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Therapy of oral cancer from chemo-resistance to side effects: nutraceuticals and new perspectives

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1. Introduction and aim of the research

Lip, oral cavity and oropharyngeal cancer is still responsible of about 3.8% of cancer cases and about 3.6% of cancer deaths [1].

More specifically oral squamous cell carcinoma represents the 90% of malignancies affecting the oral cavity and the 3% of all human malignancies. OSCC can affect different areas of the mouth and tongue including lips, alveolar ridge, oral floor, oral tongue, hard palate, posterior molar triangle and buccal mucosa [2]. The 5-year survival rate remained stable below 50% and has not improved in the past two decades even though an early diagnosis can play a fundamental role in reducing mortality and life expectancy [3]. There are several risk factors involved in the development of oral squamous cell carcinoma (OSCC): tobacco smoke, alcohol consumption, reverse smoke and betel chewing. The 8 edition of AJCC TNM staging manual has added the depth of invasion as a further criteria for prognostic accuracy of OSCC based on the evidence that tumor depth has a critical importance for prognosis of OSCC [4].

Moreover oral squamous cell carcinoma has the ability to invade and metastasize to lymph nodes and distant organs even if the mechanism is still poorly understood.

Surgery still represents treatment of choice for OSCC followed by radiotherapy and chemotherapy. The breakthrough of induction chemotherapy was highly promising for treatment of oral cancer. Reducing volume tumor prior to treatment with radiotherapy could enhance efficacy and tolerability with the reduction of the disfiguring effects of surgery and radiation [5].

However the emergence of chemotherapy resistances is one of the biggest issues in treatment of cancer. This can be due to several molecular mechanisms and can play a significant role in reducing the survival of OSCC patients [6].

A study showed the potential genes involved in cisplatin (NOTCH1, JUN, CTNNB1, CEBPA, and ETS1)[6]. There are two main mechanisms of resistance described in cancer treatment: the intrinsic or de novo drug resistance where the cells are inherently insensitive to chemotherapy and the acquired

or adaptive drug resistance that develops after prolonged exposure to chemotherapeutic drugs. Enhanced DNA repair, increased drug efflux, overexpression of drug resistance genes and evasion from apoptosis are the mechanisms most commonly responsible for chemotherapy resistance [7].

Nevertheless, in the last decades the introduction of new therapies radically changed the overall prognosis of numerous malignancies but scarce results were achieved in the survival rate of OSCC.

Cisplatin is an alkylating agent that targets DNA and results in bulky adducts as well as intra- and inter-strand crosslink. Its activity has been especially interesting since the discover of its anticancer activity in several solid tumors including head and neck cancer. De novo and acquired resistance of cancer cells to cisplatin are the two main causes of treatment failure [8].

Among anticancer drugs, also 5-fluorouracil has a wide clinical application in several solid tumors including OSCC. However also 5-fluorouracil showed mechanisms of resistance with an unclear development.

Conventional chemotherapy however does not distinguish between normal and cancer cells. Thus it is characterized by several side effects related to the damage inflicted on normal tissue[9]. This is often responsible for delays or interruption of therapy. The introduction of targeted therapy at the beginning of 2000'aimed to lower the incidence of side effects related to chemotherapy with a significant incidence on patients quality of life and survival rates. This therapy is based on targeting specific enzymes, growth factor receptors and signal transducers. Unfortunately, several studies soon showed that even these kind of therapy was characterized by several side effects.

Our group carried out several research to evaluate the incidence of side effects due to targeted therapy.

1.1 Oral stomatitis and mTOR inhibitors: A review of current evidence in 20,915 patients

Traditional treatment of malignancies with chemotherapeutic agents is often affected by the damage inflicted on non-cancerous cells. Toxicities of the oral cavity, such as mucositis and stomatitis are

some of the most significant and unavoidable toxicities associated with anti-cancer therapies. For such reason, in the last decades, newer targeted agents have been developed aiming to decrease the rates of side effects on healthy cells. Unfortunately, targeted anti-cancer therapies also showed significant rate of toxicity on healthy tissues.

mTOR inhibitors are a class of drugs that inhibit the mechanistic target of rapamycin (mTOR), a serine/threonine-specific protein kinase that belongs to the family of phosphatidylinositol-3 kinase (PI3K) related kinases (PIKKs). mTOR regulates cellular metabolism, growth, and proliferation by forming and signaling through two protein complexes, mTORC1 and mTORC2. These drugs are useful against various tumor types. This class showed some adverse events, such as hyperglycaemia, hyperlipidemia, hypophosphatemia, hematologic toxicities, and mucocutaneous eruption, but the most important are still stomatitis and skin rash, often reported as dose-limiting side effects.

We performed a search of the literature on the PubMed online database using the following keywords: “sirolimus OR “everolimus” OR “temsirolimus” OR “deforolimus” OR “ridaforolimus” combined with the Boolean operator AND with the terms “stomatitis” OR “mucositis” OR “oral pain”. Titles and abstracts of 382 potentially relevant studies were screened; of these, 114 studies were excluded because they did not fulfill the inclusion criteria. In the second round, 268 studies were read in full-text, but only 135 reported the inclusion criteria and were included for data extraction. Of the included studies, 95 referred to everolimus use, 16 to ridaforolimus, and 26 to temsirolimus (two studies referred to both everolimus and temsirolimus)

The incidence rate of stomatitis according to the agent used was 25.07% (3,959/15,787) for everolimus, 27,02% (724/2,679) for temsirolimus, and 54,76% (598/1,092) for ridaforolimus. All the three agents analyzed showed high rates of low-grade stomatitis (G1-G2) while the onset of severe stomatitis was rare. Analysis of the reports with patients treated with everolimus, temsirolimus and ridaforolimus showed a clear prevalence of stomatitis grade 1 or 2. These data differ from that of

patients treated with conventional chemotherapy in which mucositis is predominantly of grade 3 or 4.

1.2 Stomatitis and VEGFR- Tyrosine Kinase Inhibitors (VR-TKIs): A review of current literature in 4369 patients.

We analyzed another class of drugs used in targeted therapy. Multitargeted tyrosine kinase inhibitors (TKIs) represent a new class of target-specific antineoplastic agents. These agents show some specific adverse events such as fatigue/asthenia, anorexia/loss of appetite, dysgeusia, diarrhea/abdominal pain, hypothyroidism, hypertension, myelosuppression, and stomatitis.

We performed a systematic search on PubMed online database using a combination of MESH terms and free text words, “sunitinib” OR “sorafenib” OR “axitinib” OR “cabozantinib” OR “pazopanib” OR “regorafenib” OR “nintedanib” OR “vatalanib” combined through the use of Boolean operator AND with the key words “stomatitis” OR “mucositis,” (i) on human subjects, (ii) written in the English language, and (iii) reporting about the incidence of stomatitis or oral mucositis.

The incidence of stomatitis of any grade was 35.2% for sunitinib, 20.52% for sorafenib, 20.63% for axitinib, and 34.21% for cabozantinib. All the agents showed high rates of low- grade stomatitis (G1-G2), while the onset of severe stomatitis (G3-G4) was very low. Analysis of the reports with patients treated with sunitinib, sorafenib, axitinib, and cabozantinib showed a clear prevalence of stomatitis grade 1 or grade 2. These data differ from those of patients treated with conventional chemotherapy in which mucositis is predominantly of grade 3 or grade 4.

1.3 Stomatitis and Everolimus: A review of current literature on 8,201 patients.

We performed a new study on the incidence of stomatitis in patients treated with everolimus conducting a systematic search on the PubMed and Medline online databases using a combination of MESH terms and free text: “everolimus” (MESH) AND “side effects” OR “toxicities” OR “adverse events”. Only studies fulfilling the following inclusion criteria were considered eligible for inclusion in this study: performed on human subjects, reporting on the use of everolimus (even if in combination with other drugs or ionizing radiation), written in the English language, and reporting the incidence of side effects. The analysis of literature revealed that the overall incidence of stomatitis after treatment with everolimus was 42.6% (3,493) and that of stomatitis grade G1/2 84.02% (2,935), while G3/4 was 15.97% (558). Results of the analysis showed that the incidence of stomatitis of grade 1 or 2 is higher than grade 3 or 4. However, it must be taken into account that it is not possible to say if side effects are entirely due to everolimus therapy or combinations with other drugs.

1.4 Nutraceuticals

Cancerous phenotypes often derive from the dysregulation of more than 5 hundred genes at multiple steps in signaling pathways. Therefore pharmaceutical companies focused in developing multitargeted therapies. Nutraceuticals are plant-derived dietary agents that have multitargeting properties.

Nutraceuticals are natural or chemical compounds which have other than a nutritional role, also a health promoting, disease curing or prevention properties. The term dates back to Stephen DeFelice in 1989 [10]. Classification of nutraceuticals is based on their chemical constitution: antioxidants, dietary fibers, inorganic mineral supplements, phytochemicals, prebiotic probiotics and herbs [11].

They showed a promising role in treatment of cardiovascular diseases, diabetes, atherosclerosis and cancer [11].

1.5 Systematic review of the literature concerning the adjunctive effects of nutraceuticals in overcoming conventional chemotherapy resistance

This systematic review was performed to evaluate the use of nutraceutical agents such as curcumin, resveratrol, indole-3-carbinole, epigallocatechin-3-gallate and lycopene could sensitize Oral cancer cell lines to cisplatin and 5-Fluorouracil chemotherapy.

A systematic review was performed on the online database PubMed and Medline using the following terms (("curcumin" OR "resveratrol" OR "indole-3-carbinole" OR "epigallocatechin-3-gallate" OR "lycopene")) AND ("cisplatin" OR "cisplatin resistance" OR "5-FU" OR "5-Fluorouracil").

The inclusion criteria for this systematic review were: original studies on human tumor cell lines where the effects of the above-mentioned nutraceutical agents were evaluated.

For every article the following information were extracted: author, year, title, cell type, kind of investigation, a primary outcome and a possible secondary outcome.

During the first round 291 potentially relevant articles were retrieved. After duplicate discard only 55 articles fulfilled the inclusion criteria and were read in full text. At the end of the selection process only 23 articles were included for qualitative synthesis while 18 articles were excluded. Results of the analysis of literature are showed in Table I.

Table I Results of the analysis of literature on the effects of nutraceuticals on different cancer cell lines

	Author	Year	Title	Cell Type	Investigations	Results	Secondary results
1.	Hernandez-Valencia et al.	2018	Induction of p53 Phosphorylation at Serine 20 by Resveratrol Is Required to Activate p53 Target Genes, Restoring Apoptosis in MCF-7 Cells Resistant to Cisplatin	MCF-7 human breast cancer cells (ATCC) MCF-7R	Cell Viability Assay Apoptosis Analysis	Resv Overcome CDDP-Resistance and Induces Apoptosis in MCF-7R Cells	Resv Induces Sensitivity to CDDP in MCF-7R Cells Down-Regulation of p53 Expression and Inhibition of the p53 Protein Activity Enhances Resistance to shRNA targeting p53 (p53-shRNA) or control (Ctrl-shRNA). Stably transfected cells were treated CDDP and Resv in MCF-7 and MCF-7R Cells Resv Induces S20 Phosphorylation and Attenuates Phosphorylation of p53 in S15 and S46 in CDDP-Treated MCF-7 Cells Resv Promotes Early Dephosphorylation of ATM, Inhibition of BCL-2, and Upregulation of BAX
2.	Zou et al.	2017	Curcumin increases breast cancer cell sensitivity to cisplatin by decreasing FEN1 expression	MCF-7, BT-474, and MDA-MB-231 breast cancer cell lines	Cell proliferation assay Flow cytometry Establishment of FEN1 stable expression cell lines	Curcumin down-regulates FEN1 expression and inhibits human breast cancer cell proliferation The combination of cisplatin and curcumin enhances breast cancer cell sensitivity to cisplatin through FEN1 down-regulation The inhibition of ERK phosphorylation is involved in the chemosensitizing effect of curcumin to cisplatin by targeting FEN1	
3.	Chang et al.	2018	Pterostilbene modulates the suppression of multidrug resistance protein 1 and triggers autophagic and apoptotic mechanisms in cisplatin-resistant human oral cancer CAR cells via AKT signaling	Cisplatin-resistant human oral cancer CAR	Cell viability assay and morphological determination Quantification of cellular apoptosis and DNA breaks Assessment of caspase-3	Pterostilbene induces cytotoxicity in cisplatin-resistant human oral cancer CAR cells.	Pterostilbene triggers the autophagy and apoptosis of CAR cells. Pterostilbene induces the expression of autophagy-associated genes and stimulates its signaling in CAR cells. The autophagy inhibitors 3-MA and CQ reverse the decrease in CAR cell viability induced by pterostilbene. Pterostilbene induces the apoptosis of CAR cells via a caspase-dependent pathway. The mitochondria-dependent pathway contributes to

					and -9 activity via colorimetric assays.		pterostilbene-induced apoptosis in CAR cells. Pterostilbene suppresses the expression of MDR1 and AKT signaling in CAR cells.
4.	Zhao et al.	2018	Curcumin sensitizes lymphoma cells to DNA damage agents through regulating Rad51-dependent homologous recombination	Murine B Lymphoma CH12F3	Cell viability assay Apoptosis assay	Curcumin suppresses growth of lymphoma cells and sensitizes tumor cells to DNA damage agents including hydroxyurea, camptothecin and cisplatin	Curcumin induces caspase3-dependent apoptosis Curcumin induces DNA breaks and down-regulates Rad51 expression Curcumin sensitizes lymphoma cells to DNA-PK and PARP inhibitors
5.	He et al.	2017	Synergistic anticancer effect of curcumin and chemotherapy regimen FP in human gastric cancer MGC-803 cells	MGC-803 human gastric cancer	Cell viability assay. Flow cytometry. Dual acridine orange/ethidium bromide (AO/EB) fluorescent staining. Colony formation assay. Transwell migration assay. Western blot analysis	All treatments significantly decreased cell viability compared with the untreated control Compared with the controls, all drug treatments significantly increased the percentage of apoptotic cells A colony formation assay demonstrated that the proliferation rate and colony numbers of the MGC-803 cells treated with curcumin and/or FP were significantly decreased compared with the control group Treatment with curcumin and/or FP significantly decreased the expression of Bcl-2 and increased the expression of Bax, compared with in the untreated control group	
6.	Wang et al.	2017	Bisdemethoxycurcumin sensitizes cisplatin-resistant lung cancer cells to chemotherapy by inhibition of CA916798 and PI3K/AKT signaling	Human cisplatin-sensitive lung adenocarcinoma A549 cells and cisplatin-resistant A549/CD DP cell lines	Cell viability assay RNA isolation and reverse transcription-polymerase chain reaction (RT-PCR) Protein extraction and western blotting	bisdemethoxycurcumin was able to sensitize cisplatin-resistant lung cancer cells to various chemotherapeutic agents, including cisplatin. The western blots showed a dose-dependent reduction of CA916798 protein in curcumin-treated cells, compared with the DMSO group	

					Protein coimmunoprecipitation and WB CA916798 protein phosphorylation assay Construction of the site-directed mutagenesis of CA917698 Cdna		
7.	Chang et al.	2017	Resveratrol-induced autophagy and apoptosis in cisplatin-resistant human oral cancer CAR cells: A key role of AMPK and Akt/mTOR signaling	CAR, a cisplatin-resistant cell line, was developed by exposing parental human tongue squamous cell carcinoma CAL 27 cell line (American Type Culture Collection, Manassas, VA, USA) to 10-80 μ M of cisplatin	Cell viability assay. Observations for autophagic vacuoles and autophagy marker. TUNEL/D API staining. Western blotting. Quantitative RT-PCR.	Resveratrol exhibits cytotoxicity and suppresses CAR cell viability. Resveratrol elicits autophagic and apoptotic death in CAR cells. Resveratrol regulates the AMPK, Akt and autophagy-related protein levels in CAR cells.	3-MA and compound c are against the autophagic effects on resveratrol-treated CAR cells. Resveratrol modulates caspase-3, caspase-9 and apoptotic-related protein levels in CAR cells. Resveratrol elicits the caspase-3/-9 activities and protective effect of pan-caspase inhibitor (Z-VAD-FMK) against resveratrol-induced caspase-dependent apoptosis on CAR cells.
8.	Hu et al.	2016	The synergistic effect of resveratrol in combination with cisplatin on apoptosis via modulating autophagy in A549 cells	Human lung adenocarcinoma cell line (A549)	Cell viability assay Analysis of combined drug effects Flow cytometry analysis Western blot analysis Transmission electron microscope	Combination of resveratrol and cisplatin results in synergistic cytotoxic effects in A549 cells Resveratrol enhances the effect of cisplatin on apoptosis in A549 cells Combination of resveratrol and cisplatin induces autophagy in A549 cells Combination of resveratrol and cisplatin induces apoptosis by modulating autophagy in A549 cells	

					Immunofluorescence analysis		
9.	Engelke et al.	2016	Ellagic Acid and Resveratrol Prevent the Development of Cisplatin Resistance in the Epithelial Ovarian Cancer Cell Line A2780	epithelial ovarian cancer cell line A2780 and its cisplatin-resistant subclone A2780CisR	MTT assay Immunoblot analysis Signal pathway analysis Measurement of reactive oxygen species Doubling time Scratch assay Cell cycle analysis Apoptosis analysis	Short term treatment (48 h) with EA or RV of the chemosensitive ovarian cancer cell line A2780 leads to moderate (2-3 fold) increase in chemosensitivity . Short term treatment (48 h) with EA or RV of cDDP-resistant A2780CisR does not improve chemosensitivity. Permanent presence over a period of 26 weeks of EA or RV, respectively, does not revert cDDP-chemoresistance of A2780CisR. However, permanent presence of EA or RV inhibits proliferation and migration of A2780CisR. Phosphorylation of ErbB2 and ErbB3 is reduced in EA or RV treated cells and may account for reduced cell migration and prevention of chemoresistance.	Permanent presence over a period of 26 weeks of EA or RV, respectively, prevents the development of chemoresistance upon weekly cDDP treatment in A2780 cells. A chemosensitive phenotype of A2780 is retained, and cell migration is inhibited.
10.	Kang et al.	2016	Theracurmin® efficiently inhibits the growth of human prostate and bladder cancer cells via induction of apoptotic cell death and cell cycle arrest	Human prostate cancer cell lines LNCaP, PC3, and DU145	Cell proliferation assay. Clonogenic assay. Flow cytometry for cell cycle analysis. Western blot analysis.	Theracurmin® significantly inhibits the proliferation of human prostate cancer cells. Theracurmin® exerts anticancer effects by inducing apoptotic cell death and cell cycle disturbance in human prostate cancer cells. Theracurmin® treatment efficiently suppresses the growth of human bladder cancer cells. Anticancer effects of Theracurmin® are induced by apoptotic cell death and cell cycle dysregulation in human bladder cancer cells.	
11.	Baharuddin et al.	2015	Curcumin improves the efficacy of	NSCLC	Spheroid assay and	Curcumin sensitization enhances the tumor	

			<p>cisplatin by targeting cancer stem-like cells through p21 and cyclin D1-mediated tumor cell inhibition in non-small cell lung cancer cell lines</p>	<p>cell lines, A549 (ATCC[®] CRL-185TM) and H2170 (ATCC[®] CRL-5928TM)</p>	<p>self-renewal capacity. Preparation of curcumin and cisplatin stock. Inhibitory concentration (IC50) of single treatments (curcumin and/or cisplatin) in the NSCLC cell lines. IC50 of curcumin sensitization prior to cisplatin treatment in the NSCLC cell lines. Apoptosis assay. Scratch-wound/migration assay. Quantitative real time-polymerase chain reaction (RT-qPCR).</p>	<p>growth inhibitory effect of low dose cisplatin. Combination of curcumin and cisplatin enriches the CD166+/EpCAM+ CSC subpopulation. Curcumin enhances the cisplatin-induced inhibition of the metastasis of the highly migratory CSC subpopulation (CD166+/EpCAM+) in the NSCLC cell lines. Curcumin together with cisplatin increases the positive expression of apoptotic and cell cycle-regulating genes in the sorted cells.</p>	
12.	Kim et al.	2015	<p>Curcumin-induced downregulation of Axl receptor tyrosine kinase inhibits cell proliferation and circumvents chemoresistance in non-small lung cancer cells</p>	<p>A549 and H460 cells</p>	<p>Reverse transcription PCR Promoter activity test. Western blot analysis. Cell viability measurement. Clonogenic assay.</p>	<p>Curcumin inhibits activation of Axl upon the growth arrest-specific gene 6 stimulation. Curcumin targets Axl to inhibit cell proliferation. Curcumin suppresses proliferation of both cisplatin- and paclitaxel-resistant lung cancer cells and results in the elevation of p21 as well as reduction of XIAP expression.</p>	
13.	Ma et al.	2015	<p>Resveratrol enhanced anticancer effects of cisplatin</p>	<p>Human lung cancer</p>	<p>Cell growth</p>	<p>extremely low dose of resveratrol (<40 µg/ml) exhibited a mild</p>	

			on non-small cell lung cancer cell lines by inducing mitochondrial dysfunction and cell apoptosis	cell lines, H838 and H520	inhibition assay. Examination of morphological changes of cells Measurement of mitochondrial membrane potential (MMP) Cell apoptosis analysis by flow cytometry. Western blot analysis.	enhancing effect on the proliferation of H520 cells, while higher dose of resveratrol (>50 µg/ml) inhibited the proliferation of H838 and H520 cells Resveratrol induces apoptosis in H838 and H520 cells Resveratrol enhances the effects of cisplatin on MMP and cell apoptosis. Resveratrol promotes cisplatin-induced cytochrome c release. Resveratrol promotes the effects of cisplatin on apoptosis regulators.	
14.	Osman et al.	2015	Modulatory role of resveratrol on cytotoxic activity of cisplatin, sensitization and modification of cisplatin resistance in colorectal cancer cells	HCT-116 human CRC cells	Assessment of cytotoxic activity. Flow-cytometric assay of apoptosis. Cell cycle analysis. Assessment of CIS cellular uptake	The addition of RSVL (15 µg/ml), in combination with the same doses of CIS, resulted in a significant increase in the percentage of cells in early apoptosis The treatment of the cells with RSVL (15 µg/ml) resulted in a preferential accumulation of the cells in G0 and S phases The uptake of CIS was significantly increased in the presence of 15 µg/ml RSVL, to 16.2 and 4.33 ng/106 cells respectively	
15.	Kilic et al.	2015	Enhancement of cisplatin sensitivity in human cervical cancer: epigallocatechin-3-gallate	HeLa cells, the human cervical cancer cell line,	Cell viability assay Western blot analysis	Egcg enhances the inhibitory effect of cisplatin on the proliferation of HeLa cells Egcg enhances cisplatin-induced apoptosis in HeLa cells	Egcg reduces cisplatin-induced oxidative stress in HeLa cells Egcg inhibits cisplatin-induced activation of mtor pathway in HeLa cells

16.	Zhang et al.	2013	Curcumin enhances the effectiveness of cisplatin by suppressing CD133+ cancer stem cells in laryngeal carcinoma treatment	human laryngeal squamous cancer cell line, HEP-2,	MTT assay. Colony formation assay. Apoptosis assay. Flow cytometry assays and fluorescence-activated cell sorting (FACS) of CD133+ cells. Western blotting.	cisplatin led to enrichment of the CD133+ population in HEP-2 cells and that the enrichment was significantly suppressed by combined treatment with curcumin. Curcumin induces apoptosis of HEP-2 cells. Curcumin suppresses the proliferation of HEP-2 cells.	
17.	Mazumder et al.	2012	A2780 (cisplatin-sensitive, parental cell line), A2780cisR (cisplatin-resistant) and A2780ZD0473R (ZD0473-resistant) ovarian cancer cell lines and multi-drug resistant SKOV-3 [Sloan-Kettering human epidermal growth factor receptor 2 (HER2) 3+ ovarian cancer cell line	Cytotoxicity assays.	It was found that for the 0/4 h combination of cisplatin with EGCG in parental A2780 and cisplatin-resistant A2780cisR cell lines, both the cellular accumulation of platinum and level of platinum-DNA binding are greater than those from the 0/0 h combination and also from that of cisplatin-alone.	Both the CIs and dose-response curves show that administration of anethole or curcumin and platinum drug	

18.	Nessa et al.	2012	Studies on Combination of Platinum Drugs Cisplatin and Oxaliplatin with Phytochemicals Anethole and Curcumin in Ovarian Tumor Models	Human ovarian cancer cell lines A2780 (parent), A2780cis R (cisplatin - resistant) and A2780Z D0473R (ZD0473 - resistant)	Cytotoxicity assays.	Both the CIs and dose-response curves show that administration of anethole or curcumin and platinum drug with a 2 h time gap produces much greater cell kill than the bolus administration and that the combined drug action is greater when phytochemicals are added first rather than the converse.	
19.	Ye et al.	2012	Curcumin reverses cis-platin resistance and promotes human lung adenocarcinoma A549/DDP cell apoptosis through HIF-1 α and caspase-3 mechanisms	human lung adenocarcinoma A549 cells and the cisplatin resistant A549/DDP cells	Cell proliferation assay Cell death and apoptosis determination DNA fragmentation analysis Caspase-3 activity assay Transient transfection and flow cytometry Measurement of HIF-1 α and P-glycoprotein	Curcumin inhibits A549 and A549/DDP cells proliferation and enhances chemotherapeutic effect of DDP Curcumin promotes A549/DDP cell apoptosis Curcumin triggers caspase-3 activation HIF-1 α plays critical roles in DDP resistance HIF-1 α as a target for curcumin to reverse DDP resistance	
20.	Abuzeid et al.	2011	Sensitization of Head and Neck Cancer to Cisplatin Through the Use of a Novel Curcumin Analog	UM-SCC-29 and UM-SCC-74B cell lines were originally derived from human head and neck tumor explants	50% inhibitory concentration determination Wb	The key finding was that combination therapy with FLLL32 and cisplatin (1.56 μ M) induced a suppressive effect comparable with cisplatin monotherapy at 6.25 μ M and an enhanced cytotoxic effect vs cisplatin monotherapy at doses of 1.56 μ M to 3.25 μ M (P .01) in cisplatin-resistant UM-SCC-29 cells. These findings suggest that FLLL32 sensitizes both cisplatin-sensitive cells and, critically, intrinsically cisplatin-	FLLL32 can potentiate apoptosis induced by cisplatin in both cisplatin-resistant and cisplatin-sensitive cell lines.

						resistant UM-SCC-29 HNSCC cells to treatment with low concentrations of cisplatin.	
21.	Chanvorachote et al.	2009	Curcumin Sensitizes Lung Cancer Cells to Cisplatin-Induced Apoptosis Through Superoxide Anion-Mediated Bcl-2 Degradation	Human non-small cell lung cancer (NCI-H460) cells	Apoptosis and cytotoxicity assays ROS detection Western blot analysis	Curcumin enhances cisplatin-induced apoptosis in H460 cells Curcumin induces intracellular ROS generation in H460 cells Curcumin reverses cisplatin resistance in Bcl-2 overexpressing cells	
22.	Montopoli et al.	2009	Cell-cycle inhibition and apoptosis induced by curcumin and cisplatin or oxaliplatin in human ovarian carcinoma cells	Wild-type (2008) cells derived from human ovary carcinoma and its parental cisplatin-resistant variant (C13) cells	Cell-cycle analysis by flow cytometry Annexin V/propidium iodide staining for apoptosis Intracellular glutathione assay Reactive oxygen species intracellular assay	Cells were exposed for 24, 48 or 72 h to curcumin or to either cisplatin or oxaliplatin at (0.01 μm –100 μm) concentration range, and cell viability measured by MTT assay. All compounds caused concentration-dependent inhibition of cell viability, which persisted after 72 h curcumin concentration-dependent increased apoptosis and cell-cycle parameter alterations, both in absence and in presence of cisplatin or oxaliplatin.	Curcumin, in a concentration-dependent fashion, caused reduction of glutathione after 2 h incubation, whereas it increased glutathione after 24 h. These effects of curcumin were similar both in wild type 2008 and C13 cells.
23.	Weir et al.	2007	Curcumin Induces G2/M Arrest and Apoptosis in Cisplatin-Resistant Human Ovarian Cancer Cells by Modulating Akt and p38 MAPK	Cisplatin-resistant (CR) and cisplatin-sensitive (CS) human ovarian cancer cells	Cell proliferation assay Cell cycle analysis by flow cytometry	Curcumin inhibited both CS and CR cell proliferation in a dose-dependent manner curcumin induced cell cycle arrest within 12-h of incubation and apoptosis after 24 h of incubation.	

Analysis of the literature, showed that Resveratrol could play a role in preventing the emergence of resistances to Cisplatin therapy in several tumors and in enhancing tumor response to chemotherapy. Moreover in cancer cells incubated with Resveratrol, it showed a grade of cytotoxicity even without the addition of Cisplatin.

1.6 Resveratrol

Resveratrol (3,4',5-trihydroxy-trans-stilbene) is a polyphenolic compound that can be found in plants and foods. It is produced by plants as a self-defense agent. Resveratrol can be found in Grapevine and Wine and in more than 70 plant species (Polygonum Cuspidatum, Eucalyptus and Picea excelsa). It is composed of two phenol rings linked through a styrene double bond to form 3,4,5 trihydroxystilbene. In grape and wine resveratrol was found as free species and glycosylated form production of Resveratrol in grapevine is related to biotic and abiotic stress [12].

Resveratrol attracted general interest in 1992 for its cardioprotective properties in the *French paradox*. [13] It shown a wide spectrum of biological activities (anti-oxidant, anti-inflammatory, anti-atherosclerotic) but was first identified for its anti-tumor properties [14].

Several studies proved that resveratrol is a free radical scavenger and an antioxidant that can counteract the oxidative stress associated with multiple chronic and acute diseases. Resveratrol was found to have a potential use in cancer treatment. Studies indicate that resveratrol has a potential role in inhibiting pathways that contribute to cell proliferation and through induction of apoptosis and G2/M cell cycle phase arrest [15].

