LITHUANIAN UNIVERSITY OF HEALTH SCIENCES

The radiosensitizer potential of resveratrol on MDA-MB-231 breast cancer cell line

1st CERN Baltic Conference (CBC 2021)

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Background

- **Breast cancer** has posed a major threat to female health worldwide, and its morbidity shows an increasing trend every year.
- So far **radiation therapy** has been applied in the treatment of breast cancer.
- However, **radioresistance** and side effects have been limiting factors of this practice.
- Therefore, studying phytochemicals that can enhance the radiation effect and, at the same time, protect normal cells is extremely relevant.

Background

- One of these phytochemicals is **RESVERATROL** (RSV).

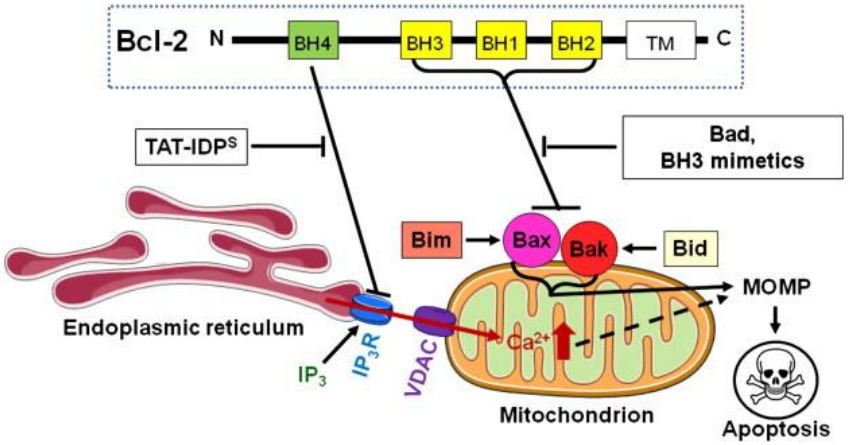
- Resveratrol is a polyphenol produced by several plants, including **grapes**, **red wine**, **berries** and **peanuts** and is a phytoestrogen that possesses anti-oxidant, anti-inflammatory, cardioprotective, and anti-cancer properties.

- Studies with this substance show its ability to inhibit the expression of cancer-specific genes, induce changes in the cell cycle, and activate apoptosis.

Background

- ***BCL2*** is the milestone of apoptosis-regulatory gene. It contributes to tumorigenesis by blocking programmed cell death and promoting cell survival.

- The aberrant expression of BCL2 gene is strongly associated with resistance to chemotherapy and radiation.

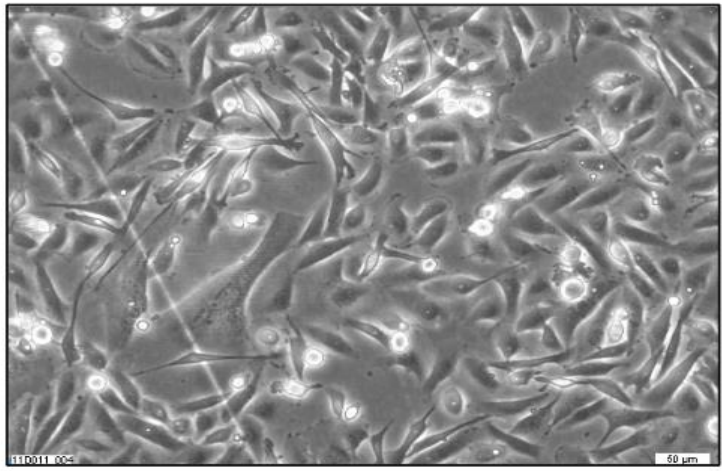


- The **aim** of the study was to investigate the *in vitro* effects of RSV on cellular radiosensitivity and the expression of anti-apoptotic gene *BCL2*.

