



**Una mela al giorno toglie
il medico di turno e...
ti fa ricrescere i capelli!**

**Studi recenti hanno dimostrato i
benefici della Mela Annurca
Campana IGP per chi ha problemi di
calvizie.**

"In questo articolo troverai l'intervento del professore Ettore Novellino della facoltà di Farmacia dell'Università Federico II di Napoli al 43° congresso del S.I. Tri (Società italiana di Tricologia). Devi sapere che il professor Novellino ha scoperto i benefici della Mela Annurca Campana IGP sui capelli, per saperne di più non ti resta che leggere..."

Il concetto di salute oggi



***“La salute è
un completo stato di benessere
fisico, mentale e sociale
e non soltanto
l’assenza di malattia...”***

***... il mantenimento
dello stato di ben-essere e bell-essere
per piacere ed accettarsi”***

Non solo 'anni alla vita' ma anche 'vita agli anni'



Aspettativa di vita



Qualità della vita



'Ciascun uomo desidera vivere a lungo, ma nessun uomo desidera invecchiare'

J. Swift



L'INDUSTRIA DEL FARMACO PER

L'OROLOGIO DELLA VITA

17:52:39

ORE MIN. SEC.

Dal 1951 ricerca, nuovi farmaci, corretti stili di vita e progressi della medicina hanno contribuito ad aumentare la tua aspettativa di vita di 3 mesi ogni anno*.

6 ORE AL GIORNO, ANCHE OGGI

* Elaborazioni su dati Istat riferiti all'Italia.

**GUARDA QUANTO TEMPO HAI GUADAGNATO DAL 1 GENNAIO,
GIORNO DI ATTIVAZIONE DI QUESTO OROLOGIO.**

24:22:13:09

GG ORE MIN. SEC.

VIVERE DI PIÙ E MEGLIO

L'industria del farmaco, innovazione continua



Come prevenire una malattia?

Farmaci



40%

MEDICINA D'ATTESA

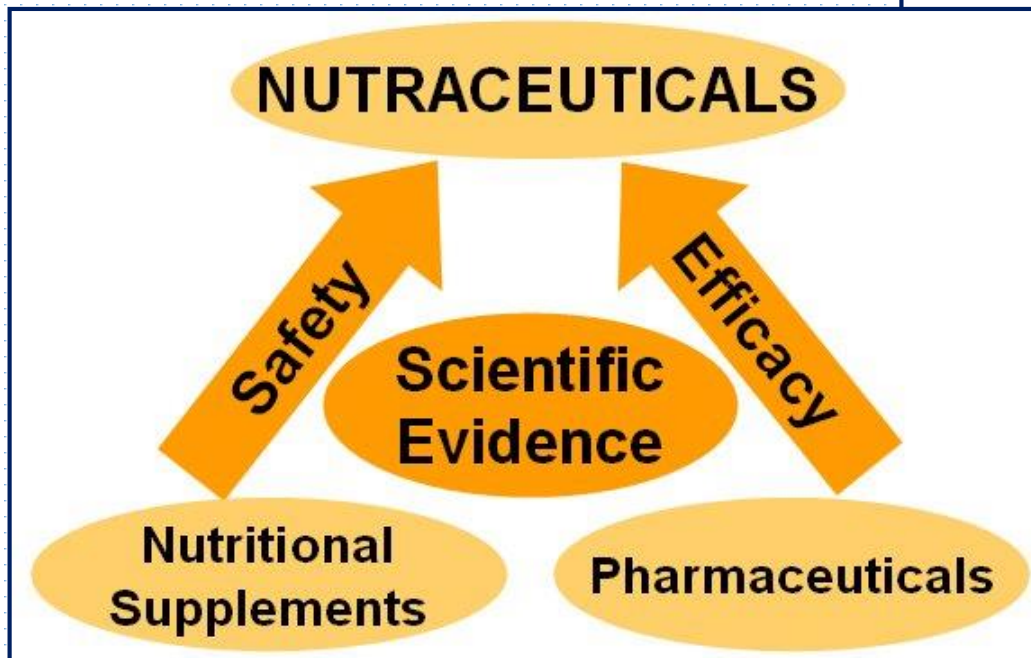
Nutraceutica



60%

MEDICINA D'INIZIATIVA

Da alimenti funzionali a nutraceutici



A statin a day keeps the doctor away: comparative proverb assessment modelling study

Adam D M Briggs *academic clinical fellow*, Anja Mizdrak *researcher*, Peter Scarborough *senior researcher*

BHF Health Promotion Research Group, Nuffield Department of Population Health, University of Oxford, Headington, Oxford OX3 7LF, UK

Objective To model the effect on UK vascular mortality of all adults over 50 years old being prescribed either a statin or an apple a day.

Design Comparative proverb assessment modelling study.

Setting United Kingdom.

Population Adults aged over 50 years.

Intervention Either a statin a day for people not already taking a statin or an apple a day for everyone, assuming 70% compliance and no change in calorie consumption. The modelling used routinely available UK population datasets; parameters describing the relations between statins, apples, and health were derived from meta-analyses.

Main outcome measure Mortality due to vascular disease.

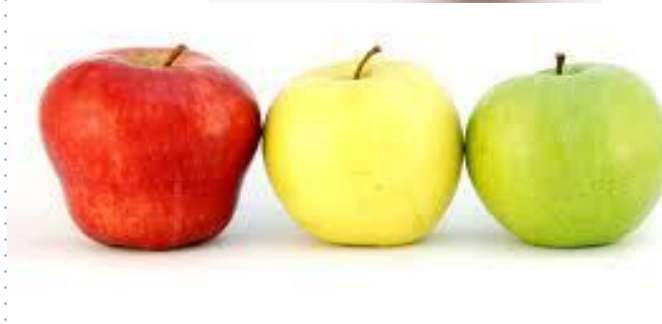
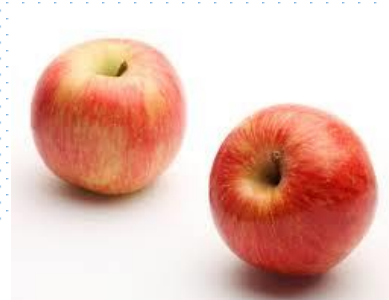
Results The estimated annual reduction in deaths from vascular disease of a statin a day, assuming 70% compliance and a reduction in vascular mortality of 12% (95% confidence interval 9% to 16%) per 1.0 mmol/L reduction in low density lipoprotein cholesterol, is 9400 (7000 to 12 500). The equivalent reduction from an apple a day, modelled using the PRIME model (assuming an apple weighs 100 g and that overall calorie consumption remains constant) is 8500 (95% credible interval 6200 to 10 800).

Conclusions Both nutritional and pharmaceutical approaches to the prevention of vascular disease may have the potential to reduce UK mortality significantly. With similar reductions in mortality, a 150 year old health promotion message is able to match modern medicine and is likely to have fewer side effects.

