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**Investigation of oxidative stress and programmed cell  
death pathways in cancer cell lines**

Ph.D. theses

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## **Introduction**

Cell death is an essential biological process for the proper functioning of an organism. Cell death processes can be classified into two major categories. Necrosis is the unregulated, passive form of cell death, usually triggered by severe physical, mechanical, or chemical damage. In contrast, in the case of programmed cell death, the destruction and elimination of the cell are carried out through strictly defined and regulated molecular processes. This regulation allows for potential intervention, whether it be inhibition or induction. However, precisely understanding the specific cell death mechanism is essential for this intervention. Numerous triggers and molecular mechanisms have been identified to date. Still, new forms of cell death are continuously being described, and even among the already known cell death processes, there are molecules and regulatory pathways with unknown roles. Many human diseases are also linked to abnormal cell death processes, and a detailed understanding of the underlying programmed cell deaths involved can contribute to the comprehension and treatment of these diseases.

Redox homeostasis is maintained by oxidant and antioxidant systems. A disruption in the balance of these systems in favor of oxidants is called oxidative stress, which can result from increased production of oxidants, such as reactive oxygen species (ROS), or a reduction in antioxidant levels. The oxidation of important macromolecules, such as DNA, proteins, or lipids, can lead to a loss of function and may even trigger cell death.

Unsurprisingly, oxidative stress and programmed cell death processes are subjects of intense scientific interest. Numerous research groups are working on identifying the molecular background and modulatory pathways of specific cell death types. Furthermore, increasing emphasis is being placed on understanding the molecular mechanisms of potential therapeutic agents. These could contribute to the development of more effective therapeutic approaches.

Our research aimed to understand various potential anti-tumor agents' mechanisms of action and the background of programmed cell death processes, with particular focus on ferroptosis, a recently described (in 2012), iron-dependent, oxidative form of cell death (Dixon *et al.*, 2012).

## Background

In contrast to necrosis, in the case of programmed cell death forms, the destruction and elimination of the cell is a strictly defined and regulated molecular process. Programmed cell death can occur without external damaging factors or be triggered by harmful intracellular or environmental stimuli. Today, numerous types of genetically regulated forms of programmed cell death are known. For a long time, it was believed that these cell death pathways operate independently and in parallel with each other. With recent findings, it is believed that they exhibit significant overlaps, and ultimately, the fate of a cell results from the interaction of these processes (Shen, Shao and Li, 2023).

Ferroptosis was first described in 2012 by Brent Stockwell's research group while searching for agents selectively killing RAS-mutant tumor cells (Dixon *et al.*, 2012). Later, it was revealed that cell death by ferroptosis is not limited to RAS-mutant tumor cells. Its role has been demonstrated in neurodegenerative disorders such as Alzheimer's disease, Huntington's disease, and Parkinson's disease, as well as in kidney injury, hematological diseases, and ischemia-reperfusion injury. In these cases, the inhibition of ferroptosis may be beneficial for managing symptoms. In contrast, inducing ferroptosis could be a potential therapeutic strategy to kill cancer cells (Han *et al.*, 2020). The mechanism of ferroptosis is not yet fully understood. The detailed mechanisms of its regulation and progression could contribute to its therapeutic exploitation in related diseases. Ferroptosis differs from previously described forms of programmed cell deaths. Morphologically it is characterized by mitochondrial shrinkage, increased mitochondrial membrane density and disappearance of internal cristae, while the plasma membrane remains intact. It is an oxidative form of cell death, with key biochemical features including intracellular glutathione (GSH) depletion and decreased glutathione peroxidase 4 (GPX4) activity, elevated intracellular free iron levels, increased quantity of reactive oxygen species (ROS), and lipid peroxidation (Dixon *et al.*, 2012). Ferroptosis can be induced by inhibiting antioxidant defense systems or by increasing the intracellular free iron level, which plays a key role in ROS formation through the Fenton reaction.

Regulation of the redox homeostasis is essential for maintaining normal cellular functions and ensuring the cell's survival. Redox balance is maintained by an equilibrium between oxidants and antioxidant systems. Oxidative stress occurs when the amount of oxidants exceeds the capacity of the antioxidant defense systems, leading to macromolecular damage and potentially cell death. Under normal conditions, reactive oxygen species can be generated as byproducts of oxygen metabolism, but various environmental stressors, such as UV radiation, ionizing

radiation, heavy metals, xenobiotics, and drugs can significantly increase ROS production. Excessive ROS levels have been associated with numerous diseases, although they are essential at strictly regulated levels. ROS plays a role in various physiological processes such as signal transduction pathways (Pizzino *et al.*, 2017).

