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ABSTRACT BOOK

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LEVELS OF MOLECULAR CHAPERONES ON TUMOR AND NORMAL SAMPLES OF TRUE VOCAL CORDS

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Laryngeal squamous cell carcinoma represents 4.5% of all malignancies and is the most common type of head and neck cancer in male subjects. Tumor biology, clinical behavior, and prognosis differ based on their location: glottis, supraglottis, or subglottis region. Between 85% and 95% of laryngeal cancer is squamous cell carcinoma. In the United States, approximately 13,150 cases of laryngeal cancer were diagnosed in 2018, resulting in roughly 3710 deaths. The male-to-female incidence ratio is 3.9:1 for laryngeal cancer. Tobacco and alcohol use are the two primary risk factors for cancer of the larynx. The risk is proportional to the intensity and duration of tobacco or alcohol consumption, and the risk decreases slowly after cessation. It takes 15 years to return to baseline risk levels. Consequently, the clinical treatments vary according to location and the stage of the disease. Organ preservation strategies are based on several operative techniques such as radiotherapy, transoral laser microsurgery (TLM), and open horizontal partial laryngectomy to definitive surgery (total laryngectomy). Surgical treatment, whether carried out for diagnostic or therapeutic purposes, provides essential information about the biology of the tumor and the patient's course of treatment. The correct histological classification of the neoplasm and accurate knowledge of the tumour's biology is relevant. Several studies have shown that heat shock proteins (HSPs) can be associated as prognostic markers in specific carcinomas. The objective posed in this experimental study is to evaluate the localization and tissue levels of Heat Shock Protein 10, 27, 60, and 90 at three different pathophysiological moments of the vocal cord carcinogenic process: healthy mucosa, mucosa with moderate-grade dysplasia, and squamous cell carcinoma, by immunohistochemistry techniques. Through the preliminary data obtained by immunohistochemical experiments, we can attribute to Hsps a possible role in the process of vocal cord oncogenesis. These molecular chaperones are found to be increased and displaced within the tumor cell compared with their physiological location in healthy tissue.

HEPATIC ALTERATIONS IN THE MOUSE MODEL OF AUTISM SPECTRUM DISORDERS: A POSSIBLE IMPROVEMENT WITH MELATONIN

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The role of the liver in autism spectrum disorders (ASD), a neurodevelopmental disease characterized by impairments in social interactions and repetitive or stereotyped behaviors, has been poorly investigated. In ASD, it has been shown a dysregulation of gut-brain crosstalk, a communication system that can influence metabolic homeostasis, as well as brain development, mood, and cognitive functions [1]. Additionally, redox imbalance and oxidative stress seems to play a critical role in ASD pathophysiology [2]. The liver is a central vital organ that helps to regulate vital events and to detect and destroy pathogens that enter the organism throughout the intestines. Based on the above, this study aims to explore the pathophysiology of ASD in liver open the way for new therapeutic strategies. We used as autistic model BTBR T+Itpr3tf/J mice (or BTBR mice) treated and not treated by melatonin, an indolamine that has many important functions [3]. The control group shows a normal liver morphology; the hepatocytes display central nucleus with a regular shape and cytoplasm with a diffuse localization of glycogen in the cytoplasm of the same cells. On the contrary, even if the hepatic cytoarchitecture is preserved, hepatocytes of BTBR mice show many intracellular vacuoles and very low presence of glycogen droplets. In BTBR mice treated with melatonin the number of vacuoles appears to be reduced. We analyzed oxidative stress by immunohistochemical evaluation of oxidative and pro-inflammatory markers, such as HO-1 and IL-1β, and observed variation in the expression of these markers among the different groups of mice studied. Evidence from morphological and immunohistochemical analysis confirmed liver involvement in autism spectrum disorders and showed a possible beneficial role of melatonin in the ameliorating autism-induced liver alterations in mice.

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EFFECTS OF A PSORIATIC INFLAMMATORY MICROENVIRONMENT ON KERATINOCYTE MORPHOLOGY IN 3D AND 2D BIOLOGICAL EXPERIMENTAL MODELS OF NORMAL HUMAN SKIN

