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ABSTRACT BOOK

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ity on epidermal keratinocytes. To evaluate cell proliferation, three hours before the end of the experiment, 5-bromo-2'-deoxyuridine (BrdU), a non-radioactive thymidine analogue selectively incorporated in DNA of S-phase cells, is added (400 µmol L^{-1}) to the culture medium. After 24, 48, and 72 hours of culture, samples are processed in parallel for histological examination by light and transmission electron microscopy. Indirect immunofluorescence analysis is performed on paraffin sections. BrdU incorporation is revealed using a monoclonal antibody and keratin 10 and 17 are considered as differentiation markers. We observed that IL-22 early impairs keratinocyte maturation as regarding keratin 10 expression, without affecting keratinocyte proliferation, highlighting its prevalent homeostatic role. On the other hand, the combination of the three cytokines induces a progressive and statistically significant decrease of keratinocyte proliferation at all considered time-points and no effects on cell differentiation are evident. The hypothesis herein advanced is that IL-22 profoundly affects keratinocyte terminal differentiation, whereas, in order to induce a proliferation impairment, a more complex psoriatic-like microenvironment should be present. As most of the data concerning IL-22 immunomodulating activity are obtained from mouse models, this work offers a new perspective on its clinical role. Further studies are needed in order to establish which clinical step better correlates with IL-22 increase in order to precisely tailor biological treatment.

MAP KINASES INVOLVEMENT IN STRESS SIGNALING DURING THE COLONIAL BLASTOGENETIC CYCLE OF *BOTRYLLUS SCHLOSSERI*

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Botryllus schlosseri is a colonial ascidian easily found in the Lagoon of Venice, which undergoes weekly generation changes called take-overs (TOs) [1]. A blastogenetic cycle is defined as the period between two successive TOs. During this phase, lasting 24-36 h, a diffuse apoptosis occurs in tissues of old zooids, which will be replaced by their primary buds representing the new generation [2]. An increase in oxygen consumption (respiratory burst) is observed, due to phagocytes removing apoptotic cells, which causes the production of reactive oxygen species (ROS) [3]. In order to protect the new zooid generation from ROS damages, these animals have evolved stress defense mechanisms, which imply the activation of anti-stress proteins through stress signaling transduction pathways, possible driven by mitogen-activated protein kinases (MAPKs). MAPKs are a family of highly conserved serine-threonine protein kinases important for the regulation of cell growth and differentiation and apoptosis [4]. With this study, through the use of specific inhibitors for Erk, JNK and p38, the three main MAPK subfamilies, directly microinjected in *Botryllus* circulation, we want to evaluate the importance of MAPKs in the regulation of the blastogenetic cycle both from a morphological and a molecular point of view. Differences in transcription levels of stress-related genes, *i.e.* superoxide dismutase (*sod*), glutathione synthase (*gs*), glutathione peroxidases (*gpxs*), tia-1 related nucleolysin (*tiar*) and tristetraprolin (*ttp*), have been evaluated by quantitative real time PCR (qRT-PCR). The last two genes are involved in the formation of stress granules, important cell foci involved in post-transcriptional control of stress-related genes [5].

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POTENTIALITY OF OXYGEN-OZONE THERAPY IN SKIN REGENERATION FOR TROPICAL DISEASES: PROTOCOL FOR THE TREATMENT OF BURULI ULCER

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If 2019 brings the signature of the medicine Nobel for "discovery of how cells sense oxygen", oxygen/ozone (O2-O3) therapy acquires a prestigious position. Indeed, if the low availability of O2 leads the cell to rise growth factors (*VEGF, Vascular Endothelial Growth Factor; PDGF, Platelet-derived growth factor; HIF, Hypoxia Inducible Factors*) genes expression, some papers demonstrated that O3 increases itself the levels of these factors, replacing the work of the cell. During regeneration processes, the mesenchymal stem cells release various paracrine factors that play key roles in mitogenesis, apoptosis, angiogenesis and scarring. Interestingly, several studies demonstrated the positive effect of O3 on Epidermal Growth Factor (EGF), Transforming Growth Factor α, β, Insulin Growth Factor (IGF-1), Fibroblast Growth Factor, Brain Derived Neurotrophic Factor increasing their levels. O3 treatment promotes the fibroblasts migration, increases the levels of collagen, α-smooth muscle actin αSMA), TGFβ and inhibits the inflammation in injured fibroblasts. Another important property of O3 is its anti-bacterial/virus/fungi activity. In relation to skin diseases, it has been demonstrated that O3 can have topic effects on the skin, producing an antioxidant response, blocking the pro-inflammatory pathway and promoting wound healing processes. Moreover, O3 can have systemic effects on platelet activity increasing the production of VEGF, PDGF and TGFβ. Particularly focusing on skin tropical diseases, we stipulated an official memorandum regarding the application of O2/O3 therapy for Buruli Ulcer (BU), one of the most widespread skin related neglected tropical diseases. As BU aetiology involves inflammatory-immune reactions that are equally implicated in the action mechanisms of O3, it is reasonable to speculate that the molecules underlying these mechanisms could represent potential therapeutic targets for the cure of this devastating skin tropical disease by O3 application, taking in consideration also its strong anti-bacterial activity. To this aim, we setup a nursery protocol for the implementation of the O2-O3 therapy in a center around Abidjian, in Cote d'Ivoire. By this procedure, it is possible to reduce the healing times, antiseptics, disinfectants, antibiotics, painkillers anti-inflammatories administration, limit the medications cost, use one device to treat up to 100 patients per day, reduce the reconstructive plastic surgery, minimum maintenance of the appliance, easy to apply and no negligible side effects. We believe that this therapy will represent a new therapeutic option capable of being easily used by local healthcare providers in the poorly assisted areas.

IMPACT OF CIGARETTE SMOKE ON INFLAMMASOME-DEPENDENT RESPONSES IN HUMAN LUNG FIBROBLASTS

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