Tumor development is a complex process requiring both cellular and molecular changes, which are mediated by endogenous and/or exogenous triggers. It is well established that oxidative stress can lead to increased oxidative DNA damage, further promoting the development of oncogenic properties in tumor cells. Persistent oxidative stress is a common characteristic of tumor cells, which can have numerous potential causes, including increased metabolic activity, mitochondrial dysfunction, increased peroxisomal activity, altered signaling pathways, increased activity of certain enzymes, or interactions with infiltrating immune cells. (Szarka *et al.*, 2021). In cancer, oxidative stress plays a dual role: low or moderate ROS levels may promote tumor formation and adaptation to the microenvironment through modifications of cell proliferation, migration, invasion, and angiogenesis, whereas high ROS levels can trigger cell death (Nakamura and Takada, 2021). Prooxidants are often considered potential chemotherapeutic agents and are sometimes they are used in cancer therapy (e.g., sorafenib) (An *et al.*, 2024).

Potential tumor-suppressive prooxidant agents include RSL3 and erastin, the first known specific inducers of ferroptosis. The canonical ferroptosis induction pathway involves inhibition of the key antioxidant defense enzyme, GPX4. Erastin can bind to SLC7A11, inhibiting the protein that transports the precursor of GSH, the cofactor of GPX4, into the cell's cytoplasm (Dixon *et al.*, 2012). RSL3 acts through its chloroacetamide part to form a covalent bond with the selenocysteine side chain of GPX4, directly and irreversibly inhibiting the enzyme's peroxidase activity (Wang, Chen and Yan, 2022).

Vitamin C (L-ascorbic acid, ascorbate) is a low molecular weight antioxidant essential for maintaining normal cell functions. Beyond its role in maintaining redox homeostasis, it plays key roles in numerous biochemical pathways. Contrary to its antioxidant function, at high concentrations (1–20 mM) it acts as a prooxidant (Szarka, Lőrincz and Hajdinák, 2022). At such concentrations, it is called pharmacological ascorbate (Ph-Asc). In the human body these high levels can only be achieved by intravenous administration (Padayatty *et al.*, 2004). It was shown that as a prooxidant, it can selectively kill tumor cells, suggesting a promising anticancer therapeutic option in combination with other chemotherapeutics or radiation therapy (Zaher *et al.*, 2022). It is believed that the antitumor and prooxidant effect of Ph-Asc comes from the

generation of H<sub>2</sub>O<sub>2</sub> via the Fenton reaction (Buranasudja *et al.*, 2019; Szarka, Lőrincz and Hajdinák, 2022).

Chloroquine (CQ) is a well-known antimalarial drug that has been used for a long time (Ciak and Hahn, 1966). Numerous examples exist of CQ being used for non-antimalarial purposes, although its exact mechanism is not always clear. Many studies have applied it in tumor cells to sensitize them to chemotherapy (Bryant *et al.*, 2019). Its anticancer effect is usually attributed to its ability to inhibit autophagy. CQ inhibits the fusion of autophagosomes with lysosomes, thereby reducing the autophagic flux (Mauthe *et al.*, 2018).

Resveratrol (RES) is a naturally occurring non-flavonoid polyphenol, which can be found in various plants. RES exerts its effects by modulating oxidative stress and several signaling pathways, such as cell death processes, enzyme expression, and inflammatory responses (Meng *et al.*, 2020). Its antitumor effects have been linked to numerous cellular signaling pathways, including cell cycle arrest, inhibition of tumor cell proliferation, induction of apoptosis (Brockmueller *et al.*, 2023), and reduction of inflammatory processes (De Sá Coutinho *et al.*, 2018).

Menadione (2-methyl-1,4-naphthoquinone) is a synthetic vitamin K compound. It is a precursor of vitamins K1 and K2, but numerous studies have demonstrated its other wide-ranging biological activities, including antitumor, antibacterial, antifungal, and antimalarial properties (Dasari *et al.*, 2017; de Souza *et al.*, 2022). Its potential anticancer effects have been studied in vitro experiments, both alone and as a chemosensitizing agent (Bajor *et al.*, 2020; Zoughaib *et al.*, 2024). Its antitumor effect is attributed to the ROS generated by the redox cycling of menadione (de Souza *et al.*, 2022).