Methods

Cell culture

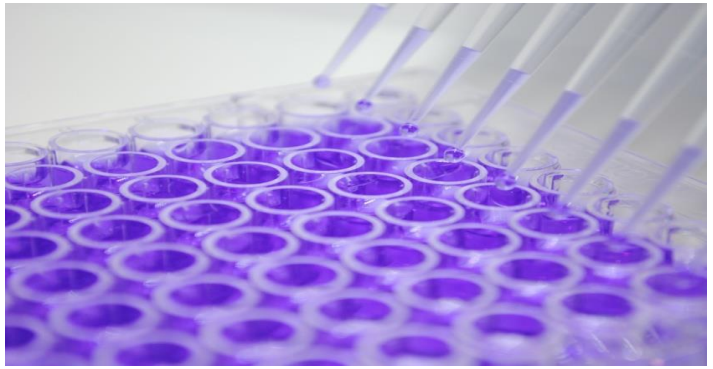
- In this study the **MDA-MB-231** breast cancer cell line has been used.
- Cells were grown in DMEM medium supplemented with 10% FBS, 1% glutamine and 100 IU/ml penicillin-streptomycin solution at 37^0C, humidified and filled with 5% CO2air conditions.
- MDA-MB-231 is a highly aggressive, invasive and poorly differentiated triple-negative breast cancer (TNBC) cell line.



MDA-MB-231 cells in culture

MTT assay

- The anti-proliferative effect of resveratrol against MDA-MB-231 breast cancer cells was determined using the colorimetric MTT assay.

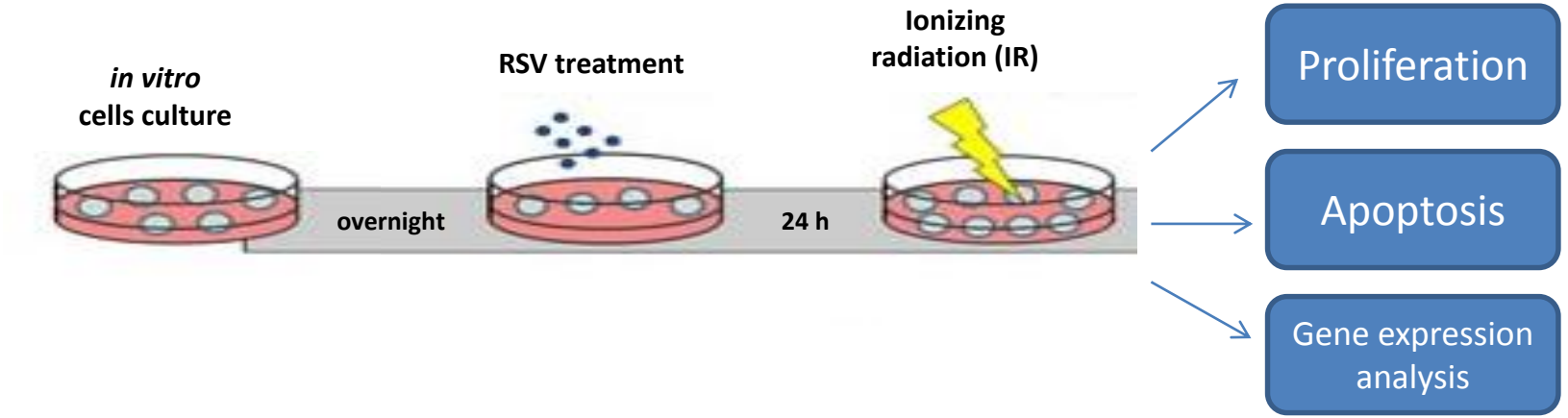


Methods

Irradiation (IR)