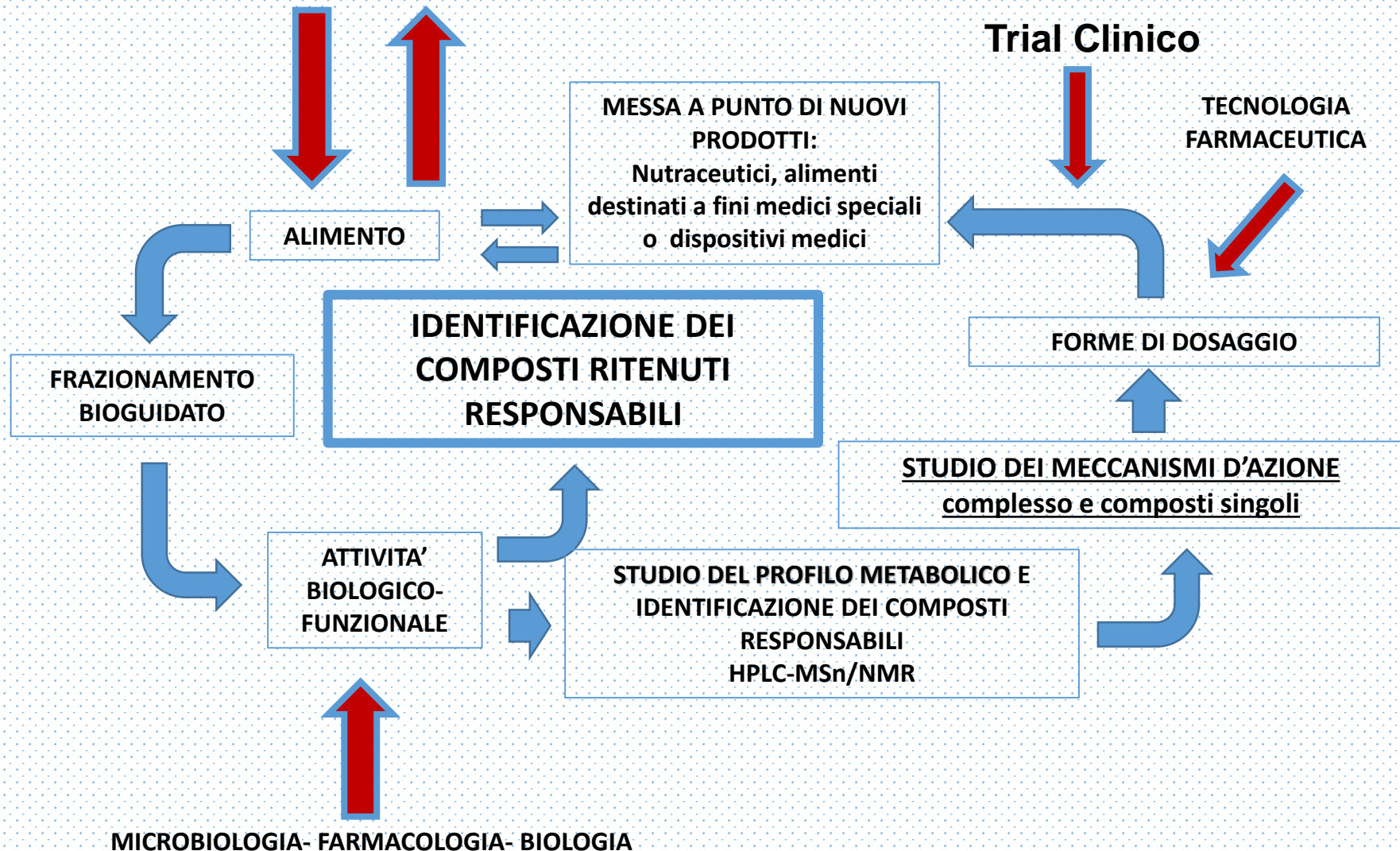
What this study adds

An apple a day or a statin a day is equally likely to keep the doctor away

*“Una mela al giorno toglie ...
il medico di turno!”*



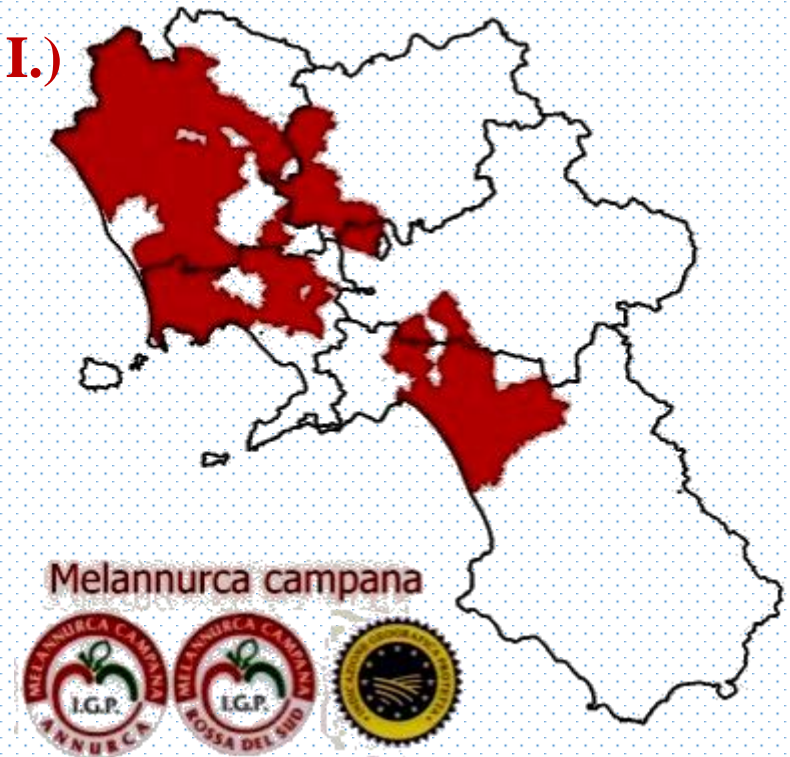
Target epidemiologico



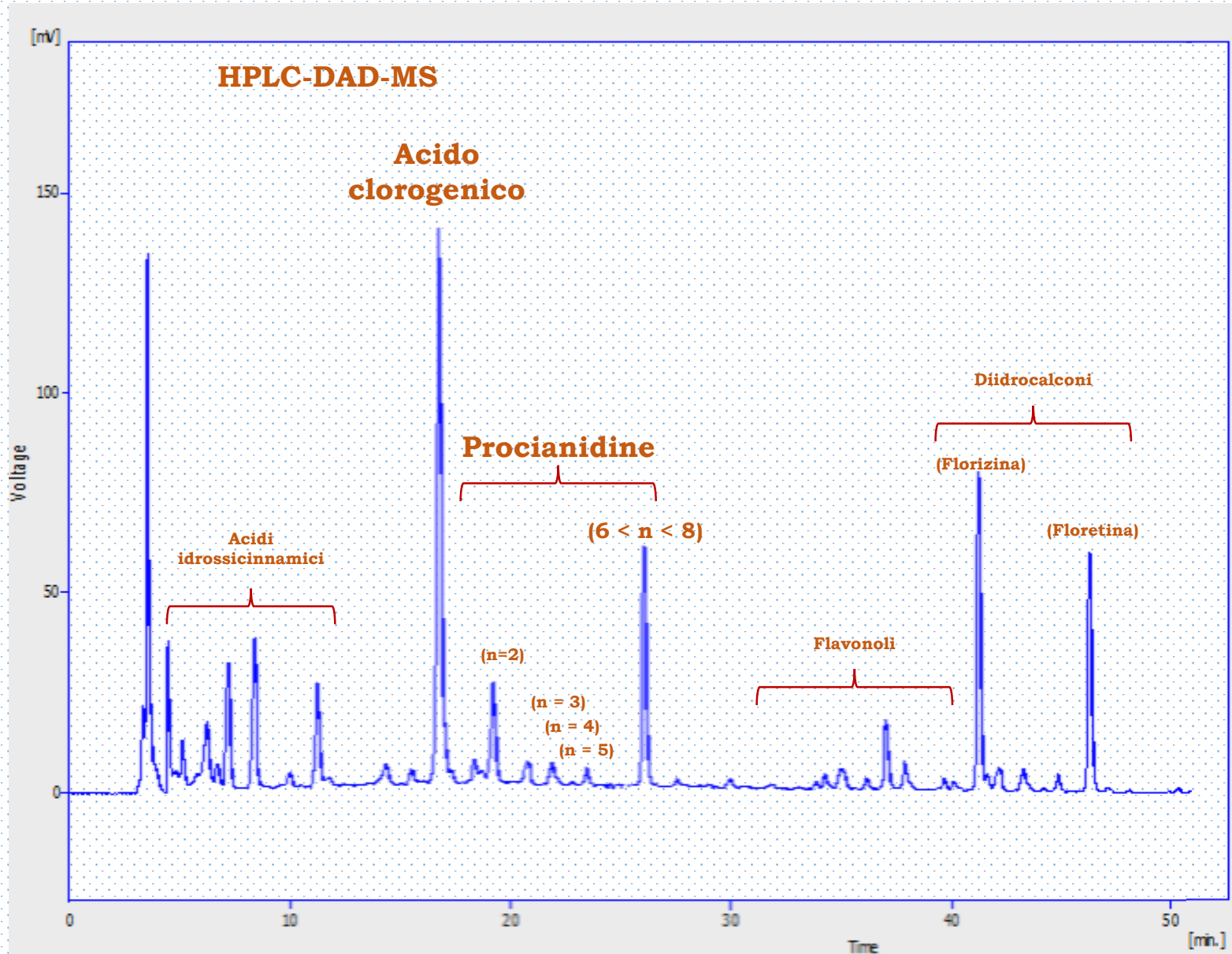


nobile come le sue origini

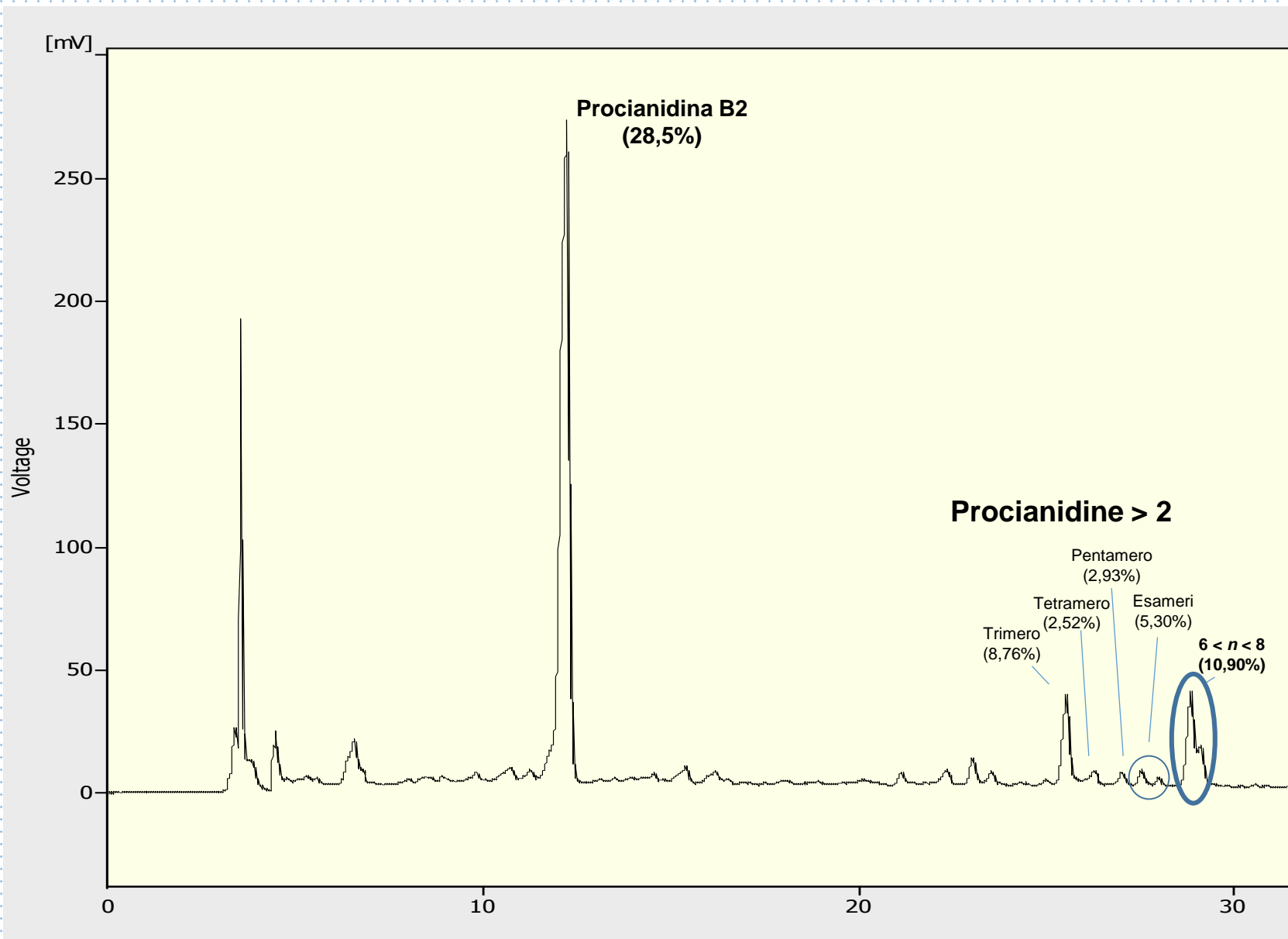
Protected Geographical Indication (P. G. I.)
“Melannurca Campana”
Reg. EU n. 417/2006