## Objectives

To better understand the molecular mechanism of ferroptosis, we investigated a hypothesized link between the JNK pathway and ferroptosis. The two processes have several similarities, suggesting a link between them: they are regulated by reactive oxygen species (ROS) (Ueda *et al.*, 2002; Shen and Liu, 2006), they can be inhibited by lipid peroxide scavengers (Shrivastava and Aggarwal, 1999; Ueda *et al.*, 2002), and RAS mutations may play a role in the initiation of both pathways (McCubrey, Lahair and Franklin, 2006). In the second part of the studies, we investigated the mechanism of a previously described synergistic cytotoxic effect of Ph-Asc, CQ, and RES. Furthermore, we compared the mechanism of action of several potential anti-tumor agents, believed to cause oxidative stress.

Our objectives were:

1. Investigation of the hypothesized link between ferroptosis and the JNK signaling pathway.
2. Investigation of the mechanism behind the synergistic cytotoxic effect of pharmacological ascorbate (Ph-Asc), chloroquine (CQ), and resveratrol (RES) combination treatment.
3. Comparison of the effects of Ph-Asc and the inorganic Fenton reagent ( $\text{H}_2\text{O}_2 + \text{FeSO}_4$ ).
4. Investigation of mechanisms of potentially oxidative stress-induced cell deaths by Ph-Asc, CQ, RES, RSL3, and menadione.

## Methods

- Measurement of cell viability with MTT assay
- Flow Cytometry:
  - Determination of ROS levels and lipid peroxidation
  - Determination of apoptosis markers
  - Determination of cell cycle distribution
  - Determination of lysosome quantity
  - Determination of FSP1 levels using fluorescently labelled antibody
- Determination of the quantity and intracellular distribution of FSP1 by microscopy using fluorescently labelled antibody
- Determination of caspase-3/7 activity by fluorescent enzyme activity assay
- HPLC-UV/Vis:
  - Determination of reduced glutathione quantity
  - Determination of ATP and  $\text{NAD}^+$  quantity
- Protein isolation and protein concentration measurement
- Western blot

## Results and discussion

### The investigation of the possible link between the JNK pathway and ferroptosis

Ferroptosis and the JNK signaling pathway have several similarities, which suggest a link between them:

- i. Both processes are ROS mediated (Ueda *et al.*, 2002; Shen and Liu, 2006)
- ii. Both can be inhibited by lipid peroxide scavengers (Shrivastava and Aggarwal, 1999; Ueda *et al.*, 2002)
- iii. RAS mutations may play a role in the initiation of both pathways (McCubrey, Lahair and Franklin, 2006)

We aimed to investigate this hypothesized link between the JNK signaling pathway and ferroptosis. Since ferroptosis was first described using HT-1080 cells (Dixon *et al.*, 2012), and most studies on ferroptosis have been performed using this cell line, we also chose this cell line for our studies.

The JNK inhibitors alone did not cause cell death, but when co-treated with ferroptosis inducers, they further reduced cell viability compared to RSL3 or erastin treatment alone. When ferroptosis was induced with RSL3, we observed phosphorylation of c-Jun protein, the main substrate of the JNK protein. These results confirmed the link between the two pathways.

After this, we aimed to elucidate the background of this link and the synergistic cytotoxic effect of RSL3 and JNK inhibitors. We investigated which specific inhibitors of known cell death types could prevent cell death caused by RSL3 and JNK inhibitors. The apoptosis inhibitor Z-VAD-FMK did not protect against cell death induced by the combination of RSL3 and JNK inhibitors, nor did inhibition of JNK cause any change in the markers of apoptosis (caspase-3/7 activity and annexin V labeling). We therefore concluded that apoptosis does not play a role in this synergistic cytotoxicity. We did not find a cell death pathway whose inhibition counteracts only the effect of the JNK inhibitors. Only by completely preventing ferroptosis could we achieve an increase in cell viability after treatment with the combination of RSL3 and JNK inhibitors. We concluded that JNK inhibitors alone are unable to induce cell death in the HT-1080 cell line and do not induce a secondary cell death, such as apoptosis, but they do amplify the effect of ferroptosis inducers. RSL3 treatment significantly increased both ROS levels and lipid peroxidation, but this elevated lipid peroxidation and ROS levels were not further affected by the JNK inhibitors, so increased ROS production is not the underlying cause of the synergy.

