In vivo effects of olive oil, coffee extract, Chinese bayberry extract, green tea extract, polyphenol extract and trans-fatty acids on miR-134, miR-132, miR-124-1, miR-9-3 and mTORC1 gene expression in a DMBA-treated mouse model

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1. Introduction

Nowadays, the incidence and mortality of malignant tumorous diseases in high-income countries is decreasing, but in the low- and middle-income countries the trend-line is still supposed to increase slightly. According to the WHO's assessment, 30–50% of cancer cases could have been prevented.

Environmental factors, such as smoking and inadequate level and composition of fat intake, are a major cause of cancer. Therefore, the chemical carcinogen 7,12-dimethylbenz(a)anthracene (DMBA), also found in tobacco smoke, has been used for decades to induce tumorous lesions in experimental animals. Furthermore, trans-3-hexadecenoic acid, a transfatty acid (TFA) used in my research has been reported in several studies to have harmful effects on animal organs.

However, *in vitro*, *in vivo* and epidemiological studies suggest that chemopreventive polyphenols reduce the probability of tumor formation. Of these, flavonoids are particularly promising chemopreventive substances. Therefore I examined the chemopreventive effects of extra virgin olive oil (Oleaeuropaea), of green tea (Camellia sinensis) extract, of Japanese waxberry (Myrica rubra) extract, of coffee (Coffea arabica) extract and of a polyphenol (mainly containing resveratrol and flavonoids) extract, as well as the harmful effects of DMBA and TFA in my study.

These effects are expected to be properly monitored by measuring the expression of miR-134, miR-132, miR-124-1, miR-9 microRNAs (miRNAs) and of the m-TOR gene, because their expression is increased by DMBA-induced damage, which may be enhanced by TFA, while the mentioned chemopreventive substances decrease it.

2. Objective

In my study I examined the expression of four miRNAs (miR-134, miR-132, miR-124-1, miR-9-3) and the mTORC1 gene in organs (liver, spleen, kidney) of DMBA-treated animals, to study the effects of different substances in the human diet on them. This miRNA and gene expression panel was found to be a reliable early biomarker of carcinogenicity in a previous study. I wanted to explore whether the chemopreventive agents studied are able to prevent the gene and miRNA expression changes caused by carcinogenic DMBA and whether it would be useful to include them in the diet for preventive purposes. In the case of TFA, the aim of the study was to confirm or to exclude a potential carcinogenic effect.

3. Materials and methods

3.1 Materials used:

1. extra virgin oil cold pressed from the berries of olive oil (Oleaeuropaea)

2. green tea (Camellia sinensis) extract

3. Chinese bayberry (Myrica rubra) extract

4. polyphenol extract (wine grape (Vitis vinifera "Cabernet Sauvignon"), thornless blackberry (Rubus fruticosus "Thornfree"), blackcurrant (Ribes nigrum) seeds and peel, added resveratrol content: 4 grams/100 ml decoction),

5. coffee (Coffee arabica) extract

6. TFA (trans-3-hexadecenoic acid)

Treatment of the groups studied and components of the substances consumed are summarised in Table 1.