Studies on resveratrol were conducted mainly in vitro and in vivo on animal models that proved the role of resveratrol in modulating signal transduction pathways that control cell division and growth, apoptosis, inflammation, angiogenesis and metastasis [16].

For these reasons we decided to investigate its potential role in human resistant oral cancer cells to further determine its role in overcoming cisplatin and 5-FU resistant cells.

2. Materials and methods

Our purpose was to evaluate the potential role of resveratrol in overcoming cisplatin and 5-fluorouracil resistance in different human squamous oral carcinoma cell lines.

The cell lines selected were HSC-3, HSC-4, SAS and HOC621.

In the first phase of the study we compared the basic carcinogenic characteristics of the four oral squamous cell carcinoma cell lines HSC-3, HSC-4, SAS and HOC621.

HSC-3, HSC-4, SAS and HOC621 cell lines were grown in Dulbecco's modified Eagle's medium with 500 mg/L glucose will be supplemented with 10% fetal bovine serum, 5% L-glutamine (2 mM) and penicillin–streptomycin (100 U/ml). All cell lines were maintained at 37°C in a 5% CO₂ humidified atmosphere. Cell proliferation was evaluated at 24, 48 and 72h with MTT assay standard protocol[17]. The experiment was performed three times and cells were seeded in triplicate. Results are reported as a mean of the three experiments.

In the second phase of the study, the HSC-3 and SAS cell lines were grown in Dulbecco's modified Eagles medium with 500 mg/L glucose supplemented with 10% fetal bovine serum, 5% L-glutamine (2mM) and penicillin-streptomycin (100 U/ml). All cell lines were maintained at 37°C in a 5% CO₂ atmosphere.

Cells were tested with both resveratrol alone and in combination with Cisplatin and 5-Fluorouracil at 24h, 48h and 72h with MTT assay standard protocol [17].

The MTT assay is based on the ability of viable cells to reduce the reagent 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide to colored formazan compounds. Because the transformation is only possible in viable cells, the amount of blue formazan is proportional to the number of viable cells and thus, a linear dependence exists between cell activity and absorbance [18].

The experiments were performed three times each and results were reported as the mean of the three experiments. Resveratrol and DMSO were obtained from Sigma-Aldrich (St. Louis, MO, USA).

At different time-points after the start of treatment (24, 48 and 72 h), the medium was eliminated and the cells were incubated with MTT (Sigma-Aldrich Chemistry, S.A.) (1 mg/ml) for 4 h, after which the non-metabolized MTT was discarded and 100 µl of DMSO was added to each well. Absorbance in each well was measured with an enzyme-linked immunosorbent assay (ELISA), using a plate spectrophotometer (Multiskan MCC/340P, Labsystems, Helsinki, Finland) at a reading wavelength of 540 nm and a reference wavelength of 690 nm. This evaluation was performed in triplicate.

A concentration of Cisplatin 0.5 mg/mL was chosen to evaluate efficacy in HSC-3 cell viability. In both HSC-3 and SAS ANOVA one-way comparison was used to examine the effect of different pharmacological principles and concentrations on cell viability: Bonferroni-HOLM post-hoc test showed a difference between various treatments.

The choice of the two cell lines was performed based on the results of the experiments conducted previously on cell viability.

The effects of the administration of resveratrol in combination with cisplatin and 5-Fluorouracil were analyzed separately on both HSC-3 and SAS.

3.Results

3.1 Cell viability evaluation

HSC-3 and SAS showed to have a higher proliferation rate with respect to the other cell lines that were analyzed, HOC 621 and HSC-4. This result was taken into consideration for the subsequent experiment, since this different proliferation rate could explain a different biological behavior, reflecting a different response rate to chemotherapy.

The results of MTT assay at two different dosages of both Cisplatin and 5-FU showed that there was no statistically significant difference between the two dosages used. (*Table II*) For the HSC-3 both Cisplatin and 5-FU were effective at 5 µg/ml and 20 µg/ml without statistically significant difference between the two-different concentration. Same results were observed for HSC-4, HOC 621 and SAS. HSC-3 and SAS resulted to have a higher proliferation rate (0.9765 and 0.7595 was the mean absorbance respectively) while the mean absorbance of HSC-4 and HOC 621 was respectively 0.6025 and 0.5333 at 72h.

The doubling time of HSC-3 in our test seems to confirm the literature in which the doubling time is of around 20 hours[19]. Same results were obtained for the SAS, where the doubling time was around 33 hours (mean at 24 h 0,282; mean at 48 h 0,4435). For both HSC-4 and HOC 621 literature does not report the doubling time. In our analysis, the doubling time for both HSC-4 and HOC621 is of around 30 hours. SAS, HOC621 and HSC-4 show similar doubling times at 48 hours. Results of the MTT assay on the four cell lines at the different time points are synthetized in *Figure I*.

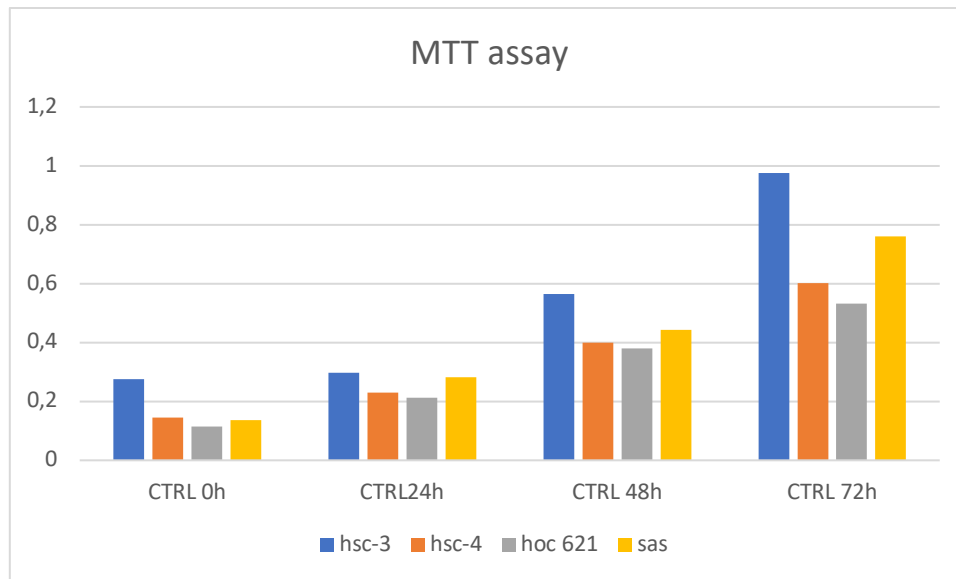


Figure I: Results of the MTT assay on four different cell lines

We evaluated cell viability for the four cell lines (HSC-2, HSC-4, SAS and HOC 621) after administration of Cisplatin and 5-Fluorouracil with MTT-assay. Different concentrations were used to evaluate viability, such as 5 $\mu\text{g/ml}$ and 20 $\mu\text{g/ml}$. For control comparison, normal medium was added against Cisplatin, meanwhile DMSO was used at 0.1% when comparing to 5-FU. In HSC-3 and SAS ANOVA one-way comparison was used to examine the effect of different pharmacological principles and concentrations on cell viability: Bonferroni-HOLM post-hoc test showed a difference between various treatments. For the purpose of the study, it can be concluded that a lower and less toxic dosage of cisplatin and 5-FU could be used to evaluate whether the additional use of nutraceutical compounds such as curcumin and resveratrol can result in a synergistic and enhancing effect.

Results of the Bonferroni-HOLM post-hoc test are resumed in *Table II*.

Table II: Bonferroni-HOLM post-hoc test

(I) Type_of_Treat		Differenza fra medie (I-J)	Errore std.	Sig.	Intervallo di confidenza 95%	
					Limite inferiore	Limite superiore
HSC3Ctrl	HSC35CIS	110,66667 [*]	16,64784	,000	42,3126	179,0207
	HSC320CIS	111,00000 [*]	16,64784	,000	42,6459	179,3541
	HSC35FUCTRL	-61,66667	16,64784	,184	-130,0207	6,6874
	HSC3FUDMSO	-43,00000	16,64784	1,000	-111,3541	25,3541
	HSC3FU5	100,33333 [*]	16,64784	,000	31,9793	168,6874
	HSC3FU20	102,33333 [*]	16,64784	,000	33,9793	170,6874
	HSC4_Ctrl	-167,33333 [*]	16,64784	,000	-235,6874	-98,9793
	HSC4_5Cis	95,66667 [*]	16,64784	,000	27,3126	164,0207
	HSC4_20Cis	98,00000 [*]	16,64784	,000	29,6459	166,3541
	HSC4_5FU_Ctrl	-242,33333 [*]	16,64784	,000	-310,6874	-173,9793
	HSC4_5FU_DMSO	-93,66667 [*]	16,64784	,000	-162,0207	-25,3126
	HSC4_5FU_5u	35,00000	16,64784	1,000	-33,3541	103,3541
	HSC4_5FU_20u	43,66667	16,64784	1,000	-24,6874	112,0207
	HOC621_Ctrl	-471,33333 [*]	16,64784	,000	-539,6874	-402,9793
	HOC621_5Cis	86,66667 [*]	16,64784	,001	18,3126	155,0207
	HOC621_20Cis	99,66667 [*]	16,64784	,000	31,3126	168,0207
	HOC621_5FU_Ctrl	-328,00000 [*]	16,64784	,000	-396,3541	-259,6459
	HOC621_5FU_DMSO	-334,00000 [*]	16,64784	,000	-402,3541	-265,6459
	HOC621_5FU_5u	59,66667	16,64784	,268	-8,6874	128,0207
	HOC621_5FU_20u	93,66667 [*]	16,64784	,000	25,3126	162,0207
	SAS_Ctrl	-423,00000 [*]	16,64784	,000	-491,3541	-354,6459
	SAS_5Cis	101,33333 [*]	16,64784	,000	32,9793	169,6874
	SAS_20Cis	96,66667 [*]	16,64784	,000	28,3126	165,0207
	SAS_5FU_Ctrl	-497,00000 [*]	16,64784	,000	-565,3541	-428,6459
	SAS_5FU_DMSO	-325,33333 [*]	16,64784	,000	-393,6874	-256,9793
	SAS_5FU_5	37,00000	16,64784	1,000	-31,3541	105,3541
	SAS_5FU_20	58,17667	16,64784	,354	-10,1774	126,5307

HSC35CIS	HSC3Ctrl	-	16,64784	,000	-	-42,3126
		110,66667			179,0207	
	HSC320CIS	,33333	16,64784	1,000	-68,0207	68,6874
	HSC35FUCTRL	-	16,64784	,000	-	-
		172,33333			240,6874	103,9793
	HSC3FUDMSO	-	16,64784	,000	-	-85,3126
		153,66667			222,0207	
	HSC3FU5	-10,33333	16,64784	1,000	-78,6874	58,0207
	HSC3FU20	-8,33333	16,64784	1,000	-76,6874	60,0207
	HSC4_Ctrl	-	16,64784	,000	-	-
		278,00000			346,3541	209,6459
	HSC4_5Cis	-15,00000	16,64784	1,000	-83,3541	53,3541
	HSC4_20Cis	-12,66667	16,64784	1,000	-81,0207	55,6874
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		353,00000			421,3541	284,6459
	HSC4_5FU_DMSO	-	16,64784	,000	-	-
		204,33333			272,6874	135,9793
	HSC4_5FU_5u	-75,66667	16,64784	,011	-	-7,3126
					144,0207	
	HSC4_5FU_20u	-67,00000	16,64784	,065	-	1,3541
					135,3541	
	HOC621_Ctrl	-	16,64784	,000	-	-
		582,00000			650,3541	513,6459
	HOC621_5Cis	-24,00000	16,64784	1,000	-92,3541	44,3541
	HOC621_20Cis	-11,00000	16,64784	1,000	-79,3541	57,3541
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		438,66667			507,0207	370,3126
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		444,66667			513,0207	376,3126
HOC621_5FU_5u	-51,00000	16,64784	1,000	-	17,3541	
				119,3541		
HOC621_5FU_20u	-17,00000	16,64784	1,000	-85,3541	51,3541	
SAS_Ctrl	-	16,64784	,000	-	-	
	533,66667			602,0207	465,3126	
SAS_5Cis	-9,33333	16,64784	1,000	-77,6874	59,0207	
SAS_20Cis	-14,00000	16,64784	1,000	-82,3541	54,3541	
SAS_5FU_Ctrl	-	16,64784	,000	-	-	
	607,66667			676,0207	539,3126	
SAS_5FU_DMSO	-	16,64784	,000	-	-	
	436,00000			504,3541	367,6459	
SAS_5FU_5	-73,66667	16,64784	,017	-	-5,3126	
				142,0207		
SAS_5FU_20	-52,49000	16,64784	,982	-	15,8641	
				120,8441		
HSC320CIS	HSC3Ctrl	-	16,64784	,000	-	-42,6459
		111,00000			179,3541	
	HSC35CIS	-,33333	16,64784	1,000	-68,6874	68,0207
HSC35FUCTRL	-	16,64784	,000	-	-	
	172,66667			241,0207	104,3126	

	HSC3FUDMSO	-	16,64784	,000	-	-85,6459
		154,00000*			222,3541	
	HSC3FU5	-10,66667	16,64784	1,000	-79,0207	57,6874
	HSC3FU20	-8,66667	16,64784	1,000	-77,0207	59,6874
	HSC4_Ctrl	-	16,64784	,000	-	-
		278,33333*			346,6874	209,9793
	HSC4_5Cis	-15,33333	16,64784	1,000	-83,6874	53,0207
	HSC4_20Cis	-13,00000	16,64784	1,000	-81,3541	55,3541
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		353,33333*			421,6874	284,9793
	HSC4_5FU_DMSO	-	16,64784	,000	-	-
		204,66667*			273,0207	136,3126
	HSC4_5FU_5u	-76,00000*	16,64784	,011	-	-7,6459
					144,3541	
	HSC4_5FU_20u	-67,33333	16,64784	,061	-	1,0207
					135,6874	
	HOC621_Ctrl	-	16,64784	,000	-	-
		582,33333*			650,6874	513,9793
	HOC621_5Cis	-24,33333	16,64784	1,000	-92,6874	44,0207
	HOC621_20Cis	-11,33333	16,64784	1,000	-79,6874	57,0207
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		439,00000*			507,3541	370,6459
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		445,00000*			513,3541	376,6459
	HOC621_5FU_5u	-51,33333	16,64784	1,000	-	17,0207
					119,6874	
	HOC621_5FU_20u	-17,33333	16,64784	1,000	-85,6874	51,0207
	SAS_Ctrl	-	16,64784	,000	-	-
		534,00000*			602,3541	465,6459
	SAS_5Cis	-9,66667	16,64784	1,000	-78,0207	58,6874
	SAS_20Cis	-14,33333	16,64784	1,000	-82,6874	54,0207
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		608,00000*			676,3541	539,6459
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		436,33333*			504,6874	367,9793
	SAS_5FU_5	-74,00000*	16,64784	,016	-	-5,6459
					142,3541	
	SAS_5FU_20	-52,82333	16,64784	,926	-	15,5307
					121,1774	
HSC35FUCTRL	HSC3Ctrl	61,66667	16,64784	,184	-6,6874	130,0207
	HSC35CIS	172,33333*	16,64784	,000	103,9793	240,6874
	HSC320CIS	172,66667*	16,64784	,000	104,3126	241,0207
	HSC3FUDMSO	18,66667	16,64784	1,000	-49,6874	87,0207
	HSC3FU5	162,00000*	16,64784	,000	93,6459	230,3541
	HSC3FU20	164,00000*	16,64784	,000	95,6459	232,3541
	HSC4_Ctrl	-	16,64784	,000	-	-37,3126
		105,66667*			174,0207	
	HSC4_5Cis	157,33333*	16,64784	,000	88,9793	225,6874

	HSC4_20Cis	159,66667 [†]	16,64784	,000	91,3126	228,0207
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		180,66667 [†]			249,0207	112,3126
	HSC4_5FU_DMSO	-32,00000	16,64784	1,000	-	36,3541
					100,3541	
	HSC4_5FU_5u	96,66667 [†]	16,64784	,000	28,3126	165,0207
	HSC4_5FU_20u	105,33333 [†]	16,64784	,000	36,9793	173,6874
	HOC621_Ctrl	-	16,64784	,000	-	-
		409,66667 [†]			478,0207	341,3126
	HOC621_5Cis	148,33333 [†]	16,64784	,000	79,9793	216,6874
	HOC621_20Cis	161,33333 [†]	16,64784	,000	92,9793	229,6874
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		266,33333 [†]			334,6874	197,9793
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		272,33333 [†]			340,6874	203,9793
	HOC621_5FU_5u	121,33333 [†]	16,64784	,000	52,9793	189,6874
	HOC621_5FU_20u	155,33333 [†]	16,64784	,000	86,9793	223,6874
	SAS_Ctrl	-	16,64784	,000	-	-
		361,33333 [†]			429,6874	292,9793
	SAS_5Cis	163,00000 [†]	16,64784	,000	94,6459	231,3541
	SAS_20Cis	158,33333 [†]	16,64784	,000	89,9793	226,6874
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		435,33333 [†]			503,6874	366,9793
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		263,66667 [†]			332,0207	195,3126
	SAS_5FU_5	98,66667 [†]	16,64784	,000	30,3126	167,0207
	SAS_5FU_20	119,84333 [†]	16,64784	,000	51,4893	188,1974
HSC3FUDMSO	HSC3Ctrl	43,00000	16,64784	1,000	-25,3541	111,3541
	HSC35CIS	153,66667 [†]	16,64784	,000	85,3126	222,0207
	HSC320CIS	154,00000 [†]	16,64784	,000	85,6459	222,3541
	HSC35FUCTRL	-18,66667	16,64784	1,000	-87,0207	49,6874
	HSC3FU5	143,33333 [†]	16,64784	,000	74,9793	211,6874
	HSC3FU20	145,33333 [†]	16,64784	,000	76,9793	213,6874
	HSC4_Ctrl	-	16,64784	,000	-	-55,9793
		124,33333 [†]			192,6874	
	HSC4_5Cis	138,66667 [†]	16,64784	,000	70,3126	207,0207
	HSC4_20Cis	141,00000 [†]	16,64784	,000	72,6459	209,3541
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		199,33333 [†]			267,6874	130,9793
	HSC4_5FU_DMSO	-50,66667	16,64784	1,000	-	17,6874
					119,0207	

	HSC4_5FU_5u	78,00000 ⁺	16,64784	,007	9,6459	146,3541
	HSC4_5FU_20u	86,66667 ⁺	16,64784	,001	18,3126	155,0207
	HOC621_Ctrl	-	16,64784	,000	-	-
		428,33333 ⁺			496,6874	359,9793
	HOC621_5Cis	129,66667 ⁺	16,64784	,000	61,3126	198,0207
	HOC621_20Cis	142,66667 ⁺	16,64784	,000	74,3126	211,0207
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		285,00000 ⁺			353,3541	216,6459
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		291,00000 ⁺			359,3541	222,6459
	HOC621_5FU_5u	102,66667 ⁺	16,64784	,000	34,3126	171,0207
	HOC621_5FU_20u	136,66667 ⁺	16,64784	,000	68,3126	205,0207
	SAS_Ctrl	-	16,64784	,000	-	-
		380,00000 ⁺			448,3541	311,6459
	SAS_5Cis	144,33333 ⁺	16,64784	,000	75,9793	212,6874
	SAS_20Cis	139,66667 ⁺	16,64784	,000	71,3126	208,0207
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		454,00000 ⁺			522,3541	385,6459
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		282,33333 ⁺			350,6874	213,9793
	SAS_5FU_5	80,00000 ⁺	16,64784	,005	11,6459	148,3541
	SAS_5FU_20	101,17667 ⁺	16,64784	,000	32,8226	169,5307
HSC3FU5	HSC3Ctrl	-	16,64784	,000	-	-31,9793
		100,33333 ⁺			168,6874	
	HSC35CIS	10,33333	16,64784	1,000	-58,0207	78,6874
	HSC320CIS	10,66667	16,64784	1,000	-57,6874	79,0207
	HSC35FUCTRL	-	16,64784	,000	-	-93,6459
		162,00000 ⁺			230,3541	
	HSC3FUDMSO	-	16,64784	,000	-	-74,9793
		143,33333 ⁺			211,6874	
	HSC3FU20	2,00000	16,64784	1,000	-66,3541	70,3541
	HSC4_Ctrl	-	16,64784	,000	-	-
		267,66667 ⁺			336,0207	199,3126
	HSC4_5Cis	-4,66667	16,64784	1,000	-73,0207	63,6874
	HSC4_20Cis	-2,33333	16,64784	1,000	-70,6874	66,0207
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		342,66667 ⁺			411,0207	274,3126
	HSC4_5FU_DMSO	-	16,64784	,000	-	-
		194,00000 ⁺			262,3541	125,6459
	HSC4_5FU_5u	-65,33333	16,64784	,091	-	3,0207
					133,6874	
	HSC4_5FU_20u	-56,66667	16,64784	,466	-	11,6874
					125,0207	

	HOC621_Ctrl	-	16,64784	,000	-	-
		571,66667			640,0207	503,3126
	HOC621_5Cis	-13,66667	16,64784	1,000	-82,0207	54,6874
	HOC621_20Cis	-,66667	16,64784	1,000	-69,0207	67,6874
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		428,33333			496,6874	359,9793
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		434,33333			502,6874	365,9793
	HOC621_5FU_5u	-40,66667	16,64784	1,000	-	27,6874
					109,0207	
	HOC621_5FU_20u	-6,66667	16,64784	1,000	-75,0207	61,6874
	SAS_Ctrl	-	16,64784	,000	-	-
		523,33333			591,6874	454,9793
	SAS_5Cis	1,00000	16,64784	1,000	-67,3541	69,3541
	SAS_20Cis	-3,66667	16,64784	1,000	-72,0207	64,6874
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		597,33333			665,6874	528,9793
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		425,66667			494,0207	357,3126
	SAS_5FU_5	-63,33333	16,64784	,134	-	5,0207
					131,6874	
	SAS_5FU_20	-42,15667	16,64784	1,000	-	26,1974
					110,5107	
HSC3FU20	HSC3Ctrl	-	16,64784	,000	-	-33,9793
		102,33333			170,6874	
	HSC35CIS	8,33333	16,64784	1,000	-60,0207	76,6874
	HSC320CIS	8,66667	16,64784	1,000	-59,6874	77,0207
	HSC35FUCTRL	-	16,64784	,000	-	-95,6459
		164,00000			232,3541	
	HSC3FUDMSO	-	16,64784	,000	-	-76,9793
		145,33333			213,6874	
	HSC3FU5	-2,00000	16,64784	1,000	-70,3541	66,3541
	HSC4_Ctrl	-	16,64784	,000	-	-
		269,66667			338,0207	201,3126
	HSC4_5Cis	-6,66667	16,64784	1,000	-75,0207	61,6874
	HSC4_20Cis	-4,33333	16,64784	1,000	-72,6874	64,0207
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		344,66667			413,0207	276,3126
	HSC4_5FU_DMSO	-	16,64784	,000	-	-
		196,00000			264,3541	127,6459
	HSC4_5FU_5u	-67,33333	16,64784	,061	-	1,0207
					135,6874	
	HSC4_5FU_20u	-58,66667	16,64784	,323	-	9,6874
					127,0207	
	HOC621_Ctrl	-	16,64784	,000	-	-
		573,66667			642,0207	505,3126
	HOC621_5Cis	-15,66667	16,64784	1,000	-84,0207	52,6874

	HOC621_20Cis	-2,66667	16,64784	1,000	-71,0207	65,6874
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		430,33333 [†]			498,6874	361,9793
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		436,33333 [†]			504,6874	367,9793
	HOC621_5FU_5u	-42,66667	16,64784	1,000	-	25,6874
					111,0207	
	HOC621_5FU_20u	-8,66667	16,64784	1,000	-77,0207	59,6874
	SAS_Ctrl	-	16,64784	,000	-	-
		525,33333 [†]			593,6874	456,9793
	SAS_5Cis	-1,00000	16,64784	1,000	-69,3541	67,3541
	SAS_20Cis	-5,66667	16,64784	1,000	-74,0207	62,6874
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		599,33333 [†]			667,6874	530,9793
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		427,66667 [†]			496,0207	359,3126
	SAS_5FU_5	-65,33333	16,64784	,091	-	3,0207
					133,6874	
	SAS_5FU_20	-44,15667	16,64784	1,000	-	24,1974
					112,5107	
HSC4_Ctrl	HSC3Ctrl	167,33333 [†]	16,64784	,000	98,9793	235,6874
	HSC35CIS	278,00000 [†]	16,64784	,000	209,6459	346,3541
	HSC320CIS	278,33333 [†]	16,64784	,000	209,9793	346,6874
	HSC35FUCTRL	105,66667 [†]	16,64784	,000	37,3126	174,0207
	HSC3FUDMSO	124,33333 [†]	16,64784	,000	55,9793	192,6874
	HSC3FU5	267,66667 [†]	16,64784	,000	199,3126	336,0207
	HSC3FU20	269,66667 [†]	16,64784	,000	201,3126	338,0207
	HSC4_5Cis	263,00000 [†]	16,64784	,000	194,6459	331,3541
	HSC4_20Cis	265,33333 [†]	16,64784	,000	196,9793	333,6874
	HSC4_5FU_Ctrl	-75,00000 [†]	16,64784	,013	-	-6,6459
					143,3541	
	HSC4_5FU_DMSO	73,66667 [†]	16,64784	,017	5,3126	142,0207
	HSC4_5FU_5u	202,33333 [†]	16,64784	,000	133,9793	270,6874
	HSC4_5FU_20u	211,00000 [†]	16,64784	,000	142,6459	279,3541
	HOC621_Ctrl	-	16,64784	,000	-	-
		304,00000 [†]			372,3541	235,6459
	HOC621_5Cis	254,00000 [†]	16,64784	,000	185,6459	322,3541
	HOC621_20Cis	267,00000 [†]	16,64784	,000	198,6459	335,3541
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-92,3126
		160,66667 [†]			229,0207	
	HOC621_5FU_DMSO	-	16,64784	,000	-	-98,3126
		166,66667 [†]			235,0207	

	HOC621_5FU_5u	227,00000*	16,64784	,000	158,6459	295,3541
	HOC621_5FU_20u	261,00000*	16,64784	,000	192,6459	329,3541
	SAS_Ctrl	-	16,64784	,000	-	-
		255,66667*			324,0207	187,3126
	SAS_5Cis	268,66667*	16,64784	,000	200,3126	337,0207
	SAS_20Cis	264,00000*	16,64784	,000	195,6459	332,3541
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		329,66667*			398,0207	261,3126
	SAS_5FU_DMSO	-	16,64784	,000	-	-89,6459
		158,00000*			226,3541	
	SAS_5FU_5	204,33333*	16,64784	,000	135,9793	272,6874
	SAS_5FU_20	225,51000*	16,64784	,000	157,1559	293,8641
HSC4_5Cis	HSC3Ctrl	-95,66667*	16,64784	,000	-	-27,3126
					164,0207	
	HSC35CIS	15,00000	16,64784	1,000	-53,3541	83,3541
	HSC320CIS	15,33333	16,64784	1,000	-53,0207	83,6874
	HSC35FUCTRL	-	16,64784	,000	-	-88,9793
		157,33333*			225,6874	
	HSC3FUDMSO	-	16,64784	,000	-	-70,3126
		138,66667*			207,0207	
	HSC3FU5	4,66667	16,64784	1,000	-63,6874	73,0207
	HSC3FU20	6,66667	16,64784	1,000	-61,6874	75,0207
	HSC4_Ctrl	-	16,64784	,000	-	-
		263,00000*			331,3541	194,6459
	HSC4_20Cis	2,33333	16,64784	1,000	-66,0207	70,6874
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		338,00000*			406,3541	269,6459
	HSC4_5FU_DMSO	-	16,64784	,000	-	-
		189,33333*			257,6874	120,9793
	HSC4_5FU_5u	-60,66667	16,64784	,222	-	7,6874
					129,0207	
	HSC4_5FU_20u	-52,00000	16,64784	1,000	-	16,3541
					120,3541	
	HOC621_Ctrl	-	16,64784	,000	-	-
		567,00000*			635,3541	498,6459
	HOC621_5Cis	-9,00000	16,64784	1,000	-77,3541	59,3541
	HOC621_20Cis	4,00000	16,64784	1,000	-64,3541	72,3541
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		423,66667*			492,0207	355,3126
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		429,66667*			498,0207	361,3126
	HOC621_5FU_5u	-36,00000	16,64784	1,000	-	32,3541
					104,3541	
	HOC621_5FU_20u	-2,00000	16,64784	1,000	-70,3541	66,3541
	SAS_Ctrl	-	16,64784	,000	-	-
		518,66667*			587,0207	450,3126

	SAS_5Cis	5,66667	16,64784	1,000	-62,6874	74,0207
	SAS_20Cis	1,00000	16,64784	1,000	-67,3541	69,3541
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		592,66667			661,0207	524,3126
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		421,00000			489,3541	352,6459
	SAS_5FU_5	-58,66667	16,64784	,323	-	9,6874
					127,0207	
	SAS_5FU_20	-37,49000	16,64784	1,000	-	30,8641
					105,8441	
HSC4_20Cis	HSC3Ctrl	-98,00000	16,64784	,000	-	-29,6459
					166,3541	
	HSC35CIS	12,66667	16,64784	1,000	-55,6874	81,0207
	HSC320CIS	13,00000	16,64784	1,000	-55,3541	81,3541
	HSC35FUCTRL	-	16,64784	,000	-	-91,3126
		159,66667			228,0207	
	HSC3FUDMSO	-	16,64784	,000	-	-72,6459
		141,00000			209,3541	
	HSC3FU5	2,33333	16,64784	1,000	-66,0207	70,6874
	HSC3FU20	4,33333	16,64784	1,000	-64,0207	72,6874
	HSC4_Ctrl	-	16,64784	,000	-	-
		265,33333			333,6874	196,9793
	HSC4_5Cis	-2,33333	16,64784	1,000	-70,6874	66,0207
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		340,33333			408,6874	271,9793
	HSC4_5FU_DMSO	-	16,64784	,000	-	-
		191,66667			260,0207	123,3126
	HSC4_5FU_5u	-63,00000	16,64784	,143	-	5,3541
					131,3541	
	HSC4_5FU_20u	-54,33333	16,64784	,710	-	14,0207
					122,6874	
	HOC621_Ctrl	-	16,64784	,000	-	-
		569,33333			637,6874	500,9793
	HOC621_5Cis	-11,33333	16,64784	1,000	-79,6874	57,0207
	HOC621_20Cis	1,66667	16,64784	1,000	-66,6874	70,0207
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		426,00000			494,3541	357,6459
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		432,00000			500,3541	363,6459
	HOC621_5FU_5u	-38,33333	16,64784	1,000	-	30,0207
					106,6874	
	HOC621_5FU_20u	-4,33333	16,64784	1,000	-72,6874	64,0207
	SAS_Ctrl	-	16,64784	,000	-	-
		521,00000			589,3541	452,6459
	SAS_5Cis	3,33333	16,64784	1,000	-65,0207	71,6874
	SAS_20Cis	-1,33333	16,64784	1,000	-69,6874	67,0207
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		595,00000			663,3541	526,6459
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		423,33333			491,6874	354,9793

