Subject: Upregulationsthese
Posted by reinforcement on Mon, 16 Oct 2006 11:49:35 GMT
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Mir geht seid einiger Zeit diese These nicht mehr aus dem Kopf.

Haarausfall bemerkt man doch nicht so, dass man heute in den Spiegel schaut und sagt.....heut sind mit ein paar Haare ausgefallen.....morgen sagt man, mit ist ein bisschen mehr ausgefallen

sonder:
Man schaut immer nach geraumer Zeit etwas deutlicher in den Spiegel und plötzlich trifft einen der Blitz wie viel plötlzich ausgefallen ist!

So.....als der Haarausfall verläuft ja meißtens schleichend!

Jetzt nehmen wir an das die ganzen Medikamente die wir uns reinpfeifen es nur schaffen den Haarausfall zu verlangsamen.
Wenn man sonst sag ich mal alle 2 JAhre einen Norwood schritt macht.....macht man diesen schritt mit Fin oder dem anderen Zeugs in sag ich mal 6 Jahren.

Nach 6 Jahren schaut man erschrocken auf ein Bild das man von sich hatte, als man mit der Behandlung angefangen hat und bemerkt die rapide Veränderung! Obwohl die Veränderung ja schleichend kam!

Trozdem kommt man zu dem Schluss .....Finasterid kann nicht mehr wirken (weil man vorher falsch dachte, dass die Haare gehalten sind) und plötzlich sind sie ja weg!
Ich mein kaum einer hat eine Tonsur ja wachsen sehen.....die ist ja meißt plötzlich da und man weiß nicht woher die kam!
Und tata.....man baut einen riesen mist indem man auf was anderes setzt?

Obwohl ich das mit dem Körper anpassen irgendwie auch logisch finde! Ist halt die Frage wie rapide man plötzlich dann den Haarausfall hat!

Trozdem glaub ich das Upregulation aus den 2 Faktoren besteht!

Subject: Re: Upregulationsthese
Posted by fixt on Mon, 16 Oct 2006 13:00:28 GMT
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Ist relativ schwer zu sagen...natürlich nur Spekulationen. Was relativ sicher anzunehmen ist ist das man mit Finasterid in den meisten Fällen wohl die Haare nicht ewig halten kann(auch Leute ohne AGA verlieren über die Jahre Haare). Finasterid hemmt 70% des DHT und dieser Effekt wird NIE abgeschwächt. Mit den Rezeptoren ist das bekanntlich anders...diese nehmen wohl zu...bedenke aber bitte das die Studie mit den Rezeptoren nur einmalig nach etwa 6Monaten der Einnahme durchgeführt wurde. Ob die Rezeptoren später immer weiter zu nehmen ist absolut unbekannt. Ist natürlich möglich...andererseits die berechtigte Frage: Stellt der Körper sich auf eine veränderte Hormonlage wirklich so langsam um?Das er so langsam upreguliert das er

erst nach 6 Jahren die Umstellung vollzogen hat?

Dann gibt es die Vermutung das ja eine Alopezie in Schüben abläuft und Propecia diese Schübe deutlich abschwächt aber nicht bei allen vollständig abstellen kann. Deswegen denken vielleicht manche wenn sie nach einigen Jahren Finasterid von einem Schub erwischt werden das Fin nicht mehr wirkt. Alles ehr schwer zu sagen.

Die Meinungen gehen auseinander....Pilos hält die Upregulation für den hauptsächlichen Grund des Wirkungsverlustes(korrigier mich falls das nicht stimmt Pilos), andere Experten(z.B. einer aus den amerikanischen Foren hält die Upregulation für ziemlich bedeutungslos.

Bedenke bitte auch folgendes: Wenn jemand zu Therapiebeginn einen DHT-Spiegel von z.B. 95 (16-110) hat dann hat er mit Fin immer noch einen Spiegel von um die 30. Das heißt DHT ist immer noch im Umlauf. Aber es ist immer noch DHT da was die Haare schädigt.