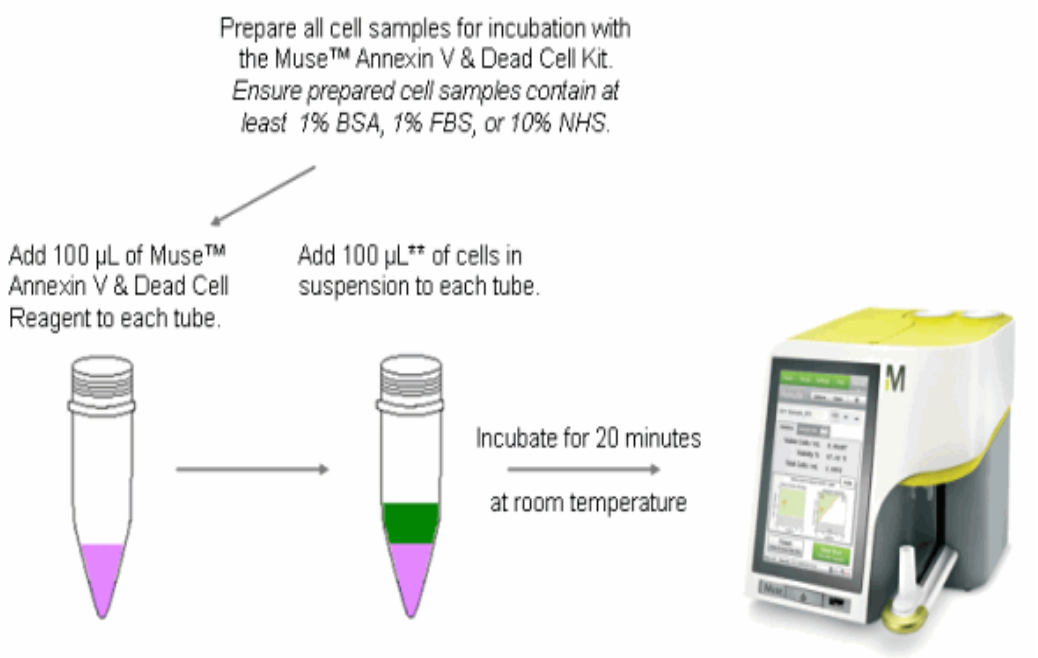
- Cells were seeded into culture plates, incubated overnight and treated with resveratrol. After 24 h the media was removed and replaced with fresh resveratrol-free culture media.

- Cell irradiations were performed with photon beams (X-rays) of 6 MV nominal energy and doses of 2 and 10 Gy, using a medical linear accelerator *Clinac 2100C/D*.



Methods

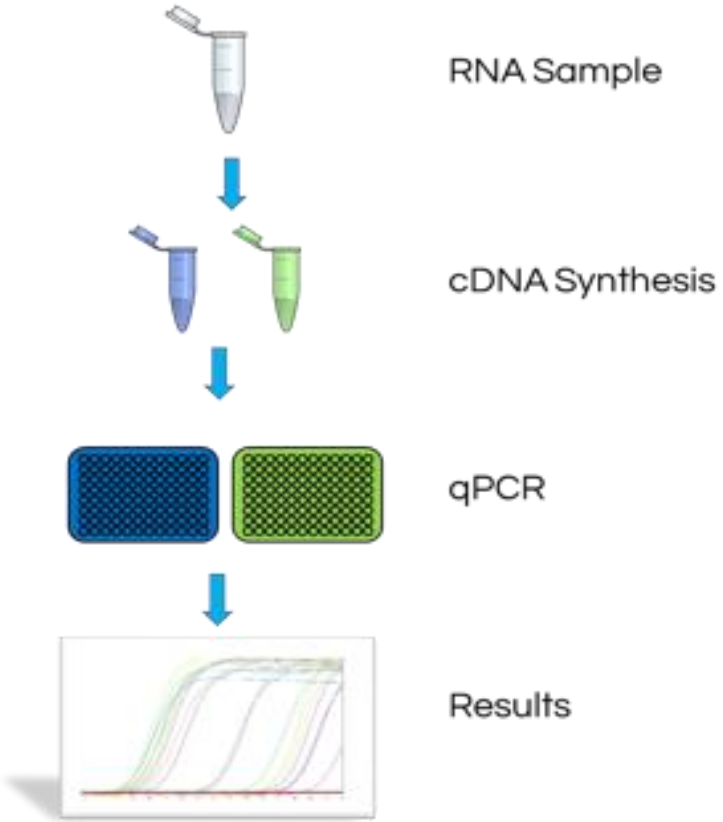
- **Apoptosis analysis.** The assay was performed according to the instructions of *Muse Annexin V & Dead Cell Kit* on a *Guava Muse Cell Analyzer*.