	SAS_5FU_5	-61,00000	16,64784	,209	-	7,3541
					129,3541	
	SAS_5FU_20	-39,82333	16,64784	1,000	-	28,5307
					108,1774	
HSC4_5FU_Ctrl	HSC3Ctrl	242,33333 [†]	16,64784	,000	173,9793	310,6874
	HSC35CIS	353,00000 [†]	16,64784	,000	284,6459	421,3541
	HSC320CIS	353,33333 [†]	16,64784	,000	284,9793	421,6874
	HSC35FUCTRL	180,66667 [†]	16,64784	,000	112,3126	249,0207
	HSC3FUDMSO	199,33333 [†]	16,64784	,000	130,9793	267,6874
	HSC3FU5	342,66667 [†]	16,64784	,000	274,3126	411,0207
	HSC3FU20	344,66667 [†]	16,64784	,000	276,3126	413,0207
	HSC4_Ctrl	75,00000 [†]	16,64784	,013	6,6459	143,3541
	HSC4_5Cis	338,00000 [†]	16,64784	,000	269,6459	406,3541
	HSC4_20Cis	340,33333 [†]	16,64784	,000	271,9793	408,6874
	HSC4_5FU_DMSO	148,66667 [†]	16,64784	,000	80,3126	217,0207
	HSC4_5FU_5u	277,33333 [†]	16,64784	,000	208,9793	345,6874
	HSC4_5FU_20u	286,00000 [†]	16,64784	,000	217,6459	354,3541
	HOC621_Ctrl	-	16,64784	,000	-	-
		229,00000 [†]			297,3541	160,6459
	HOC621_5Cis	329,00000 [†]	16,64784	,000	260,6459	397,3541
	HOC621_20Cis	342,00000 [†]	16,64784	,000	273,6459	410,3541
	HOC621_5FU_Ctrl	-85,66667 [†]	16,64784	,001	-	-17,3126
					154,0207	
	HOC621_5FU_DMSO	-91,66667 [†]	16,64784	,000	-	-23,3126
					160,0207	
	HOC621_5FU_5u	302,00000 [†]	16,64784	,000	233,6459	370,3541
	HOC621_5FU_20u	336,00000 [†]	16,64784	,000	267,6459	404,3541
	SAS_Ctrl	-	16,64784	,000	-	-
		180,66667 [†]			249,0207	112,3126
	SAS_5Cis	343,66667 [†]	16,64784	,000	275,3126	412,0207
	SAS_20Cis	339,00000 [†]	16,64784	,000	270,6459	407,3541
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		254,66667 [†]			323,0207	186,3126
	SAS_5FU_DMSO	-83,00000 [†]	16,64784	,002	-	-14,6459
					151,3541	
	SAS_5FU_5	279,33333 [†]	16,64784	,000	210,9793	347,6874
	SAS_5FU_20	300,51000 [†]	16,64784	,000	232,1559	368,8641
HSC4_5FU_DMSO	HSC3Ctrl	93,66667 [†]	16,64784	,000	25,3126	162,0207
	HSC35CIS	204,33333 [†]	16,64784	,000	135,9793	272,6874

	HSC320CIS	204,66667 [†]	16,64784	,000	136,3126	273,0207
	HSC35FUCTRL	32,00000	16,64784	1,000	-36,3541	100,3541
	HSC3FUDMSO	50,66667	16,64784	1,000	-17,6874	119,0207
	HSC3FU5	194,00000 [†]	16,64784	,000	125,6459	262,3541
	HSC3FU20	196,00000 [†]	16,64784	,000	127,6459	264,3541
	HSC4_Ctrl	-73,66667 [†]	16,64784	,017	-	-5,3126
	HSC4_5Cis	189,33333 [†]	16,64784	,000	142,0207	257,6874
	HSC4_20Cis	191,66667 [†]	16,64784	,000	120,9793	260,0207
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-80,3126
	HSC4_5FU_5u	148,66667 [†]			217,0207	
	HSC4_5FU_5u	128,66667 [†]	16,64784	,000	60,3126	197,0207
	HSC4_5FU_20u	137,33333 [†]	16,64784	,000	68,9793	205,6874
	HOC621_Ctrl	-	16,64784	,000	-	-
	HOC621_5Cis	377,66667 [†]			446,0207	309,3126
	HOC621_5Cis	180,33333 [†]	16,64784	,000	111,9793	248,6874
	HOC621_20Cis	193,33333 [†]	16,64784	,000	124,9793	261,6874
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
	HOC621_5FU_DMSO	234,33333 [†]			302,6874	165,9793
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
	HOC621_5FU_5u	240,33333 [†]			308,6874	171,9793
	HOC621_5FU_5u	153,33333 [†]	16,64784	,000	84,9793	221,6874
	HOC621_5FU_20u	187,33333 [†]	16,64784	,000	118,9793	255,6874
	SAS_Ctrl	-	16,64784	,000	-	-
	SAS_5Cis	329,33333 [†]			397,6874	260,9793
	SAS_5Cis	195,00000 [†]	16,64784	,000	126,6459	263,3541
	SAS_20Cis	190,33333 [†]	16,64784	,000	121,9793	258,6874
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
	SAS_5FU_DMSO	403,33333 [†]			471,6874	334,9793
	SAS_5FU_DMSO	-	16,64784	,000	-	-
	SAS_5FU_5	231,66667 [†]			300,0207	163,3126
	SAS_5FU_5	130,66667 [†]	16,64784	,000	62,3126	199,0207
	SAS_5FU_20	151,84333 [†]	16,64784	,000	83,4893	220,1974
HSC4_5FU_5u	HSC3Ctrl	-35,00000	16,64784	1,000	-	33,3541
	HSC35CIS	75,66667 [†]	16,64784	,011	103,3541	144,0207
	HSC320CIS	76,00000 [†]	16,64784	,011	7,3126	144,3541
	HSC35FUCTRL	-96,66667 [†]	16,64784	,000	7,6459	-28,3126
	HSC3FUDMSO	-78,00000 [†]	16,64784	,007	-	-9,6459
					165,0207	
					146,3541	

	HSC3FU5	65,33333	16,64784	,091	-3,0207	133,6874
	HSC3FU20	67,33333	16,64784	,061	-1,0207	135,6874
	HSC4_Ctrl	-	16,64784	,000	-	-
	HSC4_5Cis	202,33333	16,64784	,222	270,6874	133,9793
	HSC4_20Cis	60,66667	16,64784	,143	-7,6874	129,0207
	HSC4_5FU_Ctrl	63,00000	16,64784	,000	-5,3541	131,3541
	HSC4_5FU_DMSO	-	16,64784	,000	-	-
	HSC4_5FU_20u	277,33333	16,64784	,000	345,6874	208,9793
	HSC4_5FU_20u	-	16,64784	,000	-	-60,3126
	HOC621_Ctrl	128,66667	16,64784	1,000	197,0207	77,0207
	HOC621_5Cis	8,66667	16,64784	,000	-59,6874	77,0207
	HOC621_20Cis	-	16,64784	,000	-	-
	HOC621_5FU_Ctrl	506,33333	16,64784	1,000	574,6874	437,9793
	HOC621_5FU_DMSO	51,66667	16,64784	,103	-16,6874	120,0207
	HOC621_5FU_5u	64,66667	16,64784	,000	-3,6874	133,0207
	HOC621_5FU_20u	-	16,64784	,000	-	-
	SAS_Ctrl	363,00000	16,64784	,000	431,3541	294,6459
	SAS_5Cis	-	16,64784	,000	-	-
	SAS_20Cis	369,00000	16,64784	1,000	437,3541	300,6459
	SAS_5FU_Ctrl	24,66667	16,64784	,323	-43,6874	93,0207
	SAS_5FU_DMSO	58,66667	16,64784	,000	-9,6874	127,0207
	SAS_5FU_5	-	16,64784	,000	-	-
	SAS_5FU_20	458,00000	16,64784	,075	526,3541	389,6459
	HSC4_5FU_20u	66,33333	16,64784	,184	-2,0207	134,6874
	HSC3Ctrl	61,66667	16,64784	,000	-6,6874	130,0207
	HSC35CIS	-	16,64784	,000	-	-
	HSC320CIS	532,00000	16,64784	,000	600,3541	463,6459
	HSC35FUCTRL	-	16,64784	,000	-	-
	HSC3FUDMSO	360,33333	16,64784	,001	428,6874	291,9793
	HSC3FU5	2,00000	16,64784	1,000	-66,3541	70,3541
	HSC3FU20	23,17667	16,64784	1,000	-45,1774	91,5307
	HSC4_Ctrl	-43,66667	16,64784	1,000	-	24,6874
	HSC4_5Cis	67,00000	16,64784	,065	112,0207	135,3541
	HSC4_5Cis	67,33333	16,64784	,061	-1,3541	135,6874
	HSC4_5Cis	-	16,64784	,000	-	-36,9793
	HSC4_5Cis	105,33333	16,64784	,001	173,6874	-18,3126
	HSC4_5Cis	-86,66667	16,64784	,466	155,0207	125,0207
	HSC4_5Cis	56,66667	16,64784	,323	-11,6874	127,0207
	HSC4_5Cis	58,66667	16,64784	,000	-9,6874	127,0207
	HSC4_5Cis	-	16,64784	,000	-	-
	HSC4_5Cis	211,00000	16,64784	1,000	279,3541	142,6459
	HSC4_5Cis	52,00000	16,64784	1,000	-16,3541	120,3541

	HSC4_20Cis	54,33333	16,64784	,710	-14,0207	122,6874
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		286,00000 [†]			354,3541	217,6459
	HSC4_5FU_DMSO	-	16,64784	,000	-	-68,9793
		137,33333 [†]			205,6874	
	HSC4_5FU_5u	-8,66667	16,64784	1,000	-77,0207	59,6874
	HOC621_Ctrl	-	16,64784	,000	-	-
		515,00000 [†]			583,3541	446,6459
	HOC621_5Cis	43,00000	16,64784	1,000	-25,3541	111,3541
	HOC621_20Cis	56,00000	16,64784	,526	-12,3541	124,3541
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		371,66667 [†]			440,0207	303,3126
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		377,66667 [†]			446,0207	309,3126
	HOC621_5FU_5u	16,00000	16,64784	1,000	-52,3541	84,3541
	HOC621_5FU_20u	50,00000	16,64784	1,000	-18,3541	118,3541
	SAS_Ctrl	-	16,64784	,000	-	-
		466,66667 [†]			535,0207	398,3126
	SAS_5Cis	57,66667	16,64784	,389	-10,6874	126,0207
	SAS_20Cis	53,00000	16,64784	,898	-15,3541	121,3541
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		540,66667 [†]			609,0207	472,3126
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		369,00000 [†]			437,3541	300,6459
	SAS_5FU_5	-6,66667	16,64784	1,000	-75,0207	61,6874
	SAS_5FU_20	14,51000	16,64784	1,000	-53,8441	82,8641
HOC621_Ctrl	HSC3Ctrl	471,33333 [†]	16,64784	,000	402,9793	539,6874
	HSC35CIS	582,00000 [†]	16,64784	,000	513,6459	650,3541
	HSC320CIS	582,33333 [†]	16,64784	,000	513,9793	650,6874
	HSC35FUCTRL	409,66667 [†]	16,64784	,000	341,3126	478,0207
	HSC3FUDMSO	428,33333 [†]	16,64784	,000	359,9793	496,6874
	HSC3FU5	571,66667 [†]	16,64784	,000	503,3126	640,0207
	HSC3FU20	573,66667 [†]	16,64784	,000	505,3126	642,0207
	HSC4_Ctrl	304,00000 [†]	16,64784	,000	235,6459	372,3541
	HSC4_5Cis	567,00000 [†]	16,64784	,000	498,6459	635,3541
	HSC4_20Cis	569,33333 [†]	16,64784	,000	500,9793	637,6874
	HSC4_5FU_Ctrl	229,00000 [†]	16,64784	,000	160,6459	297,3541
	HSC4_5FU_DMSO	377,66667 [†]	16,64784	,000	309,3126	446,0207

	HSC4_5FU_5u	506,33333 [†]	16,64784	,000	437,9793	574,6874
	HSC4_5FU_20u	515,00000 [†]	16,64784	,000	446,6459	583,3541
	HOC621_5Cis	558,00000 [†]	16,64784	,000	489,6459	626,3541
	HOC621_20Cis	571,00000 [†]	16,64784	,000	502,6459	639,3541
	HOC621_5FU_Ctrl	143,33333 [†]	16,64784	,000	74,9793	211,6874
	HOC621_5FU_DMSO	137,33333 [†]	16,64784	,000	68,9793	205,6874
	HOC621_5FU_5u	531,00000 [†]	16,64784	,000	462,6459	599,3541
	HOC621_5FU_20u	565,00000 [†]	16,64784	,000	496,6459	633,3541
	SAS_Ctrl	48,33333	16,64784	1,000	-20,0207	116,6874
	SAS_5Cis	572,66667 [†]	16,64784	,000	504,3126	641,0207
	SAS_20Cis	568,00000 [†]	16,64784	,000	499,6459	636,3541
	SAS_5FU_Ctrl	-25,66667	16,64784	1,000	-94,0207	42,6874
	SAS_5FU_DMSO	146,00000 [†]	16,64784	,000	77,6459	214,3541
	SAS_5FU_5	508,33333 [†]	16,64784	,000	439,9793	576,6874
	SAS_5FU_20	529,51000 [†]	16,64784	,000	461,1559	597,8641
HOC621_5Cis	HSC3Ctrl	-86,66667 [†]	16,64784	,001	-	-18,3126
					155,0207	
	HSC35CIS	24,00000	16,64784	1,000	-44,3541	92,3541
	HSC320CIS	24,33333	16,64784	1,000	-44,0207	92,6874
	HSC35FUCTRL	-	16,64784	,000	-	-79,9793
		148,33333 [†]			216,6874	
	HSC3FUDMSO	-	16,64784	,000	-	-61,3126
		129,66667 [†]			198,0207	
	HSC3FU5	13,66667	16,64784	1,000	-54,6874	82,0207
	HSC3FU20	15,66667	16,64784	1,000	-52,6874	84,0207
	HSC4_Ctrl	-	16,64784	,000	-	-
		254,00000 [†]			322,3541	185,6459
	HSC4_5Cis	9,00000	16,64784	1,000	-59,3541	77,3541
	HSC4_20Cis	11,33333	16,64784	1,000	-57,0207	79,6874
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		329,00000 [†]			397,3541	260,6459
	HSC4_5FU_DMSO	-	16,64784	,000	-	-
		180,33333 [†]			248,6874	111,9793
	HSC4_5FU_5u	-51,66667	16,64784	1,000	-	16,6874
					120,0207	
	HSC4_5FU_20u	-43,00000	16,64784	1,000	-	25,3541
					111,3541	
	HOC621_Ctrl	-	16,64784	,000	-	-
		558,00000 [†]			626,3541	489,6459

	HOC621_20Cis	13,00000	16,64784	1,000	-55,3541	81,3541
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		414,66667 [†]			483,0207	346,3126
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		420,66667 [†]			489,0207	352,3126
	HOC621_5FU_5u	-27,00000	16,64784	1,000	-95,3541	41,3541
	HOC621_5FU_20u	7,00000	16,64784	1,000	-61,3541	75,3541
	SAS_Ctrl	-	16,64784	,000	-	-
		509,66667 [†]			578,0207	441,3126
	SAS_5Cis	14,66667	16,64784	1,000	-53,6874	83,0207
	SAS_20Cis	10,00000	16,64784	1,000	-58,3541	78,3541
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		583,66667 [†]			652,0207	515,3126
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		412,00000 [†]			480,3541	343,6459
	SAS_5FU_5	-49,66667	16,64784	1,000	-	18,6874
					118,0207	
	SAS_5FU_20	-28,49000	16,64784	1,000	-96,8441	39,8641
HOC621_20Cis	HSC3Ctrl	-99,66667 [†]	16,64784	,000	-	-31,3126
					168,0207	
	HSC35CIS	11,00000	16,64784	1,000	-57,3541	79,3541
	HSC320CIS	11,33333	16,64784	1,000	-57,0207	79,6874
	HSC35FUCTRL	-	16,64784	,000	-	-92,9793
		161,33333 [†]			229,6874	
	HSC3FUDMSO	-	16,64784	,000	-	-74,3126
		142,66667 [†]			211,0207	
	HSC3FU5	,66667	16,64784	1,000	-67,6874	69,0207
	HSC3FU20	2,66667	16,64784	1,000	-65,6874	71,0207
	HSC4_Ctrl	-	16,64784	,000	-	-
		267,00000 [†]			335,3541	198,6459
	HSC4_5Cis	-4,00000	16,64784	1,000	-72,3541	64,3541
	HSC4_20Cis	-1,66667	16,64784	1,000	-70,0207	66,6874
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		342,00000 [†]			410,3541	273,6459
	HSC4_5FU_DMSO	-	16,64784	,000	-	-
		193,33333 [†]			261,6874	124,9793
	HSC4_5FU_5u	-64,66667	16,64784	,103	-	3,6874
					133,0207	
	HSC4_5FU_20u	-56,00000	16,64784	,526	-	12,3541
					124,3541	
	HOC621_Ctrl	-	16,64784	,000	-	-
		571,00000 [†]			639,3541	502,6459
	HOC621_5Cis	-13,00000	16,64784	1,000	-81,3541	55,3541
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		427,66667 [†]			496,0207	359,3126
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		433,66667 [†]			502,0207	365,3126

	HOC621_5FU_5u	-40,00000	16,64784	1,000	-	28,3541
					108,3541	
	HOC621_5FU_20u	-6,00000	16,64784	1,000	-74,3541	62,3541
	SAS_Ctrl	-	16,64784	,000	-	-
		522,66667*			591,0207	454,3126
	SAS_5Cis	1,66667	16,64784	1,000	-66,6874	70,0207
	SAS_20Cis	-3,00000	16,64784	1,000	-71,3541	65,3541
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		596,66667*			665,0207	528,3126
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		425,00000*			493,3541	356,6459
	SAS_5FU_5	-62,66667	16,64784	,152	-	5,6874
					131,0207	
	SAS_5FU_20	-41,49000	16,64784	1,000	-	26,8641
					109,8441	
HOC621_5FU_Ctrl	HSC3Ctrl	328,00000*	16,64784	,000	259,6459	396,3541
	HSC35CIS	438,66667*	16,64784	,000	370,3126	507,0207
	HSC320CIS	439,00000*	16,64784	,000	370,6459	507,3541
	HSC35FUCTRL	266,33333*	16,64784	,000	197,9793	334,6874
	HSC3FUDMSO	285,00000*	16,64784	,000	216,6459	353,3541
	HSC3FU5	428,33333*	16,64784	,000	359,9793	496,6874
	HSC3FU20	430,33333*	16,64784	,000	361,9793	498,6874
	HSC4_Ctrl	160,66667*	16,64784	,000	92,3126	229,0207
	HSC4_5Cis	423,66667*	16,64784	,000	355,3126	492,0207
	HSC4_20Cis	426,00000*	16,64784	,000	357,6459	494,3541
	HSC4_5FU_Ctrl	85,66667*	16,64784	,001	17,3126	154,0207
	HSC4_5FU_DMSO	234,33333*	16,64784	,000	165,9793	302,6874
	HSC4_5FU_5u	363,00000*	16,64784	,000	294,6459	431,3541
	HSC4_5FU_20u	371,66667*	16,64784	,000	303,3126	440,0207
	HOC621_Ctrl	-	16,64784	,000	-	-74,9793
		143,33333*			211,6874	
	HOC621_5Cis	414,66667*	16,64784	,000	346,3126	483,0207
	HOC621_20Cis	427,66667*	16,64784	,000	359,3126	496,0207
	HOC621_5FU_DMSO	-6,00000	16,64784	1,000	-74,3541	62,3541
	HOC621_5FU_5u	387,66667*	16,64784	,000	319,3126	456,0207
	HOC621_5FU_20u	421,66667*	16,64784	,000	353,3126	490,0207
	SAS_Ctrl	-95,00000*	16,64784	,000	-	-26,6459
					163,3541	
	SAS_5Cis	429,33333*	16,64784	,000	360,9793	497,6874

	SAS_20Cis	424,66667*	16,64784	,000	356,3126	493,0207
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		169,00000*			237,3541	100,6459
	SAS_5FU_DMSO	2,66667	16,64784	1,000	-65,6874	71,0207
	SAS_5FU_5	365,00000*	16,64784	,000	296,6459	433,3541
	SAS_5FU_20	386,17667*	16,64784	,000	317,8226	454,5307
HOC621_5FU_DMSO	HSC3Ctrl	334,00000*	16,64784	,000	265,6459	402,3541
	HSC35CIS	444,66667*	16,64784	,000	376,3126	513,0207
	HSC320CIS	445,00000*	16,64784	,000	376,6459	513,3541
	HSC35FUCTRL	272,33333*	16,64784	,000	203,9793	340,6874
	HSC3FUDMSO	291,00000*	16,64784	,000	222,6459	359,3541
	HSC3FU5	434,33333*	16,64784	,000	365,9793	502,6874
	HSC3FU20	436,33333*	16,64784	,000	367,9793	504,6874
	HSC4_Ctrl	166,66667*	16,64784	,000	98,3126	235,0207
	HSC4_5Cis	429,66667*	16,64784	,000	361,3126	498,0207
	HSC4_20Cis	432,00000*	16,64784	,000	363,6459	500,3541
	HSC4_5FU_Ctrl	91,66667*	16,64784	,000	23,3126	160,0207
	HSC4_5FU_DMSO	240,33333*	16,64784	,000	171,9793	308,6874
	HSC4_5FU_5u	369,00000*	16,64784	,000	300,6459	437,3541
	HSC4_5FU_20u	377,66667*	16,64784	,000	309,3126	446,0207
	HOC621_Ctrl	-	16,64784	,000	-	-68,9793
		137,33333*			205,6874	
	HOC621_5Cis	420,66667*	16,64784	,000	352,3126	489,0207
	HOC621_20Cis	433,66667*	16,64784	,000	365,3126	502,0207
	HOC621_5FU_Ctrl	6,00000	16,64784	1,000	-62,3541	74,3541
	HOC621_5FU_5u	393,66667*	16,64784	,000	325,3126	462,0207
	HOC621_5FU_20u	427,66667*	16,64784	,000	359,3126	496,0207
	SAS_Ctrl	-89,00000*	16,64784	,001	-	-20,6459
					157,3541	
	SAS_5Cis	435,33333*	16,64784	,000	366,9793	503,6874
	SAS_20Cis	430,66667*	16,64784	,000	362,3126	499,0207
	SAS_5FU_Ctrl	-	16,64784	,000	-	-94,6459
		163,00000*			231,3541	
	SAS_5FU_DMSO	8,66667	16,64784	1,000	-59,6874	77,0207
	SAS_5FU_5	371,00000*	16,64784	,000	302,6459	439,3541

	SAS_5FU_20	392,17667 ⁷	16,64784	,000	323,8226	460,5307
HOC621_5FU_5u	HSC3Ctrl	-59,66667	16,64784	,268	-	8,6874
	HSC35CIS	51,00000	16,64784	1,000	128,0207	119,3541
	HSC320CIS	51,33333	16,64784	1,000	-17,3541	119,6874
	HSC35FUCTRL	-	16,64784	,000	-	-52,9793
		121,33333 ⁷			189,6874	
	HSC3FUDMSO	-	16,64784	,000	-	-34,3126
		102,66667 ⁷			171,0207	
	HSC3FU5	40,66667	16,64784	1,000	-27,6874	109,0207
	HSC3FU20	42,66667	16,64784	1,000	-25,6874	111,0207
	HSC4_Ctrl	-	16,64784	,000	-	-
		227,00000 ⁷			295,3541	158,6459
	HSC4_5Cis	36,00000	16,64784	1,000	-32,3541	104,3541
	HSC4_20Cis	38,33333	16,64784	1,000	-30,0207	106,6874
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		302,00000 ⁷			370,3541	233,6459
	HSC4_5FU_DMSO	-	16,64784	,000	-	-84,9793
		153,33333 ⁷			221,6874	
	HSC4_5FU_5u	-24,66667	16,64784	1,000	-93,0207	43,6874
	HSC4_5FU_20u	-16,00000	16,64784	1,000	-84,3541	52,3541
	HOC621_Ctrl	-	16,64784	,000	-	-
		531,00000 ⁷			599,3541	462,6459
	HOC621_5Cis	27,00000	16,64784	1,000	-41,3541	95,3541
	HOC621_20Cis	40,00000	16,64784	1,000	-28,3541	108,3541
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		387,66667 ⁷			456,0207	319,3126
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		393,66667 ⁷			462,0207	325,3126
	HOC621_5FU_20u	34,00000	16,64784	1,000	-34,3541	102,3541
	SAS_Ctrl	-	16,64784	,000	-	-
		482,66667 ⁷			551,0207	414,3126
	SAS_5Cis	41,66667	16,64784	1,000	-26,6874	110,0207
	SAS_20Cis	37,00000	16,64784	1,000	-31,3541	105,3541
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		556,66667 ⁷			625,0207	488,3126
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		385,00000 ⁷			453,3541	316,6459
	SAS_5FU_5	-22,66667	16,64784	1,000	-91,0207	45,6874
	SAS_5FU_20	-1,49000	16,64784	1,000	-69,8441	66,8641
HOC621_5FU_20u	HSC3Ctrl	-93,66667 ⁷	16,64784	,000	-	-25,3126
	HSC35CIS	17,00000	16,64784	1,000	162,0207	85,3541
					-51,3541	

	HSC320CIS	17,33333	16,64784	1,000	-51,0207	85,6874
	HSC35FUCTRL	-	16,64784	,000	-	-86,9793
		155,33333 [†]			223,6874	
	HSC3FUDMSO	-	16,64784	,000	-	-68,3126
		136,66667 [†]			205,0207	
	HSC3FU5	6,66667	16,64784	1,000	-61,6874	75,0207
	HSC3FU20	8,66667	16,64784	1,000	-59,6874	77,0207
	HSC4_Ctrl	-	16,64784	,000	-	-
		261,00000 [†]			329,3541	192,6459
	HSC4_5Cis	2,00000	16,64784	1,000	-66,3541	70,3541
	HSC4_20Cis	4,33333	16,64784	1,000	-64,0207	72,6874
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		336,00000 [†]			404,3541	267,6459
	HSC4_5FU_DMSO	-	16,64784	,000	-	-
		187,33333 [†]			255,6874	118,9793
	HSC4_5FU_5u	-58,66667	16,64784	,323	-	9,6874
					127,0207	
	HSC4_5FU_20u	-50,00000	16,64784	1,000	-	18,3541
					118,3541	
	HOC621_Ctrl	-	16,64784	,000	-	-
		565,00000 [†]			633,3541	496,6459
	HOC621_5Cis	-7,00000	16,64784	1,000	-75,3541	61,3541
	HOC621_20Cis	6,00000	16,64784	1,000	-62,3541	74,3541
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		421,66667 [†]			490,0207	353,3126
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		427,66667 [†]			496,0207	359,3126
	HOC621_5FU_5u	-34,00000	16,64784	1,000	-	34,3541
					102,3541	
	SAS_Ctrl	-	16,64784	,000	-	-
		516,66667 [†]			585,0207	448,3126
	SAS_5Cis	7,66667	16,64784	1,000	-60,6874	76,0207
	SAS_20Cis	3,00000	16,64784	1,000	-65,3541	71,3541
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		590,66667 [†]			659,0207	522,3126
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		419,00000 [†]			487,3541	350,6459
	SAS_5FU_5	-56,66667	16,64784	,466	-	11,6874
					125,0207	
	SAS_5FU_20	-35,49000	16,64784	1,000	-	32,8641
					103,8441	
SAS_Ctrl	HSC3Ctrl	423,00000 [†]	16,64784	,000	354,6459	491,3541
	HSC35CIS	533,66667 [†]	16,64784	,000	465,3126	602,0207
	HSC320CIS	534,00000 [†]	16,64784	,000	465,6459	602,3541
	HSC35FUCTRL	361,33333 [†]	16,64784	,000	292,9793	429,6874
	HSC3FUDMSO	380,00000 [†]	16,64784	,000	311,6459	448,3541