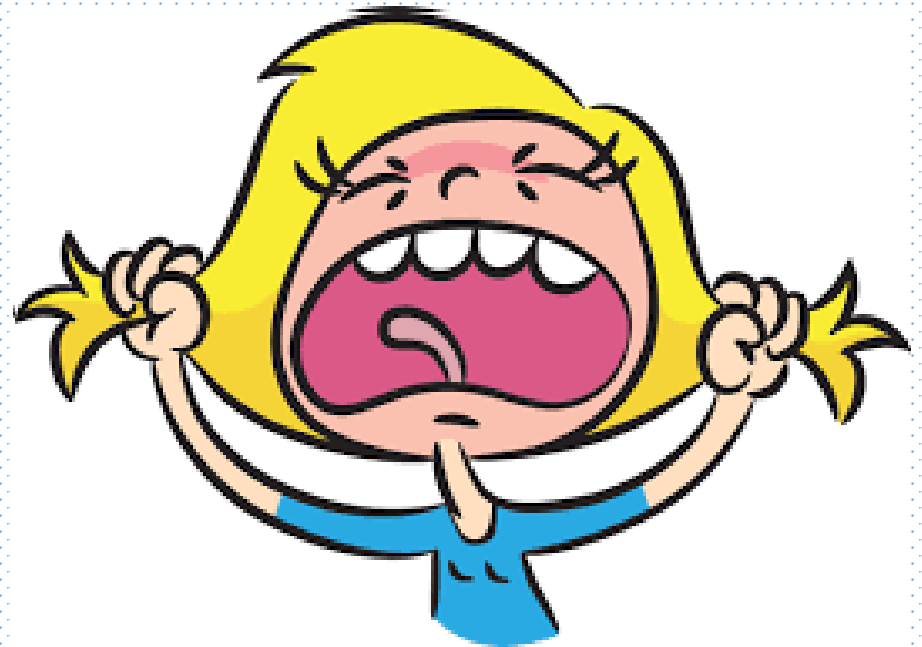
Caratterizzazione estratto



Caratterizzazione estratto



Effetti Concomitanti....



Le **Procianidine** presenti nelle mele:

- > promuovono la **crescita** dei capelli
- > Aumentano notevolmente il **numero di capelli**
- > Aumentano la crescita **sin dalla radice**
- > Aumentano di **oltre 80% lo spessore** dei capelli sia alla radice che alle punte
- > Attivano intensamente la **vitalità dei bulbi piliferi**
- > Hanno un'attività **superiore del 200%** rispetto al Minoxidil



Investigation of topical application of procyanidin B-2 from apple to identify its potential use as a hair growing agent

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²Watanabe Dermatological Clinic, Tokyo, Japan

PHYTOTHERAPY RESEARCH
Phytother. Res. 15, 331–336 (2001)
DOI: 10.1002/ptr.800

The First Clinical Trial of Topical Application of Procyanidin B-2 to Investigate its Potential as a Hair Growing Agent

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³Watanabe Dermatological Clinic, 1–32–16, Shinjuku, Shinjuku-ku, Tokyo 160–0022, Japan

Effetti, dopo un anno, dell'applicazione topica di una soluzione al 1% di Procianidina B2

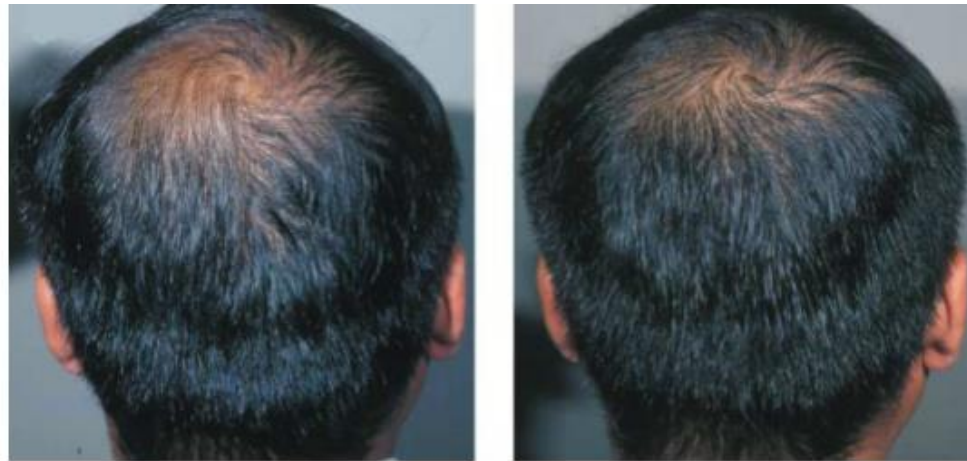


Figure 3 Clinical photographs of a subject before (a) and after (b) 12-month treatment of procyanidin agent.

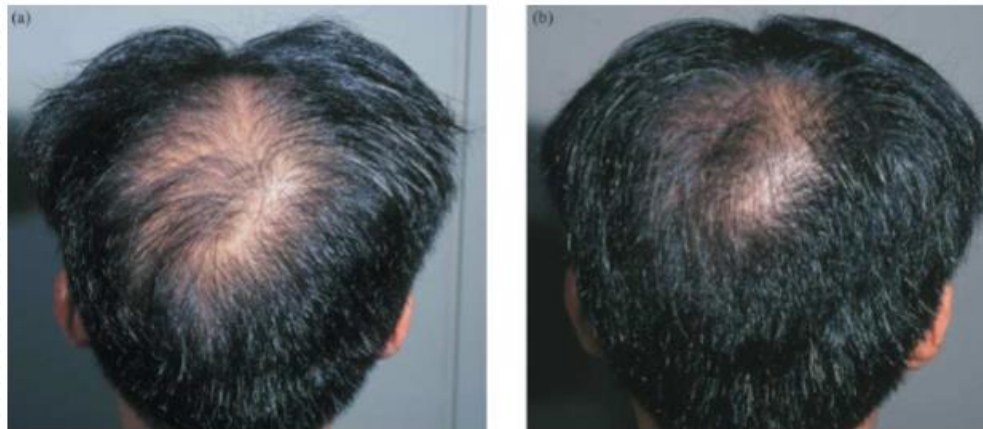


Figure 4 Clinical photographs of a subject before (a) and after (b) 12-month treatment of procyanidin agent.