Based on these findings, we hypothesized that the JNK pathway may influence a defense mechanism against ferroptosis. Two main pathways are defending against ferroptosis. Inhibition of these pathways is known to increase sensitivity to ferroptosis. It has been well established that the inhibition of the GSH-GPX4 antioxidant system through glutathione (GSH) depletion or inhibition of the enzyme GPX4 plays a central role in the induction of ferroptosis (Dixon *et al.*, 2012). In addition, FSP1 also contributes to ferroptosis defense. FSP1 is a membrane-bound oxidoreductase enzyme that catalyzes the regeneration of ubiquinone, also known as coenzyme Q10 (Q10, CoQ10), using NAD(P)H. Q10 is a lipophilic antioxidant, and with the continuous regeneration by the membrane-associated FSP1, it can inhibit lipid peroxidation locally at the cell membrane (Doll *et al.*, 2019). Pharmacological inhibition of FSP1 using its inhibitor iFSP1 had synergistic cytotoxicity with ferroptosis inducers (RSL3, FIN56, erastin). Similar to JNK inhibitors, iFSP1 did not influence ROS levels or lipid peroxidation. Although inhibition of both JNK and FSP1 showed similar outcomes, our results suggest that JNK inhibition does not affect the FSP1–CoQ10–NAD(P)H pathway. JNK inhibitors did not affect the quantity or intracellular localization of FSP1.

We next investigated the relationship between the JNK pathway and the key antioxidant in ferroptosis defense, GSH. Treatment with BSO (buthionine sulfoximine) inhibits GSH synthesis. BSO treatment completely depleted the cellular GSH content, though on its own, it did not affect cell viability. However, we observed a significant decrease in cell viability when cells were treated with JNK inhibitors after BSO treatment, even though neither compound alone induced cell death. Based on these results, GSH may play a central role in the ferroptosis-sensitizing effect of JNK inhibitors, however, further experiments are required to confirm and to understand the background of this phenomenon.

### **Investigating the mechanism of action of potential cancer therapeutics**

Drug development is a time- and resource-consuming process, so different strategies have been developed to reduce the costs. One such strategy is the use of an already approved drug for a new disease, which often exploits unknown (side)effects. Another option is to combine drugs, which can increase efficacy, trigger multiple pathways in the cells, and reduce the development of drug resistance, thus allowing lower doses.

Our research group has previously built an *in silico* model containing the main elements of the regulatory network in KRAS mutant cancer cells (Kapuy, Makk-Merczel and Szarka, 2021). Based on this model, the combined treatment with Ph-Asc and CQ in KRAS-mutant tumors could be a potential therapeutic approach through the inhibition of the Warburg effect, the

KRAS pathway, and autophagy. Ph-Asc was shown to induce a decrease in GLUT1 expression (Aguilera *et al.*, 2016), and CQ inhibits autophagy (Cai *et al.*, 2018).

Our results showed that the combined treatment with Ph-Asc and CQ indeed resulted in a synergistic cytotoxic effect on KRAS-mutant cells, however, further experiments have shown that Ph-Asc does not exert its effects through the KRAS pathway or GLUT1 expression (Makk-Merczel *et al.*, 2024).

In our experiments, we confirmed the autophagy inhibitory effect of CQ but found its synergistic cytotoxic effect to be independent of its autophagy inhibitor ability. We compared the mechanism of action of several other potential anti-tumor agents. RES significantly reduced viability in MIA PaCa-2 cells, and showed synergistic cytotoxic effects in combination with Ph-Asc and CQ. Both Ph-Asc (Szarka *et al.*, 2021), CQ (Besaratina, Caliri and Tommasi, 2021) and RES (Woods and Turchi, 2013) have been shown to cause DNA damage. We confirmed these results and showed the DNA-damaging ability of RSL3, menadione, and H<sub>2</sub>O<sub>2</sub>. All potential antitumor agents tested caused DNA damage, which is a common point in their mechanism of action, and this could be behind the synergistic cytotoxicity of Ph-Asc, CQ and RES.

