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Angiosarcoma of the scalp with fatal outcome

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Angiosarcoma is a rare malignant tumor, accounting for only 1%-5% of all soft tissue sarcomas. It spread out from the endothelial cells of vessels. Cutaneous angiosarcoma is the most common presentation of this neoplasm, which affects the facial skin and scalp regions. Head and neck angiosarcoma is usually seen in people >60 years old. Patients generally describe pain and swelling at the primary lesion site. The pathology usually follow an aggressive course with progressive local extension and early metastasis. It is well known that this tumor frequently metastasizes to the lung, often including repeated neumothorax and/or hemothorax as a result of rupture of enlarged cystic tumors arising in the peripheral lung field. We describe a case of angiosarcoma in the scalp with lymph nodes, lung and liver metastasis at the moment of diagnosis. The highly progressive course of the disease caused the death of the patient in a few months. Previous reports have emphasized the poor prognosis of the disease. Some of them have indicated that multimodal treatments including surgery and radiotherapy were effective in improving overall survival for patients with these tumors, and the addition of chemotherapy and immunotherapy may further improve. However, effective treatment strategies have yet to be elucidated. The optimization of angiosarcoma treatment remains a future goal.

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Antiglycation effect of unique topical facial cream containing carnosine and alteromonas ferment extract in epidermis and dermis of human skin explants

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During aging, end-products of nonenzymatic reaction between sugar molecules and proteins accumulate in the skin. This accumulation of advanced glycation end-products (AGEs) results in loss of flexibility of dermal proteins constituting the extracellular matrix (ECM) and loss of skin suppleness. Carboxymethyl lysine (CML) and pentosidine (PD) are AGEs used as markers for glycation in the present skin. Methylglyoxal (MG) induce glycation in vitro.

Objective: To study effect of topical treatment with a face cream (FC) containing carnosine and alteromonas ferment extract (AFE) on AGE levels in human skin explants with MG-induced glycation.

Method: Human skin explants obtained from abdominoplasty were maintained in culture media over 9 days. Skin explants were divided into the following treatment groups: untreated control, MG-treated control and MG+FC-treated. MG-treated group received MG through culture media whereas FC was applied topically (2 $\mu g/cm^2$). At day 9 all tissues were harvested and processed for sectioning and immunohistochemistry for CML and PD using specific monoclonal antibodies. Image analysis of stained sections was conducted to determine the percentage of area positive for CML or PD. Antiglycation effect was mathematically calculated and expressed as percentage of change induced by MG inhibited by FC.

Results: CML results: CML staining was observed both in epidermis and dermis. MG treatment led to a significant increase in CML staining compared with untreated control group (31% and 413% increase in epidermis and dermis, respectively). The topical treatment with FC of MG-treated skin explants induced a 58% and 91% decrease in CML staining in the epidermis and dermis, respectively, compared with MG-treated control. PD results: MG treatment led to a significant increase in PD staining in epidermis and dermis by 37% and 41%, respectively. Topically applied FC was able to reduce this increase by 18% in the epidermis and 41% in the dermis. Antiglycation effect of FC was calculated to be 150% and 122% in epidermis and dermis, respectively for CML and 108% and 136% in epidermis and dermis, respectively, for PD.

Conclusion: FC containing carnosine and AFE inhibits or reverses the MG-induced formation of CML and PD in human skin explants in both epidermis and dermis after topical application during 9 days in an ex vivo study. This innovative FC may help prevent the appearance of signs related to the accumulation of AGE in the skin.