	HSC3FU5	523,33333 [†]	16,64784	,000	454,9793	591,6874
	HSC3FU20	525,33333 [†]	16,64784	,000	456,9793	593,6874
	HSC4_Ctrl	255,66667 [†]	16,64784	,000	187,3126	324,0207
	HSC4_5Cis	518,66667 [†]	16,64784	,000	450,3126	587,0207
	HSC4_20Cis	521,00000 [†]	16,64784	,000	452,6459	589,3541
	HSC4_5FU_Ctrl	180,66667 [†]	16,64784	,000	112,3126	249,0207
	HSC4_5FU_DMSO	329,33333 [†]	16,64784	,000	260,9793	397,6874
	HSC4_5FU_5u	458,00000 [†]	16,64784	,000	389,6459	526,3541
	HSC4_5FU_20u	466,66667 [†]	16,64784	,000	398,3126	535,0207
	HOC621_Ctrl	-48,33333	16,64784	1,000	-	20,0207
					116,6874	
	HOC621_5Cis	509,66667 [†]	16,64784	,000	441,3126	578,0207
	HOC621_20Cis	522,66667 [†]	16,64784	,000	454,3126	591,0207
	HOC621_5FU_Ctrl	95,00000 [†]	16,64784	,000	26,6459	163,3541
	HOC621_5FU_DMSO	89,00000 [†]	16,64784	,001	20,6459	157,3541
	HOC621_5FU_5u	482,66667 [†]	16,64784	,000	414,3126	551,0207
	HOC621_5FU_20u	516,66667 [†]	16,64784	,000	448,3126	585,0207
	SAS_5Cis	524,33333 [†]	16,64784	,000	455,9793	592,6874
	SAS_20Cis	519,66667 [†]	16,64784	,000	451,3126	588,0207
	SAS_5FU_Ctrl	-74,00000 [†]	16,64784	,016	-	-5,6459
					142,3541	
	SAS_5FU_DMSO	97,66667 [†]	16,64784	,000	29,3126	166,0207
	SAS_5FU_5	460,00000 [†]	16,64784	,000	391,6459	528,3541
	SAS_5FU_20	481,17667 [†]	16,64784	,000	412,8226	549,5307
SAS_5Cis	HSC3Ctrl	-	16,64784	,000	-	-32,9793
		101,33333 [†]			169,6874	
	HSC35CIS	9,33333	16,64784	1,000	-59,0207	77,6874
	HSC320CIS	9,66667	16,64784	1,000	-58,6874	78,0207
	HSC35FUCTRL	-	16,64784	,000	-	-94,6459
		163,00000 [†]			231,3541	
	HSC3FUDMSO	-	16,64784	,000	-	-75,9793
		144,33333 [†]			212,6874	
	HSC3FU5	-1,00000	16,64784	1,000	-69,3541	67,3541
	HSC3FU20	1,00000	16,64784	1,000	-67,3541	69,3541
	HSC4_Ctrl	-	16,64784	,000	-	-
		268,66667 [†]			337,0207	200,3126
	HSC4_5Cis	-5,66667	16,64784	1,000	-74,0207	62,6874

	HSC4_20Cis	-3,33333	16,64784	1,000	-71,6874	65,0207
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		343,66667 [†]			412,0207	275,3126
	HSC4_5FU_DMSO	-	16,64784	,000	-	-
		195,00000 [†]			263,3541	126,6459
	HSC4_5FU_5u	-66,33333	16,64784	,075	-	2,0207
					134,6874	
	HSC4_5FU_20u	-57,66667	16,64784	,389	-	10,6874
					126,0207	
	HOC621_Ctrl	-	16,64784	,000	-	-
		572,66667 [†]			641,0207	504,3126
	HOC621_5Cis	-14,66667	16,64784	1,000	-83,0207	53,6874
	HOC621_20Cis	-1,66667	16,64784	1,000	-70,0207	66,6874
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		429,33333 [†]			497,6874	360,9793
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		435,33333 [†]			503,6874	366,9793
	HOC621_5FU_5u	-41,66667	16,64784	1,000	-	26,6874
					110,0207	
	HOC621_5FU_20u	-7,66667	16,64784	1,000	-76,0207	60,6874
	SAS_Ctrl	-	16,64784	,000	-	-
		524,33333 [†]			592,6874	455,9793
	SAS_20Cis	-4,66667	16,64784	1,000	-73,0207	63,6874
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		598,33333 [†]			666,6874	529,9793
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		426,66667 [†]			495,0207	358,3126
	SAS_5FU_5	-64,33333	16,64784	,110	-	4,0207
					132,6874	
	SAS_5FU_20	-43,15667	16,64784	1,000	-	25,1974
					111,5107	
SAS_20Cis	HSC3Ctrl	-96,66667 [†]	16,64784	,000	-	-28,3126
					165,0207	
	HSC35CIS	14,00000	16,64784	1,000	-54,3541	82,3541
	HSC320CIS	14,33333	16,64784	1,000	-54,0207	82,6874
	HSC35FUCTRL	-	16,64784	,000	-	-89,9793
		158,33333 [†]			226,6874	
	HSC3FUDMSO	-	16,64784	,000	-	-71,3126
		139,66667 [†]			208,0207	
	HSC3FU5	3,66667	16,64784	1,000	-64,6874	72,0207
	HSC3FU20	5,66667	16,64784	1,000	-62,6874	74,0207
	HSC4_Ctrl	-	16,64784	,000	-	-
		264,00000 [†]			332,3541	195,6459
	HSC4_5Cis	-1,00000	16,64784	1,000	-69,3541	67,3541
	HSC4_20Cis	1,33333	16,64784	1,000	-67,0207	69,6874
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		339,00000 [†]			407,3541	270,6459

	HSC4_5FU_DMSO	-	16,64784	,000	-	-
		190,33333*			258,6874	121,9793
	HSC4_5FU_5u	-61,66667	16,64784	,184	-	6,6874
					130,0207	
	HSC4_5FU_20u	-53,00000	16,64784	,898	-	15,3541
					121,3541	
	HOC621_Ctrl	-	16,64784	,000	-	-
		568,00000*			636,3541	499,6459
	HOC621_5Cis	-10,00000	16,64784	1,000	-78,3541	58,3541
	HOC621_20Cis	3,00000	16,64784	1,000	-65,3541	71,3541
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		424,66667*			493,0207	356,3126
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		430,66667*			499,0207	362,3126
	HOC621_5FU_5u	-37,00000	16,64784	1,000	-	31,3541
					105,3541	
	HOC621_5FU_20u	-3,00000	16,64784	1,000	-71,3541	65,3541
	SAS_Ctrl	-	16,64784	,000	-	-
		519,66667*			588,0207	451,3126
	SAS_5Cis	4,66667	16,64784	1,000	-63,6874	73,0207
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		593,66667*			662,0207	525,3126
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		422,00000*			490,3541	353,6459
	SAS_5FU_5	-59,66667	16,64784	,268	-	8,6874
					128,0207	
	SAS_5FU_20	-38,49000	16,64784	1,000	-	29,8641
					106,8441	
SAS_5FU_Ctrl	HSC3Ctrl	497,00000*	16,64784	,000	428,6459	565,3541
	HSC35CIS	607,66667*	16,64784	,000	539,3126	676,0207
	HSC320CIS	608,00000*	16,64784	,000	539,6459	676,3541
	HSC35FUCTRL	435,33333*	16,64784	,000	366,9793	503,6874
	HSC3FUDMSO	454,00000*	16,64784	,000	385,6459	522,3541
	HSC3FU5	597,33333*	16,64784	,000	528,9793	665,6874
	HSC3FU20	599,33333*	16,64784	,000	530,9793	667,6874
	HSC4_Ctrl	329,66667*	16,64784	,000	261,3126	398,0207
	HSC4_5Cis	592,66667*	16,64784	,000	524,3126	661,0207
	HSC4_20Cis	595,00000*	16,64784	,000	526,6459	663,3541
	HSC4_5FU_Ctrl	254,66667*	16,64784	,000	186,3126	323,0207
	HSC4_5FU_DMSO	403,33333*	16,64784	,000	334,9793	471,6874
	HSC4_5FU_5u	532,00000*	16,64784	,000	463,6459	600,3541
	HSC4_5FU_20u	540,66667*	16,64784	,000	472,3126	609,0207

	HOC621_Ctrl	25,66667	16,64784	1,000	-42,6874	94,0207
	HOC621_5Cis	583,66667	16,64784	,000	515,3126	652,0207
	HOC621_20Cis	596,66667	16,64784	,000	528,3126	665,0207
	HOC621_5FU_Ctrl	169,00000	16,64784	,000	100,6459	237,3541
	HOC621_5FU_DMSO	163,00000	16,64784	,000	94,6459	231,3541
	HOC621_5FU_5u	556,66667	16,64784	,000	488,3126	625,0207
	HOC621_5FU_20u	590,66667	16,64784	,000	522,3126	659,0207
	SAS_Ctrl	74,00000	16,64784	,016	5,6459	142,3541
	SAS_5Cis	598,33333	16,64784	,000	529,9793	666,6874
	SAS_20Cis	593,66667	16,64784	,000	525,3126	662,0207
	SAS_5FU_DMSO	171,66667	16,64784	,000	103,3126	240,0207
	SAS_5FU_5	534,00000	16,64784	,000	465,6459	602,3541
	SAS_5FU_20	555,17667	16,64784	,000	486,8226	623,5307
SAS_5FU_DMSO	HSC3Ctrl	325,33333	16,64784	,000	256,9793	393,6874
	HSC35CIS	436,00000	16,64784	,000	367,6459	504,3541
	HSC320CIS	436,33333	16,64784	,000	367,9793	504,6874
	HSC35FUCTRL	263,66667	16,64784	,000	195,3126	332,0207
	HSC3FUDMSO	282,33333	16,64784	,000	213,9793	350,6874
	HSC3FU5	425,66667	16,64784	,000	357,3126	494,0207
	HSC3FU20	427,66667	16,64784	,000	359,3126	496,0207
	HSC4_Ctrl	158,00000	16,64784	,000	89,6459	226,3541
	HSC4_5Cis	421,00000	16,64784	,000	352,6459	489,3541
	HSC4_20Cis	423,33333	16,64784	,000	354,9793	491,6874
	HSC4_5FU_Ctrl	83,00000	16,64784	,002	14,6459	151,3541
	HSC4_5FU_DMSO	231,66667	16,64784	,000	163,3126	300,0207
	HSC4_5FU_5u	360,33333	16,64784	,000	291,9793	428,6874
	HSC4_5FU_20u	369,00000	16,64784	,000	300,6459	437,3541
	HOC621_Ctrl	-	16,64784	,000	-	-77,6459
		146,00000			214,3541	
	HOC621_5Cis	412,00000	16,64784	,000	343,6459	480,3541
	HOC621_20Cis	425,00000	16,64784	,000	356,6459	493,3541

	HOC621_5FU_Ctrl	-2,66667	16,64784	1,000	-71,0207	65,6874
	HOC621_5FU_DMSO	-8,66667	16,64784	1,000	-77,0207	59,6874
	HOC621_5FU_5u	385,00000 ⁺	16,64784	,000	316,6459	453,3541
	HOC621_5FU_20u	419,00000 ⁺	16,64784	,000	350,6459	487,3541
	SAS_Ctrl	-97,66667 ⁺	16,64784	,000	-	-29,3126
	SAS_5Cis	426,66667 ⁺	16,64784	,000	166,0207	495,0207
	SAS_20Cis	422,00000 ⁺	16,64784	,000	358,3126	490,3541
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
	SAS_5FU_5	171,66667 ⁺			240,0207	103,3126
	SAS_5FU_20	362,33333 ⁺	16,64784	,000	293,9793	430,6874
	SAS_5FU_5	383,51000 ⁺	16,64784	,000	315,1559	451,8641
SAS_5FU_5	HSC3Ctrl	-37,00000	16,64784	1,000	-	31,3541
	HSC35CIS	73,66667 ⁺	16,64784	,017	105,3541	142,0207
	HSC320CIS	74,00000 ⁺	16,64784	,016	5,3126	142,3541
	HSC35FUCTRL	-98,66667 ⁺	16,64784	,000	-	-30,3126
	HSC3FUDMSO	-80,00000 ⁺	16,64784	,005	167,0207	-11,6459
	HSC3FU5	63,33333	16,64784	,134	148,3541	131,6874
	HSC3FU20	65,33333	16,64784	,091	-5,0207	133,6874
	HSC4_Ctrl	-	16,64784	,000	-3,0207	-
	HSC4_5Cis	204,33333 ⁺			-	135,9793
	HSC4_20Cis	58,66667	16,64784	,323	272,6874	127,0207
	HSC4_5FU_Ctrl	61,00000	16,64784	,209	-9,6874	129,3541
	HSC4_5FU_DMSO	-	16,64784	,000	-	-
	HSC4_5FU_5u	279,33333 ⁺			347,6874	210,9793
	HSC4_5FU_20u	-	16,64784	,000	-	-62,3126
	HOC621_Ctrl	130,66667 ⁺			199,0207	66,3541
	HOC621_5Cis	-2,00000	16,64784	1,000	-70,3541	75,0207
	HOC621_20Cis	6,66667	16,64784	1,000	-61,6874	-
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
	HOC621_5FU_DMSO	508,33333 ⁺			576,6874	439,9793
	HOC621_5FU_5u	49,66667	16,64784	1,000	-18,6874	118,0207
	HOC621_5FU_20u	62,66667	16,64784	,152	-5,6874	131,0207
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
	HOC621_5FU_DMSO	365,00000 ⁺			433,3541	296,6459
	HOC621_5FU_5u	-	16,64784	,000	-	-
	HOC621_5FU_20u	371,00000 ⁺			439,3541	302,6459
	HOC621_5FU_5u	22,66667	16,64784	1,000	-45,6874	91,0207

	HOC621_5FU_20u	56,66667	16,64784	,466	-11,6874	125,0207
	SAS_Ctrl	-	16,64784	,000	-	-
		460,00000 [†]			528,3541	391,6459
	SAS_5Cis	64,33333	16,64784	,110	-4,0207	132,6874
	SAS_20Cis	59,66667	16,64784	,268	-8,6874	128,0207
	SAS_5FU_Ctrl	-	16,64784	,000	-	-
		534,00000 [†]			602,3541	465,6459
	SAS_5FU_DMSO	-	16,64784	,000	-	-
		362,33333 [†]			430,6874	293,9793
	SAS_5FU_20	21,17667	16,64784	1,000	-47,1774	89,5307
SAS_5FU_20	HSC3Ctrl	-58,17667	16,64784	,354	-	10,1774
					126,5307	
	HSC35CIS	52,49000	16,64784	,982	-15,8641	120,8441
	HSC320CIS	52,82333	16,64784	,926	-15,5307	121,1774
	HSC35FUCTRL	-	16,64784	,000	-	-51,4893
		119,84333 [†]			188,1974	
	HSC3FUDMSO	-	16,64784	,000	-	-32,8226
		101,17667 [†]			169,5307	
	HSC3FU5	42,15667	16,64784	1,000	-26,1974	110,5107
	HSC3FU20	44,15667	16,64784	1,000	-24,1974	112,5107
	HSC4_Ctrl	-	16,64784	,000	-	-
		225,51000 [†]			293,8641	157,1559
	HSC4_5Cis	37,49000	16,64784	1,000	-30,8641	105,8441
	HSC4_20Cis	39,82333	16,64784	1,000	-28,5307	108,1774
	HSC4_5FU_Ctrl	-	16,64784	,000	-	-
		300,51000 [†]			368,8641	232,1559
	HSC4_5FU_DMSO	-	16,64784	,000	-	-83,4893
		151,84333 [†]			220,1974	
	HSC4_5FU_5u	-23,17667	16,64784	1,000	-91,5307	45,1774
	HSC4_5FU_20u	-14,51000	16,64784	1,000	-82,8641	53,8441
	HOC621_Ctrl	-	16,64784	,000	-	-
		529,51000 [†]			597,8641	461,1559
	HOC621_5Cis	28,49000	16,64784	1,000	-39,8641	96,8441
	HOC621_20Cis	41,49000	16,64784	1,000	-26,8641	109,8441
	HOC621_5FU_Ctrl	-	16,64784	,000	-	-
		386,17667 [†]			454,5307	317,8226
	HOC621_5FU_DMSO	-	16,64784	,000	-	-
		392,17667 [†]			460,5307	323,8226
	HOC621_5FU_5u	1,49000	16,64784	1,000	-66,8641	69,8441
	HOC621_5FU_20u	35,49000	16,64784	1,000	-32,8641	103,8441
	SAS_Ctrl	-	16,64784	,000	-	-
		481,17667 [†]			549,5307	412,8226

SAS_5Cis	43,15667	16,64784	1,000	-25,1974	111,5107
SAS_20Cis	38,49000	16,64784	1,000	-29,8641	106,8441
SAS_5FU_Ctrl	-	16,64784	,000	-	-
	555,17667			623,5307	486,8226
SAS_5FU_DMSO	-	16,64784	,000	-	-
	383,51000			451,8641	315,1559
SAS_5FU_5	-21,17667	16,64784	1,000	-89,5307	47,1774

3.2 HSC-3

HSC-3 cell line was tested with resveratrol in combination with both Cisplatin and 5-Fluorouracil separately. The effects of the combination were evaluated at 24, 48 and 72 hours.

Results of the effects of resveratrol in combination with cisplatin or 5-Fluorouracil on reducing cell viability at different time points are shown in *Figure II*.

3.2.1 Twenty-four hours incubation

The combination of cisplatin and resveratrol evaluated after 24 hours incubation does not provide a statistically significant benefit in comparison with both Cisplatin alone and Cisplatin plus Resveratrol ($P=1,000$).

3.2.2 Forty-eight hours incubation

The combination of cisplatin and resveratrol at 48 hours evaluation provides a reduction in viability. The combination of Cisplatin and resveratrol on cell proliferation evaluated at 48 hours resulted to be statistically significant in reducing cell proliferation with respect to Cisplatin alone (at 24h and 48h). Resveratrol and Fluorouracil at 48 hours evaluation do not provide a statistically significant positive effect in comparison to fluorouracil alone at 24h and 48h evaluation ($P=1,000$) (*table III*).

3.2.3 Seventy-two hours incubation

The combination of Cisplatin and Resveratrol has the greatest efficacy after 72 hours incubation when compared to Resveratrol alone at 72 hours (Mean value $-0,2500000$) ($P < 0,05$)

5-Fluorouracil and Resveratrol are more effective at 72h evaluation with a mean value of $-0,2286667$ with respect to 5-Fluorouracil alone.

The combination of Cisplatin and Resveratrol in reducing cell viability is highest at 72 hours with a mean value of $0,089$ (*Figure II*).

Regarding 5-Fluorouracil and resveratrol the efficacy in reducing cell viability at 72 hours is statistically significant when compared to efficacy at 24 hours and 48 hours.

The combination between Resveratrol and 5-Fluorouracil is effective in reducing viability with respect to 5-Fluorouracil alone at both 48 and 72 hours.

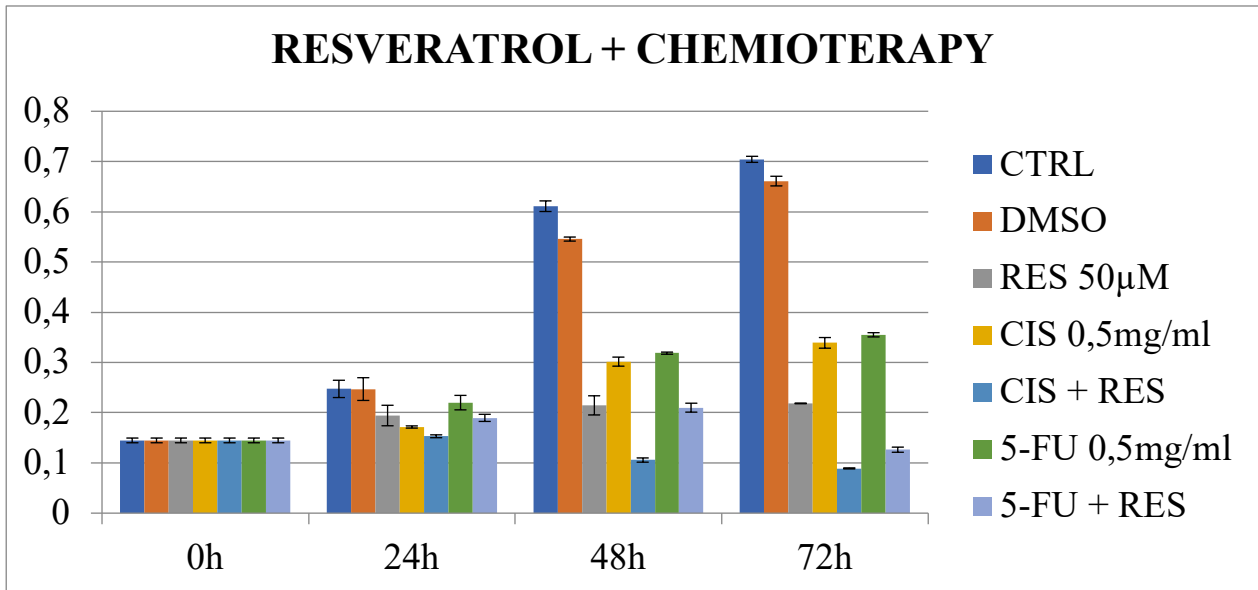


Figure II: Results of the MTT assay after administration of Resveratrol in addition to Cisplatin or 5-Fluorouracil to HSC-3 cell line

3.3 SAS

SAS cell line was tested with resveratrol in combination with both Cisplatin and 5-Fluorouracil separately. The effects of the combination were evaluated at 24, 48 and 72 hours.

Results of the effects of resveratrol in combination with cisplatin or 5-Fluorouracil on reducing cell viability at different time points are shown in *Figure III*.

3.3.1 Twenty-four hours evaluation

The combination of Cisplatin and Resveratrol after 24 hours incubation does not reduce cell viability in a statistically significant manner, in comparison with Cisplatin alone evaluated at 24 hours ($P=1,000$).

In cells treated with 5-Fluorouracil, the combination with resveratrol provides reduction in cell viability in comparison with conventional chemotherapy alone.

3.3.2 Forty-eight hours evaluation

At 48 hours evaluation either the combination of Resveratrol and Cisplatin or Resveratrol and 5-Fluorouracil and do not have a statistically significant effect in comparison with Resveratrol alone ($P=1,000$).

3.3.3 Seventy-two hours evaluation

The combination of Resveratrol and Cisplatin has the most relevant effect on cell viability after 72 hours incubation with a mean value of $-,1420000$ with a P value $<0,05$ (Table 3).

Also the combination of 5-Fluorouracil and Resveratrol has a relevant effect in decreasing cell viability after 72 hours with a mean value of $-,1295000$ (Figure III).

The combination between Cisplatin and Resveratrol did not show a statistically relevant effect in reducing cell viability when compared to Cisplatin alone and to Cisplatin and resveratrol.

At 72h we have a reduction in cell viability if compared to Cisplatin alone ($P<0,009$).

From this result we can hypothesize that we have an increase of efficacy of resveratrol over time.

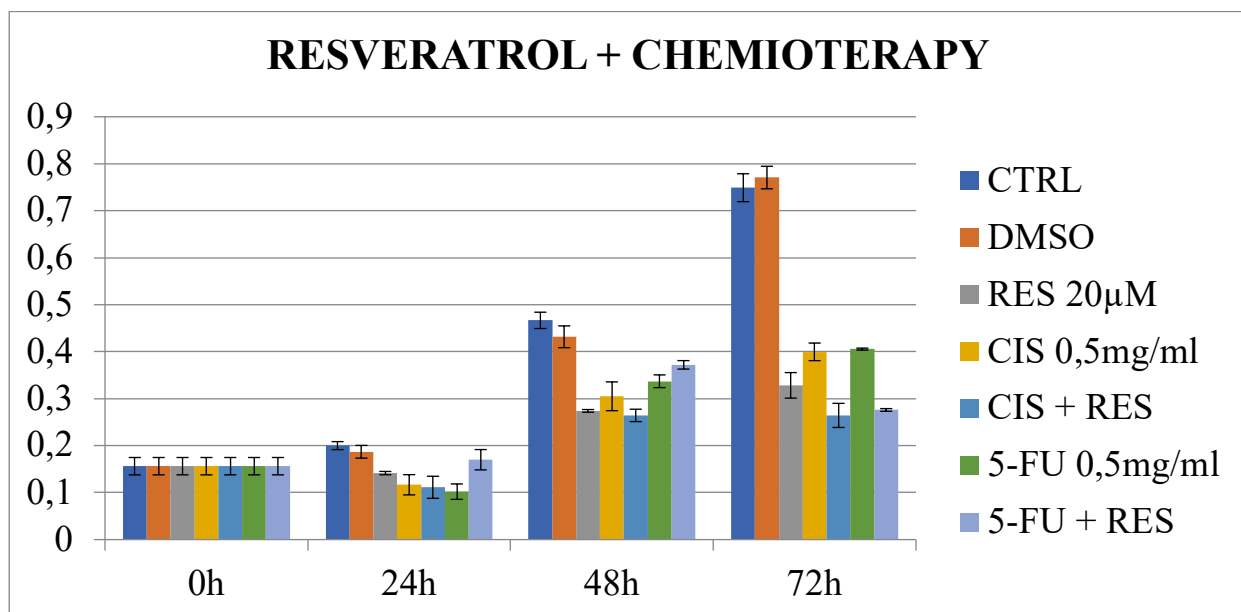


Figure III: Results of the MTT assay after administration of Resveratrol in addition to Cisplatin or 5-Fluorouracil to SAS cell line

The results of the MTT show that the addition of Resveratrol to both Cisplatin and 5-Fluorouracil is effective in reducing cell viability when compared to the substances alone.

Moreover the beneficial increases over time being most effective after 72 hours.

Regarding SAS cell line, the combination of Cisplatin and Resveratrol does not provide significant benefit in reducing cell viability.

Results of the Bonferroni-HOLM post-hoc test are resumed in *Table IV*.

Table III Bonferroni-HOLM post-hoc test

©	Differenza fra medie (I-J)	Errore std.	Sig.	Intervallo di confidenza 95%		
				Limite inferiore	Limite superiore	
Contro_t0	DMSO_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Res50_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Cis05_t0	0,0000000	,0047775	1,000	-,019331	,019331
	CisRes_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Fu05_t0	0,0000000	,0047775	1,000	-,019331	,019331
	FuRes_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Contro_t1	-,1025000*	,0058512	,000	-,126176	-,078824
	DMSO_t1	-,1021667*	,0067564	,000	-,129505	-,074828
	Res50_t1	-,0495000*	,0058512	,000	-,073176	-,025824
	Cis05_t1	-,0266667	,0067564	,070	-,054005	,000672
	CisRes_t1	-,0081667	,0067564	1,000	-,035505	,019172
	Fu05_t1	-,0751667*	,0058512	,000	-,098842	-,051491
	FuRes_t1	-,0448333*	,0058512	,000	-,068509	-,021158
	Control_t2	-,4661667*	,0058512	,000	-,489842	-,442491
	DMSO_t2	-,4008333*	,0058512	,000	-,424509	-,377158
	Res50_t2	-,0696667*	,0067564	,000	-,097005	-,042328
	Cis05_t2	-,1568333*	,0058512	,000	-,180509	-,133158
	CisRes_t2	,0391667*	,0058512	,000	,015491	,062842
	Fu05_t2	-,1736667*	,0067564	,000	-,201005	-,146328
	FuRes_t2	-,0651667*	,0058512	,000	-,088842	-,041491
	Control_t3	-,5595000*	,0058512	,000	-,583176	-,535824
	DMSO_t3	-,5161667*	,0058512	,000	-,539842	-,492491
	Res50_t3	-,0736667*	,0067564	,000	-,101005	-,046328
	Cis05_t3	-,1941667*	,0058512	,000	-,217842	-,170491
	CisRes_t3	,0558333*	,0058512	,000	,032158	,079509

	Fu05_t3	-,2101667*	,0067564	,000	-,237505	-,182828
	FuRes_t3	,0185000	,0058512	,876	-,005176	,042176
DMSO_t0	Contro_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Res50_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Cis05_t0	0,0000000	,0047775	1,000	-,019331	,019331
	CisRes_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Fu05_t0	0,0000000	,0047775	1,000	-,019331	,019331
	FuRes_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Contro_t1	-,1025000*	,0058512	,000	-,126176	-,078824
	DMSO_t1	-,1021667*	,0067564	,000	-,129505	-,074828
	Res50_t1	-,0495000*	,0058512	,000	-,073176	-,025824
	Cis05_t1	-,0266667	,0067564	,070	-,054005	,000672
	CisRes_t1	-,0081667	,0067564	1,000	-,035505	,019172
	Fu05_t1	-,0751667*	,0058512	,000	-,098842	-,051491
	FuRes_t1	-,0448333*	,0058512	,000	-,068509	-,021158
	Control_t2	-,4661667*	,0058512	,000	-,489842	-,442491
	DMSO_t2	-,4008333*	,0058512	,000	-,424509	-,377158
	Res50_t2	-,0696667*	,0067564	,000	-,097005	-,042328
	Cis05_t2	-,1568333*	,0058512	,000	-,180509	-,133158
	CisRes_t2	,0391667*	,0058512	,000	,015491	,062842
	Fu05_t2	-,1736667*	,0067564	,000	-,201005	-,146328
	FuRes_t2	-,0651667*	,0058512	,000	-,088842	-,041491
	Control_t3	-,5595000*	,0058512	,000	-,583176	-,535824
	DMSO_t3	-,5161667*	,0058512	,000	-,539842	-,492491
	Res50_t3	-,0736667*	,0067564	,000	-,101005	-,046328
	Cis05_t3	-,1941667*	,0058512	,000	-,217842	-,170491
	CisRes_t3	,0558333*	,0058512	,000	,032158	,079509
	Fu05_t3	-,2101667*	,0067564	,000	-,237505	-,182828
	FuRes_t3	,0185000	,0058512	,876	-,005176	,042176
Res50_t0	Contro_t0	0,0000000	,0047775	1,000	-,019331	,019331
	DMSO_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Cis05_t0	0,0000000	,0047775	1,000	-,019331	,019331
	CisRes_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Fu05_t0	0,0000000	,0047775	1,000	-,019331	,019331
	FuRes_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Contro_t1	-,1025000*	,0058512	,000	-,126176	-,078824
	DMSO_t1	-,1021667*	,0067564	,000	-,129505	-,074828
	Res50_t1	-,0495000*	,0058512	,000	-,073176	-,025824
	Cis05_t1	-,0266667	,0067564	,070	-,054005	,000672
	CisRes_t1	-,0081667	,0067564	1,000	-,035505	,019172
	Fu05_t1	-,0751667*	,0058512	,000	-,098842	-,051491
	FuRes_t1	-,0448333*	,0058512	,000	-,068509	-,021158
	Control_t2	-,4661667*	,0058512	,000	-,489842	-,442491
	DMSO_t2	-,4008333*	,0058512	,000	-,424509	-,377158
	Res50_t2	-,0696667*	,0067564	,000	-,097005	-,042328
	Cis05_t2	-,1568333*	,0058512	,000	-,180509	-,133158
	CisRes_t2	,0391667*	,0058512	,000	,015491	,062842

