Subject: neues von der EHRS
Posted by tino on Sat, 21 Apr 2007 20:05:58 GMT
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Wieder mal einige Arbeiten die voll und ganz meine These untermauern.

Dort(insbesondere Abstract 1),bestaetigt sich genau das,was ich erstmalig schon vor langer Zeit auf meiner Seite beschrieben habe....

Irgendwo dort schwirrt auch eine kleine Studie über Roxithromicyn am Menschen rum.

. Role of reactive oxygen species (ROS) on androgen-inducible TGF-beta1 regulation of dermal papilla cells.
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Little is known about the roles of androgen on the regulation of redox state in the dermal papilla cells, a cellular process known to profoundly increase with aging. The androgen receptor (AR) has been reported to modulate TGF-beta1/Smad signaling and to be overexpressed in androgen-dependent scalp area of the patients with androgenetic alopecia. The rat vibrissae dermal papilla cell line (DP-6) overexpressed with AR was investigated to evaluate the role of ROS on androgen-induced increase of TGF-beta1 secretion. The AR stably-transfected DP-6 cells were incubated with R1881 or dihydrotestosterone (DHT). Flow cytometry and laser scanning confocal microscopy were undergone to measure ROS production and ELISA assay to evaluate TGF-beta1 secretion after androgen treatment. TGF-beta1 promoter activity assay was also performed whether to be influenced by pretreatment of ROS scavengers. Androgen markedly increased ROS generation and the androgen-inducible ROS augmented TGF-beta1 secretion from dermal papilla cells. Treatment with ROS scavenger or several species of inhibitors decreased ROS production and TGF-beta1 expression. Luciferase reporter assays showed suppression of TGF-beta1 promoter signaling by ROS scavengers. In conclusion, our study shows for the first time that androgen-induced TGF-beta1 accumulation in dermal papilla cells would be mediated by ROS production and prevented by antioxidants or ROS inhibitors.

Zwar shows for the first time,weil halt Nachweis per Experiment,..aber ganz sicher nicht aufgeschrieben weil klug gedacht for the first time...

7. Immortalisation and characterisation of balding and non-balding dermal papilla cell lines and their response to oxidative stress.
Adiam W Bahta, Dermatology (QMUL), London, UK

The dermal papilla (DP) expresses androgen receptors and is known to control normal hair growth. The paradox of androgen action in human hair growth is well established but the molecular mechanisms in hair follicles are poorly understood. DP cells derived from frontal (balding) human scalp hair follicles (BDPC) are used to study Androgenetic alopecia. However,

cultured BDPC are very difficult to obtain, grow very slowly in vitro and have a limited life span of 2-6 passages before they senescence (see other abstract). We have recently shown that BDPC express senescence-associated beta galactosidase activity at PH-6. Moreover, stress induced premature senescence was induced with more prominent characteristic behaviour in BDPC than non balding DPC (NBDPC) after exposure to sub-cytotoxic levels of H2O2. However, the limited life span of BDPC represents a substantial obstacle for biochemical analysis, genetic manipulation and screens. We therefore, generated immortalized balding and non-balding human DP cells (IBDPC, INBDPC) by ectopic expression of human telomerase. The IBDPC have undergone more than 90 passages without showing any phenotypic changes. As with the primary DPC, the IBDPC maintained their aggregating characteristics and expressed wnt7a, wnt3a, androgen receptor and 5 alpha reductase type 2 mRNA. We established an in vitro co-culture system by growing IBDPC and INBDPC with keratinocytes (KC) to study the androgen effects in hair follicles. Androgen suppressed the growth of KC when grown with IBDPC and this could be partially reversed using a neutralising antibody to TGF-beta1. In addition we have also observed that IBDPC retains increased sensitivity towards H2O2 than INBDPC cell lines. Therefore, immortalised DP cell lines show similar characteristics to primary DPC and they will be of major help to us in our attempt to understand the actions of androgens on hair growth and enable the development of better treatment for androgen dependent hair disorders.

6. Study of cell senescence in cultured primary balding and non-balding dermal papilla cells.
Adiam W Bahta, Dermatology (QMUL), London, UK

The dermal papilla (DP) expresses androgen receptors and is known to control normal hair growth. The paradox of androgen action in human hair growth is well established but the molecular mechanisms are poorly understood. DP cells derived from frontal (balding) human scalp hair follicles (BDPC) are used to study Androgenetic alopecia. Cultured BDPC are known to have a much slower rate of growth in vitro than DP from non balding sites (NBDPC), however, the cause of this has not been reported. In this study we have investigated the growth of human BDPC and NBDPC in vitro. We observed that BDPC have a limited life span of 2-6 passages. We observed that from passage 2 onwards BDPC but not NBDPC showed a large flattened morphology characteristic of senescent fibroblasts and that once they had assumed this morphology they could no longer be passaged. We showed that these BDPC but not NBDPC of the same passage expressed senescence-associated beta-galactosidase activity at PH-6. Moreover, stress induced premature senescence was induced with more prominent characteristic behaviour in BDPC than NBDPC after exposure to sub-cytotoxic levels of H2O2 a known inducer of oxidative stress. Finally BDPC also expressed a wide range of oxidative stress markers including HSP27, Super Oxide Dismutase and Catalase. These data suggest that the well documented, slower in vitro proliferative rate of BDPC is due in part to premature senescence. Moreover, our observation that cultured BDPC express markers of oxidative stress and their response to H2O2 suggest that oxidative stress may play a major role in male pattern hair loss. Others and we have observed that DHT is able to induce TGF-beta1 in BDPC. TGF-beta1 is known to induce oxidative stress and this may therefore, link androgens with oxidative stress and help explain the paradox of androgen action on hair growth.

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