	ip. DMBA		**Experimental material**			
Name of the group		**Daily dose/animal**	**Manufacturer/Product**	**Name of the group**		**Daily dose/animal**
negatíve control	-			**negatíve control**	-	
positive control	+		Sigma Aldrich Ltd.	**positive control**	+	
polypheno extract	+	30 mg	SC Vita Crystal Research SRL. FruitCafe™	**polyphenol extract**	+	30 mg
				Eritrit	(2R,3S)-bután-1,2,3,4-tetraol	12000 mg / 100 ml forrázat
				rezveratrol	transz-3,5,4'-trihidroxisztilbén	4000 mg / 100 ml forrázat
				fekete szeder mag, héj	*Rubus fruticosus „Thornfree"*	2000 mg / 100 ml forrázat
				fekete ribiszke mag, héj	*Ribes nigrum*	2000 mg / 100 ml forrázat
				összes polifenol		4000-5000 mg / 100 ml forrázat
coffee extract	+	30 mg	Xi'an Longze Biotechnology Co. Ltd.	**coffee extract**	+	30 mg
				klorogénsav	3-kaffeoil sav	5,03%
				Koffein	1,3,7-trimetilxantin	1,21%
green tea extract	+	4 mg	Xi'an Longze Biotechnology Co. Ltd.	**green tea extract**	+	4 mg
				összes polifenol		98,53%
				összes katekin		80,42%
				EGCG	epigallokatekin-3-gallát	50,45%
				Koffein	1,3,7-trimetilxantin	0,28%
Chinese bayberry extract	+	2,5 mg	Xi'an Longze Biotechnology Co. Ltd.	**Chinese bayberry extract**	+	2,5 mg
				Myricetin	3,5,7,3',4',5'-hexahidroxiflavon	80,42%
Extra virgin olive oil	+	300 mg	Agraria Riva Del Garda SCA	**Extra virgin olive oil**	+	300 mg
Trans-fatty acid	+	300 mg	Sigma Aldrich Ltd.	**Trans-fatty acid**	+	300 mg

Table 1: Treatment of the groups studied and components of the substances consumed

3.2 Treatment of animals

In our study we used 6-8 week old female CBA/Ca mice and each group was housed in separate cages. The groups of animals (n=6) received olive oil at a dose of 300 mg/animal/day, trans fatty acid at a dose of 300 mg/animal/day, green tea extract at a dose of 4 mg/animal/day, Chinese bayberry extract at a dose of 2.5 mg/animal/day, polyphenol extract at a dose of 30 mg/animal/day and coffee extract at a dose of 30 mg/animal/day (150 ml) mixed into their diet for 14 days. The above groups were treated intraperitoneally (i.p.) with 20 mg DMBA/kg bw dissolved in 0.1ml of corn oil. In addition, a positive control group (n=6) was administered DMBA alone, as described above. After 24 h of DMBA exposure, the mice were euthanized, cervical dislocation was performed, and their livers, kidneys, and spleens were removed. The mice were treated according to the protocols for animal experimentation. Ethical approval number of the experiment: BA02/200-79/2017.

3.3 Isolation of RNA

Total cellular RNA isolation was performed using TRIZOL reagent (MRTR118-20 Nucleotest Bio Ltd.) according to the manufacturer's instructions. The RNA quality was checked by nanodrop absorbtion photometry and only RNA fractions with A > 2.0 at 260/280 nm were used for the RT-PCR process.

3.4 Reverse transcription polymerase chain reaction (RT-PCR)

The one-step PCR (reverse transcription, target amplification) was performed on a LightCycler 480 qPCR platform in a 96-well plate with the use of the Kapa SYBR FAST One-step RTQPCR kit (Kapa Biosystems).

The temperature programme was set according to the following protocol:

a) incubation at 42°C for 5 min,
b) incubation at 95°C for 3 minutes,
c) 45 cycles (95°C – 5 s, 56°C – 15 s, 72°C – 5 s) with a fluorescence reading at the end of each cycle.

The runs were performed by melting curve analysis (95°C – 5 s, 65°C – 60 s, 97°C ∞) to confirm the amplification specificity. The reaction mixture was the following: 10µl KAPA SYBR FASTqPCR Master Mix, 0.4µl KAPA RT Mix, 0.4µl dUTP, 0.4µl primers, 5µl miRNA template supplemented with sterile double-distilled water to a total volume of 20 µl.

The primer sequences of the miRNAs examined (miR-134, miR-132a, miR-124-1, mir-9-3), as well as of mTORC1 and of the internal control gene (mouse U6) are summarized in Table 2. Primers were synthesized by Integrated DNA Technologies (Bio-Sciences). Sequences were determined on the basis of previous studies.