	Fu05_t2	-,1736667*	,0067564	,000	-,201005	-,146328
	FuRes_t2	-,0651667*	,0058512	,000	-,088842	-,041491
	Control_t3	-,5595000*	,0058512	,000	-,583176	-,535824
	DMSO_t3	-,5161667*	,0058512	,000	-,539842	-,492491
	Res50_t3	-,0736667*	,0067564	,000	-,101005	-,046328
	Cis05_t3	-,1941667*	,0058512	,000	-,217842	-,170491
	CisRes_t3	,0558333*	,0058512	,000	,032158	,079509
	Fu05_t3	-,2101667*	,0067564	,000	-,237505	-,182828
	FuRes_t3	,0185000	,0058512	,876	-,005176	,042176
Cis05_t0	Contro_t0	0,0000000	,0047775	1,000	-,019331	,019331
	DMSO_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Res50_t0	0,0000000	,0047775	1,000	-,019331	,019331
	CisRes_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Fu05_t0	0,0000000	,0047775	1,000	-,019331	,019331
	FuRes_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Contro_t1	-,1025000*	,0058512	,000	-,126176	-,078824
	DMSO_t1	-,1021667*	,0067564	,000	-,129505	-,074828
	Res50_t1	-,0495000*	,0058512	,000	-,073176	-,025824
	Cis05_t1	-,0266667	,0067564	,070	-,054005	,000672
	CisRes_t1	-,0081667	,0067564	1,000	-,035505	,019172
	Fu05_t1	-,0751667*	,0058512	,000	-,098842	-,051491
	FuRes_t1	-,0448333*	,0058512	,000	-,068509	-,021158
	Control_t2	-,4661667*	,0058512	,000	-,489842	-,442491
	DMSO_t2	-,4008333*	,0058512	,000	-,424509	-,377158
	Res50_t2	-,0696667*	,0067564	,000	-,097005	-,042328
	Cis05_t2	-,1568333*	,0058512	,000	-,180509	-,133158
	CisRes_t2	,0391667*	,0058512	,000	,015491	,062842
	Fu05_t2	-,1736667*	,0067564	,000	-,201005	-,146328
	FuRes_t2	-,0651667*	,0058512	,000	-,088842	-,041491
	Control_t3	-,5595000*	,0058512	,000	-,583176	-,535824
	DMSO_t3	-,5161667*	,0058512	,000	-,539842	-,492491
	Res50_t3	-,0736667*	,0067564	,000	-,101005	-,046328
	Cis05_t3	-,1941667*	,0058512	,000	-,217842	-,170491
	CisRes_t3	,0558333*	,0058512	,000	,032158	,079509
	Fu05_t3	-,2101667*	,0067564	,000	-,237505	-,182828
	FuRes_t3	,0185000	,0058512	,876	-,005176	,042176
CisRes_t0	Contro_t0	0,0000000	,0047775	1,000	-,019331	,019331
	DMSO_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Res50_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Cis05_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Fu05_t0	0,0000000	,0047775	1,000	-,019331	,019331
	FuRes_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Contro_t1	-,1025000*	,0058512	,000	-,126176	-,078824
	DMSO_t1	-,1021667*	,0067564	,000	-,129505	-,074828
	Res50_t1	-,0495000*	,0058512	,000	-,073176	-,025824
	Cis05_t1	-,0266667	,0067564	,070	-,054005	,000672
	CisRes_t1	-,0081667	,0067564	1,000	-,035505	,019172

	Fu05_t1	-,0751667*	,0058512	,000	-,098842	-,051491
	FuRes_t1	-,0448333*	,0058512	,000	-,068509	-,021158
	Control_t2	-,4661667*	,0058512	,000	-,489842	-,442491
	DMSO_t2	-,4008333*	,0058512	,000	-,424509	-,377158
	Res50_t2	-,0696667*	,0067564	,000	-,097005	-,042328
	Cis05_t2	-,1568333*	,0058512	,000	-,180509	-,133158
	CisRes_t2	,0391667*	,0058512	,000	,015491	,062842
	Fu05_t2	-,1736667*	,0067564	,000	-,201005	-,146328
	FuRes_t2	-,0651667*	,0058512	,000	-,088842	-,041491
	Control_t3	-,5595000*	,0058512	,000	-,583176	-,535824
	DMSO_t3	-,5161667*	,0058512	,000	-,539842	-,492491
	Res50_t3	-,0736667*	,0067564	,000	-,101005	-,046328
	Cis05_t3	-,1941667*	,0058512	,000	-,217842	-,170491
	CisRes_t3	,0558333*	,0058512	,000	,032158	,079509
	Fu05_t3	-,2101667*	,0067564	,000	-,237505	-,182828
	FuRes_t3	,0185000	,0058512	,876	-,005176	,042176
Fu05_t0	Contro_t0	0,0000000	,0047775	1,000	-,019331	,019331
	DMSO_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Res50_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Cis05_t0	0,0000000	,0047775	1,000	-,019331	,019331
	CisRes_t0	0,0000000	,0047775	1,000	-,019331	,019331
	FuRes_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Contro_t1	-,1025000*	,0058512	,000	-,126176	-,078824
	DMSO_t1	-,1021667*	,0067564	,000	-,129505	-,074828
	Res50_t1	-,0495000*	,0058512	,000	-,073176	-,025824
	Cis05_t1	-,0266667	,0067564	,070	-,054005	,000672
	CisRes_t1	-,0081667	,0067564	1,000	-,035505	,019172
	Fu05_t1	-,0751667*	,0058512	,000	-,098842	-,051491
	FuRes_t1	-,0448333*	,0058512	,000	-,068509	-,021158
	Control_t2	-,4661667*	,0058512	,000	-,489842	-,442491
	DMSO_t2	-,4008333*	,0058512	,000	-,424509	-,377158
	Res50_t2	-,0696667*	,0067564	,000	-,097005	-,042328
	Cis05_t2	-,1568333*	,0058512	,000	-,180509	-,133158
	CisRes_t2	,0391667*	,0058512	,000	,015491	,062842
	Fu05_t2	-,1736667*	,0067564	,000	-,201005	-,146328
	FuRes_t2	-,0651667*	,0058512	,000	-,088842	-,041491
	Control_t3	-,5595000*	,0058512	,000	-,583176	-,535824
	DMSO_t3	-,5161667*	,0058512	,000	-,539842	-,492491
	Res50_t3	-,0736667*	,0067564	,000	-,101005	-,046328
	Cis05_t3	-,1941667*	,0058512	,000	-,217842	-,170491
	CisRes_t3	,0558333*	,0058512	,000	,032158	,079509
	Fu05_t3	-,2101667*	,0067564	,000	-,237505	-,182828
	FuRes_t3	,0185000	,0058512	,876	-,005176	,042176
FuRes_t0	Contro_t0	0,0000000	,0047775	1,000	-,019331	,019331
	DMSO_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Res50_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Cis05_t0	0,0000000	,0047775	1,000	-,019331	,019331

	CisRes_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Fu05_t0	0,0000000	,0047775	1,000	-,019331	,019331
	Contro_t1	-,1025000*	,0058512	,000	-,126176	-,078824
	DMSO_t1	-,1021667*	,0067564	,000	-,129505	-,074828
	Res50_t1	-,0495000*	,0058512	,000	-,073176	-,025824
	Cis05_t1	-,0266667	,0067564	,070	-,054005	,000672
	CisRes_t1	-,0081667	,0067564	1,000	-,035505	,019172
	Fu05_t1	-,0751667*	,0058512	,000	-,098842	-,051491
	FuRes_t1	-,0448333*	,0058512	,000	-,068509	-,021158
	Control_t2	-,4661667*	,0058512	,000	-,489842	-,442491
	DMSO_t2	-,4008333*	,0058512	,000	-,424509	-,377158
	Res50_t2	-,0696667*	,0067564	,000	-,097005	-,042328
	Cis05_t2	-,1568333*	,0058512	,000	-,180509	-,133158
	CisRes_t2	,0391667*	,0058512	,000	,015491	,062842
	Fu05_t2	-,1736667*	,0067564	,000	-,201005	-,146328
	FuRes_t2	-,0651667*	,0058512	,000	-,088842	-,041491
	Control_t3	-,5595000*	,0058512	,000	-,583176	-,535824
	DMSO_t3	-,5161667*	,0058512	,000	-,539842	-,492491
	Res50_t3	-,0736667*	,0067564	,000	-,101005	-,046328
	Cis05_t3	-,1941667*	,0058512	,000	-,217842	-,170491
	CisRes_t3	,0558333*	,0058512	,000	,032158	,079509
	Fu05_t3	-,2101667*	,0067564	,000	-,237505	-,182828
	FuRes_t3	,0185000	,0058512	,876	-,005176	,042176
Contro_t1	Contro_t0	,1025000*	,0058512	,000	,078824	,126176
	DMSO_t0	,1025000*	,0058512	,000	,078824	,126176
	Res50_t0	,1025000*	,0058512	,000	,078824	,126176
	Cis05_t0	,1025000*	,0058512	,000	,078824	,126176
	CisRes_t0	,1025000*	,0058512	,000	,078824	,126176
	Fu05_t0	,1025000*	,0058512	,000	,078824	,126176
	FuRes_t0	,1025000*	,0058512	,000	,078824	,126176
	DMSO_t1	,0003333	,0075539	1,000	-,030232	,030898
	Res50_t1	,0530000*	,0067564	,000	,025662	,080338
	Cis05_t1	,0758333*	,0075539	,000	,045268	,106398
	CisRes_t1	,0943333*	,0075539	,000	,063768	,124898
	Fu05_t1	,0273333	,0067564	,050	-,000005	,054672
	FuRes_t1	,0576667*	,0067564	,000	,030328	,085005
	Control_t2	-,3636667*	,0067564	,000	-,391005	-,336328
	DMSO_t2	-,2983333*	,0067564	,000	-,325672	-,270995
	Res50_t2	,0328333*	,0075539	,017	,002268	,063398
	Cis05_t2	-,0543333*	,0067564	,000	-,081672	-,026995
	CisRes_t2	,1416667*	,0067564	,000	,114328	,169005
	Fu05_t2	-,0711667*	,0075539	,000	-,101732	-,040602
	FuRes_t2	,0373333*	,0067564	,000	,009995	,064672
	Control_t3	-,4570000*	,0067564	,000	-,484338	-,429662
	DMSO_t3	-,4136667*	,0067564	,000	-,441005	-,386328
	Res50_t3	,0288333	,0075539	,109	-,001732	,059398
	Cis05_t3	-,0916667*	,0067564	,000	-,119005	-,064328

	CisRes_t3	,1583333*	,0067564	,000	,130995	,185672
	Fu05_t3	-,1076667*	,0075539	,000	-,138232	-,077102
	FuRes_t3	,1210000*	,0067564	,000	,093662	,148338
DMSO_t1	Contro_t0	,1021667*	,0067564	,000	,074828	,129505
	DMSO_t0	,1021667*	,0067564	,000	,074828	,129505
	Res50_t0	,1021667*	,0067564	,000	,074828	,129505
	Cis05_t0	,1021667*	,0067564	,000	,074828	,129505
	CisRes_t0	,1021667*	,0067564	,000	,074828	,129505
	Fu05_t0	,1021667*	,0067564	,000	,074828	,129505
	FuRes_t0	,1021667*	,0067564	,000	,074828	,129505
	Contro_t1	-,0003333	,0075539	1,000	-,030898	,030232
	Res50_t1	,0526667*	,0075539	,000	,022102	,083232
	Cis05_t1	,0755000*	,0082749	,000	,042018	,108982
	CisRes_t1	,0940000*	,0082749	,000	,060518	,127482
	Fu05_t1	,0270000	,0075539	,242	-,003565	,057565
	FuRes_t1	,0573333*	,0075539	,000	,026768	,087898
	Control_t2	-,3640000*	,0075539	,000	-,394565	-,333435
	DMSO_t2	-,2986667*	,0075539	,000	-,329232	-,268102
	Res50_t2	,0325000	,0082749	,075	-,000982	,065982
	Cis05_t2	-,0546667*	,0075539	,000	-,085232	-,024102
	CisRes_t2	,1413333*	,0075539	,000	,110768	,171898
	Fu05_t2	-,0715000*	,0082749	,000	-,104982	-,038018
	FuRes_t2	,0370000*	,0075539	,002	,006435	,067565
	Control_t3	-,4573333*	,0075539	,000	-,487898	-,426768
	DMSO_t3	-,4140000*	,0075539	,000	-,444565	-,383435
	Res50_t3	,0285000	,0082749	,367	-,004982	,061982
	Cis05_t3	-,0920000*	,0075539	,000	-,122565	-,061435
	CisRes_t3	,1580000*	,0075539	,000	,127435	,188565
	Fu05_t3	-,1080000*	,0082749	,000	-,141482	-,074518
	FuRes_t3	,1206667*	,0075539	,000	,090102	,151232
Res50_t1	Contro_t0	,0495000*	,0058512	,000	,025824	,073176
	DMSO_t0	,0495000*	,0058512	,000	,025824	,073176
	Res50_t0	,0495000*	,0058512	,000	,025824	,073176
	Cis05_t0	,0495000*	,0058512	,000	,025824	,073176
	CisRes_t0	,0495000*	,0058512	,000	,025824	,073176
	Fu05_t0	,0495000*	,0058512	,000	,025824	,073176
	FuRes_t0	,0495000*	,0058512	,000	,025824	,073176
	Contro_t1	-,0530000*	,0067564	,000	-,080338	-,025662
	DMSO_t1	-,0526667*	,0075539	,000	-,083232	-,022102
	Cis05_t1	,0228333	,0075539	1,000	-,007732	,053398
	CisRes_t1	,0413333*	,0075539	,000	,010768	,071898
	Fu05_t1	-,0256667	,0067564	,116	-,053005	,001672
	FuRes_t1	,0046667	,0067564	1,000	-,022672	,032005
	Control_t2	-,4166667*	,0067564	,000	-,444005	-,389328
	DMSO_t2	-,3513333*	,0067564	,000	-,378672	-,323995
	Res50_t2	-,0201667	,0075539	1,000	-,050732	,010398
	Cis05_t2	-,1073333*	,0067564	,000	-,134672	-,079995

	CisRes_t2	,0886667*	,0067564	,000	,061328	,116005
	Fu05_t2	-,1241667*	,0075539	,000	-,154732	-,093602
	FuRes_t2	-,0156667	,0067564	1,000	-,043005	,011672
	Control_t3	-,5100000*	,0067564	,000	-,537338	-,482662
	DMSO_t3	-,4666667*	,0067564	,000	-,494005	-,439328
	Res50_t3	-,0241667	,0075539	,783	-,054732	,006398
	Cis05_t3	-,1446667*	,0067564	,000	-,172005	-,117328
	CisRes_t3	,1053333*	,0067564	,000	,077995	,132672
	Fu05_t3	-,1606667*	,0075539	,000	-,191232	-,130102
	FuRes_t3	,0680000*	,0067564	,000	,040662	,095338
Cis05_t1	Contro_t0	,0266667	,0067564	,070	-,000672	,054005
	DMSO_t0	,0266667	,0067564	,070	-,000672	,054005
	Res50_t0	,0266667	,0067564	,070	-,000672	,054005
	Cis05_t0	,0266667	,0067564	,070	-,000672	,054005
	CisRes_t0	,0266667	,0067564	,070	-,000672	,054005
	Fu05_t0	,0266667	,0067564	,070	-,000672	,054005
	FuRes_t0	,0266667	,0067564	,070	-,000672	,054005
	Contro_t1	-,0758333*	,0075539	,000	-,106398	-,045268
	DMSO_t1	-,0755000*	,0082749	,000	-,108982	-,042018
	Res50_t1	-,0228333	,0075539	1,000	-,053398	,007732
	CisRes_t1	,0185000	,0082749	1,000	-,014982	,051982
	Fu05_t1	-,0485000*	,0075539	,000	-,079065	-,017935
	FuRes_t1	-,0181667	,0075539	1,000	-,048732	,012398
	Control_t2	-,4395000*	,0075539	,000	-,470065	-,408935
	DMSO_t2	-,3741667*	,0075539	,000	-,404732	-,343602
	Res50_t2	-,0430000*	,0082749	,001	-,076482	-,009518
	Cis05_t2	-,1301667*	,0075539	,000	-,160732	-,099602
	CisRes_t2	,0658333*	,0075539	,000	,035268	,096398
	Fu05_t2	-,1470000*	,0082749	,000	-,180482	-,113518
	FuRes_t2	-,0385000*	,0075539	,001	-,069065	-,007935
	Control_t3	-,5328333*	,0075539	,000	-,563398	-,502268
	DMSO_t3	-,4895000*	,0075539	,000	-,520065	-,458935
	Res50_t3	-,0470000*	,0082749	,000	-,080482	-,013518
	Cis05_t3	-,1675000*	,0075539	,000	-,198065	-,136935
	CisRes_t3	,0825000*	,0075539	,000	,051935	,113065
	Fu05_t3	-,1835000*	,0082749	,000	-,216982	-,150018
	FuRes_t3	,0451667*	,0075539	,000	,014602	,075732
CisRes_t1	Contro_t0	,0081667	,0067564	1,000	-,019172	,035505
	DMSO_t0	,0081667	,0067564	1,000	-,019172	,035505
	Res50_t0	,0081667	,0067564	1,000	-,019172	,035505
	Cis05_t0	,0081667	,0067564	1,000	-,019172	,035505
	CisRes_t0	,0081667	,0067564	1,000	-,019172	,035505
	Fu05_t0	,0081667	,0067564	1,000	-,019172	,035505
	FuRes_t0	,0081667	,0067564	1,000	-,019172	,035505
	Contro_t1	-,0943333*	,0075539	,000	-,124898	-,063768
	DMSO_t1	-,0940000*	,0082749	,000	-,127482	-,060518
	Res50_t1	-,0413333*	,0075539	,000	-,071898	-,010768

	Cis05_t1	-,0185000	,0082749	1,000	-,051982	,014982
	Fu05_t1	-,0670000*	,0075539	,000	-,097565	-,036435
	FuRes_t1	-,0366667*	,0075539	,003	-,067232	-,006102
	Control_t2	-,4580000*	,0075539	,000	-,488565	-,427435
	DMSO_t2	-,3926667*	,0075539	,000	-,423232	-,362102
	Res50_t2	-,0615000*	,0082749	,000	-,094982	-,028018
	Cis05_t2	-,1486667*	,0075539	,000	-,179232	-,118102
	CisRes_t2	,0473333*	,0075539	,000	,016768	,077898
	Fu05_t2	-,1655000*	,0082749	,000	-,198982	-,132018
	FuRes_t2	-,0570000*	,0075539	,000	-,087565	-,026435
	Control_t3	-,5513333*	,0075539	,000	-,581898	-,520768
	DMSO_t3	-,5080000*	,0075539	,000	-,538565	-,477435
	Res50_t3	-,0655000*	,0082749	,000	-,098982	-,032018
	Cis05_t3	-,1860000*	,0075539	,000	-,216565	-,155435
	CisRes_t3	,0640000*	,0075539	,000	,033435	,094565
	Fu05_t3	-,2020000*	,0082749	,000	-,235482	-,168518
	FuRes_t3	,0266667	,0075539	,279	-,003898	,057232
Fu05_t1	Contro_t0	,0751667*	,0058512	,000	,051491	,098842
	DMSO_t0	,0751667*	,0058512	,000	,051491	,098842
	Res50_t0	,0751667*	,0058512	,000	,051491	,098842
	Cis05_t0	,0751667*	,0058512	,000	,051491	,098842
	CisRes_t0	,0751667*	,0058512	,000	,051491	,098842
	Fu05_t0	,0751667*	,0058512	,000	,051491	,098842
	FuRes_t0	,0751667*	,0058512	,000	,051491	,098842
	Contro_t1	-,0273333	,0067564	,050	-,054672	,000005
	DMSO_t1	-,0270000	,0075539	,242	-,057565	,003565
	Res50_t1	,0256667	,0067564	,116	-,001672	,053005
	Cis05_t1	,0485000*	,0075539	,000	,017935	,079065
	CisRes_t1	,0670000*	,0075539	,000	,036435	,097565
	FuRes_t1	,0303333*	,0067564	,010	,002995	,057672
	Control_t2	-,3910000*	,0067564	,000	-,418338	-,363662
	DMSO_t2	-,3256667*	,0067564	,000	-,353005	-,298328
	Res50_t2	,0055000	,0075539	1,000	-,025065	,036065
	Cis05_t2	-,0816667*	,0067564	,000	-,109005	-,054328
	CisRes_t2	,1143333*	,0067564	,000	,086995	,141672
	Fu05_t2	-,0985000*	,0075539	,000	-,129065	-,067935
	FuRes_t2	,0100000	,0067564	1,000	-,017338	,037338
	Control_t3	-,4843333*	,0067564	,000	-,511672	-,456995
	DMSO_t3	-,4410000*	,0067564	,000	-,468338	-,413662
	Res50_t3	,0015000	,0075539	1,000	-,029065	,032065
	Cis05_t3	-,1190000*	,0067564	,000	-,146338	-,091662
	CisRes_t3	,1310000*	,0067564	,000	,103662	,158338
	Fu05_t3	-,1350000*	,0075539	,000	-,165565	-,104435
	FuRes_t3	,0936667*	,0067564	,000	,066328	,121005
FuRes_t1	Contro_t0	,0448333*	,0058512	,000	,021158	,068509
	DMSO_t0	,0448333*	,0058512	,000	,021158	,068509
	Res50_t0	,0448333*	,0058512	,000	,021158	,068509

	Cis05_t0	,0448333*	,0058512	,000	,021158	,068509
	CisRes_t0	,0448333*	,0058512	,000	,021158	,068509
	Fu05_t0	,0448333*	,0058512	,000	,021158	,068509
	FuRes_t0	,0448333*	,0058512	,000	,021158	,068509
	Contro_t1	-,0576667*	,0067564	,000	-,085005	-,030328
	DMSO_t1	-,0573333*	,0075539	,000	-,087898	-,026768
	Res50_t1	-,0046667	,0067564	1,000	-,032005	,022672
	Cis05_t1	,0181667	,0075539	1,000	-,012398	,048732
	CisRes_t1	,0366667*	,0075539	,003	,006102	,067232
	Fu05_t1	-,0303333*	,0067564	,010	-,057672	-,002995
	Control_t2	-,4213333*	,0067564	,000	-,448672	-,393995
	DMSO_t2	-,3560000*	,0067564	,000	-,383338	-,328662
	Res50_t2	-,0248333	,0075539	,598	-,055398	,005732
	Cis05_t2	-,1120000*	,0067564	,000	-,139338	-,084662
	CisRes_t2	,0840000*	,0067564	,000	,056662	,111338
	Fu05_t2	-,1288333*	,0075539	,000	-,159398	-,098268
	FuRes_t2	-,0203333	,0067564	1,000	-,047672	,007005
	Control_t3	-,5146667*	,0067564	,000	-,542005	-,487328
	DMSO_t3	-,4713333*	,0067564	,000	-,498672	-,443995
	Res50_t3	-,0288333	,0075539	,109	-,059398	,001732
	Cis05_t3	-,1493333*	,0067564	,000	-,176672	-,121995
	CisRes_t3	,1006667*	,0067564	,000	,073328	,128005
	Fu05_t3	-,1653333*	,0075539	,000	-,195898	-,134768
	FuRes_t3	,0633333*	,0067564	,000	,035995	,090672
Control_t2	Contro_t0	,4661667*	,0058512	,000	,442491	,489842
	DMSO_t0	,4661667*	,0058512	,000	,442491	,489842
	Res50_t0	,4661667*	,0058512	,000	,442491	,489842
	Cis05_t0	,4661667*	,0058512	,000	,442491	,489842
	CisRes_t0	,4661667*	,0058512	,000	,442491	,489842
	Fu05_t0	,4661667*	,0058512	,000	,442491	,489842
	FuRes_t0	,4661667*	,0058512	,000	,442491	,489842
	Contro_t1	,3636667*	,0067564	,000	,336328	,391005
	DMSO_t1	,3640000*	,0075539	,000	,333435	,394565
	Res50_t1	,4166667*	,0067564	,000	,389328	,444005
	Cis05_t1	,4395000*	,0075539	,000	,408935	,470065
	CisRes_t1	,4580000*	,0075539	,000	,427435	,488565
	Fu05_t1	,3910000*	,0067564	,000	,363662	,418338
	FuRes_t1	,4213333*	,0067564	,000	,393995	,448672
	DMSO_t2	,0653333*	,0067564	,000	,037995	,092672
	Res50_t2	,3965000*	,0075539	,000	,365935	,427065
	Cis05_t2	,3093333*	,0067564	,000	,281995	,336672
	CisRes_t2	,5053333*	,0067564	,000	,477995	,532672
	Fu05_t2	,2925000*	,0075539	,000	,261935	,323065
	FuRes_t2	,4010000*	,0067564	,000	,373662	,428338
	Control_t3	-,0933333*	,0067564	,000	-,120672	-,065995
	DMSO_t3	-,0500000*	,0067564	,000	-,077338	-,022662
	Res50_t3	,3925000*	,0075539	,000	,361935	,423065

	Cis05_t3	,2720000*	,0067564	,000	,244662	,299338
	CisRes_t3	,5220000*	,0067564	,000	,494662	,549338
	Fu05_t3	,2560000*	,0075539	,000	,225435	,286565
	FuRes_t3	,4846667*	,0067564	,000	,457328	,512005
DMSO_t2	Contro_t0	,4008333*	,0058512	,000	,377158	,424509
	DMSO_t0	,4008333*	,0058512	,000	,377158	,424509
	Res50_t0	,4008333*	,0058512	,000	,377158	,424509
	Cis05_t0	,4008333*	,0058512	,000	,377158	,424509
	CisRes_t0	,4008333*	,0058512	,000	,377158	,424509
	Fu05_t0	,4008333*	,0058512	,000	,377158	,424509
	FuRes_t0	,4008333*	,0058512	,000	,377158	,424509
	Contro_t1	,2983333*	,0067564	,000	,270995	,325672
	DMSO_t1	,2986667*	,0075539	,000	,268102	,329232
	Res50_t1	,3513333*	,0067564	,000	,323995	,378672
	Cis05_t1	,3741667*	,0075539	,000	,343602	,404732
	CisRes_t1	,3926667*	,0075539	,000	,362102	,423232
	Fu05_t1	,3256667*	,0067564	,000	,298328	,353005
	FuRes_t1	,3560000*	,0067564	,000	,328662	,383338
	Control_t2	-,0653333*	,0067564	,000	-,092672	-,037995
	Res50_t2	,3311667*	,0075539	,000	,300602	,361732
	Cis05_t2	,2440000*	,0067564	,000	,216662	,271338
	CisRes_t2	,4400000*	,0067564	,000	,412662	,467338
	Fu05_t2	,2271667*	,0075539	,000	,196602	,257732
	FuRes_t2	,3356667*	,0067564	,000	,308328	,363005
	Control_t3	-,1586667*	,0067564	,000	-,186005	-,131328
	DMSO_t3	-,1153333*	,0067564	,000	-,142672	-,087995
	Res50_t3	,3271667*	,0075539	,000	,296602	,357732
	Cis05_t3	,2066667*	,0067564	,000	,179328	,234005
	CisRes_t3	,4566667*	,0067564	,000	,429328	,484005
	Fu05_t3	,1906667*	,0075539	,000	,160102	,221232
	FuRes_t3	,4193333*	,0067564	,000	,391995	,446672
Res50_t2	Contro_t0	,0696667*	,0067564	,000	,042328	,097005
	DMSO_t0	,0696667*	,0067564	,000	,042328	,097005
	Res50_t0	,0696667*	,0067564	,000	,042328	,097005
	Cis05_t0	,0696667*	,0067564	,000	,042328	,097005
	CisRes_t0	,0696667*	,0067564	,000	,042328	,097005
	Fu05_t0	,0696667*	,0067564	,000	,042328	,097005
	FuRes_t0	,0696667*	,0067564	,000	,042328	,097005
	Contro_t1	-,0328333*	,0075539	,017	-,063398	-,002268
	DMSO_t1	-,0325000	,0082749	,075	-,065982	,000982
	Res50_t1	,0201667	,0075539	1,000	-,010398	,050732
	Cis05_t1	,0430000*	,0082749	,001	,009518	,076482
	CisRes_t1	,0615000*	,0082749	,000	,028018	,094982
	Fu05_t1	-,0055000	,0075539	1,000	-,036065	,025065
	FuRes_t1	,0248333	,0075539	,598	-,005732	,055398
	Control_t2	-,3965000*	,0075539	,000	-,427065	-,365935
	DMSO_t2	-,3311667*	,0075539	,000	-,361732	-,300602