Subject: Re: Upregulationsthese
Posted by fixt on Mon, 16 Oct 2006 13:07:17 GMT
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Bedenke noch etwas: Wie manche schon sagten Du wirst hier eher die Leute treffen bei denen es eher nicht super über mega lange Zeit wirkt. Die Frage ist wieviele Männer Propecia nehmen? Es gibt etwa 42millionen Männer in Deutschland. Davon vielleicht 12mill. unter 18Jahren und 18mill. über 50 Jahren.

Bleiben etwa 12mill. im Bereich 18-50 Jahren. Wenn von diesen auch nur 100000 Finasterid nehmen würden (entpricht weniger als 1%) wären wohl noch immer die meisten sehr zufrieden. Ich denke dieses Forum hat über die letzten 5Jahre oder so nicht viel mehr als 3000 user gehabt.

Subject: Re: Upregulationsthese
Posted by kkoo on Mon, 16 Oct 2006 14:10:31 GMT
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fixt schrieb am Mon, 16 Oktober 2006 15:00Mit den Rezeptoren ist das bekanntlich anders...diese nehmen wohl zu...bedenke aber bitte das die Studie mit den Rezeptoren nur einmalig nach etwa 6Monaten der Einnahme durchgeführt wurde. Ob die Rezeptoren später immer weiter zu nehmen ist absolut unbekannt....

fixt, hast du eine studie, wo man ersieht, dass die ARs zunehmen?

ich kenne nur eine, die die allgem. verteilung bei männl. u. weibl. unterscheidet, aber leider nicht altersabhängig unterscheidet:

Localization of androgen receptors in human skin by immunohistochemistry: implications for the

hormonal regulation of hair growth, sebaceous glands and sweat glands.
Choudhry R, Hodgins MB, Van der Kwast TH, Brinkmann AO, Boersma WJ.

Department of Dermatology, University of Glasgow, U.K.

A mouse monoclonal antibody against the N-terminal region of human androgen receptor (AR) was used to identify receptors by immunoperoxidase staining in frozen serial sections of skin from scalp, face, limb and genitalia of men and women aged 30-80 years. AR staining was restricted to cell nuclei. In sebaceous glands, AR were identified in basal and differentiating sebocytes. The percentage of receptor-positive basal sebocyte nuclei in the temple/forehead region was greater in males (65%) than in females (29%). AR staining was restricted to the cells of dermal papillae in anagen and telogen hair follicles. The percentage of dermal papillae containing AR was greater in males (58%) than in females (20%). The number of positively stained dermal papillae was lowest in female scalp skin. In 163 hair follicles sectioned, AR were absent from germinative matrix, outer root sheath (including the bulge region), inner root sheath, hair shaft and hair bulb, and from the capillaries present in some large dermal papillae. AR were present in pilosebaceous duct keratinocytes, suggesting that androgens may influence pilosebaceous duct keratinization. AR were also identified in interfollicular epidermal keratinocytes and dermal fibroblasts although, in both cell types, intensity and frequency of staining were greatest in genital skin. AR were identified in luminal epithelial cells of apocrine glands in genital skin and in certain cells of the secretory coils of eccrine sweat glands in all body sites. This study indicates that androgens regulate sebaceous gland and hair growth by acting upon two different types of target cells, the epithelial sebocytes of sebaceous glands and the mesenchymal cells of the hair follicle dermal papilla.

wobei die sebocyten anscheinend eine sonderrolle haben:

Sebocytes are the key regulators of androgen homeostasis in human skin.
Fritsch M, Orfanos CE, Zouboulis CC.

Department of Dermatology, University Medical Center Benjamin Franklin, The Free University of Berlin, Berlin, Germany.