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Antiaging effects of retinoid hydroxypinacolone retinoate on skin models

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Tretinoin, also known as all-trans retinoic acid (ATRA), is well known for its antiaging effects on skin. However, skin irritation, photochemical instability, and concerns about toxicity have hindered the use of ATRA in cosmetic products. Typically, milder retinoid derivatives are used, which must first be metabolized to more active forms by several enzymatic steps in the skin, which reduces their potency. Therefore, it is desirable to find new molecules that have increased retinoic acid–like activity without the negative side-effects. Hydroxypinacolone retinoate (HPR), a cosmetic grade ester of ATRA, is unique in that it processes innate retinoic acid activity, binding directly with retinoid receptors without the need for metabolic breakdown to more biologically active forms. It has been demonstrated to be more stable and cause less skin irritation than retinol. Here, we compared levels of gene transcription by HPR, ATRA, retinol (Rol), retinaldehyde (Ral), and retinyl palmitate (RP) by evaluating binding of the retinoic acid receptor to retinoid acid responsive elements (RARE) in DNA using a RARE reporter assay. In addition, we compared the antiaging properties of HPR to ATRA by testing the effects on collagen levels and skin irritation in organotypic skin models. Skin models were treated for 5 days with three doses of HPR and ATRA; vehicle controls skins were treated with vehicle alone. Basal media was collected for procollagen and 1L-1α ELISA analysis. On day 5, skins were fixed, paraffin embedded, sectioned, and stained with Masson trichrome (for collagen). RARE assay results showed that HPR had greater levels of gene transcription than Rol, Ral, and RP at the same concentrations, and was less cytotoxic to cells at a 10 times higher concentration; however, HPR did not achieve gene transcription levels of ATRA. Procollagen ELISA results showed that skins treated with HPR significantly increased procollagen production compared with untreated control skins, and was similar to ATRA. Qualitative assessment of collagen levels from histologic staining of skins corroborated these results, with the highest dose of HPR out-performing ATRA. IL-1α ELISA analysis showed that HPR did not induce more (or less) inflammatory response than either ATRA or the vehicle control. Together these data suggest that HPR is an effective alternative to ATRA and other less potent retinoids in the treatment of aging skin without the detrimental side-effects.

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Anti–laminin-γ1-pemphigoid: A missing link between bullous pemphigoid and mucous membrane pemphigoid

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Background: Bullous pemphigoid (BP) predominantly involves the skin with autoantibodies targeting basement membrane zone (BMZ) antigens, BPAg1 and BPAg2. Mucous membrane pemphigoid (MMP) mostly affects the mucosal surfaces, about 25% have skin involvement as well. The target BMZ antigens are BPAg2, human $\alpha 6\beta 4$ integrins, and laminin 332. A subset of pemphigoid was described in 1996 called anti–p200 pemphigoid, now referred to as anti–laminin-γ1-pemphigoid. Sera of reported cases show autoantibodies against laminin-γ1.

Objective: To define a possible relationship among BP, MMP, and anti–laminin-γ1-pemphigoid.

Methods: Analysis of published cases of anti–laminin-γ1-pemphigoid for clinical features, treatment and clinical outcomes. Data included histopathology, direct and indirect immunofluorescence, ELISA, and immunoblot studies.

Discussion: Patients with anti–laminin-γ1-pemphigoid have tense cutaneous bullae similar to BP. These patients also resemble those with MMP with involvement of nasopharyngeal, oral, anogenital and conjunctival mucosa. The clinical difference between anti–laminin-γ1-pemphigoid and MMP is the lack of scarring in the former. Laminin γ1 is a member of a family of extracellular matrix glycoproteins that are major noncollagenous constituents of the lower lamina lucida. In anti–laminin-γ1-pemphigoid, indirect immunofluorescence (IIF) with salt split skin shows binding of antibody to the dermal side. This binding differentiates it from BP but not from patients with laminin 332 pemphigoid (subtype of MMP) whose sera also bind to the dermal side of the split. However, in anti–laminin-γ1-pemphigoid, there is absent binding to BPAg1/BPAg2 as well as to $\alpha 6\beta 4$/laminin 332 antigens on immunoblot analysis and by ELISA testing. Presence of autoantibodies to both the p200 antigen and laminin was demonstrated on immunoblot studies in one case report. Treatment options are comparable with those used in BP and MMP such as topical steroids, prednisone, dapsone, and occasionally intravenous immunoglobulin. Prognosis was favorable, because scarring was absent.

Conclusion: These observations indicate anti–laminin-γ1-pemphigoid have many features of both BP and MMP with overlap. The target antigen is molecularly distinct and lies between the target antigens of BP and MMP. This may represent the missing link between BP and MMP.

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