	Cis05_t2	-,0871667*	,0075539	,000	-,117732	-,056602
	CisRes_t2	,1088333*	,0075539	,000	,078268	,139398
	Fu05_t2	-,1040000*	,0082749	,000	-,137482	-,070518
	FuRes_t2	,0045000	,0075539	1,000	-,026065	,035065
	Control_t3	-,4898333*	,0075539	,000	-,520398	-,459268
	DMSO_t3	-,4465000*	,0075539	,000	-,477065	-,415935
	Res50_t3	-,0040000	,0082749	1,000	-,037482	,029482
	Cis05_t3	-,1245000*	,0075539	,000	-,155065	-,093935
	CisRes_t3	,1255000*	,0075539	,000	,094935	,156065
	Fu05_t3	-,1405000*	,0082749	,000	-,173982	-,107018
	FuRes_t3	,0881667*	,0075539	,000	,057602	,118732
Cis05_t2	Contro_t0	,1568333*	,0058512	,000	,133158	,180509
	DMSO_t0	,1568333*	,0058512	,000	,133158	,180509
	Res50_t0	,1568333*	,0058512	,000	,133158	,180509
	Cis05_t0	,1568333*	,0058512	,000	,133158	,180509
	CisRes_t0	,1568333*	,0058512	,000	,133158	,180509
	Fu05_t0	,1568333*	,0058512	,000	,133158	,180509
	FuRes_t0	,1568333*	,0058512	,000	,133158	,180509
	Contro_t1	,0543333*	,0067564	,000	,026995	,081672
	DMSO_t1	,0546667*	,0075539	,000	,024102	,085232
	Res50_t1	,1073333*	,0067564	,000	,079995	,134672
	Cis05_t1	,1301667*	,0075539	,000	,099602	,160732
	CisRes_t1	,1486667*	,0075539	,000	,118102	,179232
	Fu05_t1	,0816667*	,0067564	,000	,054328	,109005
	FuRes_t1	,1120000*	,0067564	,000	,084662	,139338
	Control_t2	-,3093333*	,0067564	,000	-,336672	-,281995
	DMSO_t2	-,2440000*	,0067564	,000	-,271338	-,216662
	Res50_t2	,0871667*	,0075539	,000	,056602	,117732
	CisRes_t2	,1960000*	,0067564	,000	,168662	,223338
	Fu05_t2	-,0168333	,0075539	1,000	-,047398	,013732
	FuRes_t2	,0916667*	,0067564	,000	,064328	,119005
	Control_t3	-,4026667*	,0067564	,000	-,430005	-,375328
	DMSO_t3	-,3593333*	,0067564	,000	-,386672	-,331995
	Res50_t3	,0831667*	,0075539	,000	,052602	,113732
	Cis05_t3	-,0373333*	,0067564	,000	-,064672	-,009995
	CisRes_t3	,2126667*	,0067564	,000	,185328	,240005
	Fu05_t3	-,0533333*	,0075539	,000	-,083898	-,022768
	FuRes_t3	,1753333*	,0067564	,000	,147995	,202672
CisRes_t2	Contro_t0	-,0391667*	,0058512	,000	-,062842	-,015491
	DMSO_t0	-,0391667*	,0058512	,000	-,062842	-,015491
	Res50_t0	-,0391667*	,0058512	,000	-,062842	-,015491
	Cis05_t0	-,0391667*	,0058512	,000	-,062842	-,015491
	CisRes_t0	-,0391667*	,0058512	,000	-,062842	-,015491
	Fu05_t0	-,0391667*	,0058512	,000	-,062842	-,015491
	FuRes_t0	-,0391667*	,0058512	,000	-,062842	-,015491
	Contro_t1	-,1416667*	,0067564	,000	-,169005	-,114328
	DMSO_t1	-,1413333*	,0075539	,000	-,171898	-,110768

	Res50_t1	-,0886667*	,0067564	,000	-,116005	-,061328
	Cis05_t1	-,0658333*	,0075539	,000	-,096398	-,035268
	CisRes_t1	-,0473333*	,0075539	,000	-,077898	-,016768
	Fu05_t1	-,1143333*	,0067564	,000	-,141672	-,086995
	FuRes_t1	-,0840000*	,0067564	,000	-,111338	-,056662
	Control_t2	-,5053333*	,0067564	,000	-,532672	-,477995
	DMSO_t2	-,4400000*	,0067564	,000	-,467338	-,412662
	Res50_t2	-,1088333*	,0075539	,000	-,139398	-,078268
	Cis05_t2	-,1960000*	,0067564	,000	-,223338	-,168662
	Fu05_t2	-,2128333*	,0075539	,000	-,243398	-,182268
	FuRes_t2	-,1043333*	,0067564	,000	-,131672	-,076995
	Control_t3	-,5986667*	,0067564	,000	-,626005	-,571328
	DMSO_t3	-,5553333*	,0067564	,000	-,582672	-,527995
	Res50_t3	-,1128333*	,0075539	,000	-,143398	-,082268
	Cis05_t3	-,2333333*	,0067564	,000	-,260672	-,205995
	CisRes_t3	,0166667	,0067564	1,000	-,010672	,044005
	Fu05_t3	-,2493333*	,0075539	,000	-,279898	-,218768
	FuRes_t3	-,0206667	,0067564	1,000	-,048005	,006672
Fu05_t2	Contro_t0	,1736667*	,0067564	,000	,146328	,201005
	DMSO_t0	,1736667*	,0067564	,000	,146328	,201005
	Res50_t0	,1736667*	,0067564	,000	,146328	,201005
	Cis05_t0	,1736667*	,0067564	,000	,146328	,201005
	CisRes_t0	,1736667*	,0067564	,000	,146328	,201005
	Fu05_t0	,1736667*	,0067564	,000	,146328	,201005
	FuRes_t0	,1736667*	,0067564	,000	,146328	,201005
	Contro_t1	,0711667*	,0075539	,000	,040602	,101732
	DMSO_t1	,0715000*	,0082749	,000	,038018	,104982
	Res50_t1	,1241667*	,0075539	,000	,093602	,154732
	Cis05_t1	,1470000*	,0082749	,000	,113518	,180482
	CisRes_t1	,1655000*	,0082749	,000	,132018	,198982
	Fu05_t1	,0985000*	,0075539	,000	,067935	,129065
	FuRes_t1	,1288333*	,0075539	,000	,098268	,159398
	Control_t2	-,2925000*	,0075539	,000	-,323065	-,261935
	DMSO_t2	-,2271667*	,0075539	,000	-,257732	-,196602
	Res50_t2	,1040000*	,0082749	,000	,070518	,137482
	Cis05_t2	,0168333	,0075539	1,000	-,013732	,047398
	CisRes_t2	,2128333*	,0075539	,000	,182268	,243398
	FuRes_t2	,1085000*	,0075539	,000	,077935	,139065
	Control_t3	-,3858333*	,0075539	,000	-,416398	-,355268
	DMSO_t3	-,3425000*	,0075539	,000	-,373065	-,311935
	Res50_t3	,1000000*	,0082749	,000	,066518	,133482
	Cis05_t3	-,0205000	,0075539	1,000	-,051065	,010065
	CisRes_t3	,2295000*	,0075539	,000	,198935	,260065
	Fu05_t3	-,0365000*	,0082749	,014	-,069982	-,003018
	FuRes_t3	,1921667*	,0075539	,000	,161602	,222732
FuRes_t2	Contro_t0	,0651667*	,0058512	,000	,041491	,088842
	DMSO_t0	,0651667*	,0058512	,000	,041491	,088842

	Res50_t0	,0651667*	,0058512	,000	,041491	,088842
	Cis05_t0	,0651667*	,0058512	,000	,041491	,088842
	CisRes_t0	,0651667*	,0058512	,000	,041491	,088842
	Fu05_t0	,0651667*	,0058512	,000	,041491	,088842
	FuRes_t0	,0651667*	,0058512	,000	,041491	,088842
	Contro_t1	-,0373333*	,0067564	,000	-,064672	-,009995
	DMSO_t1	-,0370000*	,0075539	,002	-,067565	-,006435
	Res50_t1	,0156667	,0067564	1,000	-,011672	,043005
	Cis05_t1	,0385000*	,0075539	,001	,007935	,069065
	CisRes_t1	,0570000*	,0075539	,000	,026435	,087565
	Fu05_t1	-,0100000	,0067564	1,000	-,037338	,017338
	FuRes_t1	,0203333	,0067564	1,000	-,007005	,047672
	Control_t2	-,4010000*	,0067564	,000	-,428338	-,373662
	DMSO_t2	-,3356667*	,0067564	,000	-,363005	-,308328
	Res50_t2	-,0045000	,0075539	1,000	-,035065	,026065
	Cis05_t2	-,0916667*	,0067564	,000	-,119005	-,064328
	CisRes_t2	,1043333*	,0067564	,000	,076995	,131672
	Fu05_t2	-,1085000*	,0075539	,000	-,139065	-,077935
	Control_t3	-,4943333*	,0067564	,000	-,521672	-,466995
	DMSO_t3	-,4510000*	,0067564	,000	-,478338	-,423662
	Res50_t3	-,0085000	,0075539	1,000	-,039065	,022065
	Cis05_t3	-,1290000*	,0067564	,000	-,156338	-,101662
	CisRes_t3	,1210000*	,0067564	,000	,093662	,148338
	Fu05_t3	-,1450000*	,0075539	,000	-,175565	-,114435
	FuRes_t3	,0836667*	,0067564	,000	,056328	,111005
Control_t3	Contro_t0	,5595000*	,0058512	,000	,535824	,583176
	DMSO_t0	,5595000*	,0058512	,000	,535824	,583176
	Res50_t0	,5595000*	,0058512	,000	,535824	,583176
	Cis05_t0	,5595000*	,0058512	,000	,535824	,583176
	CisRes_t0	,5595000*	,0058512	,000	,535824	,583176
	Fu05_t0	,5595000*	,0058512	,000	,535824	,583176
	FuRes_t0	,5595000*	,0058512	,000	,535824	,583176
	Contro_t1	,4570000*	,0067564	,000	,429662	,484338
	DMSO_t1	,4573333*	,0075539	,000	,426768	,487898
	Res50_t1	,5100000*	,0067564	,000	,482662	,537338
	Cis05_t1	,5328333*	,0075539	,000	,502268	,563398
	CisRes_t1	,5513333*	,0075539	,000	,520768	,581898
	Fu05_t1	,4843333*	,0067564	,000	,456995	,511672
	FuRes_t1	,5146667*	,0067564	,000	,487328	,542005
	Control_t2	,0933333*	,0067564	,000	,065995	,120672
	DMSO_t2	,1586667*	,0067564	,000	,131328	,186005
	Res50_t2	,4898333*	,0075539	,000	,459268	,520398
	Cis05_t2	,4026667*	,0067564	,000	,375328	,430005
	CisRes_t2	,5986667*	,0067564	,000	,571328	,626005
	Fu05_t2	,3858333*	,0075539	,000	,355268	,416398
	FuRes_t2	,4943333*	,0067564	,000	,466995	,521672
	DMSO_t3	,0433333*	,0067564	,000	,015995	,070672

	Res50_t3	,4858333*	,0075539	,000	,455268	,516398
	Cis05_t3	,3653333*	,0067564	,000	,337995	,392672
	CisRes_t3	,6153333*	,0067564	,000	,587995	,642672
	Fu05_t3	,3493333*	,0075539	,000	,318768	,379898
	FuRes_t3	,5780000*	,0067564	,000	,550662	,605338
DMSO_t3	Contro_t0	,5161667*	,0058512	,000	,492491	,539842
	DMSO_t0	,5161667*	,0058512	,000	,492491	,539842
	Res50_t0	,5161667*	,0058512	,000	,492491	,539842
	Cis05_t0	,5161667*	,0058512	,000	,492491	,539842
	CisRes_t0	,5161667*	,0058512	,000	,492491	,539842
	Fu05_t0	,5161667*	,0058512	,000	,492491	,539842
	FuRes_t0	,5161667*	,0058512	,000	,492491	,539842
	Contro_t1	,4136667*	,0067564	,000	,386328	,441005
	DMSO_t1	,4140000*	,0075539	,000	,383435	,444565
	Res50_t1	,4666667*	,0067564	,000	,439328	,494005
	Cis05_t1	,4895000*	,0075539	,000	,458935	,520065
	CisRes_t1	,5080000*	,0075539	,000	,477435	,538565
	Fu05_t1	,4410000*	,0067564	,000	,413662	,468338
	FuRes_t1	,4713333*	,0067564	,000	,443995	,498672
	Control_t2	,0500000*	,0067564	,000	,022662	,077338
	DMSO_t2	,1153333*	,0067564	,000	,087995	,142672
	Res50_t2	,4465000*	,0075539	,000	,415935	,477065
	Cis05_t2	,3593333*	,0067564	,000	,331995	,386672
	CisRes_t2	,5553333*	,0067564	,000	,527995	,582672
	Fu05_t2	,3425000*	,0075539	,000	,311935	,373065
	FuRes_t2	,4510000*	,0067564	,000	,423662	,478338
	Control_t3	-,0433333*	,0067564	,000	-,070672	-,015995
	Res50_t3	,4425000*	,0075539	,000	,411935	,473065
	Cis05_t3	,3220000*	,0067564	,000	,294662	,349338
	CisRes_t3	,5720000*	,0067564	,000	,544662	,599338
	Fu05_t3	,3060000*	,0075539	,000	,275435	,336565
	FuRes_t3	,5346667*	,0067564	,000	,507328	,562005
Res50_t3	Contro_t0	,0736667*	,0067564	,000	,046328	,101005
	DMSO_t0	,0736667*	,0067564	,000	,046328	,101005
	Res50_t0	,0736667*	,0067564	,000	,046328	,101005
	Cis05_t0	,0736667*	,0067564	,000	,046328	,101005
	CisRes_t0	,0736667*	,0067564	,000	,046328	,101005
	Fu05_t0	,0736667*	,0067564	,000	,046328	,101005
	FuRes_t0	,0736667*	,0067564	,000	,046328	,101005
	Contro_t1	-,0288333	,0075539	,109	-,059398	,001732
	DMSO_t1	-,0285000	,0082749	,367	-,061982	,004982
	Res50_t1	,0241667	,0075539	,783	-,006398	,054732
	Cis05_t1	,0470000*	,0082749	,000	,013518	,080482
	CisRes_t1	,0655000*	,0082749	,000	,032018	,098982
	Fu05_t1	-,0015000	,0075539	1,000	-,032065	,029065
	FuRes_t1	,0288333	,0075539	,109	-,001732	,059398
	Control_t2	-,3925000*	,0075539	,000	-,423065	-,361935

	DMSO_t2	-,3271667*	,0075539	,000	-,357732	-,296602
	Res50_t2	,0040000	,0082749	1,000	-,029482	,037482
	Cis05_t2	-,0831667*	,0075539	,000	-,113732	-,052602
	CisRes_t2	,1128333*	,0075539	,000	,082268	,143398
	Fu05_t2	-,1000000*	,0082749	,000	-,133482	-,066518
	FuRes_t2	,0085000	,0075539	1,000	-,022065	,039065
	Control_t3	-,4858333*	,0075539	,000	-,516398	-,455268
	DMSO_t3	-,4425000*	,0075539	,000	-,473065	-,411935
	Cis05_t3	-,1205000*	,0075539	,000	-,151065	-,089935
	CisRes_t3	,1295000*	,0075539	,000	,098935	,160065
	Fu05_t3	-,1365000*	,0082749	,000	-,169982	-,103018
	FuRes_t3	,0921667*	,0075539	,000	,061602	,122732
Cis05_t3	Contro_t0	,1941667*	,0058512	,000	,170491	,217842
	DMSO_t0	,1941667*	,0058512	,000	,170491	,217842
	Res50_t0	,1941667*	,0058512	,000	,170491	,217842
	Cis05_t0	,1941667*	,0058512	,000	,170491	,217842
	CisRes_t0	,1941667*	,0058512	,000	,170491	,217842
	Fu05_t0	,1941667*	,0058512	,000	,170491	,217842
	FuRes_t0	,1941667*	,0058512	,000	,170491	,217842
	Contro_t1	,0916667*	,0067564	,000	,064328	,119005
	DMSO_t1	,0920000*	,0075539	,000	,061435	,122565
	Res50_t1	,1446667*	,0067564	,000	,117328	,172005
	Cis05_t1	,1675000*	,0075539	,000	,136935	,198065
	CisRes_t1	,1860000*	,0075539	,000	,155435	,216565
	Fu05_t1	,1190000*	,0067564	,000	,091662	,146338
	FuRes_t1	,1493333*	,0067564	,000	,121995	,176672
	Control_t2	-,2720000*	,0067564	,000	-,299338	-,244662
	DMSO_t2	-,2066667*	,0067564	,000	-,234005	-,179328
	Res50_t2	,1245000*	,0075539	,000	,093935	,155065
	Cis05_t2	,0373333*	,0067564	,000	,009995	,064672
	CisRes_t2	,2333333*	,0067564	,000	,205995	,260672
	Fu05_t2	,0205000	,0075539	1,000	-,010065	,051065
	FuRes_t2	,1290000*	,0067564	,000	,101662	,156338
	Control_t3	-,3653333*	,0067564	,000	-,392672	-,337995
	DMSO_t3	-,3220000*	,0067564	,000	-,349338	-,294662
	Res50_t3	,1205000*	,0075539	,000	,089935	,151065
	CisRes_t3	,2500000*	,0067564	,000	,222662	,277338
	Fu05_t3	-,0160000	,0075539	1,000	-,046565	,014565
	FuRes_t3	,2126667*	,0067564	,000	,185328	,240005
CisRes_t3	Contro_t0	-,0558333*	,0058512	,000	-,079509	-,032158
	DMSO_t0	-,0558333*	,0058512	,000	-,079509	-,032158
	Res50_t0	-,0558333*	,0058512	,000	-,079509	-,032158
	Cis05_t0	-,0558333*	,0058512	,000	-,079509	-,032158
	CisRes_t0	-,0558333*	,0058512	,000	-,079509	-,032158
	Fu05_t0	-,0558333*	,0058512	,000	-,079509	-,032158
	FuRes_t0	-,0558333*	,0058512	,000	-,079509	-,032158
	Contro_t1	-,1583333*	,0067564	,000	-,185672	-,130995

	DMSO_t1	-,1580000*	,0075539	,000	-,188565	-,127435
	Res50_t1	-,1053333*	,0067564	,000	-,132672	-,077995
	Cis05_t1	-,0825000*	,0075539	,000	-,113065	-,051935
	CisRes_t1	-,0640000*	,0075539	,000	-,094565	-,033435
	Fu05_t1	-,1310000*	,0067564	,000	-,158338	-,103662
	FuRes_t1	-,1006667*	,0067564	,000	-,128005	-,073328
	Control_t2	-,5220000*	,0067564	,000	-,549338	-,494662
	DMSO_t2	-,4566667*	,0067564	,000	-,484005	-,429328
	Res50_t2	-,1255000*	,0075539	,000	-,156065	-,094935
	Cis05_t2	-,2126667*	,0067564	,000	-,240005	-,185328
	CisRes_t2	-,0166667	,0067564	1,000	-,044005	,010672
	Fu05_t2	-,2295000*	,0075539	,000	-,260065	-,198935
	FuRes_t2	-,1210000*	,0067564	,000	-,148338	-,093662
	Control_t3	-,6153333*	,0067564	,000	-,642672	-,587995
	DMSO_t3	-,5720000*	,0067564	,000	-,599338	-,544662
	Res50_t3	-,1295000*	,0075539	,000	-,160065	-,098935
	Cis05_t3	-,2500000*	,0067564	,000	-,277338	-,222662
	Fu05_t3	-,2660000*	,0075539	,000	-,296565	-,235435
	FuRes_t3	-,0373333*	,0067564	,000	-,064672	-,009995
Fu05_t3	Contro_t0	,2101667*	,0067564	,000	,182828	,237505
	DMSO_t0	,2101667*	,0067564	,000	,182828	,237505
	Res50_t0	,2101667*	,0067564	,000	,182828	,237505
	Cis05_t0	,2101667*	,0067564	,000	,182828	,237505
	CisRes_t0	,2101667*	,0067564	,000	,182828	,237505
	Fu05_t0	,2101667*	,0067564	,000	,182828	,237505
	FuRes_t0	,2101667*	,0067564	,000	,182828	,237505
	Contro_t1	,1076667*	,0075539	,000	,077102	,138232
	DMSO_t1	,1080000*	,0082749	,000	,074518	,141482
	Res50_t1	,1606667*	,0075539	,000	,130102	,191232
	Cis05_t1	,1835000*	,0082749	,000	,150018	,216982
	CisRes_t1	,2020000*	,0082749	,000	,168518	,235482
	Fu05_t1	,1350000*	,0075539	,000	,104435	,165565
	FuRes_t1	,1653333*	,0075539	,000	,134768	,195898
	Control_t2	-,2560000*	,0075539	,000	-,286565	-,225435
	DMSO_t2	-,1906667*	,0075539	,000	-,221232	-,160102
	Res50_t2	,1405000*	,0082749	,000	,107018	,173982
	Cis05_t2	,0533333*	,0075539	,000	,022768	,083898
	CisRes_t2	,2493333*	,0075539	,000	,218768	,279898
	Fu05_t2	,0365000*	,0082749	,014	,003018	,069982
	FuRes_t2	,1450000*	,0075539	,000	,114435	,175565
	Control_t3	-,3493333*	,0075539	,000	-,379898	-,318768
	DMSO_t3	-,3060000*	,0075539	,000	-,336565	-,275435
	Res50_t3	,1365000*	,0082749	,000	,103018	,169982
	Cis05_t3	,0160000	,0075539	1,000	-,014565	,046565
	CisRes_t3	,2660000*	,0075539	,000	,235435	,296565
	FuRes_t3	,2286667*	,0075539	,000	,198102	,259232

FuRes_t3	Contro_t0	-,0185000	,0058512	,876	-,042176	,005176
	DMSO_t0	-,0185000	,0058512	,876	-,042176	,005176
	Res50_t0	-,0185000	,0058512	,876	-,042176	,005176
	Cis05_t0	-,0185000	,0058512	,876	-,042176	,005176
	CisRes_t0	-,0185000	,0058512	,876	-,042176	,005176
	Fu05_t0	-,0185000	,0058512	,876	-,042176	,005176
	FuRes_t0	-,0185000	,0058512	,876	-,042176	,005176
	Contro_t1	-,1210000*	,0067564	,000	-,148338	-,093662
	DMSO_t1	-,1206667*	,0075539	,000	-,151232	-,090102
	Res50_t1	-,0680000*	,0067564	,000	-,095338	-,040662
	Cis05_t1	-,0451667*	,0075539	,000	-,075732	-,014602
	CisRes_t1	-,0266667	,0075539	,279	-,057232	,003898
	Fu05_t1	-,0936667*	,0067564	,000	-,121005	-,066328
	FuRes_t1	-,0633333*	,0067564	,000	-,090672	-,035995
	Control_t2	-,4846667*	,0067564	,000	-,512005	-,457328
	DMSO_t2	-,4193333*	,0067564	,000	-,446672	-,391995
	Res50_t2	-,0881667*	,0075539	,000	-,118732	-,057602
	Cis05_t2	-,1753333*	,0067564	,000	-,202672	-,147995
	CisRes_t2	,0206667	,0067564	1,000	-,006672	,048005
	Fu05_t2	-,1921667*	,0075539	,000	-,222732	-,161602
	FuRes_t2	-,0836667*	,0067564	,000	-,111005	-,056328
	Control_t3	-,5780000*	,0067564	,000	-,605338	-,550662
	DMSO_t3	-,5346667*	,0067564	,000	-,562005	-,507328
	Res50_t3	-,0921667*	,0075539	,000	-,122732	-,061602
	Cis05_t3	-,2126667*	,0067564	,000	-,240005	-,185328
	CisRes_t3	,0373333*	,0067564	,000	,009995	,064672
	Fu05_t3	-,2286667*	,0075539	,000	-,259232	-,198102

*. La differenza media è significativa al livello 0.05

Table IV Bonferroni-HOLM post-hoc test

(I) Group	Differenza fra medie (I-J)	Errore std.	Sig.	Intervallo di confidenza 95%			
				Limite inferiore	Limite superiore		
Contro_t0	DMSO_t0	0,000000	,0133262	1,000	-,054577	,054577	
	Res20_t0	0,000000	,0133262	1,000	-,054577	,054577	
	Cis05_t0	0,000000	,0133262	1,000	-,054577	,054577	
	CisRes_t0	0,000000	,0133262	1,000	-,054577	,054577	
	Fu05_t0	0,000000	,0133262	1,000	-,054577	,054577	
	FuRes_t0	0,000000	,0133262	1,000	-,054577	,054577	
	Contro_t1	-,0437500	,0143940	1,000	-,102700	,015200	
	DMSO_t1	-,0307500	,0143940	1,000	-,089700	,028200	
	Res20_t1	,0147500	,0163212	1,000	-,052093	,081593	
	Cis05_t1	,0395833	,0143940	1,000	-,019367	,098534	
	CisRes_t1	,0449167	,0143940	1,000	-,014034	,103867	
	Fu05_t1	,0542500	,0143940	,146	-,004700	,113200	
	FuRes_t1	-,0137500	,0143940	1,000	-,072700	,045200	
	Control_t2	-,3104167*	,0143940	,000	-,369367	-,251466	
	DMSO_t2	-,2754167*	,0143940	,000	-,334367	-,216466	
	Res20_t2	-,1177500*	,0163212	,000	-,184593	-,050907	
	Cis05_t2	-,1487500*	,0143940	,000	-,207700	-,089800	
	CisRes_t2	-,1080833*	,0143940	,000	-,167034	-,049133	
	Fu05_t2	-,1807500*	,0143940	,000	-,239700	-,121800	
	FuRes_t2	-,2157500*	,0143940	,000	-,274700	-,156800	
	Control_t3	-,5927500*	,0163212	,000	-,659593	-,525907	
	DMSO_t3	-,6144167*	,0143940	,000	-,673367	-,555466	
	Res20_t3	-,1720833*	,0143940	,000	-,231034	-,113133	
	Cis05_t3	-,2434167*	,0143940	,000	-,302367	-,184466	
	CisRes_t3	-,1014167*	,0143940	,000	-,160367	-,042466	
	Fu05_t3	-,2492500*	,0163212	,000	-,316093	-,182407	
	FuRes_t3	-,1197500*	,0163212	,000	-,186593	-,052907	
	DMSO_t0	Contro_t0	0,000000	,0133262	1,000	-,054577	,054577
		Res20_t0	0,000000	,0133262	1,000	-,054577	,054577
		Cis05_t0	0,000000	,0133262	1,000	-,054577	,054577
CisRes_t0		0,000000	,0133262	1,000	-,054577	,054577	
Fu05_t0		0,000000	,0133262	1,000	-,054577	,054577	
FuRes_t0		0,000000	,0133262	1,000	-,054577	,054577	
Contro_t1		-,0437500	,0143940	1,000	-,102700	,015200	
DMSO_t1		-,0307500	,0143940	1,000	-,089700	,028200	
Res20_t1		,0147500	,0163212	1,000	-,052093	,081593	
Cis05_t1		,0395833	,0143940	1,000	-,019367	,098534	
CisRes_t1		,0449167	,0143940	1,000	-,014034	,103867	
Fu05_t1		,0542500	,0143940	,146	-,004700	,113200	
FuRes_t1		-,0137500	,0143940	1,000	-,072700	,045200	

	Control_t2	-,3104167*	,0143940	,000	-,369367	-,251466
	DMSO_t2	-,2754167*	,0143940	,000	-,334367	-,216466
	Res20_t2	-,1177500*	,0163212	,000	-,184593	-,050907
	Cis05_t2	-,1487500*	,0143940	,000	-,207700	-,089800
	CisRes_t2	-,1080833*	,0143940	,000	-,167034	-,049133
	Fu05_t2	-,1807500*	,0143940	,000	-,239700	-,121800
	FuRes_t2	-,2157500*	,0143940	,000	-,274700	-,156800
	Control_t3	-,5927500*	,0163212	,000	-,659593	-,525907
	DMSO_t3	-,6144167*	,0143940	,000	-,673367	-,555466
	Res20_t3	-,1720833*	,0143940	,000	-,231034	-,113133
	Cis05_t3	-,2434167*	,0143940	,000	-,302367	-,184466
	CisRes_t3	-,1014167*	,0143940	,000	-,160367	-,042466
	Fu05_t3	-,2492500*	,0163212	,000	-,316093	-,182407
	FuRes_t3	-,1197500*	,0163212	,000	-,186593	-,052907
Res20_t0	Contro_t0	0,0000000	,0133262	1,000	-,054577	,054577
	DMSO_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Cis05_t0	0,0000000	,0133262	1,000	-,054577	,054577
	CisRes_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Fu05_t0	0,0000000	,0133262	1,000	-,054577	,054577
	FuRes_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Contro_t1	-,0437500	,0143940	1,000	-,102700	,015200
	DMSO_t1	-,0307500	,0143940	1,000	-,089700	,028200
	Res20_t1	,0147500	,0163212	1,000	-,052093	,081593
	Cis05_t1	,0395833	,0143940	1,000	-,019367	,098534
	CisRes_t1	,0449167	,0143940	1,000	-,014034	,103867
	Fu05_t1	,0542500	,0143940	,146	-,004700	,113200
	FuRes_t1	-,0137500	,0143940	1,000	-,072700	,045200
	Control_t2	-,3104167*	,0143940	,000	-,369367	-,251466
	DMSO_t2	-,2754167*	,0143940	,000	-,334367	-,216466
	Res20_t2	-,1177500*	,0163212	,000	-,184593	-,050907
	Cis05_t2	-,1487500*	,0143940	,000	-,207700	-,089800
	CisRes_t2	-,1080833*	,0143940	,000	-,167034	-,049133
	Fu05_t2	-,1807500*	,0143940	,000	-,239700	-,121800
	FuRes_t2	-,2157500*	,0143940	,000	-,274700	-,156800
	Control_t3	-,5927500*	,0163212	,000	-,659593	-,525907
	DMSO_t3	-,6144167*	,0143940	,000	-,673367	-,555466
	Res20_t3	-,1720833*	,0143940	,000	-,231034	-,113133
	Cis05_t3	-,2434167*	,0143940	,000	-,302367	-,184466
	CisRes_t3	-,1014167*	,0143940	,000	-,160367	-,042466
	Fu05_t3	-,2492500*	,0163212	,000	-,316093	-,182407
	FuRes_t3	-,1197500*	,0163212	,000	-,186593	-,052907
Cis05_t0	Contro_t0	0,0000000	,0133262	1,000	-,054577	,054577
	DMSO_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Res20_t0	0,0000000	,0133262	1,000	-,054577	,054577
	CisRes_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Fu05_t0	0,0000000	,0133262	1,000	-,054577	,054577
	FuRes_t0	0,0000000	,0133262	1,000	-,054577	,054577

