination with Ionizing Radiation** // 5th International Hematology / Oncology Colloquium : 26 June **2020**, Kaunas / Lithuania : Online Poster Abstract Book / Editor Elona Juozaitytė ; Abstracts' Reviewers Arturas Inčiūra, Rolandas Gerbutavičius, Sigita Liutkauskienė ; Kaunas Region Society of Oncologists, Hematologists and Transfusiologists. Kaunas : Eventas, 2020. ISBN 9786099616704, p. 7-8, no. 7.
- Gudoitytė, Greta; Ugenškienė, Rasa; Savukaitytė, Aistė; Bartnykaitė, Agnė; Vaitkus, Antanas; Juozaitytė, Elona. **The Effect of Resveratrol on the change in vitality of breast cancer cells in combination with ionizing radiation** // Eighth International Conference on Radiation in Various Fields of Research, Virtual Conference, **2020** : (RAD 2020) : Book of Abstracts : [July 20-24, 2020, Herceg Novi, Montenegro] / [editor Goran Ristić]. Niš : RAD Centre, 2020. ISBN 9788690115013, p. 127-127.
- Laukaitienė, Danguolė; Savukaitytė, Aistė; Vadeikienė, Roberta; Vaitkus, Antanas; Ugenškienė, Rasa; Juozaitytė, Elona; Inčiūra, Arturas. **Evaluation of resistance of different breast cancer cell lines to radiotherapy** // 1st International doctoral students' conference "Science for Health" : book of abstracts : April 13, **2018**, Kaunas, Lithuania / Lithuanian university of health sciences. LSMU Department of Research Affairs. Council of LSMU Doctoral Students ; [Edited by Indrė Šveikauskaitė]. Kaunas : Lietuvos sveikatos mokslų universiteto Leidybos namai, 2018. ISBN 9789955155300, p. 59-60.



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