Procyanidin Oligomers Counteract TGF- β_1 - and TGF- β_2 -Induced Apoptosis in Hair Epithelial Cells: An Insight into Their Mechanisms

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^cDepartment of Pathology, Toyama Medical and Pharmaceutical University, Toyama, Japan

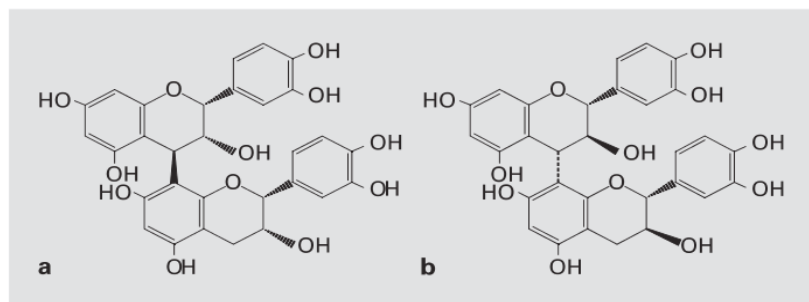
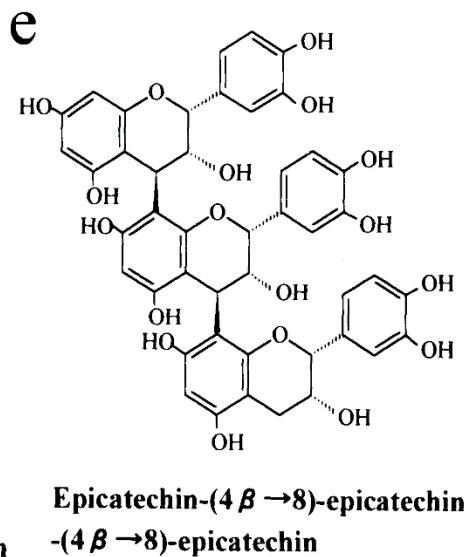
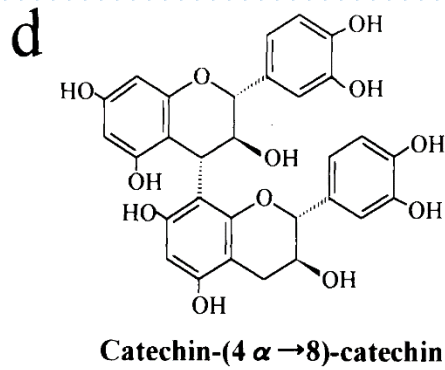
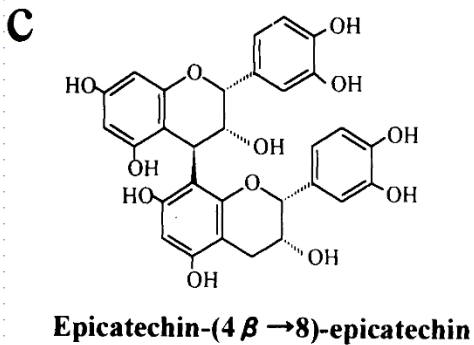
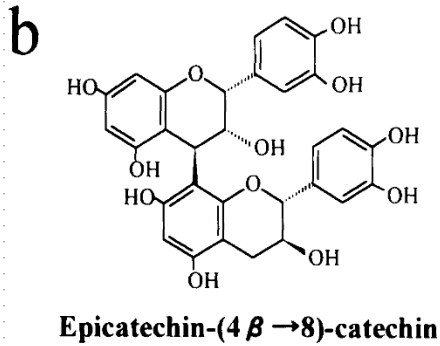
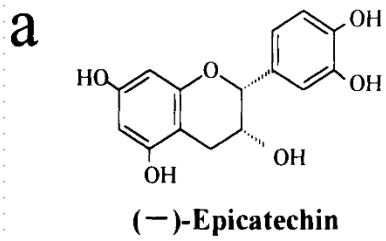


Fig. 1. Structure of procyanidin B-2 [(-)-epicatechin-(4 β →8)-(-)-epicatechin] (a) and procyanidin B-3 [(+)-catechin-(4 α →8)-(+)-catechin] (b).

1) Murine hair epithelial cells (C3H/HeNCrj mice) incubated with TGF- β_1 and TGF- β_2 → apoptosis

2) Addition of procyanidins B2 and B3 protects cells from apoptosis

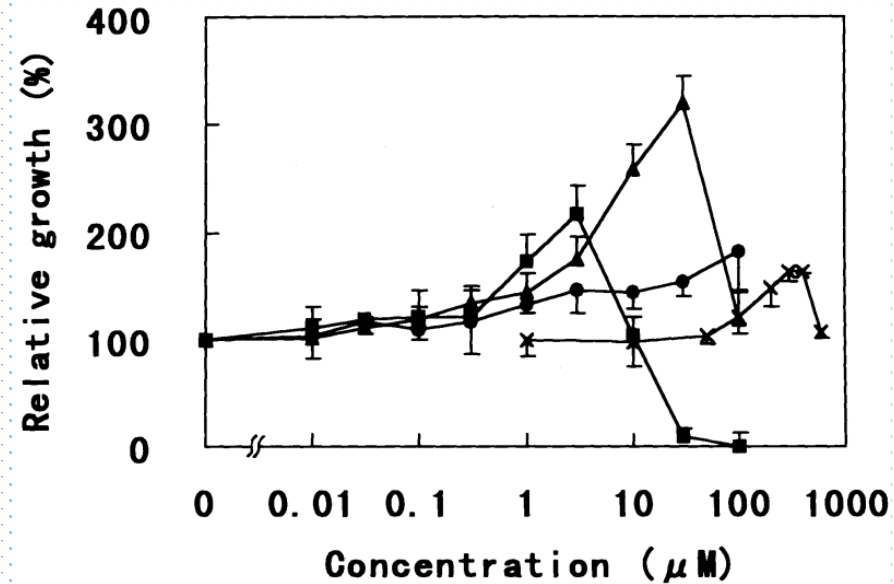
Procyanidins B2 upregulates mitogen-activated protein kinase (MAPK) cascade/extracellular signal-regulated kinase (MEK) in hair epithelial cells, protecting from TGF- β_1 and TGF- β_2 -induced apoptotic cell death (catagen phase).



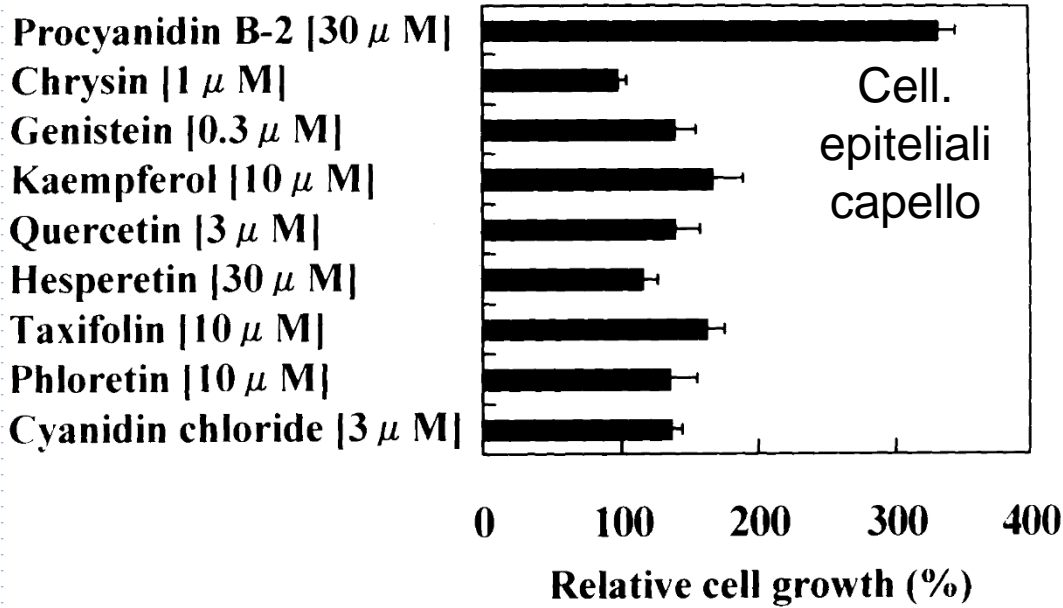
Procianidine monomeriche e oligomeriche

- (a) (-)-Epicatechin (b) proc. B-1
 (c) proc. B-2 (d) proc. B-o
 (e) proc. C-1.

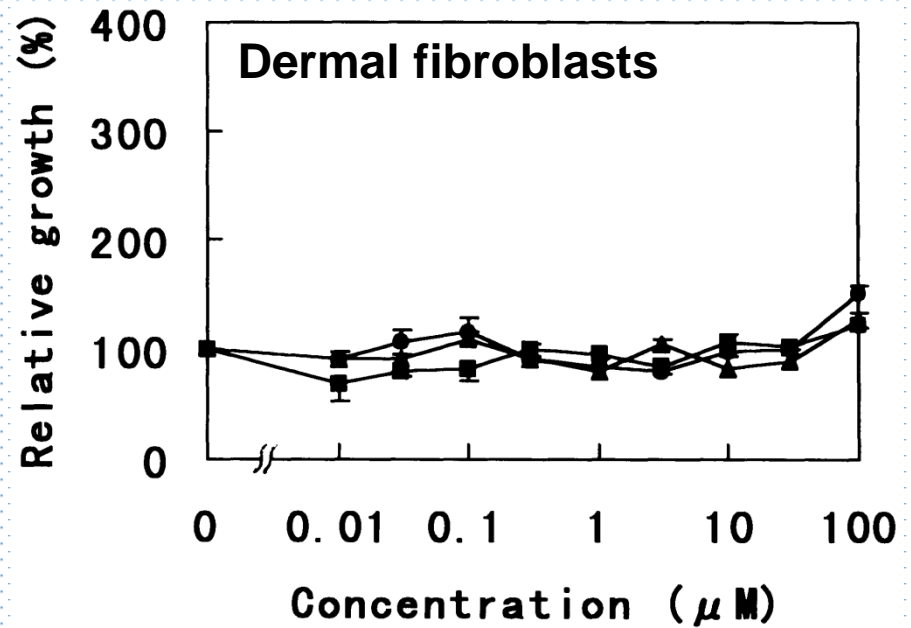
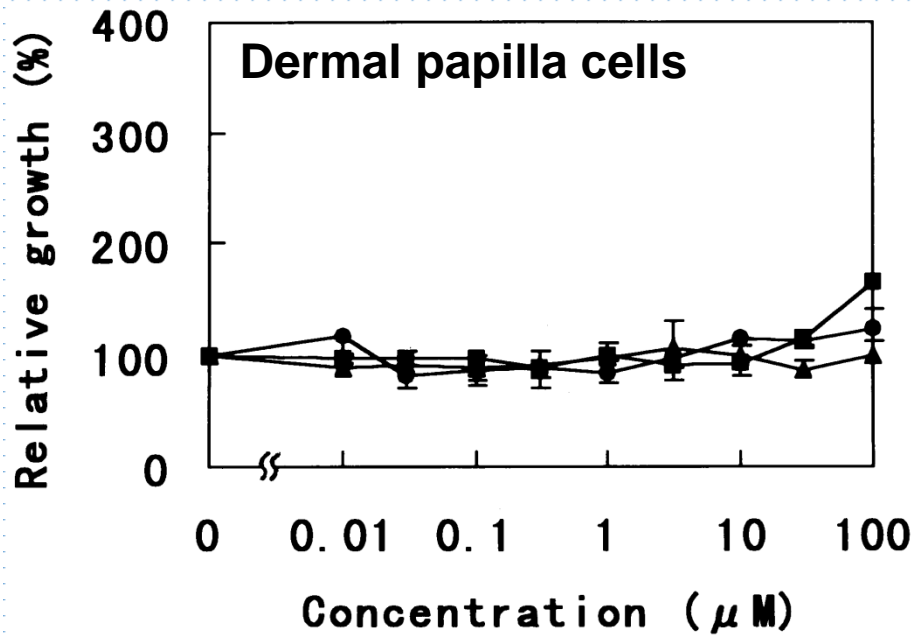
Cellule Epiteliali del Capello