Poly(ADP-ribose) polymerase 1 (PARP1), when activated by mild or moderate levels of DNA damage, helps to initiate DNA repair mechanisms and supports cell survival. However, in the case of severe DNA damage, PARP1 hyperactivity can lead to excessive consumption of NAD<sup>+</sup> and ATP, and their depletion can ultimately result in cell death (Luo and Kraus, 2012; Buranasudja *et al.*, 2019). Buranasudja and colleagues found that in the MIA PaCa-2 cells, Ph-Asc induces DNA damage, therefore, PARP1 activation, which leads to the depletion of NAD<sup>+</sup> and ATP due to their intense utilization. However, they concluded that the disruption of bioenergetics is a secondary factor in the toxicity of Ph-Asc, and damage to the DNA appears to be the primary factor (Buranasudja *et al.*, 2019). We confirmed these results and found that, unlike Ph-Asc, CQ and RES did not result in a decrease in NAD<sup>+</sup> or ATP levels despite the presence of DNA damage. This suggests a different mechanism of action than Ph-Asc.

DNA damage often causes cell cycle arrest, therefore, we examined the changes in cell cycle phase distribution after treatments with Ph-Asc, H<sub>2</sub>O<sub>2</sub>, RES, CQ, menadione, and RSL3. Although the cytotoxic effect of Ph-Asc is primarily attributed to its ability to generate H<sub>2</sub>O<sub>2</sub>, the effects of the two compounds on cell cycle distribution proved to be different. While Ph-Asc had little to no effect on the cell cycle, H<sub>2</sub>O<sub>2</sub> treatment caused a concentration-dependent and significant cell cycle arrest. Additionally, CQ, RES, menadione, and RSL3 also induced

cell cycle arrest, but the phase distribution was different, indicating partially different mechanisms of action.

Oxidative stress often causes significant damage to macromolecules, including nucleic acids, therefore, it is a common cause of DNA damage. The cytotoxic effects of Ph-Asc, H<sub>2</sub>O<sub>2</sub>, menadione, and RSL3 are explicitly attributed to their oxidative nature. CQ and RES were also shown to cause oxidative stress (Rodríguez-Enríquez *et al.*, 2019; Gregório *et al.*, 2021), but it is not clear whether oxidative stress is the underlying cause of their cytotoxicity.

In our experiments, CQ treatment did not induce oxidative stress in Mia PaCa-2 cells. CQ did not affect intracellular ROS levels and lipid peroxidation, and its cytotoxic effect could not be counteracted by co-treatment with the antioxidant N-acetylcysteine (NAC). These results suggest that ROS formation does not play a key role in CQ-induced cell death. Although RES treatment increased intracellular ROS levels, it did not cause lipid peroxidation, and its cytotoxic effect could not be counteracted by co-treatment with NAC. Suggesting that ROS formation, although present, does not play a key role in RES-induced cell death. Ph-Asc, H<sub>2</sub>O<sub>2</sub>, and menadione treatments all increased ROS levels and lipid peroxidation. H<sub>2</sub>O<sub>2</sub> treatment induced a concentration-independent and lower degree of lipid peroxidation than Ph-Asc. This is another difference in the mechanism of action of Ph-Asc and H<sub>2</sub>O<sub>2</sub>. The difference could be explained by the fact that H<sub>2</sub>O<sub>2</sub> causes a sudden, large amount of ROS formation, but it is an unstable substance and is quickly eliminated, while Ph-Asc can maintain a lower but continuous level of H<sub>2</sub>O<sub>2</sub> and oxidative stress by the Fenton reaction. Elevated ROS levels and lipid peroxidation are classic features of ferroptosis, but our research group has previously shown that ferroptosis does not play a role in Ph-Asc-induced cell death (Lőrincz *et al.*, 2019). We also found that ferroptosis does not play a role in either H<sub>2</sub>O<sub>2</sub>- or menadione-induced cell death. Cell death induced by Ph-Asc, H<sub>2</sub>O<sub>2</sub> or menadione was not inhibited by specific ferroptosis inhibitors such as liproxstatin-1 or ferrostatin-1, but cell death was prevented by co-treatment with NAC. This confirms that ROS formation plays a key role in the mechanism of cell death induced by Ph-Asc, H<sub>2</sub>O<sub>2</sub> and menadione, but ferroptosis is not involved. We found the MIA PaCa-2 cell line ferroptosis resistant, therefore confirmed that menadione does not induce ferroptosis in the known ferroptosis-sensitive cell line, HT-1080. The characteristic increased ROS levels and lipid peroxidation were present, but specific ferroptosis inhibitors did not protect against menadione-induced cell death in the HT-1080 cell line either.