Methods

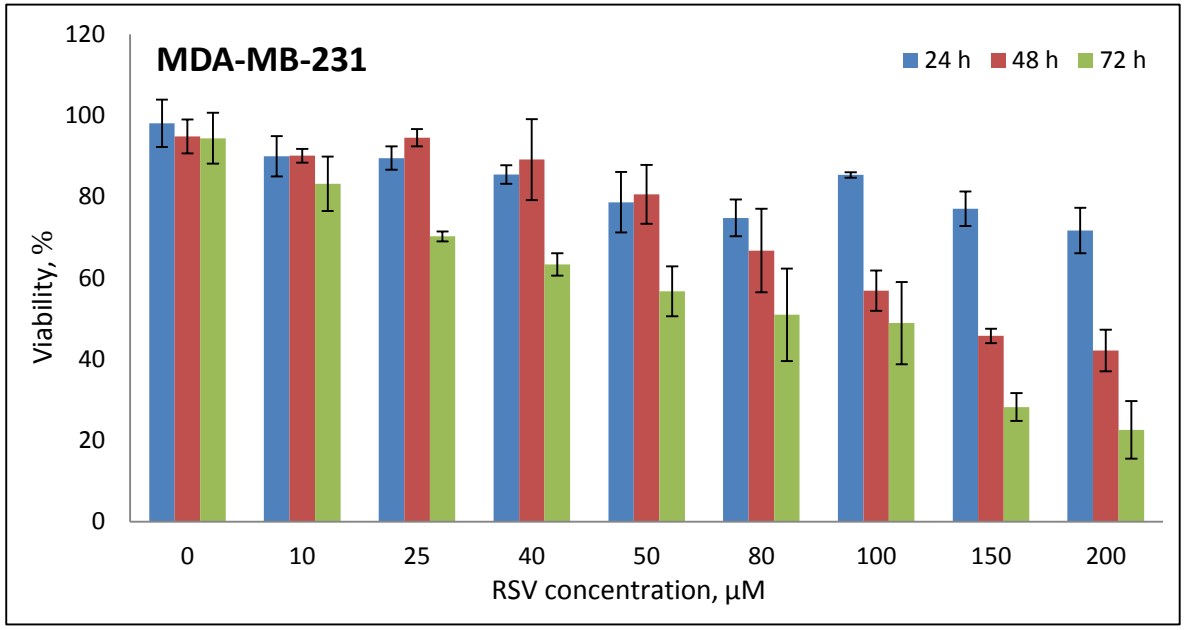
Gene expression analysis

- The expression of *BCl2* was determined by quantitative real-time PCR.
- Total RNA was extracted using *RNeasy Mini Kit*.
- One microgram of total RNA was reverse transcribed to cDNA using *High Capacity cDNA Reverse Transcription Kit with RNase Inhibitor.*



Results

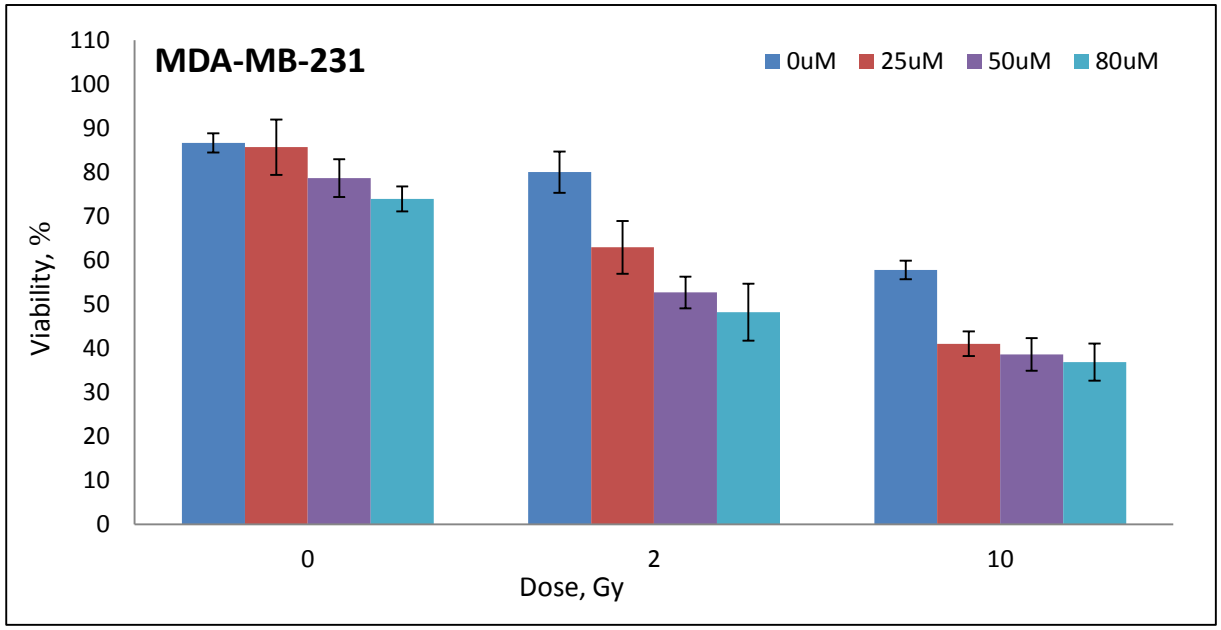
We examined the effect of resveratrol on the viability of MDA-MB-231 breast cancer cell line.