The mRNA expression patterns of the androgen receptor and the androgen metabolizing enzymes 3beta-hydroxysteroid dehydrogenase/Delta(5-4)-isomerase, 17beta-hydroxysteroid dehydrogenase, 5alpha-reductase, and 3alpha-hydroxysteroid dehydrogenase were investigated in three different cell populations originating from human skin, SZ95 sebocytes, HaCaT keratinocytes, and MeWo melanoma cells, by means of reverse transcription polymerase chain reaction. Restriction analysis of cDNA fragments was performed to identify isozymes of 3beta-hydroxysteroid dehydrogenase/Delta(5-4)-isomerase and 3alpha-hydroxysteroid dehydrogenase. In addition, 3H-dihydroepiandrosterone and 3H-testosterone were used as substrates to determine the metabolic activity of these enzymes in SZ95 sebocytes, primary sebocyte cultures, and HaCaT keratinocytes. Furthermore, the effects of the selective 5alpha-reductase type 1 and 2 inhibitors, 4,7beta-dimethyl-4-aza-5alpha-cholestan-3-one and dihydrofinasteride, respectively, and of the 3beta-hydroxysteroid dehydrogenase/Delta(5-4)-isomerase inhibitor cyproterone acetate on androgen metabolism were investigated. Androgen receptor mRNA was detected in SZ95 sebocytes and HaCaT keratinocytes but not in MeWo melanoma cells, whereas 3beta-hydroxysteroid

dehydrogenase/Delta(5-4)-isomerase isotype 1 mRNA and metabolic activity were only found in SZ95 sebocytes. The enzyme activity could be inhibited by cyproterone acetate. Type 2 17beta-hydroxysteroid dehydrogenase, type 1 5alpha-reductase, and 3alpha-hydroxysteroid dehydrogenase mRNA were expressed in all three cell populations tested, whereas type 3 17beta-hydroxysteroid dehydrogenase mRNA could only be detected in SZ95 sebocytes. The major metabolic steps of testosterone in SZ95 sebocytes, primary sebocyte cultures, and HaCaT keratinocytes were its conversion to androstenedione by 17beta-hydroxysteroid dehydrogenase and further to 5alpha-androstanedione by 5alpha-reductase. The type 1 5alpha-reductase selective inhibitor 4,7beta-dimethyl-4-aza-5alpha-cholestan-3-one, but not the type 2 selective inhibitor dihydrofinasteride, inhibited 5alpha-reductase at low concentrations in SZ95 sebocytes and HaCaT keratinocytes. 5alpha-androstanedione was degraded to androsterone by 3alpha-hydroxysteroid dehydrogenase, which exhibited a stronger activity in HaCaT keratinocytes than in SZ95 sebocytes and in primary sebocyte cultures. Lower levels of 5alpha-dihydrotestosterone and 5alpha-androstanediol were also detected in all cells tested. Our investigations show that specific enzyme expression and activity in cultured sebocytes and keratinocytes seem to allocate different duties to these cells in vitro. Sebocytes are able to synthesize testosterone from adrenal precursors and to inactivate it in order to maintain androgen homeostasis, whereas keratinocytes are responsible for androgen degradation.

Subject: Re: Upregulationsthese
Posted by fixt on Mon, 16 Oct 2006 14:15:26 GMT
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ANDROGEN RESPONSIVE GENES AS THEY AFFECT HAIR GROWTH
Marty E. Sawaya, MD, PhD, ARATEC (Alopecia Research & Associated Technologies) Clinics & University of Miami School Medicine, Florida, USA.

Androgens have profound affects on scalp hair follicles causing growth inhibitory activity hence, miniaturization of hair follicles in the case of men with Androgenetic alopecia (AGA). In human scalp hair follicles, androgens are thought to be growth inhibitory, whereas on beard and body hair, androgens upregulate hair growth. The biochemical activity and immunohistochemical expression of 5a-reductase isoenzymes type I and II has been assessed in scalp of men with AGA, as well as the cytochrome P-450 aromatase enzyme, androgen receptor (AR), estrogen receptor (ER) alpha and beta. Studies in 10 men with AGA where scalp biopsies are obtained before and after 6 months treatment with finasteride (a specific type II 5a-reductase inhibitor) reveal interesting results with regard to the effects of suppressing DHT and how it affects these androgen associated factors. Differences in expression were found for some of the enzymes as well as transcription proteins, AR, ER-alpha and beta. All scalp biopsies from patients obtained 6 months after finasteride treatment revealed intense upregulation of AR expression in comparison to pre-treatment biopsies of the same patient, whereas ERs were not affected, indicating that AR is very sensitive to the affects of 5a-R type II suppression of DHT. Results suggest that as the hair growth returns in these previously miniaturized follicles, DHT suppression also alters the expression of specific Caspase genes inhibiting programmed cell death, apoptosis. Therefore, we can learn alot about the multiple effects of DHT by looking at its suppression in human scalp hair follicle to gain a better understanding of the many androgen responsive genes involved in hair growth regulation.