	FORWARD	**REVERSE**
miR-134	TGTGACTGGTTGACCAGAGG	GTGACTAGGTGGCCCACAG
miR-132	ACCGTGGCTTTCGATTGTTA	CGACCATGGCTGTAGACTGTT
miR-124-1	TCTCTCTCCGTGTTCACAGC	ACCGCGTGCCTTAATTGTAT
miR-9-3	GCCCGTTTCTCTCTTTGGTT	TCTAGCTTTATGACGGCTCTGTGG
mTORC1	AAGGCCTGATGGGATTTGG	TGTCAAGTACACGGGGCAAG
mouse U6	CGCTTCGGCAGCACATATAC	TTCACGAATTTGCGTGTCAT

Table 2: Primer sequences (5'-3') of the mTORC1 gene, of the miRNAs examined (miR-134, miR-132, miR-124-1, miR-9-3) and of the internal control gene (mouse U6).

3.5 Calculations and statistical analysis

Relative levels of miRNA expression were calculated using the $2^{-\Delta\Delta CT}$ method and the Kolmogorov-Smirnov test was used to determine the distribution of results. Levene's F-test and t-test were used to compare means, and the analysis was performed using IBM SPSS 21 statistical software. We determined the level of statistical significance at $p < 0.05$.

4. Results

4.1. Effects of olive oil and DMB treatment in the organs studied

The liver of the group receiving the olive oil supplemented diet showed significantly decreased expression of miR-9-3 (-31.1%; $p<0.05$; SD=13.6%), of miR-124-1 (-57%; $p<0.05$; SD=10.9%), and of mTORC1 (-31%; $p<0.05$; SD=9.4%) compared to the DMBA positive control, while the decreases observed for miR-132 (5.8%; $p=0.66$; SD=17.1%) and for miR-134 (-16.9%; $p=0.21$; SD=18.6%) were not significant.

In the spleen, olive oil also caused a decrease in the expression of the studied miRs and the mTORC1 gene with a significant decrease of miR-9-3 (-42%; $p<0.05$; SD=14.7%), of miR-124-1 (-36%; $p<0.05$; SD=17.6%) and of mTORC1 (-26%; $p<0.05$; SD=7.7%), while the values for the miR-132 (-17%; $p=0.27$; SD=22.1%) and miR-134 (-8.5%; $p=0.51$; SD=19.6%) were not significant.

For kidneys, miR-9-3 (-68%; $p<0.001$; SD=6.1%), miR-124-1 (-46%; $p<0.05$; SD=15.5%), miR-132 (-65.3%; $p<0.001$; SD=7.8%) and miR-134 (-59.5%; $p<0.001$); SD=9.1%) were significantly decreased compared to the DMBA positive control, while the decrease in mTORC1 (-19%; p=0.051; SD=13.2%) gene expression was not significant following the olive oil treatment.

4.2. Effects of TFA and DMBA treatment in the organs studied

In the liver of animals, TFA consumption significantly increased the expression of miR-9-3 (423%; $p<0.001$; SD=110%), of miR-124-1 (832%; $p<0.001$; SD=243%), of miR-132 (337%; $p<0.001$; SD=124%), of miR-134 (275%; $p<0.001$; SD=98%) and of mTORC1 (69%; $p<0.001$; SD=24.2%) compared to the positive DMBA controls.

In the spleen, TFA significantly increased the expression of miR-9-3 (322%; $p<0.001$; SD=122.3%), of miR-124-1 (268%; $p<0.001$; SD=110.7%), of miR-132 (224.3%; $p<0.001$; SD=89.1%) and of miR-134 (151.8%; $p<0.001$; SD=62.5%) compared to the DMBA control.