The inhibition of cell viability significantly increased in response to resveratrol in a dose- and time-dependent manner.

Results

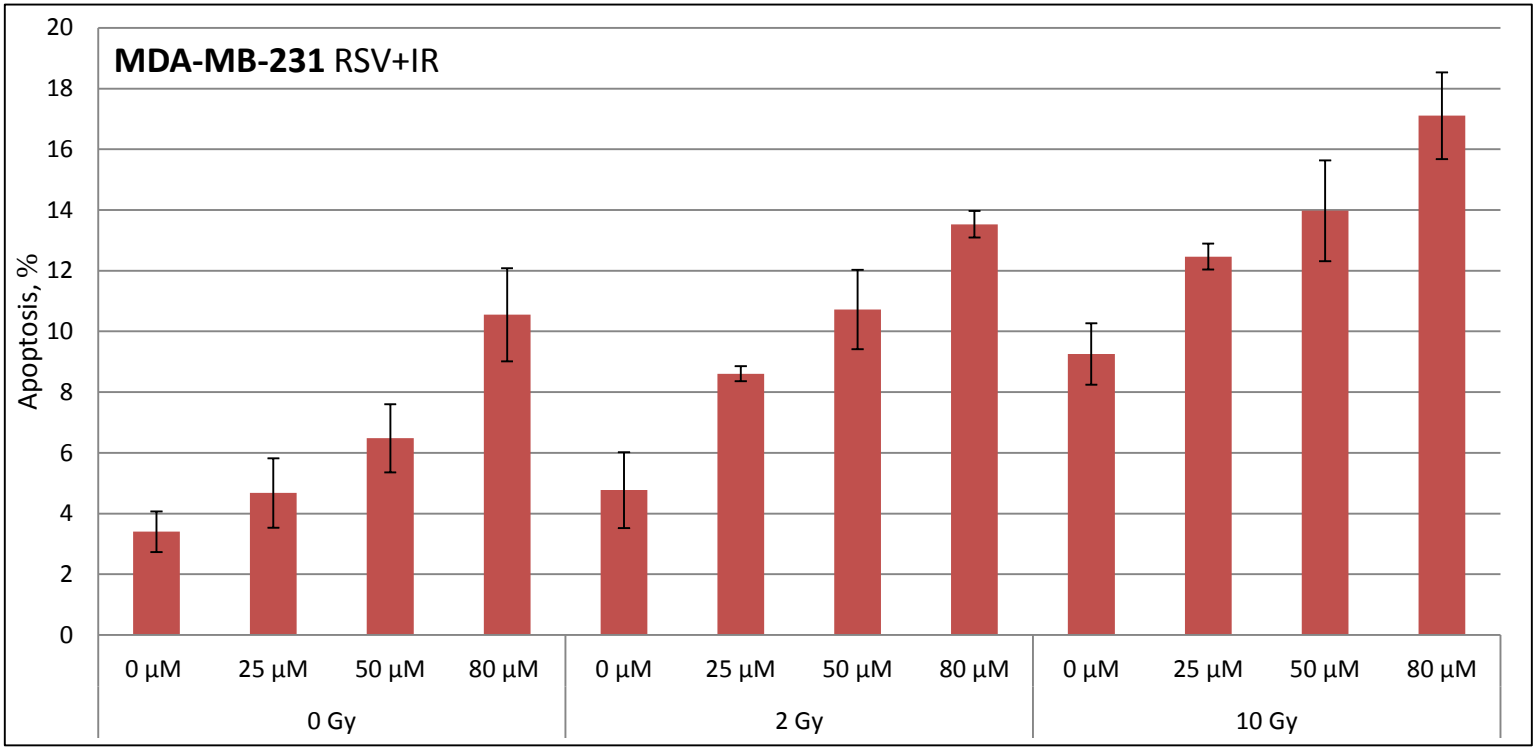
The radiosensitizing effect of resveratrol at different concentrations (25, 50, 80 μM) in 24 h cell culture irradiated at 0, 2, and 10 Gy were evaluated.