Subject: Re: Upregulationsthese
Posted by kkoo on Mon, 16 Oct 2006 14:23:53 GMT
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fixt schrieb am Mon, 16 Oktober 2006 16:15ANDROGEN RESPONSIVE GENES AS THEY AFFECT HAIR GROWTH
Marty E. Sawaya, MD, PhD, ARATEC (Alopecia Research & Associated Technologies) Clinics & University of Miami School Medicine, Florida, USA.

Androgens have profound affects on scalp hair follicles causing growth inhibitory activity hence, miniaturization of hair follicles in the case of men with Androgenetic alopecia (AGA). In human scalp hair follicles, androgens are thought to be growth inhibitory, whereas on beard and body hair, androgens upregulate hair growth. The biochemical activity and immunohistochemical expression of 5a-reductase isoenzymes type I and II has been assessed in scalp of men with AGA, as well as the cytochrome P-450 aromatase enzyme, androgen receptor (AR), estrogen receptor (ER) alpha and beta. Studies in 10 men with AGA where scalp biopsies are obtained before and after 6 months treatment with finasteride (a specific type II 5a-reductase inhibitor) reveal interesting results with regard to the effects of suppressing DHT and how it affects these androgen associated factors. Differences in expression were found for some of the enzymes as well as transcription proteins, AR, ER-alpha and beta. All scalp biopsies from patients obtained 6 months after finasteride treatment revealed intense upregulation of AR expression in comparison to pre-treatment biopsies of the same patient, whereas ERs were not affected, indicating that AR is very sensitive to the affects of 5a-R type II suppression of DHT. Results suggest that as the hair growth returns in these previously miniaturized follicles, DHT suppression also alters the expression of specific Caspase genes inhibiting programmed cell death, apoptosis. Therefore, we can learn alot about the multiple effects of DHT by looking at its suppression in human scalp hair follicle to gain a better understanding of the many androgen responsive genes involved in hair growth regulation.

aja. einmal mehr wird damit klar, dass man sich mehr mit AR-blockade bzw. AR-antagonisten befassen muss...

Subject: Re: Upregulationsthese
Posted by fixt on Mon, 16 Oct 2006 14:27:15 GMT
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aus irgendwelchen Gründen wurde diese Studie allerdings zurückgezogen glaube ich.

fixt schrieb am Mon, 16 Oktober 2006 16:27aus irgendwelchen Gründen wurde diese Studie allerdings zurückgezogen glaube ich.

mmh.

naja, jedenfalls sollte das AR-thema verfolgt werden, etwas so: würde ich mich interessieren was neue "SARMs" (Dut. und Fin. gelten auch als SARM) an den ARs der kopfhaut u. am Follikel bewirken:

zitat:

"An Orally-Active Selective Androgen Receptor Modulator is Efficacious on Bone, Muscle and Sex Function with Reduced Impact on Prostate.
Miner JN, Chang W, Chapman MS, Finn PD, Hong MH, Lopez FJ, Marschke KB, Rosen J, Schrader W, Turner R, van Oeveren A, Viveros H, Zhi L, Negro-Vilar A.

Research and Development, Ligand Pharmaceuticals, 10275 Science Center Drive, San Diego, CA 92121; NIEHS/NIH - Environmental Diseases & Medicine Program, Research Triangle Park, NC; Metabasis Therapeutics, Inc. 11119 North Torrey Pines Rd., La Jolla, CA 92037; Department of Nutrition and Exercise Sciences, Oregon State University, 127 Milam Hall, Corvallis, OR 97331.