Similarly, kidneys showed increasing results for miR-9-3 (159%; $p<0.001$; SD=63.5%), of miR-124-1 (391%; $p<0.001$; SD=121.1%), of miR-132 (432.2%; $p<0.001$; SD=122.8%)

and of miR-134 (238.4%); p<0.001; SD=67.9%), but gene expression of mTORC1 did not show significant increase in these organs, the increase was 19.5% in the spleen (p=0.07; SD=17.2%) and 18% in the kidneys (p=0.10; SD=18%).

4.3. Effects of polyphenol extract and DMBA treatment in the organs studied

In the liver of the animals, consumption of polyphenol extract significantly decreased the expression of miR-9-3 (-41%; p<0.05; SD=11.1%), of miR-124-1 (-68%; p<0.001; SD=10.1%), of miR-132 (-62.9%; p<0.001); SD=9.2%), of miR-134 (-77.9%; p<0.001; SD=5.6%) and of mTORC1 (-49%; p<0.001; SD=8.4%) compared to the positive DMBA control.

In the spleens of animals, we also observed a significant decrease in miR-9-3 (-38%; p<0.05; SD=12.1%), miR-124-1 (-59%; p<0.05), miR-124-1 (-59%; p<0.05); SD=9.8%), miR-132 (-62.4%; p<0.001; SD=8%), miR-134 (-60.4%; p<0.001; SD=8%) and mTORC1 (-39%; p<0.001; SD=8.6%) expressions compared to the positive DMBA controls.

In the kidneys of the animals, a significant decrease in miR-9-3 (-59%; p<0.001; SD=7.8%), miR-124-1 (-62%; p<0.05; SD=13.1%), miR-134 (-81.4%; p<0.001; SD=3.7%) and mTORC1 (-59%; p<0.001; SD=6.3%) expressions were observed compared to the positive DMBA control, while the values for miR 132 (-27.1%; p=0.051; SD=13.7%) were not statistically significant.

4.4. Effect of green tea extract and DMBA treatment in the organs studied

In the liver of animals, consumption of green tea extract significantly decreased the expression of miR-9-3 (-33%; p<0.05; SD=12.9%), of miR-124-1 (-69%; p<0.001; SD=7.4%), of miR-132 (-45.4%; p<0.05; SD=10.2%), of miR-134 (-59.2%; p<0.001; SD=8.9%) and of mTORC1 (-57%; p<0.001; SD=6.7%) compared to the positive DMBA controls.

In the spleen, green tea extract caused a decrease in the expression of miR-9-3 (-56%; p<0.001; SD=8.5%), of miR-124-1 (-62%; p<0.001; SD=11.3%), of miR-132 (-61.1%); p<0.001; SD=9.1%), of miR-134 (-47.6%; p<0.05; SD=11.2%) and of mTORC1 (-58%; p<0.001; SD=5.1%) compared to the positive DMBA controls.

In the kidneys, we also observed significant decreases in the expression of miR 9-3 (-48%; $p<0.05$; SD=11.4%), of miR-124-1 (-36%; $p<0.05$; SD=16.6%), of miR-132 (-59.6%; $p<0.001$; SD=10.8%), of miR-134 (-53.3%; $p<0.001$; SD = 11.1%) and of mTORC1 (-57%; $p<0.001$; SD=5.6%) compared to the positive DMBA controls in the group consuming green tea extract.

4.5. Effects of coffee extract and DMBA treatment in the organs studied

In the liver, we observed a significant decrease in miR 9-3 (-37%; $p<0.05$; SD=19.8%) and mTORC1 (-37%; $p<0.05$; SD=14%) expression in the coffee extract receiving group compared to the positive DMBA controls, while the results for miR-124-1 (-21%; $p=0.21$; SD=23.6%), for miR-132 (-16.7%; $p=0.24$; SD=19.4%) and for miR-134 (-12.7%; $p=0.32$; SD=16.7%) were not statistically significant.