The combination of resveratrol and radiation (RSV+IR) treatment produced significantly greater antitumor effects on the breast cancer cells than either treatment alone.

Results

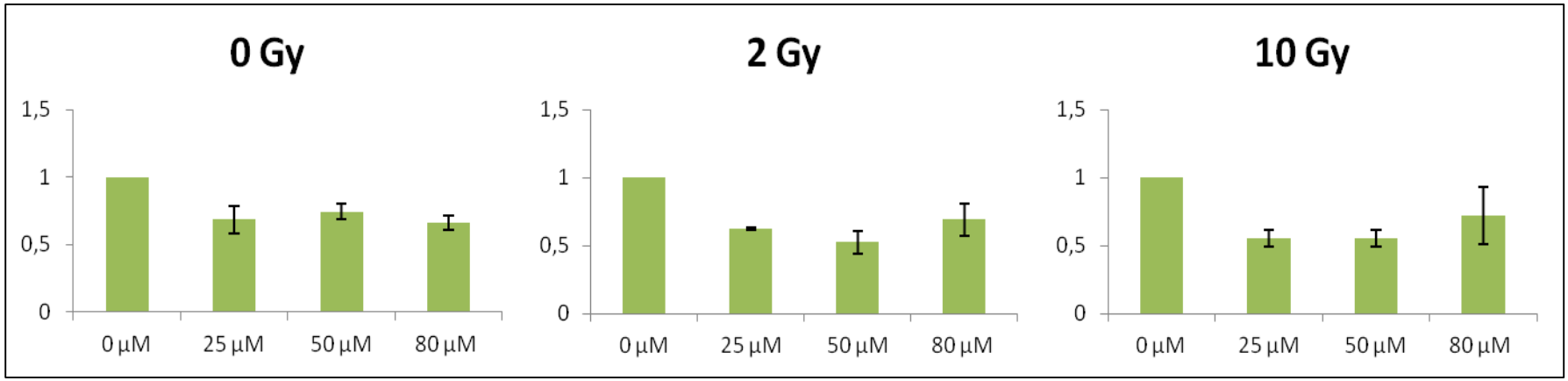
To determine whether the RSV-induced inhibition of breast cancer cells growth was due to cell apoptosis, MDA-MB-231 cells were stained with annexin V. Flow cytometry analysis showed that the apoptotic cell population increased in a dose-dependent manner.



The activation of apoptosis was also demonstrated by the combination of RSV+IR therapy. The percentage of cells undergoing apoptosis increased with radiation dose and resveratrol concentration.

Results

The combination of RSV+IR treatment significantly reduced *BCL2* gene expression than either treatment alone.



Conclusions

- So, to conclude, our study results revealed that resveratrol is a potential radiosensitizer of MDA-MB-231 breast cancer cells.

- We also demonstrated that the inhibitory effect of combination of RSV+IR cell growth was related to the induction of apoptosis and the expression reduction of anti-apoptotic gene *BCL2*.

Thanks for your attention!!!

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