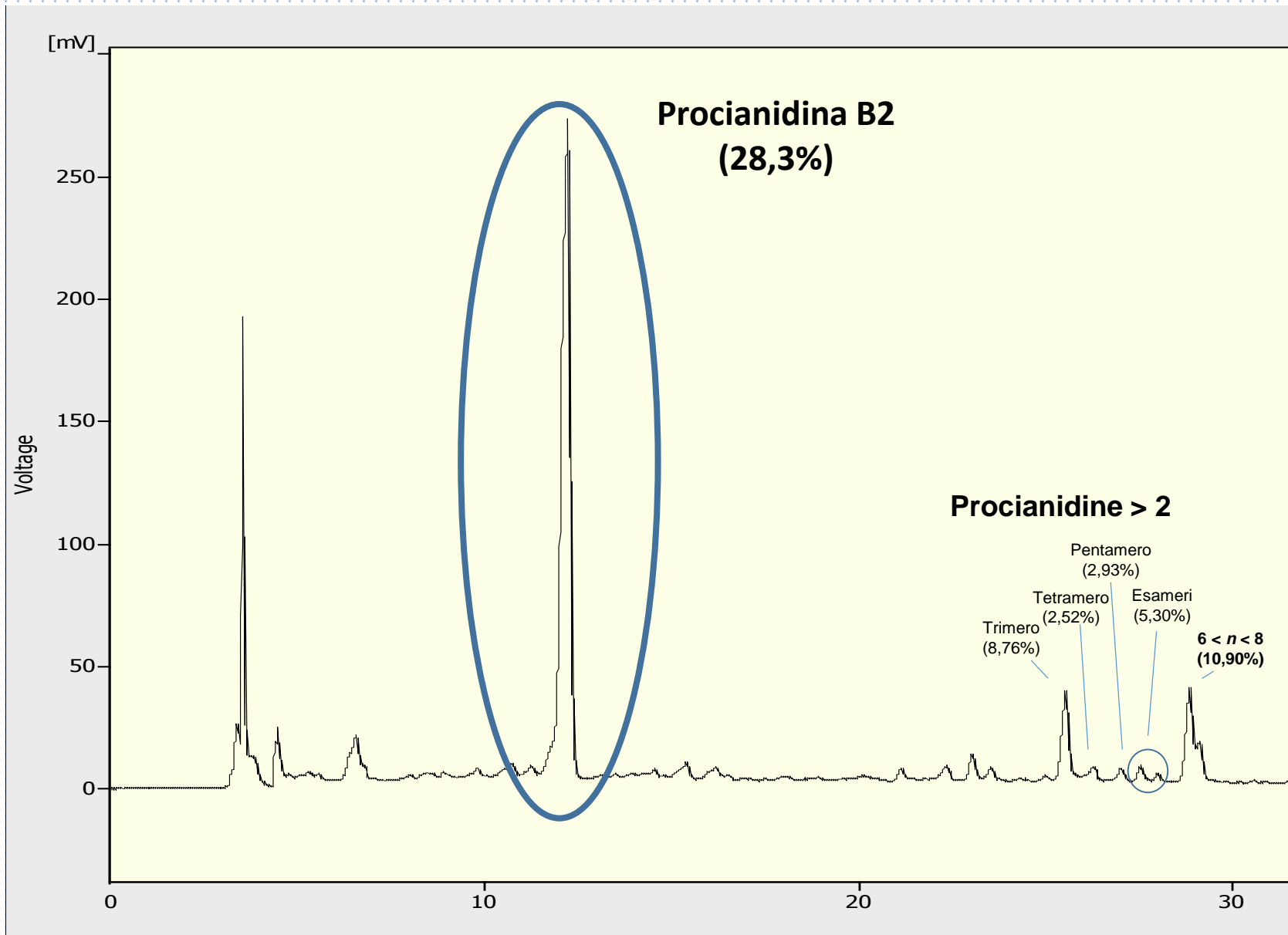
- (-)-Epicatechin
- ▲ procyanidin B-2
- procyanidin C-1
- × minoxidil.



Gli altri flavonoidi esaminati stimolano solo debolmente la crescita delle **Cellue Epiteliali** del Capello.



Caratterizzazione estratto



Composizione della frazione procianidinica di differenti cultivar di mele



| | Annurca | RD | GS | F | GD |
|----------------------|--------------------|--------------------|--------------------|--------------------|--------------------|
| Dimers | 28.3 ± 1.1 | 7.24 ± 0.7 | 10.44 ± 0.8 | 10.06 ± 0.7 | 8.70 ± 0.7 |
| Trimers | 6.85 ± 0.8 | 8.02 ± 0.9 | 11.57 ± 1.1 | 11.14 ± 1.0 | 9.64 ± 0.9 |
| Tetramers | 3.93 ± 0.5 | 5.68 ± 0.4 | 8.19 ± 0.7 | 7.88 ± 0.6 | 6.82 ± 0.5 |
| Pentamers | 2.80 ± 0.2 | 3.84 ± 0.2 | 5.55 ± 0.5 | 5.34 ± 0.4 | 4.62 ± 0.2 |
| Procyanidin polymers | 15.5 ± 1.8 | 16.8 ± 0.9 | 24.3 ± 1.3 | 23.4 ± 1.4 | 20.2 ± 1.2 |
| Total procyanidins | 64.31 ± 2.1 | 41.61 ± 1.8 | 60.04 ± 1.9 | 57.80 ± 1.0 | 50.00 ± 0.9 |

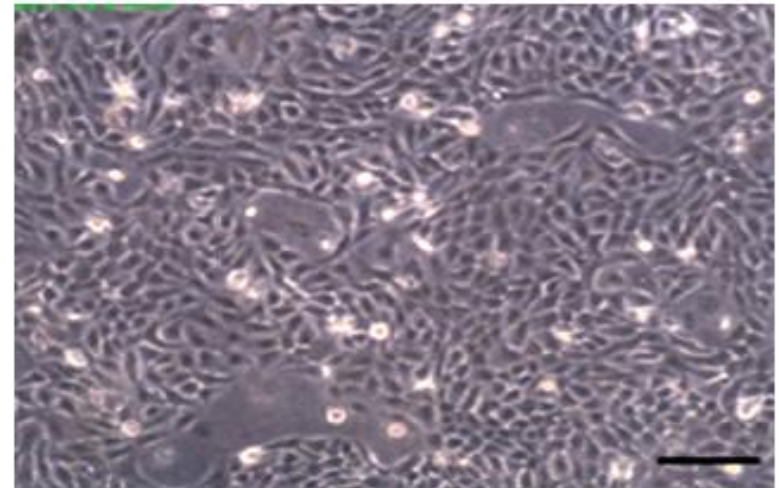
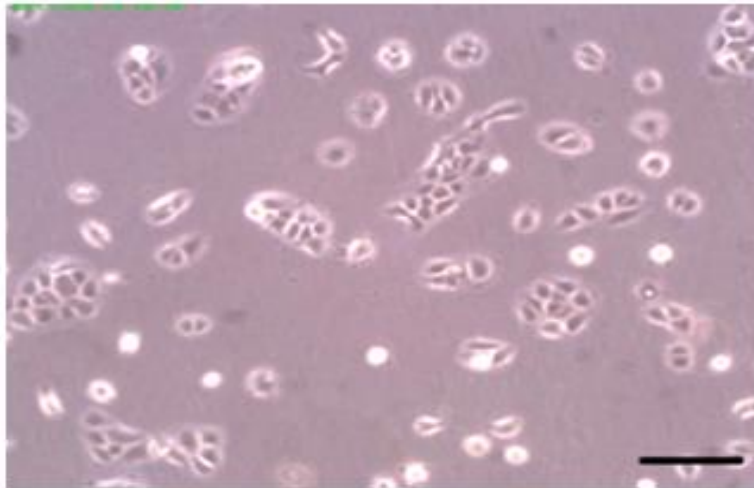
* Values are expressed as % ± SD; n = 5; results were significantly different at a level of $P = 0.001$.