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The interplay between proinflammatory circulating cytokines and keratinocytes is a crucial event in the development and progression of psoriatic lesions. However, the early phases of the pathogenesis of psoriasis are still to be elucidated, in particular regarding the epidermal barrier. A pivotal role is played by tight junctions (TJs), *i.e.* claudin-mediated intercellular attachment structures, localized in the upper granular layer. A barrier impairment associated to an alteration in TJ proteins is described in psoriasis as a response to a proinflammatory microenvironment. We investigated by immunofluorescence analysis the modulation of the expression of claudin 1 (CLDN-1), a transmembrane integral TJ protein, and of Zonula Occludens 1 (ZO-1), a scaffold plaque protein, after the incubation with MIX, a combination of interleukin (IL)-17, IL-22, IL-23, tumor necrosis factor (TNF)-alpha, for 24 (T24) and 48 (T48) hours. We considered as experimental models the standardized 3D organotypic cultures of normal human skin (n=7) and *in vitro* cultures of primary normal human keratinocytes (n=3) in basal or differentiating cell growth conditions. On skin bioptic samples, ultrastructural analysis by transmission electron microscopy (TEM) was performed. In control skin samples, CLDN-1 immunopositivity increased from the basal layer upwards, but its expression was early reduced in the basal and suprabasal layers starting from T24 in MIX-incubated group. At this time point, ZO-1 expression in control samples increased gradually, starting from the basal layers towards the epidermal surface and the incubation with MIX induced its immunopositivity in the basal and suprabasal layers. At T24, CLDN-1 expression was unaffected by MIX in undifferentiated and also calcium- differentiated keratinocytes. Unexpectedly, undifferentiated cells relocated ZO-1 at cell-cell contact points after the incubation with MIX, and in calcium-differentiated keratinocytes, ZO-1 synthesis was stimulated, too. By TEM, after MIX incubation, the overall architecture of the epidermal compartment was maintained, but apoptosis and enlargement of intercellular spaces were evident. The present results strongly suggest that the i) broadening of ZO-1 expression and ii) the downregulation of CLDN-1, typical features of psoriasis, can be induced as early as 24 hours in both models, suggesting that they represent a valid experimental approach. To complete this study, the effect of this microenvironment on keratinocyte proliferation and differentiation will be investigated, obtaining further insights into the early processes leading to the formation/progression of psoriatic plaques.

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ANTI-INFLAMMATORY ACTIVITY OF *Diospyros digyna* JACQ. FRUIT EXTRSCTS IN AN *IN VITRO* MODEL OF INTESTINAL INFLAMMATION

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Diospyros digyna Jacq. is a tropical fruit tree native to Mexico. Although it is almost completely unknown in Europe, recently, its cultivation has been successfully tested in the Mediterranean area, including Sicily. Its fruit, due to a peculiar soft and dark chocolate pulp, is called black persimmon or chocolate pudding fruit and some studies suggested that it possess an interesting nutritional and nutraceutical value (1). We previously demonstrated that black persimmon is a rich source of bioactive compounds, peculiarly distributed in the different parts of the fruit, showing notable radical scavenging and metal-reducing activity and ability to prevent oxidative damage in cells (2). Nowadays, the role of oxidative stress in human diseases is well demonstrated. In particular, several experimental data indicate that cellular oxidative damage is involved in etiology and progression of several chronic diseases, including cancer and inflammatory diseases (3). In addition, epidemiological studies show that dietary intake of antioxidants can provide a significant protection against oxidative stress-related diseases. Here we evaluated the anti-inflammatory potential of different parts of *Diospyros digyna* fruit obtained from plants grown in Sicily. For our experiment we used an *in vitro* model of intestinal inflammation consisting of differentiated Caco-2 cell monolayers subjected to proinflammatory activity of IL-1b. qRT-PCR analysis demonstrated that cell exposure to extracts from pulp, seeds, and peel of black persimmon prevents, in a concentration-dependent manner, the IL-1b-induced up-regulation of the genes encoding the main proinflammatory mediators, including soluble ones (IL-8, IL-6, IL-12, and TNF-α) and proinflammatory enzymes (iNOS, and COX-2). On the other hand, results from western blot and ELISA analysis, showed that the observed transcriptional effects result in a reduced level of the corresponding proinflammatory proteins. Interestingly, black persimmon extracts produce opposite effects on the expression of the gene encoding the anti-inflammatory cytokine, IL-10. Finally, our results showed that the observed anti-inflammatory activity of the black sapote extracts is associated with positive effects on the expression of genes encoding the main antioxidant enzymes (Cu,ZnSOD, MnSOD, and GPx) suggesting that redox-sensitive signalling pathways could be involved in the anti-inflammatory activity of fruit components. Collectively, the obtained data showed for the first time that *Diospyros digyna* fruit components, at very low concentration, are active in attenuating the inflammatory response of intestinal epithelial cells suggesting local effects at the gut lumen useful for the physiology of the gastrointestinal tract.

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COMPLEX MAGNETIC FIELDS AS STORAGE OF INFORMATION AND PROCESSING OF BIOACTIVE RESPONSES

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From the scientific literature it is known that electromagnetic signals of a certain type significantly increase the tolerance to hypoxia in post-infarction patients, have strong angiogenic properties and strongly reduce the cardiovascular risk factor. To prove this feature, *in vivo, in vitro* and cohort tests were carried out with the aim of monitoring performance and cardiopulmonary function at the same time. The first trial set involved a total of 300 mice with the aim of monitoring performance and cardiopulmonary function at the same time. The Rotarod Performance Test is a bin test that uses a rotating cylinder to test the animals' ability to balance and move their legs in a coordi-