## **Theses**

1. We have described that pharmacological inhibition of the JNK protein enhances the cytotoxic effect of ferroptosis inducers, suggesting a link between the two pathways (Varga et al., 2022).
2. We observed that pharmacological ascorbate and chloroquine have a synergistic cytotoxic effect on MIA PaCa-2 PDAC cells, but the (synergistic) cytotoxic effect of CQ is not due to its autophagy inhibitory effect (Makk-Merczel et al., 2024).
3. We have shown that pharmacological ascorbate, chloroquine, resveratrol, menadione and RSL3 all cause DNA damage, which may be the basis of the synergistic cytotoxicity of Ph-Asc, CQ and RES. For RSL3, there is no previous literature data on its DNA-damaging effects (Varga, Szentirmai and Szarka, 2025).
4. We have described the ferroptosis resistance of the MIA PaCa-2 cell line, which may be due to higher GPX4 and lower ACSL4 expression levels than in the ferroptosis-sensitive HT-1080 cell line (Varga, Szentirmai and Szarka, 2025).

## **Possible application of the results**

Inadequate regulation of redox homeostasis and programmed cell death processes, such as ferroptosis, can play a role in many diseases (Han *et al.*, 2020). Prooxidants have potential therapeutic applications and are being investigated and sometimes applied as therapeutic agents against cancer (Pizzino *et al.*, 2017). Depending on the disease, a precise understanding of the regulation of redox homeostasis, the triggers of oxidative stress, or the mechanisms of cell death may contribute to the understanding of the given disease and the development of potential therapeutic approaches. Our research helps to better understand the mechanism and regulation of oxidative stress and the oxidative-based programmed cell death, ferroptosis.

## Publications

### Publications in relation to the dissertation:

1. Dóra Varga, Péter Hajdinák, Kinga Makk-Merczel, András Szarka. The Possible Connection of Two Dual Function Processes: The Relationship of Ferroptosis and the JNK Pathway. *Int. J. Mol. Sci.* **2022**, *23*, 11004. doi: 10.3390/ijms231911004 (IF: 6,201; D1 (2022))
2. Kinga Makk-Merczel, Dóra Varga, Péter Hajdinák, András Szarka. The interlacing anticancer effect of pharmacologic ascorbate, chloroquine, and resveratrol. *Biofactors*. 2024 Mar 15. doi: 10.1002/biof.2050 (IF: 6,807; Q1 (2024))
3. Dóra Varga, Anna Szentirmai, András Szarka. Research for a Common Thread: Insights into the Mechanisms of Six Potential Anticancer Agents. *Molecules* 2025, *30*, 1031. doi: 10.3390/molecules30051031 (IF: 5,266; Q1 (2024))

### Presentations in relation to the dissertation:

1. Dóra Varga, András Szarka. Programozott sejthalál-folyamatok vizsgálata: Ferroptózis és a JNK útvonal kapcsolata (Programmed cell death pathways: The connection of ferroptosis and the JNK pathway), UNKP conference, online, 2023.06.07.
2. Dóra Varga, András Szarka, Péter Hajdinák, Kinga Makk-Merczel. A ferroptózis és a JNK jelátviteli útvonal közötti lehetséges kapcsolat (The possible connection of ferroptosis and the JNK pathway), A Magyar Szabadgyök-kutató Társaság XII. Kongresszusa, Martonvásár, 2023.08.24-25.
3. Dóra Varga, András Szarka, Péter Hajdinák, Kinga Makk-Merczel. The possible connection of ferroptosis and the JNK pathway, V. George Olah Conference, XXI Conference of the George Olah Doctoral School, Budapest, 2023.09.12.
4. Dóra Varga, András Szarka. A ferroptózis és szerepe a diabéteszben és szövődményeiben (The ferroptosis and its role in diabetes and complications of diabetes), Fiatal diabetológusok és diabetológiai témával foglalkozók tudományos találkozója, Budapest, 2024.05.17.

### Poster in relation to the dissertation:

1. Dóra Varga, András Szarka, Péter Hajdinák, Kinga Makk-Merczel. The Possible Connection of Ferroptosis and the JNK Pathway, The 2023 annual meeting of the Society for Free Radical Research – Europe (SFRR-E), Vienna, Austria, 2023.06.06-09.

### Other publication:

4. Tamás Lőrincz, Veronika Deák, Kinga Makk-Merczel, Dóra Varga, Péter Hajdinák, András Szarka. The Performance of HepG2 and HepaRG Systems through the Glass of Acetaminophen-Induced Toxicity. *Life (Basel)*. 2021 Aug 21;11(8):856. doi: 10.3390/life11080856. (IF: 3,371; Q2 (2021))

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