RD: Red Delicious; PL: Pink Lady; F: Fuji; GD: Golden Delicious.

Mela Annurca Campana IGP



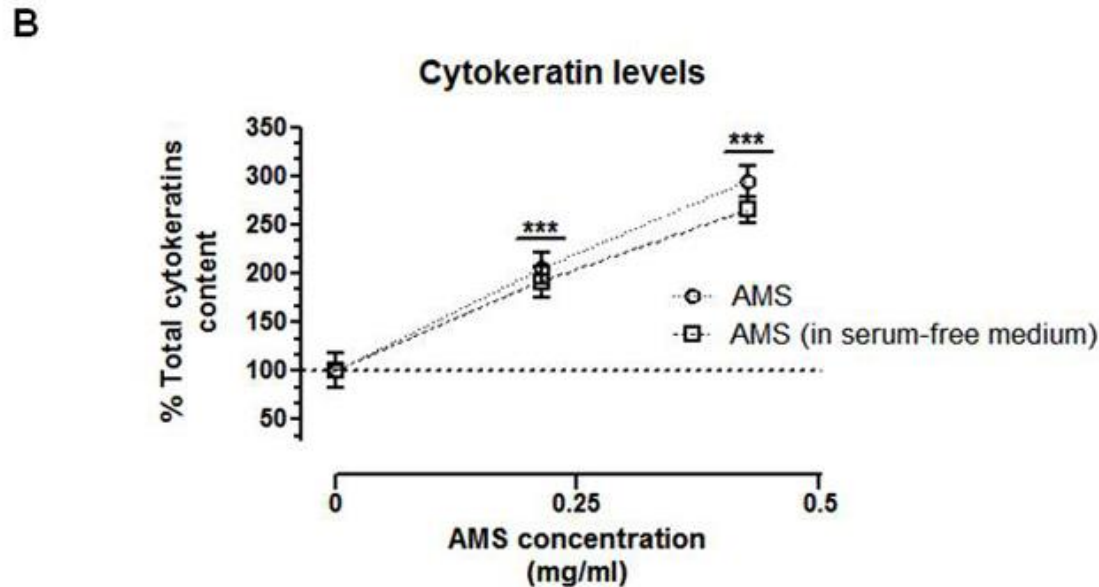
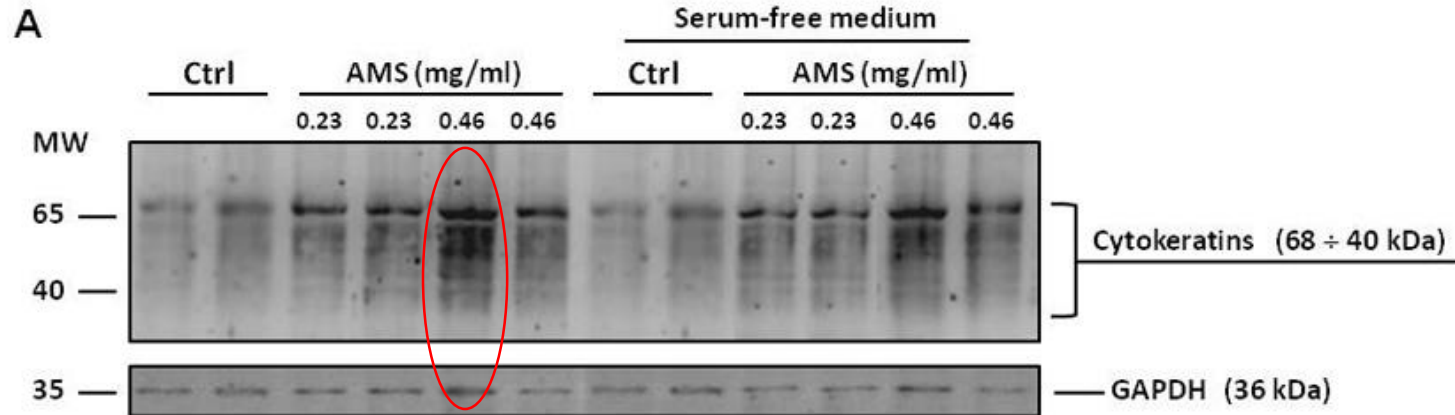
Modello sperimentale di cute umana di cheratinociti HaCaT utilizzata per studi *in vitro* su omeostasi epidermica



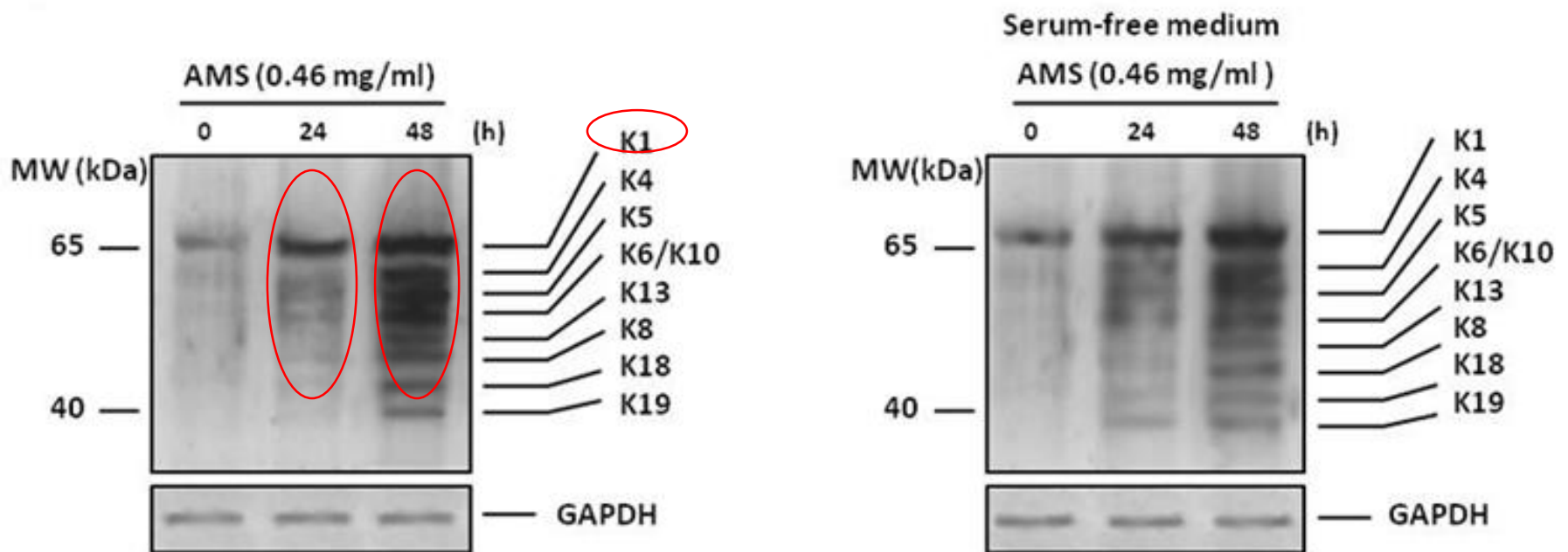
Microfotografie a contrasto di fase di cellule HaCaT, a bassa (sinistra) ed alta (destra) confluenza. Scale bars: 200 μ m

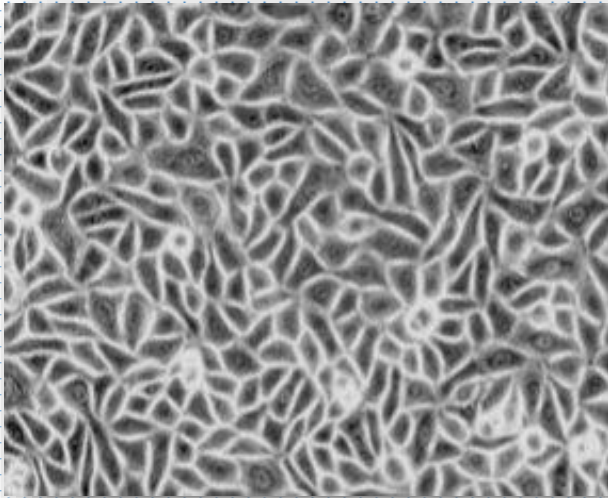
HaCaT è una linea cellulare di cheratinociti adulti umani immortalizzati. Questa linea mantiene la capacità di differenziare in vitro come quella di normali cheratinociti epidermici umani in vivo (NHEK), e rappresenta pertanto un modello adatto per studi di cheratinizzazione, di omeostasi, e di patofisiologia epidermica.