In the spleen, there was a statistically significant decrease in the expression of miR 9-3 (-46%; $p<0.05$; SD=10.7%), of miR-134 (-38.9%; $p<0.05$; SD=12.7%) and of mTORC1 (-20%; $p<0.05$; SD=8.9%) in the coffee extract receiving group compared to the positive DMBA controls, while the decrease of miR-124-1 (-15%; $p=0.37$; SD=22.9%) and the slight increase of miR-132 (13.1%; $p=0.40$; SD=23%) was not statistically significant.

In the kidneys, statistically significant decreases were observed in miR 9-3 (-31%; $p<0.05$; SD=12.8%), in miR-124-1 (-47%; $p<0.05$; SD=13.6%), in miR-134 (-31.6%; $p<0.05$; SD=13.5%) and in mTORC1 (-22%; $p<0.05$; SD=8.7%) in the coffee extract receiving group compared to the positive DMBA controls, while the slight increase in miR-132 (22.1%; $p=0.18$; SD=25.4%) was not statistically significant.

4.6. Effects of Chinese bayberry extract and DMBA treatment in the organs studied

In the liver, we observed statistically significant decreases in miR 9-3 (-58%; $p<0.001$; SD=9.1%), in miR-124-1 (-43%; $p<0.05$; SD=14.6%), in miR-134 (-40.6%; $p<0.05$; SD=16.8%) and in mTORC1 (-39%; $p<0.001$; SD=9.6%) compared to the positive DMBA controls in the Chinese bayberry extract receiving group, while the decrease in miR-132 (-19.1%; $p=0.14$; SD=14.9%) was not statistically significant.

In the spleen, we observed statistically significant decreasing trend in the changes of miR 9-3 (-46%; $p<0.05$; SD=11.1%), of miR-124-1 (-57%; $p<0.05$; SD=12.9%), of miR-132

(-32.3%; p<0.05), of miR-134 (-51.8%; p<0.001; SD=10.3%) and of mTORC1 (-32%; p<0.001; SD=8.6%) in the Chinese bayberry extract consuming group compared to the positive DMBA controls.

In the kidneys of the group consuming Chinese bayberry extract statistically significant decreases were observed in miR-9-3 (-40%; p<0,05; SD=13,2%), in miR-124-1 (-51%; p<0.05; SD=14 %), in miR-132 (-57.9%; p<0.01; SD=10,5%), in miR-134 (-28.8%; p<0.05; SD=12.8%) and in mTORC1 (-22%; p<0.05; SD=11.9%) compared to DMBA positive controls.

5. Discussion

5.1. Harmful effects of DMBA

The degradation of DMBA leads to the formation of reactive oxygen species (ROS) and this activates transcription factors (e.g. NF-κB) which ultimately induces various cytokines (e.g. IL-1β, I-L6, TNF) and depletes the protective glutathion (GSH). The presence of high levels of IL1β implies the generation of inflammatory factors (TNF, MMPs), which also increase the risk of malignant cell proliferation by inducing NF-κB, because it reduces the expression of the tumour suppressor genes miR-134 and P53. Thus, the proinflammatory and cell proliferation enhancing factors act in a way that they mutually potentiate each other.

5.2. Harmful effects of TFA

TFA consumption activates vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1), which activate NF-κB, which through the generation of ROS, activate inflammation- and proliferation-promoting NF-κB. Therefore, it can be concluded that the examined mTOR gene and the miRs showed significant overexpression both in the TFA- and DMBA-treated groups.

5.3. Effects of the chemopreventive agents studied

Flavonoids and olive oil can reduce ROS-induced cell damage due to their molecular structure. The same is true for the chlorogenic acid, hydroxycinnamic acid and caffeine content of coffee and for its melanoidin content, as well. Furthermore, polyphenols are able to inhibit indirect carcinogenic activator microsomal enzymes, through which they significantly reduce the formation of DNA adducts. Resveratrol, myricetin, GTC and chlorogenic acid also induce the protective enzymes superoxide dismutase and glutathione S-transferase (GST). Furthermore, PUFA can also indirectly increase GSH levels.