	Contro_t1	-,0437500	,0143940	1,000	-,102700	,015200
	DMSO_t1	-,0307500	,0143940	1,000	-,089700	,028200
	Res20_t1	,0147500	,0163212	1,000	-,052093	,081593
	Cis05_t1	,0395833	,0143940	1,000	-,019367	,098534
	CisRes_t1	,0449167	,0143940	1,000	-,014034	,103867
	Fu05_t1	,0542500	,0143940	,146	-,004700	,113200
	FuRes_t1	-,0137500	,0143940	1,000	-,072700	,045200
	Control_t2	-,3104167*	,0143940	,000	-,369367	-,251466
	DMSO_t2	-,2754167*	,0143940	,000	-,334367	-,216466
	Res20_t2	-,1177500*	,0163212	,000	-,184593	-,050907
	Cis05_t2	-,1487500*	,0143940	,000	-,207700	-,089800
	CisRes_t2	-,1080833*	,0143940	,000	-,167034	-,049133
	Fu05_t2	-,1807500*	,0143940	,000	-,239700	-,121800
	FuRes_t2	-,2157500*	,0143940	,000	-,274700	-,156800
	Control_t3	-,5927500*	,0163212	,000	-,659593	-,525907
	DMSO_t3	-,6144167*	,0143940	,000	-,673367	-,555466
	Res20_t3	-,1720833*	,0143940	,000	-,231034	-,113133
	Cis05_t3	-,2434167*	,0143940	,000	-,302367	-,184466
	CisRes_t3	-,1014167*	,0143940	,000	-,160367	-,042466
	Fu05_t3	-,2492500*	,0163212	,000	-,316093	-,182407
	FuRes_t3	-,1197500*	,0163212	,000	-,186593	-,052907
CisRes_t0	Contro_t0	0,0000000	,0133262	1,000	-,054577	,054577
	DMSO_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Res20_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Cis05_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Fu05_t0	0,0000000	,0133262	1,000	-,054577	,054577
	FuRes_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Contro_t1	-,0437500	,0143940	1,000	-,102700	,015200
	DMSO_t1	-,0307500	,0143940	1,000	-,089700	,028200
	Res20_t1	,0147500	,0163212	1,000	-,052093	,081593
	Cis05_t1	,0395833	,0143940	1,000	-,019367	,098534
	CisRes_t1	,0449167	,0143940	1,000	-,014034	,103867
	Fu05_t1	,0542500	,0143940	,146	-,004700	,113200
	FuRes_t1	-,0137500	,0143940	1,000	-,072700	,045200
	Control_t2	-,3104167*	,0143940	,000	-,369367	-,251466
	DMSO_t2	-,2754167*	,0143940	,000	-,334367	-,216466
	Res20_t2	-,1177500*	,0163212	,000	-,184593	-,050907
	Cis05_t2	-,1487500*	,0143940	,000	-,207700	-,089800
	CisRes_t2	-,1080833*	,0143940	,000	-,167034	-,049133
	Fu05_t2	-,1807500*	,0143940	,000	-,239700	-,121800
	FuRes_t2	-,2157500*	,0143940	,000	-,274700	-,156800
	Control_t3	-,5927500*	,0163212	,000	-,659593	-,525907
	DMSO_t3	-,6144167*	,0143940	,000	-,673367	-,555466
	Res20_t3	-,1720833*	,0143940	,000	-,231034	-,113133
	Cis05_t3	-,2434167*	,0143940	,000	-,302367	-,184466
	CisRes_t3	-,1014167*	,0143940	,000	-,160367	-,042466
	Fu05_t3	-,2492500*	,0163212	,000	-,316093	-,182407

	FuRes_t3	-,1197500*	,0163212	,000	-,186593	-,052907
Fu05_t0	Contro_t0	0,0000000	,0133262	1,000	-,054577	,054577
	DMSO_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Res20_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Cis05_t0	0,0000000	,0133262	1,000	-,054577	,054577
	CisRes_t0	0,0000000	,0133262	1,000	-,054577	,054577
	FuRes_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Contro_t1	-,0437500	,0143940	1,000	-,102700	,015200
	DMSO_t1	-,0307500	,0143940	1,000	-,089700	,028200
	Res20_t1	,0147500	,0163212	1,000	-,052093	,081593
	Cis05_t1	,0395833	,0143940	1,000	-,019367	,098534
	CisRes_t1	,0449167	,0143940	1,000	-,014034	,103867
	Fu05_t1	,0542500	,0143940	,146	-,004700	,113200
	FuRes_t1	-,0137500	,0143940	1,000	-,072700	,045200
	Control_t2	-,3104167*	,0143940	,000	-,369367	-,251466
	DMSO_t2	-,2754167*	,0143940	,000	-,334367	-,216466
	Res20_t2	-,1177500*	,0163212	,000	-,184593	-,050907
	Cis05_t2	-,1487500*	,0143940	,000	-,207700	-,089800
	CisRes_t2	-,1080833*	,0143940	,000	-,167034	-,049133
	Fu05_t2	-,1807500*	,0143940	,000	-,239700	-,121800
	FuRes_t2	-,2157500*	,0143940	,000	-,274700	-,156800
	Control_t3	-,5927500*	,0163212	,000	-,659593	-,525907
	DMSO_t3	-,6144167*	,0143940	,000	-,673367	-,555466
	Res20_t3	-,1720833*	,0143940	,000	-,231034	-,113133
	Cis05_t3	-,2434167*	,0143940	,000	-,302367	-,184466
	CisRes_t3	-,1014167*	,0143940	,000	-,160367	-,042466
	Fu05_t3	-,2492500*	,0163212	,000	-,316093	-,182407
	FuRes_t3	-,1197500*	,0163212	,000	-,186593	-,052907
FuRes_t0	Contro_t0	0,0000000	,0133262	1,000	-,054577	,054577
	DMSO_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Res20_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Cis05_t0	0,0000000	,0133262	1,000	-,054577	,054577
	CisRes_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Fu05_t0	0,0000000	,0133262	1,000	-,054577	,054577
	Contro_t1	-,0437500	,0143940	1,000	-,102700	,015200
	DMSO_t1	-,0307500	,0143940	1,000	-,089700	,028200
	Res20_t1	,0147500	,0163212	1,000	-,052093	,081593
	Cis05_t1	,0395833	,0143940	1,000	-,019367	,098534
	CisRes_t1	,0449167	,0143940	1,000	-,014034	,103867
	Fu05_t1	,0542500	,0143940	,146	-,004700	,113200
	FuRes_t1	-,0137500	,0143940	1,000	-,072700	,045200
	Control_t2	-,3104167*	,0143940	,000	-,369367	-,251466
	DMSO_t2	-,2754167*	,0143940	,000	-,334367	-,216466
	Res20_t2	-,1177500*	,0163212	,000	-,184593	-,050907
	Cis05_t2	-,1487500*	,0143940	,000	-,207700	-,089800
	CisRes_t2	-,1080833*	,0143940	,000	-,167034	-,049133
	Fu05_t2	-,1807500*	,0143940	,000	-,239700	-,121800

	FuRes_t2	-,2157500*	,0143940	,000	-,274700	-,156800
	Control_t3	-,5927500*	,0163212	,000	-,659593	-,525907
	DMSO_t3	-,6144167*	,0143940	,000	-,673367	-,555466
	Res20_t3	-,1720833*	,0143940	,000	-,231034	-,113133
	Cis05_t3	-,2434167*	,0143940	,000	-,302367	-,184466
	CisRes_t3	-,1014167*	,0143940	,000	-,160367	-,042466
	Fu05_t3	-,2492500*	,0163212	,000	-,316093	-,182407
	FuRes_t3	-,1197500*	,0163212	,000	-,186593	-,052907
Contro_t1	Contro_t0	,0437500	,0143940	1,000	-,015200	,102700
	DMSO_t0	,0437500	,0143940	1,000	-,015200	,102700
	Res20_t0	,0437500	,0143940	1,000	-,015200	,102700
	Cis05_t0	,0437500	,0143940	1,000	-,015200	,102700
	CisRes_t0	,0437500	,0143940	1,000	-,015200	,102700
	Fu05_t0	,0437500	,0143940	1,000	-,015200	,102700
	FuRes_t0	,0437500	,0143940	1,000	-,015200	,102700
	DMSO_t1	,0130000	,0153878	1,000	-,050021	,076021
	Res20_t1	,0585000	,0172041	,463	-,011959	,128959
	Cis05_t1	,0833333*	,0153878	,000	,020313	,146354
	CisRes_t1	,0886667*	,0153878	,000	,025646	,151687
	Fu05_t1	,0980000*	,0153878	,000	,034979	,161021
	FuRes_t1	,0300000	,0153878	1,000	-,033021	,093021
	Control_t2	-,2666667*	,0153878	,000	-,329687	-,203646
	DMSO_t2	-,2316667*	,0153878	,000	-,294687	-,168646
	Res20_t2	-,0740000*	,0172041	,025	-,144459	-,003541
	Cis05_t2	-,1050000*	,0153878	,000	-,168021	-,041979
	CisRes_t2	-,0643333*	,0153878	,038	-,127354	-,001313
	Fu05_t2	-,1370000*	,0153878	,000	-,200021	-,073979
	FuRes_t2	-,1720000*	,0153878	,000	-,235021	-,108979
	Control_t3	-,5490000*	,0172041	,000	-,619459	-,478541
	DMSO_t3	-,5706667*	,0153878	,000	-,633687	-,507646
	Res20_t3	-,1283333*	,0153878	,000	-,191354	-,065313
	Cis05_t3	-,1996667*	,0153878	,000	-,262687	-,136646
	CisRes_t3	-,0576667	,0153878	,156	-,120687	,005354
	Fu05_t3	-,2055000*	,0172041	,000	-,275959	-,135041
	FuRes_t3	-,0760000*	,0172041	,017	-,146459	-,005541
DMSO_t1	Contro_t0	,0307500	,0143940	1,000	-,028200	,089700
	DMSO_t0	,0307500	,0143940	1,000	-,028200	,089700
	Res20_t0	,0307500	,0143940	1,000	-,028200	,089700
	Cis05_t0	,0307500	,0143940	1,000	-,028200	,089700
	CisRes_t0	,0307500	,0143940	1,000	-,028200	,089700
	Fu05_t0	,0307500	,0143940	1,000	-,028200	,089700
	FuRes_t0	,0307500	,0143940	1,000	-,028200	,089700
	Contro_t1	-,0130000	,0153878	1,000	-,076021	,050021
	Res20_t1	,0455000	,0172041	1,000	-,024959	,115959
	Cis05_t1	,0703333*	,0153878	,010	,007313	,133354
	CisRes_t1	,0756667*	,0153878	,003	,012646	,138687
	Fu05_t1	,0850000*	,0153878	,000	,021979	,148021

	FuRes_t1	,0170000	,0153878	1,000	-,046021	,080021
	Control_t2	-,2796667*	,0153878	,000	-,342687	-,216646
	DMSO_t2	-,2446667*	,0153878	,000	-,307687	-,181646
	Res20_t2	-,0870000*	,0172041	,002	-,157459	-,016541
	Cis05_t2	-,1180000*	,0153878	,000	-,181021	-,054979
	CisRes_t2	-,0773333*	,0153878	,002	-,140354	-,014313
	Fu05_t2	-,1500000*	,0153878	,000	-,213021	-,086979
	FuRes_t2	-,1850000*	,0153878	,000	-,248021	-,121979
	Control_t3	-,5620000*	,0172041	,000	-,632459	-,491541
	DMSO_t3	-,5836667*	,0153878	,000	-,646687	-,520646
	Res20_t3	-,1413333*	,0153878	,000	-,204354	-,078313
	Cis05_t3	-,2126667*	,0153878	,000	-,275687	-,149646
	CisRes_t3	-,0706667*	,0153878	,009	-,133687	-,007646
	Fu05_t3	-,2185000*	,0172041	,000	-,288959	-,148041
	FuRes_t3	-,0890000*	,0172041	,001	-,159459	-,018541
Res20_t1	Contro_t0	-,0147500	,0163212	1,000	-,081593	,052093
	DMSO_t0	-,0147500	,0163212	1,000	-,081593	,052093
	Res20_t0	-,0147500	,0163212	1,000	-,081593	,052093
	Cis05_t0	-,0147500	,0163212	1,000	-,081593	,052093
	CisRes_t0	-,0147500	,0163212	1,000	-,081593	,052093
	Fu05_t0	-,0147500	,0163212	1,000	-,081593	,052093
	FuRes_t0	-,0147500	,0163212	1,000	-,081593	,052093
	Contro_t1	-,0585000	,0172041	,463	-,128959	,011959
	DMSO_t1	-,0455000	,0172041	1,000	-,115959	,024959
	Cis05_t1	,0248333	,0172041	1,000	-,045626	,095293
	CisRes_t1	,0301667	,0172041	1,000	-,040293	,100626
	Fu05_t1	,0395000	,0172041	1,000	-,030959	,109959
	FuRes_t1	-,0285000	,0172041	1,000	-,098959	,041959
	Control_t2	-,3251667*	,0172041	,000	-,395626	-,254707
	DMSO_t2	-,2901667*	,0172041	,000	-,360626	-,219707
	Res20_t2	-,1325000*	,0188461	,000	-,209684	-,055316
	Cis05_t2	-,1635000*	,0172041	,000	-,233959	-,093041
	CisRes_t2	-,1228333*	,0172041	,000	-,193293	-,052374
	Fu05_t2	-,1955000*	,0172041	,000	-,265959	-,125041
	FuRes_t2	-,2305000*	,0172041	,000	-,300959	-,160041
	Control_t3	-,6075000*	,0188461	,000	-,684684	-,530316
	DMSO_t3	-,6291667*	,0172041	,000	-,699626	-,558707
	Res20_t3	-,1868333*	,0172041	,000	-,257293	-,116374
	Cis05_t3	-,2581667*	,0172041	,000	-,328626	-,187707
	CisRes_t3	-,1161667*	,0172041	,000	-,186626	-,045707
	Fu05_t3	-,2640000*	,0188461	,000	-,341184	-,186816
	FuRes_t3	-,1345000*	,0188461	,000	-,211684	-,057316
Cis05_t1	Contro_t0	-,0395833	,0143940	1,000	-,098534	,019367
	DMSO_t0	-,0395833	,0143940	1,000	-,098534	,019367
	Res20_t0	-,0395833	,0143940	1,000	-,098534	,019367
	Cis05_t0	-,0395833	,0143940	1,000	-,098534	,019367
	CisRes_t0	-,0395833	,0143940	1,000	-,098534	,019367

	Fu05_t0	-,0395833	,0143940	1,000	-,098534	,019367
	FuRes_t0	-,0395833	,0143940	1,000	-,098534	,019367
	Contro_t1	-,0833333*	,0153878	,000	-,146354	-,020313
	DMSO_t1	-,0703333*	,0153878	,010	-,133354	-,007313
	Res20_t1	-,0248333	,0172041	1,000	-,095293	,045626
	CisRes_t1	,0053333	,0153878	1,000	-,057687	,068354
	Fu05_t1	,0146667	,0153878	1,000	-,048354	,077687
	FuRes_t1	-,0533333	,0153878	,378	-,116354	,009687
	Control_t2	-,3500000*	,0153878	,000	-,413021	-,286979
	DMSO_t2	-,3150000*	,0153878	,000	-,378021	-,251979
	Res20_t2	-,1573333*	,0172041	,000	-,227793	-,086874
	Cis05_t2	-,1883333*	,0153878	,000	-,251354	-,125313
	CisRes_t2	-,1476667*	,0153878	,000	-,210687	-,084646
	Fu05_t2	-,2203333*	,0153878	,000	-,283354	-,157313
	FuRes_t2	-,2553333*	,0153878	,000	-,318354	-,192313
	Control_t3	-,6323333*	,0172041	,000	-,702793	-,561874
	DMSO_t3	-,6540000*	,0153878	,000	-,717021	-,590979
	Res20_t3	-,2116667*	,0153878	,000	-,274687	-,148646
	Cis05_t3	-,2830000*	,0153878	,000	-,346021	-,219979
	CisRes_t3	-,1410000*	,0153878	,000	-,204021	-,077979
	Fu05_t3	-,2888333*	,0172041	,000	-,359293	-,218374
	FuRes_t3	-,1593333*	,0172041	,000	-,229793	-,088874
CisRes_t1	Contro_t0	-,0449167	,0143940	1,000	-,103867	,014034
	DMSO_t0	-,0449167	,0143940	1,000	-,103867	,014034
	Res20_t0	-,0449167	,0143940	1,000	-,103867	,014034
	Cis05_t0	-,0449167	,0143940	1,000	-,103867	,014034
	CisRes_t0	-,0449167	,0143940	1,000	-,103867	,014034
	Fu05_t0	-,0449167	,0143940	1,000	-,103867	,014034
	FuRes_t0	-,0449167	,0143940	1,000	-,103867	,014034
	Contro_t1	-,0886667*	,0153878	,000	-,151687	-,025646
	DMSO_t1	-,0756667*	,0153878	,003	-,138687	-,012646
	Res20_t1	-,0301667	,0172041	1,000	-,100626	,040293
	Cis05_t1	-,0053333	,0153878	1,000	-,068354	,057687
	Fu05_t1	,0093333	,0153878	1,000	-,053687	,072354
	FuRes_t1	-,0586667	,0153878	,127	-,121687	,004354
	Control_t2	-,3553333*	,0153878	,000	-,418354	-,292313
	DMSO_t2	-,3203333*	,0153878	,000	-,383354	-,257313
	Res20_t2	-,1626667*	,0172041	,000	-,233126	-,092207
	Cis05_t2	-,1936667*	,0153878	,000	-,256687	-,130646
	CisRes_t2	-,1530000*	,0153878	,000	-,216021	-,089979
	Fu05_t2	-,2256667*	,0153878	,000	-,288687	-,162646
	FuRes_t2	-,2606667*	,0153878	,000	-,323687	-,197646
	Control_t3	-,6376667*	,0172041	,000	-,708126	-,567207
	DMSO_t3	-,6593333*	,0153878	,000	-,722354	-,596313
	Res20_t3	-,2170000*	,0153878	,000	-,280021	-,153979
	Cis05_t3	-,2883333*	,0153878	,000	-,351354	-,225313
	CisRes_t3	-,1463333*	,0153878	,000	-,209354	-,083313

	Fu05_t3	-,2941667*	,0172041	,000	-,364626	-,223707
	FuRes_t3	-,1646667*	,0172041	,000	-,235126	-,094207
Fu05_t1	Contro_t0	-,0542500	,0143940	,146	-,113200	,004700
	DMSO_t0	-,0542500	,0143940	,146	-,113200	,004700
	Res20_t0	-,0542500	,0143940	,146	-,113200	,004700
	Cis05_t0	-,0542500	,0143940	,146	-,113200	,004700
	CisRes_t0	-,0542500	,0143940	,146	-,113200	,004700
	Fu05_t0	-,0542500	,0143940	,146	-,113200	,004700
	FuRes_t0	-,0542500	,0143940	,146	-,113200	,004700
	Contro_t1	-,0980000*	,0153878	,000	-,161021	-,034979
	DMSO_t1	-,0850000*	,0153878	,000	-,148021	-,021979
	Res20_t1	-,0395000	,0172041	1,000	-,109959	,030959
	Cis05_t1	-,0146667	,0153878	1,000	-,077687	,048354
	CisRes_t1	-,0093333	,0153878	1,000	-,072354	,053687
	FuRes_t1	-,0680000*	,0153878	,017	-,131021	-,004979
	Control_t2	-,3646667*	,0153878	,000	-,427687	-,301646
	DMSO_t2	-,3296667*	,0153878	,000	-,392687	-,266646
	Res20_t2	-,1720000*	,0172041	,000	-,242459	-,101541
	Cis05_t2	-,2030000*	,0153878	,000	-,266021	-,139979
	CisRes_t2	-,1623333*	,0153878	,000	-,225354	-,099313
	Fu05_t2	-,2350000*	,0153878	,000	-,298021	-,171979
	FuRes_t2	-,2700000*	,0153878	,000	-,333021	-,206979
	Control_t3	-,6470000*	,0172041	,000	-,717459	-,576541
	DMSO_t3	-,6686667*	,0153878	,000	-,731687	-,605646
	Res20_t3	-,2263333*	,0153878	,000	-,289354	-,163313
	Cis05_t3	-,2976667*	,0153878	,000	-,360687	-,234646
	CisRes_t3	-,1556667*	,0153878	,000	-,218687	-,092646
	Fu05_t3	-,3035000*	,0172041	,000	-,373959	-,233041
	FuRes_t3	-,1740000*	,0172041	,000	-,244459	-,103541
FuRes_t1	Contro_t0	,0137500	,0143940	1,000	-,045200	,072700
	DMSO_t0	,0137500	,0143940	1,000	-,045200	,072700
	Res20_t0	,0137500	,0143940	1,000	-,045200	,072700
	Cis05_t0	,0137500	,0143940	1,000	-,045200	,072700
	CisRes_t0	,0137500	,0143940	1,000	-,045200	,072700
	Fu05_t0	,0137500	,0143940	1,000	-,045200	,072700
	FuRes_t0	,0137500	,0143940	1,000	-,045200	,072700
	Contro_t1	-,0300000	,0153878	1,000	-,093021	,033021
	DMSO_t1	-,0170000	,0153878	1,000	-,080021	,046021
	Res20_t1	,0285000	,0172041	1,000	-,041959	,098959
	Cis05_t1	,0533333	,0153878	,378	-,009687	,116354
	CisRes_t1	,0586667	,0153878	,127	-,004354	,121687
	Fu05_t1	,0680000*	,0153878	,017	,004979	,131021
	Control_t2	-,2966667*	,0153878	,000	-,359687	-,233646
	DMSO_t2	-,2616667*	,0153878	,000	-,324687	-,198646
	Res20_t2	-,1040000*	,0172041	,000	-,174459	-,033541
	Cis05_t2	-,1350000*	,0153878	,000	-,198021	-,071979
	CisRes_t2	-,0943333*	,0153878	,000	-,157354	-,031313

	Fu05_t2	-,1670000*	,0153878	,000	-,230021	-,103979
	FuRes_t2	-,2020000*	,0153878	,000	-,265021	-,138979
	Control_t3	-,5790000*	,0172041	,000	-,649459	-,508541
	DMSO_t3	-,6006667*	,0153878	,000	-,663687	-,537646
	Res20_t3	-,1583333*	,0153878	,000	-,221354	-,095313
	Cis05_t3	-,2296667*	,0153878	,000	-,292687	-,166646
	CisRes_t3	-,0876667*	,0153878	,000	-,150687	-,024646
	Fu05_t3	-,2355000*	,0172041	,000	-,305959	-,165041
	FuRes_t3	-,1060000*	,0172041	,000	-,176459	-,035541
Control_t2	Contro_t0	,3104167*	,0143940	,000	,251466	,369367
	DMSO_t0	,3104167*	,0143940	,000	,251466	,369367
	Res20_t0	,3104167*	,0143940	,000	,251466	,369367
	Cis05_t0	,3104167*	,0143940	,000	,251466	,369367
	CisRes_t0	,3104167*	,0143940	,000	,251466	,369367
	Fu05_t0	,3104167*	,0143940	,000	,251466	,369367
	FuRes_t0	,3104167*	,0143940	,000	,251466	,369367
	Contro_t1	,2666667*	,0153878	,000	,203646	,329687
	DMSO_t1	,2796667*	,0153878	,000	,216646	,342687
	Res20_t1	,3251667*	,0172041	,000	,254707	,395626
	Cis05_t1	,3500000*	,0153878	,000	,286979	,413021
	CisRes_t1	,3553333*	,0153878	,000	,292313	,418354
	Fu05_t1	,3646667*	,0153878	,000	,301646	,427687
	FuRes_t1	,2966667*	,0153878	,000	,233646	,359687
	DMSO_t2	,0350000	,0153878	1,000	-,028021	,098021
	Res20_t2	,1926667*	,0172041	,000	,122207	,263126
	Cis05_t2	,1616667*	,0153878	,000	,098646	,224687
	CisRes_t2	,2023333*	,0153878	,000	,139313	,265354
	Fu05_t2	,1296667*	,0153878	,000	,066646	,192687
	FuRes_t2	,0946667*	,0153878	,000	,031646	,157687
	Control_t3	-,2823333*	,0172041	,000	-,352793	-,211874
	DMSO_t3	-,3040000*	,0153878	,000	-,367021	-,240979
	Res20_t3	,1383333*	,0153878	,000	,075313	,201354
	Cis05_t3	,0670000*	,0153878	,021	,003979	,130021
	CisRes_t3	,2090000*	,0153878	,000	,145979	,272021
	Fu05_t3	,0611667	,0172041	,287	-,009293	,131626
	FuRes_t3	,1906667*	,0172041	,000	,120207	,261126
DMSO_t2	Contro_t0	,2754167*	,0143940	,000	,216466	,334367
	DMSO_t0	,2754167*	,0143940	,000	,216466	,334367
	Res20_t0	,2754167*	,0143940	,000	,216466	,334367
	Cis05_t0	,2754167*	,0143940	,000	,216466	,334367
	CisRes_t0	,2754167*	,0143940	,000	,216466	,334367
	Fu05_t0	,2754167*	,0143940	,000	,216466	,334367
	FuRes_t0	,2754167*	,0143940	,000	,216466	,334367
	Contro_t1	,2316667*	,0153878	,000	,168646	,294687
	DMSO_t1	,2446667*	,0153878	,000	,181646	,307687
	Res20_t1	,2901667*	,0172041	,000	,219707	,360626
	Cis05_t1	,3150000*	,0153878	,000	,251979	,378021

	CisRes_t1	,3203333*	,0153878	,000	,257313	,383354
	Fu05_t1	,3296667*	,0153878	,000	,266646	,392687
	FuRes_t1	,2616667*	,0153878	,000	,198646	,324687
	Control_t2	-,0350000	,0153878	1,000	-,098021	,028021
	Res20_t2	,1576667*	,0172041	,000	,087207	,228126
	Cis05_t2	,1266667*	,0153878	,000	,063646	,189687
	CisRes_t2	,1673333*	,0153878	,000	,104313	,230354
	Fu05_t2	,0946667*	,0153878	,000	,031646	,157687
	FuRes_t2	,0596667	,0153878	,103	-,003354	,122687
	Control_t3	-,3173333*	,0172041	,000	-,387793	-,246874
	DMSO_t3	-,3390000*	,0153878	,000	-,402021	-,275979
	Res20_t3	,1033333*	,0153878	,000	,040313	,166354
	Cis05_t3	,0320000	,0153878	1,000	-,031021	,095021
	CisRes_t3	,1740000*	,0153878	,000	,110979	,237021
	Fu05_t3	,0261667	,0172041	1,000	-,044293	,096626
	FuRes_t3	,1556667*	,0172041	,000	,085207	,226126
Res20_t2	Contro_t0	,1177500*	,0163212	,000	,050907	,184593
	DMSO_t0	,1177500*	,0163212	,000	,050907	,184593
	Res20_t0	,1177500*	,0163212	,000	,050907	,184593
	Cis05_t0	,1177500*	,0163212	,000	,050907	,184593
	CisRes_t0	,1177500*	,0163212	,000	,050907	,184593
	Fu05_t0	,1177500*	,0163212	,000	,050907	,184593
	FuRes_t0	,1177500*	,0163212	,000	,050907	,184593
	Contro_t1	,0740000*	,0172041	,025	,003541	,144459
	DMSO_t1	,0870000*	,0172041	,002	,016541	,157459
	Res20_t1	,1325000*	,0188461	,000	,055316	,209684
	Cis05_t1	,1573333*	,0172041	,000	,086874	,227793
	CisRes_t1	,1626667*	,0172041	,000	,092207	,233126
	Fu05_t1	,1720000*	,0172041	,000	,101541	,242459
	FuRes_t1	,1040000*	,0172041	,000	,033541	,174459
	Control_t2	-,1926667*	,0172041	,000	-,263126	-,122207
	DMSO_t2	-,1576667*	,0172041	,000	-,228126	-,087207
	Cis05_t2	-,0310000	,0172041	1,000	-,101459	,039459
	CisRes_t2	,0096667	,0172041	1,000	-,060793	,080126
	Fu05_t2	-,0630000	,0172041	,205	-,133459	,007459
	FuRes_t2	-,0980000*	,0172041	,000	-,168459	-,027541
	Control_t3	-,4750000*	,0188461	,000	-,552184	-,397816
	DMSO_t3	-,4966667*	,0172041	,000	-,567126	-,426207
	Res20_t3	-,0543333	,0172041	,953	-,124793	,016126
	Cis05_t3	-,1256667*	,0172041	,000	-,196126	-,055207
	CisRes_t3	,0163333	,0172041	1,000	-,054126	,086793
	Fu05_t3	-,1315000*	,0188461	,000	-,208684	-,054316
	FuRes_t3	-,0020000	,0188461	1,000	-,079184	,075184
Cis05_t2	Contro_t0	,1487500*	,0143940	,000	,089800	,207700
	DMSO_t0	,1487500*	,0143940	,000	,089800	,207700
	Res20_t0	,1487500*	,0143940	,000	,089800	,207700
	Cis05_t0	,1487500*	,0143940	,000	,089800	,207700