Effetto concentrazione-dipendente di AMS sulla espressione di cheratine in cellule HaCaT



Effetto di AMS sulla espressione di specifiche citocheratine in cellule HaCaT





ScienCell® #2440

TAN Record #944

Human scalp

Gender: Male

Age: 55 years old

Race: caucasian

AMS *in vitro*

concentrazione 0.1 ÷ 3 mg/ml

tempo 24 ÷ 96 h

Valutazione degli effetti di AMS su cheratinociti follicolari umani

Cellule che esprimono in modo esclusivo cheratine che costituiscono la struttura del capello [K81-K86 (type II), K31-K40 (type I)], localizzate sia nella corteccia che nella cuticola, e pertanto rappresentano le cellule principali del follicolo pilifero responsabili della crescita del capello

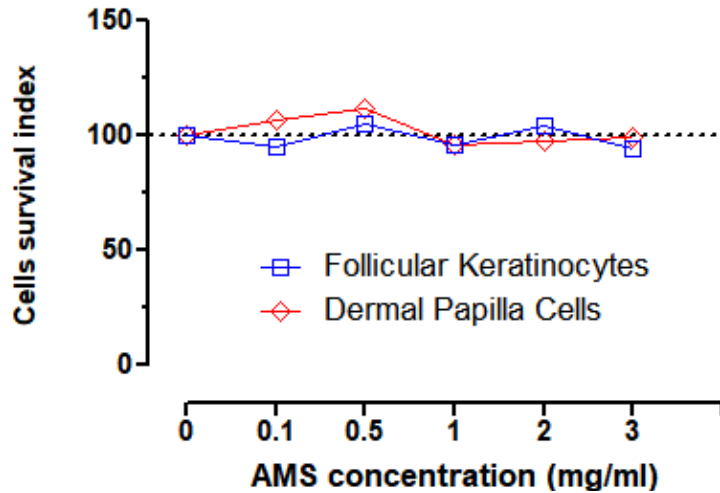
Effetti sulla proliferazione e vitalità cellulare

Effetti sul differenziamento dei cheratinociti

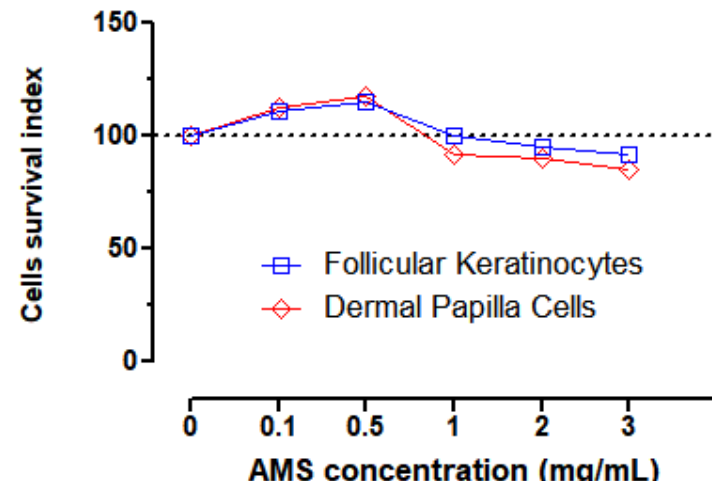
Effetti sulla biosintesi ed espressione di specifiche cheratine dei capelli

In vitro Bioscreen – Vitalità cellulare

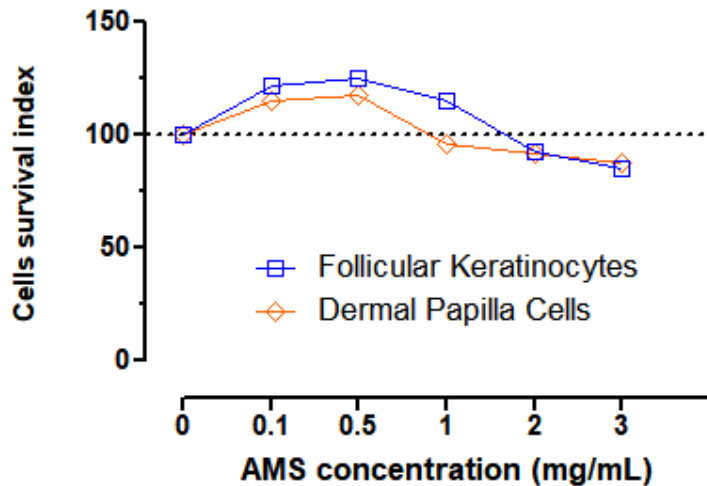
24h



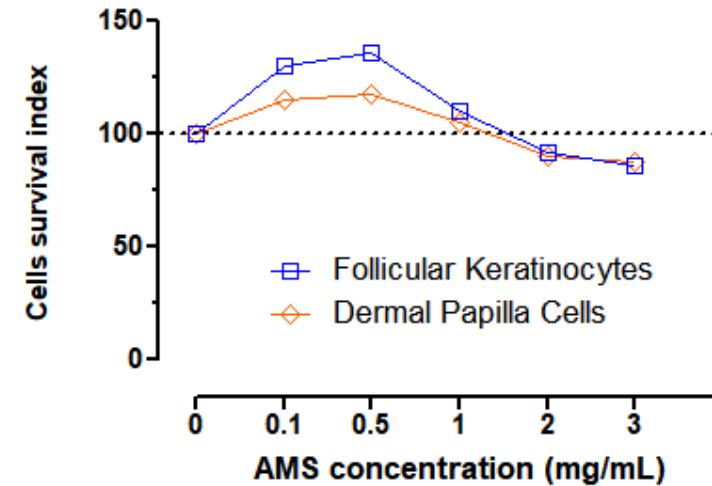
48h



72h

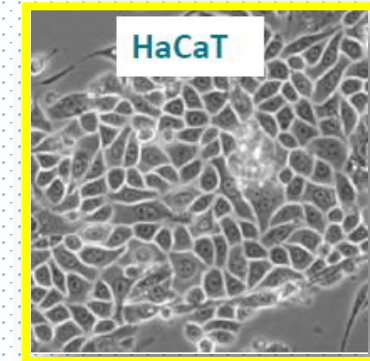


96h

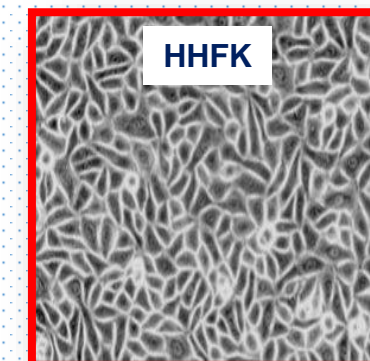
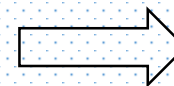


| Keratin types | Type I | | Type II | | |
|---------------------|--|-------------|----------|-------------|--------|
| | new name | former name | new name | former name | |
| Epithelial keratins | K9 | K9 | K1 | K1 | |
| | K10 | K10 | K2 | K2 | |
| | K12 | K12 | K3 | K3 | |
| | K13 | K13 | K4 | K4 | |
| | K14 | K14 | K5 | K5 | |
| | K15 | K15 | K6a | K6a | |
| | K16 | K16 | K6b | K6b | |
| | K17 | K17 | K6c | K6e/h | |
| | K18 | K18 | K7 | K7 | |
| | K19 | K19 | K8 | K8 | |
| | K20 | K20 | K76 | K2p | |
| | K23* | K23 | K77 | K1b | |
| | K24* | K24 | K78* | K5b | |
| | | | K79* | K6l | |
| | | | K80* | Kb20 | |
| | Hair follicle-specific epithelial keratins (root sheath) | K25 | K25irs1 | K71 | K6irs1 |
| | | K26 | K25irs2 | K72 | K6irs2 |
| | | K27 | K25irs3 | K73 | K6irs3 |
| | | K28 | K25irs4 | K74 | K6irs4 |
| | | | K75 | K6hf | |
| Hair keratins | K31 | Ha1 | K81 | Hb1 | |
| | K32 | Ha2 | K82 | Hb2 | |
| | K33a | Ha3-I | K83 | Hb3 | |
| | K33b | Ha3-II | K84 | Hb4 | |
| | K34 | Ha4 | K85 | Hb5 | |
| | K35 | Ha5 | K86 | Hb6 | |
| | K36 | Ha6 | | | |
| | K37 | Ha7 | | | |
| | K38 | Ha8 | | | |
| | K39 | Ka35 | | | |
| | K40 | Ka36 | | | |