5.3.1. The protective effects of olive oil

The most important antioxidant and anti-inflammatory substances in olive oil are the unsaturated fatty acids MUFA and PUFA. In addition, olive oil also contains water-

soluble substances with protective effects, the best known of which are oleuropein and oleocanthal.

5.3.2. Water soluble substances of olive oil

Oleuropein and oleocanthal are water-soluble secoiridoids with antioxidant and membrane protective effects. Oleuropein blocks NF-κB and oleocanthal protects intracellular GSH. This may lead to a decrease in miR-134, in miR-132 and in miR124-1 expression through negative feedback mechanisms, and significantly reduces the amount of overexpressed miR-9-3 due to DMBA treatment.

In the kidneys, oleuropein caused a strong and significant decrease in miR-134 and in miR-132 through the regulation of these negative feedbacks. The significantly decreased mTOR gene expression observed in both the liver and the spleen was also caused by the potent mTOR inhibitory effect of oleuropein.

5.3.2. Fat soluble substances of olive oil

PUFA has a direct β-catenin inhibitory effect, leading to a significant decrease in C-MYC expression, while C-MYC causes an increase in miR-9 expression. Furthermore, PUFA increased the amount of P300, the increase of which also leads to a decrease in miR-132 expression, as they cross-regulate each other. BIRC3 and miR-124 expression were negatively correlated, suggesting a negative feedback loop as ICAM-1 positively modulates miR-124 expression.

5.4. The protective effects of polyphenols

Polyphenols may have protected against DMBA-induced overexpressions of the biomarkers studied by inhibiting classical inflammatory interleukins (IL1, TNF-α, etc.) and, for example, the transcription factor NF-κB. For example, resveratrol decreases the expression of IL-1β, IL-6, TNF-α, among others. Resveratrol and myricetin stimulate CREB protein through the activated SIRT1-dependent signalling pathway and this leads to a decrease in miR-134, in miR-124 and in mTOR expression.

Both EGCG and resveratrol inhibit NF-κB and activate the PTEN gene. Through the former mechanisms, they decrease the expression of miR-132, of miR-124 and of miR-

9, while the latter decreases the amount of cell division protein cyclin D1. Moreover, resveratrol and EGCG also inhibit anti-apoptotic cascades by suppressing the MAPK pathway. This induces cell cycle arrest in the G0/G1 phase, which decreases the expression of miR-132 and increases the expression of miR-9.

In all the groups studied, the decrease in cyclin D1 levels may have led to the decrease of the mTOR expression by the above described mechanisms. In addition, myricetin inhibited PI3K, which also has an mTOR expression-reducing effects.

5.4.1. A kávé klorogénsav tartalma

Chlorogenic acid also decreases the gene expression of IL-1β, IL-6, TNF-α. The literary data are inconsistent with the results of our measurements suggesting that the chlorogenic acid content of coffee has a renoprotective effect by inducing miR-134 which leads to the suppression of MMP-9 and MMP-7. This ultimately reduced cyclin D1, encoded by CCND1, and its expression is inversely correlated with miR-134 – this is also inconsistent with our results suggesting a negative feedback mechanism rather than a direct support.

5.4.2. Effect of caffeine

Caffeine activates the PTEN gene, which decreases the amount of cell division protein cyclin D1, leading to the inhibition of the PI3-K/AKT/mTOR signalling pathway. In addition, caffeine induces P53-dependent apoptosis *in vitro*.

6. Conclusion and summary

It can be concluded that the chemopreventive agents studied exert their protective effects by inhibiting inflammatory and carcinogenic mechanisms. As nutritional factors, they thereby contribute to the prevention of malignant tumours. TFA has also been found to enhance inflammatory and carcinogenic effects. The aggregation of these mechanisms was properly showed by the expression of miR-134, of miR-132, of miR-124-1, of miR-9-3 and of mTORC1 gene as biomarkers.