	CisRes_t0	,1487500*	,0143940	,000	,089800	,207700
	Fu05_t0	,1487500*	,0143940	,000	,089800	,207700
	FuRes_t0	,1487500*	,0143940	,000	,089800	,207700
	Contro_t1	,1050000*	,0153878	,000	,041979	,168021
	DMSO_t1	,1180000*	,0153878	,000	,054979	,181021
	Res20_t1	,1635000*	,0172041	,000	,093041	,233959
	Cis05_t1	,1883333*	,0153878	,000	,125313	,251354
	CisRes_t1	,1936667*	,0153878	,000	,130646	,256687
	Fu05_t1	,2030000*	,0153878	,000	,139979	,266021
	FuRes_t1	,1350000*	,0153878	,000	,071979	,198021
	Control_t2	-,1616667*	,0153878	,000	-,224687	-,098646
	DMSO_t2	-,1266667*	,0153878	,000	-,189687	-,063646
	Res20_t2	,0310000	,0172041	1,000	-,039459	,101459
	CisRes_t2	,0406667	,0153878	1,000	-,022354	,103687
	Fu05_t2	-,0320000	,0153878	1,000	-,095021	,031021
	FuRes_t2	-,0670000*	,0153878	,021	-,130021	-,003979
	Control_t3	-,4440000*	,0172041	,000	-,514459	-,373541
	DMSO_t3	-,4656667*	,0153878	,000	-,528687	-,402646
	Res20_t3	-,0233333	,0153878	1,000	-,086354	,039687
	Cis05_t3	-,0946667*	,0153878	,000	-,157687	-,031646
	CisRes_t3	,0473333	,0153878	1,000	-,015687	,110354
	Fu05_t3	-,1005000*	,0172041	,000	-,170959	-,030041
	FuRes_t3	,0290000	,0172041	1,000	-,041459	,099459
CisRes_t2	Contro_t0	,1080833*	,0143940	,000	,049133	,167034
	DMSO_t0	,1080833*	,0143940	,000	,049133	,167034
	Res20_t0	,1080833*	,0143940	,000	,049133	,167034
	Cis05_t0	,1080833*	,0143940	,000	,049133	,167034
	CisRes_t0	,1080833*	,0143940	,000	,049133	,167034
	Fu05_t0	,1080833*	,0143940	,000	,049133	,167034
	FuRes_t0	,1080833*	,0143940	,000	,049133	,167034
	Contro_t1	,0643333*	,0153878	,038	,001313	,127354
	DMSO_t1	,0773333*	,0153878	,002	,014313	,140354
	Res20_t1	,1228333*	,0172041	,000	,052374	,193293
	Cis05_t1	,1476667*	,0153878	,000	,084646	,210687
	CisRes_t1	,1530000*	,0153878	,000	,089979	,216021
	Fu05_t1	,1623333*	,0153878	,000	,099313	,225354
	FuRes_t1	,0943333*	,0153878	,000	,031313	,157354
	Control_t2	-,2023333*	,0153878	,000	-,265354	-,139313
	DMSO_t2	-,1673333*	,0153878	,000	-,230354	-,104313
	Res20_t2	-,0096667	,0172041	1,000	-,080126	,060793
	Cis05_t2	-,0406667	,0153878	1,000	-,103687	,022354
	Fu05_t2	-,0726667*	,0153878	,006	-,135687	-,009646
	FuRes_t2	-,1076667*	,0153878	,000	-,170687	-,044646
	Control_t3	-,4846667*	,0172041	,000	-,555126	-,414207
	DMSO_t3	-,5063333*	,0153878	,000	-,569354	-,443313
	Res20_t3	-,0640000*	,0153878	,040	-,127021	-,000979
	Cis05_t3	-,1353333*	,0153878	,000	-,198354	-,072313

	CisRes_t3	,0066667	,0153878	1,000	-,056354	,069687
	Fu05_t3	-,1411667*	,0172041	,000	-,211626	-,070707
	FuRes_t3	-,0116667	,0172041	1,000	-,082126	,058793
Fu05_t2	Contro_t0	,1807500*	,0143940	,000	,121800	,239700
	DMSO_t0	,1807500*	,0143940	,000	,121800	,239700
	Res20_t0	,1807500*	,0143940	,000	,121800	,239700
	Cis05_t0	,1807500*	,0143940	,000	,121800	,239700
	CisRes_t0	,1807500*	,0143940	,000	,121800	,239700
	Fu05_t0	,1807500*	,0143940	,000	,121800	,239700
	FuRes_t0	,1807500*	,0143940	,000	,121800	,239700
	Contro_t1	,1370000*	,0153878	,000	,073979	,200021
	DMSO_t1	,1500000*	,0153878	,000	,086979	,213021
	Res20_t1	,1955000*	,0172041	,000	,125041	,265959
	Cis05_t1	,2203333*	,0153878	,000	,157313	,283354
	CisRes_t1	,2256667*	,0153878	,000	,162646	,288687
	Fu05_t1	,2350000*	,0153878	,000	,171979	,298021
	FuRes_t1	,1670000*	,0153878	,000	,103979	,230021
	Control_t2	-,1296667*	,0153878	,000	-,192687	-,066646
	DMSO_t2	-,0946667*	,0153878	,000	-,157687	-,031646
	Res20_t2	,0630000	,0172041	,205	-,007459	,133459
	Cis05_t2	,0320000	,0153878	1,000	-,031021	,095021
	CisRes_t2	,0726667*	,0153878	,006	,009646	,135687
	FuRes_t2	-,0350000	,0153878	1,000	-,098021	,028021
	Control_t3	-,4120000*	,0172041	,000	-,482459	-,341541
	DMSO_t3	-,4336667*	,0153878	,000	-,496687	-,370646
	Res20_t3	,0086667	,0153878	1,000	-,054354	,071687
	Cis05_t3	-,0626667	,0153878	,054	-,125687	,000354
	CisRes_t3	,0793333*	,0153878	,001	,016313	,142354
	Fu05_t3	-,0685000	,0172041	,073	-,138959	,001959
	FuRes_t3	,0610000	,0172041	,296	-,009459	,131459
FuRes_t2	Contro_t0	,2157500*	,0143940	,000	,156800	,274700
	DMSO_t0	,2157500*	,0143940	,000	,156800	,274700
	Res20_t0	,2157500*	,0143940	,000	,156800	,274700
	Cis05_t0	,2157500*	,0143940	,000	,156800	,274700
	CisRes_t0	,2157500*	,0143940	,000	,156800	,274700
	Fu05_t0	,2157500*	,0143940	,000	,156800	,274700
	FuRes_t0	,2157500*	,0143940	,000	,156800	,274700
	Contro_t1	,1720000*	,0153878	,000	,108979	,235021
	DMSO_t1	,1850000*	,0153878	,000	,121979	,248021
	Res20_t1	,2305000*	,0172041	,000	,160041	,300959
	Cis05_t1	,2553333*	,0153878	,000	,192313	,318354
	CisRes_t1	,2606667*	,0153878	,000	,197646	,323687
	Fu05_t1	,2700000*	,0153878	,000	,206979	,333021
	FuRes_t1	,2020000*	,0153878	,000	,138979	,265021
	Control_t2	-,0946667*	,0153878	,000	-,157687	-,031646
	DMSO_t2	-,0596667	,0153878	,103	-,122687	,003354
	Res20_t2	,0980000*	,0172041	,000	,027541	,168459

	Cis05_t2	,0670000*	,0153878	,021	,003979	,130021
	CisRes_t2	,1076667*	,0153878	,000	,044646	,170687
	Fu05_t2	,0350000	,0153878	1,000	-,028021	,098021
	Control_t3	-,3770000*	,0172041	,000	-,447459	-,306541
	DMSO_t3	-,3986667*	,0153878	,000	-,461687	-,335646
	Res20_t3	,0436667	,0153878	1,000	-,019354	,106687
	Cis05_t3	-,0276667	,0153878	1,000	-,090687	,035354
	CisRes_t3	,1143333*	,0153878	,000	,051313	,177354
	Fu05_t3	-,0335000	,0172041	1,000	-,103959	,036959
	FuRes_t3	,0960000*	,0172041	,000	,025541	,166459
Control_t3	Contro_t0	,5927500*	,0163212	,000	,525907	,659593
	DMSO_t0	,5927500*	,0163212	,000	,525907	,659593
	Res20_t0	,5927500*	,0163212	,000	,525907	,659593
	Cis05_t0	,5927500*	,0163212	,000	,525907	,659593
	CisRes_t0	,5927500*	,0163212	,000	,525907	,659593
	Fu05_t0	,5927500*	,0163212	,000	,525907	,659593
	FuRes_t0	,5927500*	,0163212	,000	,525907	,659593
	Contro_t1	,5490000*	,0172041	,000	,478541	,619459
	DMSO_t1	,5620000*	,0172041	,000	,491541	,632459
	Res20_t1	,6075000*	,0188461	,000	,530316	,684684
	Cis05_t1	,6323333*	,0172041	,000	,561874	,702793
	CisRes_t1	,6376667*	,0172041	,000	,567207	,708126
	Fu05_t1	,6470000*	,0172041	,000	,576541	,717459
	FuRes_t1	,5790000*	,0172041	,000	,508541	,649459
	Control_t2	,2823333*	,0172041	,000	,211874	,352793
	DMSO_t2	,3173333*	,0172041	,000	,246874	,387793
	Res20_t2	,4750000*	,0188461	,000	,397816	,552184
	Cis05_t2	,4440000*	,0172041	,000	,373541	,514459
	CisRes_t2	,4846667*	,0172041	,000	,414207	,555126
	Fu05_t2	,4120000*	,0172041	,000	,341541	,482459
	FuRes_t2	,3770000*	,0172041	,000	,306541	,447459
	DMSO_t3	-,0216667	,0172041	1,000	-,092126	,048793
	Res20_t3	,4206667*	,0172041	,000	,350207	,491126
	Cis05_t3	,3493333*	,0172041	,000	,278874	,419793
	CisRes_t3	,4913333*	,0172041	,000	,420874	,561793
	Fu05_t3	,3435000*	,0188461	,000	,266316	,420684
	FuRes_t3	,4730000*	,0188461	,000	,395816	,550184
DMSO_t3	Contro_t0	,6144167*	,0143940	,000	,555466	,673367
	DMSO_t0	,6144167*	,0143940	,000	,555466	,673367
	Res20_t0	,6144167*	,0143940	,000	,555466	,673367
	Cis05_t0	,6144167*	,0143940	,000	,555466	,673367
	CisRes_t0	,6144167*	,0143940	,000	,555466	,673367
	Fu05_t0	,6144167*	,0143940	,000	,555466	,673367
	FuRes_t0	,6144167*	,0143940	,000	,555466	,673367
	Contro_t1	,5706667*	,0153878	,000	,507646	,633687
	DMSO_t1	,5836667*	,0153878	,000	,520646	,646687
	Res20_t1	,6291667*	,0172041	,000	,558707	,699626

	Cis05_t1	,6540000*	,0153878	,000	,590979	,717021
	CisRes_t1	,6593333*	,0153878	,000	,596313	,722354
	Fu05_t1	,6686667*	,0153878	,000	,605646	,731687
	FuRes_t1	,6006667*	,0153878	,000	,537646	,663687
	Control_t2	,3040000*	,0153878	,000	,240979	,367021
	DMSO_t2	,3390000*	,0153878	,000	,275979	,402021
	Res20_t2	,4966667*	,0172041	,000	,426207	,567126
	Cis05_t2	,4656667*	,0153878	,000	,402646	,528687
	CisRes_t2	,5063333*	,0153878	,000	,443313	,569354
	Fu05_t2	,4336667*	,0153878	,000	,370646	,496687
	FuRes_t2	,3986667*	,0153878	,000	,335646	,461687
	Control_t3	,0216667	,0172041	1,000	-,048793	,092126
	Res20_t3	,4423333*	,0153878	,000	,379313	,505354
	Cis05_t3	,3710000*	,0153878	,000	,307979	,434021
	CisRes_t3	,5130000*	,0153878	,000	,449979	,576021
	Fu05_t3	,3651667*	,0172041	,000	,294707	,435626
	FuRes_t3	,4946667*	,0172041	,000	,424207	,565126
Res20_t3	Contro_t0	,1720833*	,0143940	,000	,113133	,231034
	DMSO_t0	,1720833*	,0143940	,000	,113133	,231034
	Res20_t0	,1720833*	,0143940	,000	,113133	,231034
	Cis05_t0	,1720833*	,0143940	,000	,113133	,231034
	CisRes_t0	,1720833*	,0143940	,000	,113133	,231034
	Fu05_t0	,1720833*	,0143940	,000	,113133	,231034
	FuRes_t0	,1720833*	,0143940	,000	,113133	,231034
	Contro_t1	,1283333*	,0153878	,000	,065313	,191354
	DMSO_t1	,1413333*	,0153878	,000	,078313	,204354
	Res20_t1	,1868333*	,0172041	,000	,116374	,257293
	Cis05_t1	,2116667*	,0153878	,000	,148646	,274687
	CisRes_t1	,2170000*	,0153878	,000	,153979	,280021
	Fu05_t1	,2263333*	,0153878	,000	,163313	,289354
	FuRes_t1	,1583333*	,0153878	,000	,095313	,221354
	Control_t2	-,1383333*	,0153878	,000	-,201354	-,075313
	DMSO_t2	-,1033333*	,0153878	,000	-,166354	-,040313
	Res20_t2	,0543333	,0172041	,953	-,016126	,124793
	Cis05_t2	,0233333	,0153878	1,000	-,039687	,086354
	CisRes_t2	,0640000*	,0153878	,040	,000979	,127021
	Fu05_t2	-,0086667	,0153878	1,000	-,071687	,054354
	FuRes_t2	-,0436667	,0153878	1,000	-,106687	,019354
	Control_t3	-,4206667*	,0172041	,000	-,491126	-,350207
	DMSO_t3	-,4423333*	,0153878	,000	-,505354	-,379313
	Cis05_t3	-,0713333*	,0153878	,008	-,134354	-,008313
	CisRes_t3	,0706667*	,0153878	,009	,007646	,133687
	Fu05_t3	-,0771667*	,0172041	,013	-,147626	-,006707
	FuRes_t3	,0523333	,0172041	1,000	-,018126	,122793
Cis05_t3	Contro_t0	,2434167*	,0143940	,000	,184466	,302367
	DMSO_t0	,2434167*	,0143940	,000	,184466	,302367
	Res20_t0	,2434167*	,0143940	,000	,184466	,302367

	Cis05_t0	,2434167*	,0143940	,000	,184466	,302367
	CisRes_t0	,2434167*	,0143940	,000	,184466	,302367
	Fu05_t0	,2434167*	,0143940	,000	,184466	,302367
	FuRes_t0	,2434167*	,0143940	,000	,184466	,302367
	Contro_t1	,1996667*	,0153878	,000	,136646	,262687
	DMSO_t1	,2126667*	,0153878	,000	,149646	,275687
	Res20_t1	,2581667*	,0172041	,000	,187707	,328626
	Cis05_t1	,2830000*	,0153878	,000	,219979	,346021
	CisRes_t1	,2883333*	,0153878	,000	,225313	,351354
	Fu05_t1	,2976667*	,0153878	,000	,234646	,360687
	FuRes_t1	,2296667*	,0153878	,000	,166646	,292687
	Control_t2	-,0670000*	,0153878	,021	-,130021	-,003979
	DMSO_t2	-,0320000	,0153878	1,000	-,095021	,031021
	Res20_t2	,1256667*	,0172041	,000	,055207	,196126
	Cis05_t2	,0946667*	,0153878	,000	,031646	,157687
	CisRes_t2	,1353333*	,0153878	,000	,072313	,198354
	Fu05_t2	,0626667	,0153878	,054	-,000354	,125687
	FuRes_t2	,0276667	,0153878	1,000	-,035354	,090687
	Control_t3	-,3493333*	,0172041	,000	-,419793	-,278874
	DMSO_t3	-,3710000*	,0153878	,000	-,434021	-,307979
	Res20_t3	,0713333*	,0153878	,008	,008313	,134354
	CisRes_t3	,1420000*	,0153878	,000	,078979	,205021
	Fu05_t3	-,0058333	,0172041	1,000	-,076293	,064626
	FuRes_t3	,1236667*	,0172041	,000	,053207	,194126
CisRes_t3	Contro_t0	,1014167*	,0143940	,000	,042466	,160367
	DMSO_t0	,1014167*	,0143940	,000	,042466	,160367
	Res20_t0	,1014167*	,0143940	,000	,042466	,160367
	Cis05_t0	,1014167*	,0143940	,000	,042466	,160367
	CisRes_t0	,1014167*	,0143940	,000	,042466	,160367
	Fu05_t0	,1014167*	,0143940	,000	,042466	,160367
	FuRes_t0	,1014167*	,0143940	,000	,042466	,160367
	Contro_t1	,0576667	,0153878	,156	-,005354	,120687
	DMSO_t1	,0706667*	,0153878	,009	,007646	,133687
	Res20_t1	,1161667*	,0172041	,000	,045707	,186626
	Cis05_t1	,1410000*	,0153878	,000	,077979	,204021
	CisRes_t1	,1463333*	,0153878	,000	,083313	,209354
	Fu05_t1	,1556667*	,0153878	,000	,092646	,218687
	FuRes_t1	,0876667*	,0153878	,000	,024646	,150687
	Control_t2	-,2090000*	,0153878	,000	-,272021	-,145979
	DMSO_t2	-,1740000*	,0153878	,000	-,237021	-,110979
	Res20_t2	-,0163333	,0172041	1,000	-,086793	,054126
	Cis05_t2	-,0473333	,0153878	1,000	-,110354	,015687
	CisRes_t2	-,0066667	,0153878	1,000	-,069687	,056354
	Fu05_t2	-,0793333*	,0153878	,001	-,142354	-,016313
	FuRes_t2	-,1143333*	,0153878	,000	-,177354	-,051313
	Control_t3	-,4913333*	,0172041	,000	-,561793	-,420874
	DMSO_t3	-,5130000*	,0153878	,000	-,576021	-,449979

	Res20_t3	-,0706667*	,0153878	,009	-,133687	-,007646
	Cis05_t3	-,1420000*	,0153878	,000	-,205021	-,078979
	Fu05_t3	-,1478333*	,0172041	,000	-,218293	-,077374
	FuRes_t3	-,0183333	,0172041	1,000	-,088793	,052126
Fu05_t3	Contro_t0	,2492500*	,0163212	,000	,182407	,316093
	DMSO_t0	,2492500*	,0163212	,000	,182407	,316093
	Res20_t0	,2492500*	,0163212	,000	,182407	,316093
	Cis05_t0	,2492500*	,0163212	,000	,182407	,316093
	CisRes_t0	,2492500*	,0163212	,000	,182407	,316093
	Fu05_t0	,2492500*	,0163212	,000	,182407	,316093
	FuRes_t0	,2492500*	,0163212	,000	,182407	,316093
	Contro_t1	,2055000*	,0172041	,000	,135041	,275959
	DMSO_t1	,2185000*	,0172041	,000	,148041	,288959
	Res20_t1	,2640000*	,0188461	,000	,186816	,341184
	Cis05_t1	,2888333*	,0172041	,000	,218374	,359293
	CisRes_t1	,2941667*	,0172041	,000	,223707	,364626
	Fu05_t1	,3035000*	,0172041	,000	,233041	,373959
	FuRes_t1	,2355000*	,0172041	,000	,165041	,305959
	Control_t2	-,0611667	,0172041	,287	-,131626	,009293
	DMSO_t2	-,0261667	,0172041	1,000	-,096626	,044293
	Res20_t2	,1315000*	,0188461	,000	,054316	,208684
	Cis05_t2	,1005000*	,0172041	,000	,030041	,170959
	CisRes_t2	,1411667*	,0172041	,000	,070707	,211626
	Fu05_t2	,0685000	,0172041	,073	-,001959	,138959
	FuRes_t2	,0335000	,0172041	1,000	-,036959	,103959
	Control_t3	-,3435000*	,0188461	,000	-,420684	-,266316
	DMSO_t3	-,3651667*	,0172041	,000	-,435626	-,294707
	Res20_t3	,0771667*	,0172041	,013	,006707	,147626
	Cis05_t3	,0058333	,0172041	1,000	-,064626	,076293
	CisRes_t3	,1478333*	,0172041	,000	,077374	,218293
	FuRes_t3	,1295000*	,0188461	,000	,052316	,206684
FuRes_t3	Contro_t0	,1197500*	,0163212	,000	,052907	,186593
	DMSO_t0	,1197500*	,0163212	,000	,052907	,186593
	Res20_t0	,1197500*	,0163212	,000	,052907	,186593
	Cis05_t0	,1197500*	,0163212	,000	,052907	,186593
	CisRes_t0	,1197500*	,0163212	,000	,052907	,186593
	Fu05_t0	,1197500*	,0163212	,000	,052907	,186593
	FuRes_t0	,1197500*	,0163212	,000	,052907	,186593
	Contro_t1	,0760000*	,0172041	,017	,005541	,146459
	DMSO_t1	,0890000*	,0172041	,001	,018541	,159459
	Res20_t1	,1345000*	,0188461	,000	,057316	,211684
	Cis05_t1	,1593333*	,0172041	,000	,088874	,229793
	CisRes_t1	,1646667*	,0172041	,000	,094207	,235126
	Fu05_t1	,1740000*	,0172041	,000	,103541	,244459
	FuRes_t1	,1060000*	,0172041	,000	,035541	,176459

Control_t2	-,1906667*	,0172041	,000	-,261126	-,120207
DMSO_t2	-,1556667*	,0172041	,000	-,226126	-,085207
Res20_t2	,0020000	,0188461	1,000	-,075184	,079184
Cis05_t2	-,0290000	,0172041	1,000	-,099459	,041459
CisRes_t2	,0116667	,0172041	1,000	-,058793	,082126
Fu05_t2	-,0610000	,0172041	,296	-,131459	,009459
FuRes_t2	-,0960000*	,0172041	,000	-,166459	-,025541
Control_t3	-,4730000*	,0188461	,000	-,550184	-,395816
DMSO_t3	-,4946667*	,0172041	,000	-,565126	-,424207
Res20_t3	-,0523333	,0172041	1,000	-,122793	,018126
Cis05_t3	-,1236667*	,0172041	,000	-,194126	-,053207
CisRes_t3	,0183333	,0172041	1,000	-,052126	,088793
Fu05_t3	-,1295000*	,0188461	,000	-,206684	-,052316

*. La differenza media è significativa al livello 0.05

4. Conclusion

The present study was performed to evaluate the role of Resveratrol in overcoming oral squamous cancer cell resistance to Cisplatin and 5-Fluoruracil. The study was performed on two cell lines, HSC-3 and SAS, both from human tongue squamous cell carcinoma poorly differentiated. The two lines were selected after evaluation of their basic carcinogenic characteristics. From the results of the MTT-assay, Resveratrol showed to be more effective in reducing cell viability in HSC-3 cell line than in SAS. The different response to treatment is probably due to a different expression of tumor suppressor genes or oncogenes in the two different cell lines.

Therefore further analysis are required to clarify these results.

The efficacy of Resveratrol in reducing cell viability appears to be strongly related with time of incubation. The efficacy is greater at 72 hours than at 24 and 48 hours.

In conclusion further *in vivo* studies are necessary to evaluate the efficacy of Resveratrol in reducing cell viability via both topical or intravenous administration.

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Appendix 1: Publications

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[2020]

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[2020]

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[2020]

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Appendix 2: Congress Presentations

- 1 Evaluation of *Echinophora tenuifolia* L. Extracts on HSC-2 Cell Line Arena C, Vairano M, Mascitti M, Santarelli A, Dioguardi M and Zhurakivska K

Presented at the XV National and III International Congress of the Italian Society of Oral Pathology and Medicine (SIPMO), Bari, Italy, 17–19 October 2019.

- 2 TIMELESS in Head and Neck Squamous Cell Carcinoma: A Systematic Review Saracino P, Arena C, Mascitti M, Santarelli A, Panzarella V and Lo Russo L Presented at the XV National and III International Congress of the Italian Society of Oral Pathology and Medicine (SIPMO), Bari, Italy, 17–19 October 2019.

- 3 The tumor/stroma ratio as an independent prognostic factor in patients with carcinoma of the tongue Troiano G, Mascitti M, Arena C, Testa N.F, Procaccini M, Santarelli A, Lo Muzio L
JOURNAL OF OSSEOINTEGRATION ABSTRACTS OF POSTER PRESENTATIONS -
XXVI CONGRESSO NAZIONALE CDUO

- 4 MRONJ: an 8-year retrospective study of 100 cases in a single specialist oral surgery unit
Zavaglia V, Nori A, Mazzoni F, Troiano G, Arena C, Mascitti M, Procaccini M, Santarelli A.
JOURNAL OF OSSEOINTEGRATION ABSTRACTS OF POSTER PRESENTATIONS -
XXVI CONGRESSO NAZIONALE CDUO

- 5 Bioinformatics analysis of TP53 gene in head and neck squamous cell carcinoma patients from the cancer genome atlas V. C. A. Caponio, K. Zhurakivska, C. Arena, M. Mascitti, A. Santarelli, R. Mauceri, G. Campisi, L.Lo Muzio
JOURNAL OF OSSEOINTEGRATION ABSTRACTS OF
POSTER PRESENTATIONS - XXVI CONGRESSO NAZIONALE CDUO

- 6 Principal adverse events due to everolimus therapy. A systematic review of the literature C.Arena, V. C. A.Caponio, I.Adipietro, M. Mascitti, A.Santarelli, V. Panzarella, G. Campisi, L. Lo Muzio
Italy
JOURNAL OF OSSEOINTEGRATION ABSTRACTS OF POSTER PRESENTATIONS -
XXVI CONGRESSO NAZIONALE CDUO

- 7 Osteonecrosis of the jaw prevention in oncological patients: preliminary results from a teledentistry sicilian project R. Mauceri, V. Panzarella, C. Arena, G. Troiano, G. Oteri, F. Canepa, O. Di Fede, G. JOURNAL OF OSSEOINTEGRATION ABSTRACTS OF POSTER PRESENTATIONS - XXVI CONGRESSO NAZIONALE CDUO

- 8 Immunohistochemical expression of CD56 (NCAM) in odontogenic tumors Mascitti M, Togni L, Rubini C, Lo Muzio L, Zhurakivska K, Arena C, Procaccini M, Santarelli A JOURNAL OF OSSEOINTEGRATION ATTI DEL CONGRESSO CONGRESSO NAZIONALE COLLEGIO DEI DOCENTI UNIVERSITARI DI DISCIPLINE ODONTOSTOMATOLOGICHE

- 9 Stomatitis and vR-TkI: a review of current literature in 4369 patients C. Arena , G. Campisi , V. Panzarella , M. Procaccini , K. Zhurakivska , G. Troiano , L. Lo Muzio MINERVA STOMATOLOGICA VOLUME 67 . SUPPL.1.No.2. APRIL 2018

- 10 Lynphoepithelial carcinoma in a HCv patient: a case report F. Torelli , G. Campisi , R. Mauceri , C. Arena , M. Mascitti , F. Bambini , A. Santarelli MINERVA STOMATOLOGICA VOLUME 67 . SUPPL.1.No.2. APRIL 2018

- 11 pD-11 expression in oral squamous cell carcinoma microenvironment and prognostic correlations V.C.A. Caponio , G. Troiano , M. Pace , G. Pannone , C. Arena , G. Campisi , L. Lo Muzio MINERVA STOMATOLOGICA VOLUME 67 . SUPPL.1.No.2. APRIL 2018

- 12 Oral health assessment in palliate patients: an exploratory preliminary survey V. Panzarella, G. Capocasale, C. Arena, G. Campisi, G. Peralta ANNALI DI STOMATOLOGIA 2017; Suppl. 1: 1-81

- 13 Oral stomatitis and mTOR inhibitors. A complete analysis of 21225 cases reported in literature C. Arena, M. Mascitti, G. Troiano, G. Campisi, L. Lo Muzio, Section Oral Medicine V. Margiotta, University of Palermo, Palermo, Italy ANNALI DI STOMATOLOGIA 2017; Suppl. 1: 1-81

- 14 Enrichment and characterization of cancer stem-like cells from an OSCC cell line Arena C., Dioguardi M., Giannatempo G., Capocasale G., Mastrangelo F., Lo Muzio L. JOURNAL OF OSSEOINTEGRATION ; 9(1) ATTI DEL CONGRESSO CONGRESSO

NAZIONALE COLLEGIO DEI DOCENTI UNIVERSITARI DI DISCIPLINE
ODONTOSTOMATOLOGICHE

15 What is the best surgical approach for the treatment of solid/multicystic ameloblastoma?

C. Arena , L. Laino , G. Capocasale , V. Panzarella , G. Troiano , L. Lo Muzio

ATTI DEL CONGRESSO CONGRESSO NAZIONALE COLLEGIO DEI DOCENTI

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STOMATOLOGICA VOLUME 65 . SUPPL.1.NO. 3. JUNE 2016

Appendix 3: Awards

- **IL RUOLO PROGNOSTICO DELL'INVASIONE PERINEURAL NEI PAZIENTI AFFETTI DA CARCINOMA SQUAMOCELLULARE DELLA LINGUA** Lucrezia Togni Marco Mascitti, Piermichele Saracino, Lorenzo Lo Muzio, Olga Di Fede, Claudia Arena, Maurizio Procaccini, Andrea Santarelli XXVII Congresso Nazionale Dei docenti universitari di Discipline Odontostomatologiche [2020] Miglior Poster
- **THE TUMOR/STROMA RATIO AS AN INDEPENDENT PROGNOSTIC FACTOR IN PATIENTS WITH CARCINOMA OF THE TONGUE** Troiano Giuseppe, Mascitti Marco, Arena Claudia, Testa Nunzio Francesco, Procaccini Maurizio, Santarelli Andrea, Lo Muzio Lorenzo XXVI Congresso Nazionale Dei docenti universitari di Discipline Odontostomatologiche Menzione D'Onore
- **BIOINFORMATICS ANALYSIS OF TP53 GENE IN HEAD AND NECK SQUAMOUS CELL CARCINOMA PATIENTS FROM THE CANCER GENOME ATLAS** Vito Carlo Alberto Caponio, Khrystyna Zhurakivska, Claudia Arena, Marco Mascitti, Andrea Santarelli, Rodolfo Mauceri, Giuseppina Campisi, Lorenzo Lo Muzio XXVI Congresso Nazionale Dei docenti universitari di Discipline Odontostomatologiche Miglior Poster
- **ENRICHMENT AND CHARACTERIZATION OF CANCER STEM-LIKE CELLS FROM AN OSCC CELL LINE** Arena Claudia, Dioguardi Mario, Giannatempo Giovanni, Capocasale Giorgia, Mastrangelo Filiberto, Lo Muzio Lorenzo XXIV Congresso Nazionale Collegio Dei Docenti Universitari Di Discipline Odontostomatologiche [2017]

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