A number of conditions, including osteoporosis, frailty and sexual dysfunction in both men and women have been improved using androgens. However, androgens are not widely used for these indications because of the side effects associated with these drugs. We describe an androgen receptor ligand that maintains expected anabolic activities with substantially diminished activity in the prostate. LGD2226 is a non-steroidal, non-aromatizable, highly selective ligand for the androgen receptor (AR), exhibiting virtually no affinity for the other intracellular receptors. We determined that AR bound to LGD2226 exhibits a unique pattern of protein-protein interactions compared with testosterone, fluoxymesterone (an orally available steroidal androgen) and other steroids, suggesting that LGD2226 alters the conformation of the ligand binding domain (LBD). We demonstrated that LGD2226 is fully active in cell-based models of bone and muscle. LGD2226 exhibited anabolic activity on muscle and bone with reduced impact on prostate growth in rodent models. Biomechanical testing of bones from animals treated with LGD2226 showed strong enhancement of bone strength above sham levels. LGD2226 was also efficacious in a sex behavior model in male rats measuring mounts, intromissions, ejaculations and copulation efficiency. These results with an orally-available, non-aromatizable androgen demonstrate the important role of the androgen receptor and androgens in mediating a number of beneficial effects in bone, muscle and sexual function independent from the conversion of androgens into estrogenic ligands. Taken together, these results suggest that orally-active, non-steroidal SARMs may be useful therapeutics for enhancing muscle, bone and sexual function."

quelle pubmed

oder die beinflussung von AR-kofaktoren, z.b.:

zitat:
"Degradation and beyond: Control of androgen receptor activity by the proteasome system.
Jaworski T.

Department of Cellular Biochemistry, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Pasteura 3, 02-093, Warsaw, Poland, tomasz_jaworski@poczta.onet.pl.

The androgen receptor (AR) is a transcription factor belonging to the family of nuclear receptors which mediates the action of androgens in the development of urogenital structures. AR expression is regulated post-translationally by the ubiquitin/proteasome system. This regulation involves more complex mechanisms than typical degradation. The ubiquitin/proteasome system may regulate AR via mechanisms that do not engage in receptor turnover. Given the critical role of AR in sexual development, this complex regulation is especially important. Deregulation of AR signalling may be a causal factor in prostate cancer development. AR is the main target in prostate cancer therapies. Due to the critical role of the ubiquitin/proteasome system in AR regulation, current research suggests that targeting AR degradation is a promising approach."

und als eine übersicht (wird freilich alles noch weit weg sein).

"Androgen receptor corepressors: an overview.
Wang L, Hsu CL, Chang C.

George H. Whipple Laboratory for Cancer Research, Department of Pathology, University of Rochester Medical Center, Rochester, New York, USA.

Androgens play pivotal roles in sex differentiation and development, in reproductive functions, and sexual behavior. The actions of androgens are mediated through the intracellular androgen receptor (AR), a member of the nuclear receptor (NR) superfamily, which regulates a wide range of target gene expression. Recent studies indicate that the proper transcriptional activity of AR is modulated by AR coregulators, including coactivators that can enhance AR transactivation and corepressors that can suppress AR transactivation. Here, we summarize the recent discoveries relating to AR corepressor function with the following different mechanisms: (1) corepressors that inhibit the DNA binding or nuclear translocation of AR; (2) corepressors that recruit histone deacetylases; (3) corepressors that interrupt the interaction between AR and its coactivators; (4) corepressors that interrupt the interaction between the N-terminus and C-terminus of AR; (5) corepressors that function as scaffolds for other AR coregulators; (6) corepressors that target the basal transcriptional machinery; (7) other mechanisms. The potential impact and future directions of AR corepressors are also discussed."

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Subject: Re: Upregulationsthese
Posted by lhs76 on Mon, 16 Oct 2006 18:54:07 GMT
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so sehe ich das auch reinforcement.

man stellt eben zum zeitpunkt x veränderungen fest und nicht in einem zeitraum. dann fallen vielleicht noch 3 haare mehr aus. dann schaut man genauer in den spiegel, vielleicht noch, weil mans gerade mal genau sehen will, mit hellerem licht als sonst, und siehe da, plötzlich gibts üble lichte stellen und alles ist ja plötzlich schlecht.

da gibts nur eines: fotos machen unter gleichen bedingungen und nicht nach laune.
das zeigt die unterschiede und beruhigt, wenn man sieht, dass je mehr sich zu ändern scheint, desto mehr doch gleich bleibt.