6.1. DMBA and chemopreventive agents

DMBA increased the expressions of the miRs and mTOR studied, but these expressions were significantly reduced by the consumption of green tea, Chinese bayberry and polyphenol extract. These results partially correlate with the results of coffee extract consumption.

Feeding with olive oil-containing diet inhibited DMBA-induced inflammatory and proliferation enhancing signalling pathways (TNF, IL-1, IL-6 and NF-κB).

6.2. DMBA and the TFA

Feeding diets containing TFA significantly increased the expression of all miR and mTORC1 studied in all the organs studied, except the expression of mTORC1 in the spleen and in the kidneys. In the kidneys, however, contrary to our expectations, in the animal model used in the present study design, the expression of the mTORC1 gene did not prove to be a suitable biomarker to indicate the potential chemopreventive effects of TFA consumption. It is very likely that this is because mTOR plays a central - and therefore complex - role in the regulation of inflammatory biology and in the cell cycle, the mechanisms of which can quench even the effects of each others' gene expression.

Our results suggest negative feedback regulatory mechanisms (exploration of which may be the subject of further studies) and are mainly due to cell membrane damaging, pro-inflammatory and carcinogenic properties of TFA.

7. List of publications

7.1. List of publications used as a source for the dissertation:

Molnar R, Szabo L, Tomesz A, Deutsch A, Darago R, Raposa BL, Ghodratollah N, Varjas T, Nemeth B, Orsos Z, Pozsgai E, Szentpeteri JL, Budan F, Kiss I. The Chemopreventive Effects of Polyphenols and Coffee, Based upon a DMBA Mouse Model with microRNA and mTOR Gene Expression Biomarkers. Cells. 2022 Apr 12;11(8):1300.

IF: 7.666

Molnar R, Szabo L, Tomesz A, Deutsch A, Darago R, Ghodratollah N, Varjas T, Nemeth B, Budan F, Kiss I. In vivo effects of olive oil and trans-fatty acids on miR-134, miR-132, miR-124-1, miR-9-3 and mTORC1 gene expression in a DMBA-treated mouse model. PLoS One. 2021 Feb 4;16(2):e0246022.

IF: 3.752

7.2. Other publications:

Szabo L, Molnar R, Tomesz A, Deutsch A, Darago R, Varjas T, Ritter Z, Szentpeteri JL, Andreidesz K, Mathe D, Hegedüs I, Sik A, Budan F, Kiss I. Olive Oil Improves While Trans Fatty Acids Further Aggravate the Hypomethylation of LINE-1 Retrotransposon DNA in an Environmental Carcinogen Model. Nutrients. 2022 Feb 21;14(4):908.

IF: 6.706

Szabo L, Molnar R, Tomesz A, Deutsch A, Darago R, Nowrasteh G, Varjas T, Nemeth B, Budan F, Kiss I. The effects of flavonoids, green tea polyphenols and coffee on DMBA induced LINE-1 DNA hypomethylation. PLoS One. 2021 Apr 20;16(4):e0250157.

IF: 3.752

Tomesz A, Szabo L, Molnar R, Deutsch A, Darago R, Raposa BL, Ghodratollah N, Varjas T, Nemeth B, Orsos Z, Pozsgai E, Szentpeteri JL, Budan F, Kiss I. Changes in miR-124-1, miR-212, miR-132, miR-134, and miR-155 Expression Patterns after 7,12-Dimethylbenz(a)anthracene Treatment in CBA/Ca Mice. Cells. 2022 Mar 17;11(6):1020.

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IF: 2.09

7.3. Conferences:

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Budan F, Szabo L, Molnar R, Tomesz A, Varjas T, Ritter Zs, Szentpeteri LJ, Mathe D, Hegedus I, Sik A et al. Az extraszűz olíva olaj csökkenti a karcinogén DMBA l1-RTP DNS hipometiláló hatását. 51st MEMBRANE TRANSPORT CONFERENCE POSTERS ABSTRACTS 2022.