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PS179

Human papillomavirus in the etiology of oropharyngeal carcinoma



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Aim: The aim of this retrospective survey was to investigate the association of HPV status in patients with oropharyngeal cancer with tumour staging and other clinical features.

Introduction: Infection by human papillomavirus (HPV) stands for the most frequent viral carcinogenesis in the world. Overexpression of cell oncoprotein p16 is routinely diagnosed by immunohistochemistry (IHC) as the surrogate marker of viral activity.

Methods: Records from the oropharyngeal cancer patients treated in the Department of Otorhinolaryngology-Head and Neck Surgery in Bratislava from January 2013 to December 2016 were retrospectively analysed. Patients were divided, according to IHC results on oncoprotein p16, into p16 positive, considered HPV-positive, and p16 negative as HPV-negative. The incidence of oropharyngeal carcinoma, location, T and N staging, age, gender of patients was compared based on HPV status.

Results: From 129 oropharyngeal cancer patients with p16 examination were 52 (40%) considered as HPV positive. HPV positive group consisted of 45 (86.5%) men and 7 (13.5%) women. The primary tumour in HPV-positive patients originated from the palatine tonsil and base of the tongue in 96% of cases. The peak of occurrence of HPV-associated carcinoma was found between 50 and 59 years of age. HPV positive tumours were diagnosed in early T stage (T1/2) in 52%. Both HPV positive and negative patients were predominantly diagnosed with advanced-stage cancer, 90.4% in HPV-positive and 87% in HPV-negative group.

Conclusion: Early T stage in HPV positive carcinomas was approved, as well as more advanced regional spreading and prevalence of men and non-smokers. Wide variations in numbers of diagnosed patients during years of study may be caused by relatively small size of the studied group. Survey is focusing at HPV status as the most important prognostic factor in oropharyngeal cancer and systematized introduction of HPV status examination as progressive approach to effective and targeted therapy.

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PS181

The effects of cannabinoids in exemestane-resistant breast cancer cells



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Aim: Considering that the development of resistance is the main reason for endocrine treatment failure, our group decided to explore the ability of three cannabinoids, Δ^9 -tetrahydrocannabinol (THC), cannabidiol (CBD) and anandamide (AEA), to reverse resistance to exemestane. The THC and CBD are phytocannabinoids derived from the plant *Cannabis sativa* (marijuana) whereas AEA is an endocannabinoid. For that, it was used LTEDaro cells, a long-term estrogen deprived ER+ breast cancer cell line that mimics resistance to exemestane.¹ These cells were treated with exemestane in combination with two phytocannabinoids, CBD and THC, and the endocannabinoid AEA.

Introduction: Exemestane is one of the aromatase inhibitors (AI) used as first line treatment for estrogen-receptor positive breast cancer in post-menopausal women. Exemestane acts by inhibiting aromatase, the enzyme responsible for the conversion of androgens to estrogens² and also by promoting apoptosis of breast cancer cells.³ Nevertheless, despite its therapeutic success, this AI, after prolonged treatment, can induce acquired resistance, which causes tumor relapse. Therefore, it is important to find new strategies to overcome resistance in order to improve breast cancer treatment.

Methods: The presence of CB1 and CB2 in LTEDaro cells was confirmed by Western blot analysis and the effects of the combination of cannabinoids with exemestane were evaluated by MTT and LDH assays. Cell morphology was analyzed by Giemsa and Hoechst staining.

Results: Our results demonstrate that all the cannabinoids induce a decrease in viability of exemestane-resistant cells, in a dose- and time-dependent manner, without LDH release. These results indicate that the studied cannabinoids, mainly THC and AEA, revert the resistance to exemestane, probably by inducing apoptosis, as observed in Giemsa/Hoechst stain by the presence of typical morphological features of apoptosis.

Conclusion: This study highlights the efficacy of using cannabinoids as a potential adjuvant treatment to revert resistance to AIs.

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PS184

Quantitative structure-property relationship (QSPR) of thiazolidin-4-one derivatives as RTIs of HIV virus

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Aim: The aim of this study is to build a quantitative structure-property relationship (QSPR) of 66 thiazolidin-4-one derivatives in order to predict their log P.

Introduction: Performing computational drug design is an important step for their synthesis and properties characterizations. In this work, quantitative structure-property relationship (QSPR) of 66 thiazolidin-4-one derivatives was examined in order to predict their logP which is the most commonly used measure of lipophilicity in chemical molecules. These group of compounds act as non-nucleoside reversed transcriptase inhibitors of HIV.

Methods: Two different quantum mechanics approaches including HF and DFT were applied for energy minimization of structures and different classes of molecular descriptors including quantum chemical descriptors were generated for prediction of their LogP. Numbers of descriptors which showed high correlation with each other were removed by MATLAB software. The model between structures and their LogP was built for both methods with performing Multiple Linear Regression (MLR) in Spss package

Results: Statistical results and application of developed model to the test set demonstrates that the DFT model is reliable with good predictive accuracy. ($R^2_{cal} = 0.90$, $R^2_{cv} = 0.88$) The lack of significant difference between the original and modeled values of logP reveals the validity of the built model which was built with 2D and 3D descriptors. The coefficients of model are statistically significant.

Conclusion: QSPR models can be used to predict molecular properties such as LogP. That will be beneficial in drug design processes. In this research, MLR model was built in order to correlate structure of 66 compounds with their LogP. Molecules that were optimized by DFT method showed better correlation than HF method that indicates the accuracy of the built model with 2D and 3D descriptors.

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PS185

Lung branching morphogenesis, in the chicken model, is accompanied by temporal metabolic changes



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Aim: In this work, we characterized, for the first time, the metabolic profile of chick lung branching in early stages of development: b1, b2 and b3 (1, 2 or 3 secondary bronchi, respectively).

Introduction: Pulmonary development is a complex process that depends on the activation of conserved signaling pathways that regulate cellular processes such as proliferation, differentiation and migration.^{1–3} These cellular processes require high amounts of energy and nutrients to form new biomass.^{4,5} However, the metabolic changes that occur during lung branching morphogenesis have not been described so far.

Methods: Ex vivo lung explant culture was performed and the medium collected to analyze the production/consumption of metabolic intermediates associated with glucose catabolism (lactate, acetate, alanine), by 1H-NMR. qPCR was performed to assess the expression levels of key enzymes and transporters from the correspondent metabolic pathways.

Results: The results showed that the major variations occur from stage b1 to stage b3. In b3 there is an increase in lactate and acetate production. Still, glucose consumption is maintained from b1 to b3 stage, with a concurrent decrease of glucose transporter 3 (glut3) transcript levels. Hexokinase 1 (hk1) levels also decrease in b3 stage (as compared to b2). This phenomenon suggests an increase in the glycolytic efficiency and a shift to lactic acid production (in detriment of mitochondrial respiration). In fact, we observed a decrease on pyruvate dehydrogenase B (pdhB) and an increase in lactate dehydrogenase A (ldhA) expression levels in b3 stage (as compared to b2), while lactate dehydrogenase B (ldhB) levels decrease.

Conclusion: This study describes, for the first time, the temporal metabolic changes associated with chick pulmonary branching. It seems that glycolytic efficiency is increased and Krebs cycle metabolism shifts to lactate production along development. Furthermore, acetate and lactate are potentially seen as metabolic biomarkers of lung development.