Cheratinociti epidermici



Cheratinociti follicolari



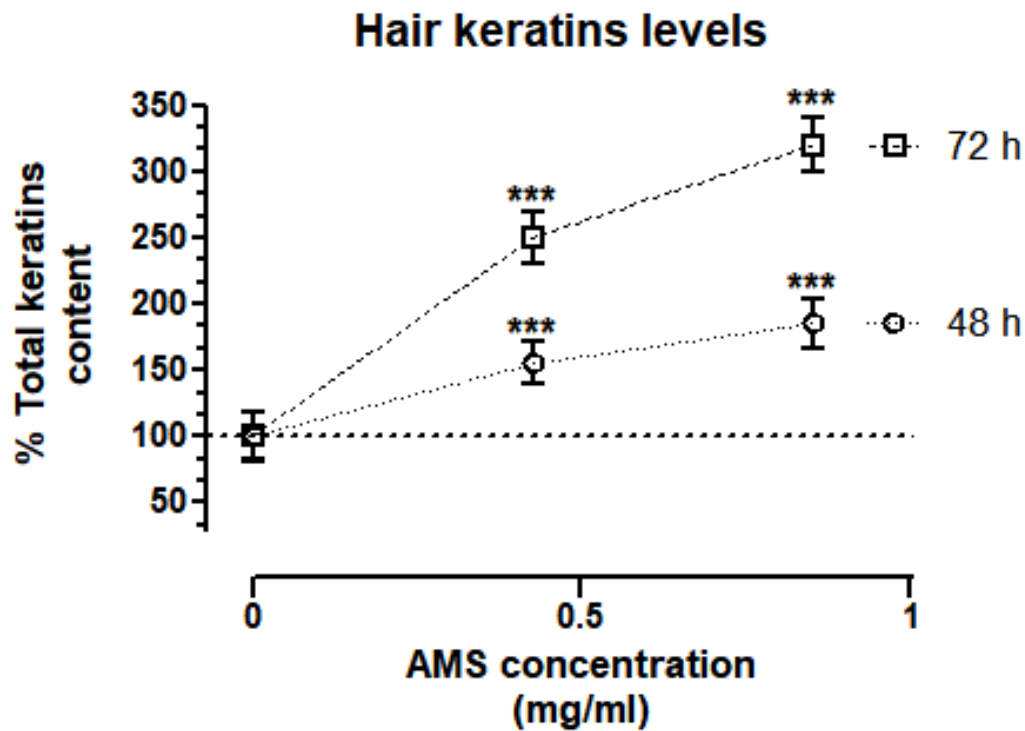
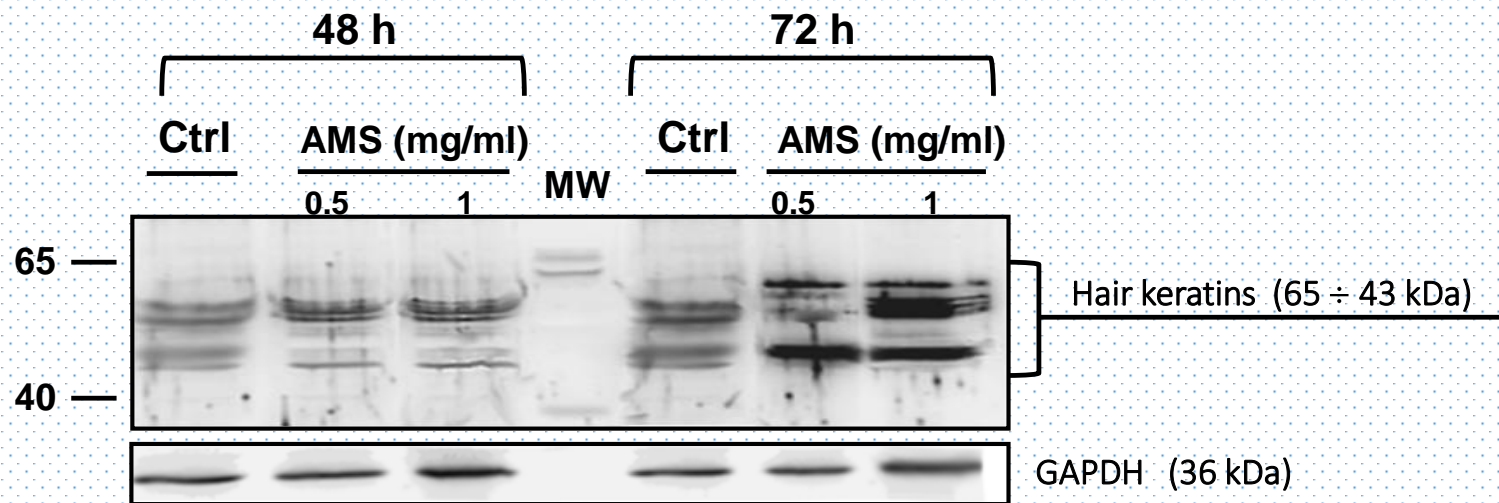


Foto al dermoscopia dopo 30 giorni di trattamento che evidenzia l'ispessimento dei capelli

T0



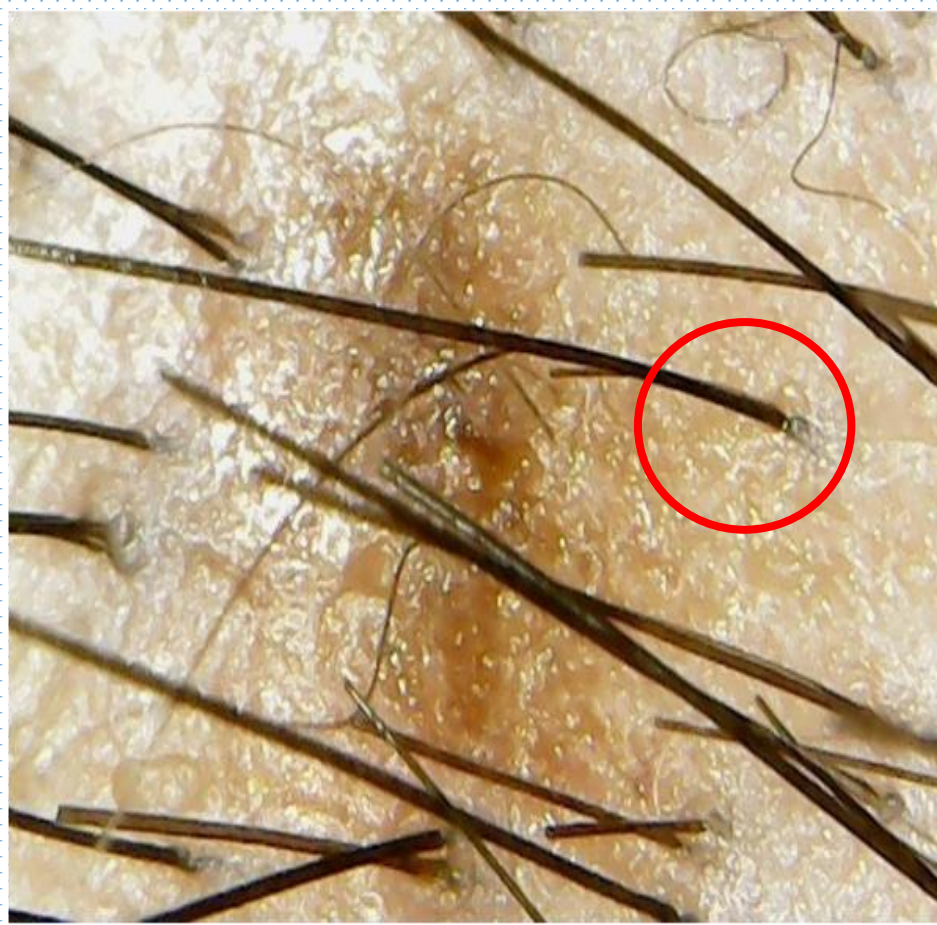
T30



Foto al dermoscopio dopo 30 giorni di trattamento che evidenzia l'ispessimento dei capelli

T0

T30



**Foto al dermoscopia dopo 30 giorni di trattamento
che evidenzia la nascita di nuovi capelli**

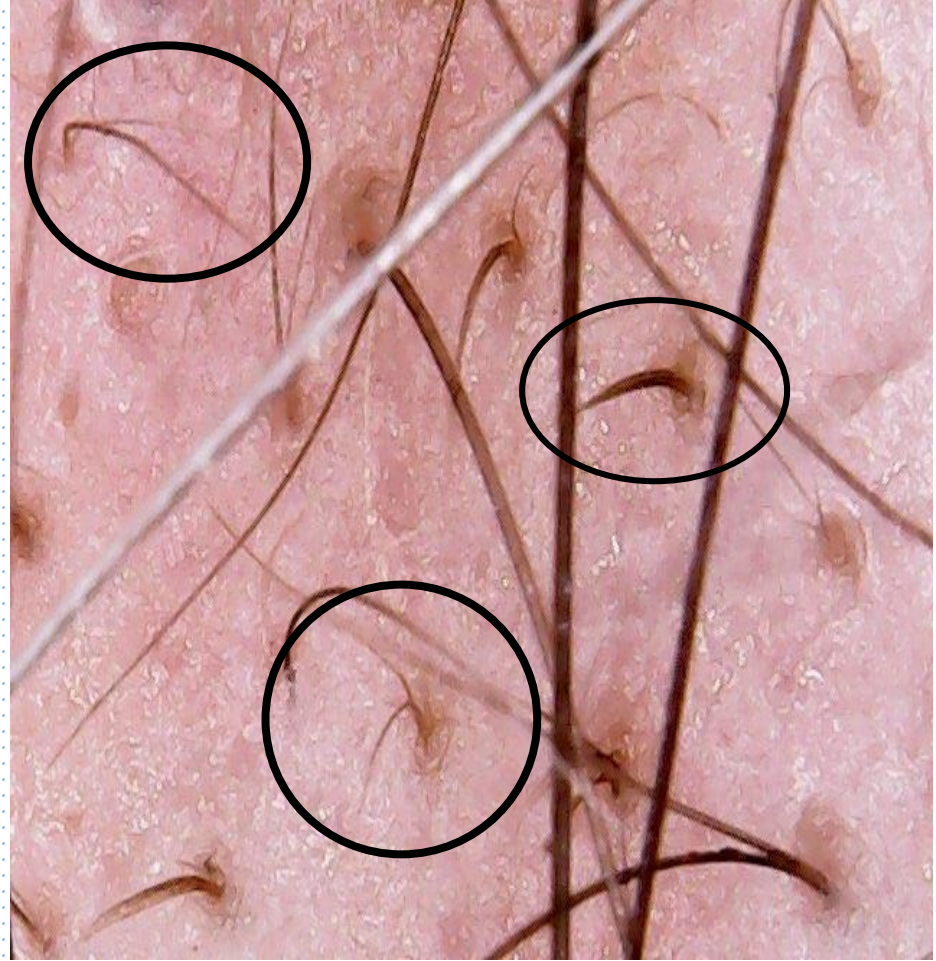
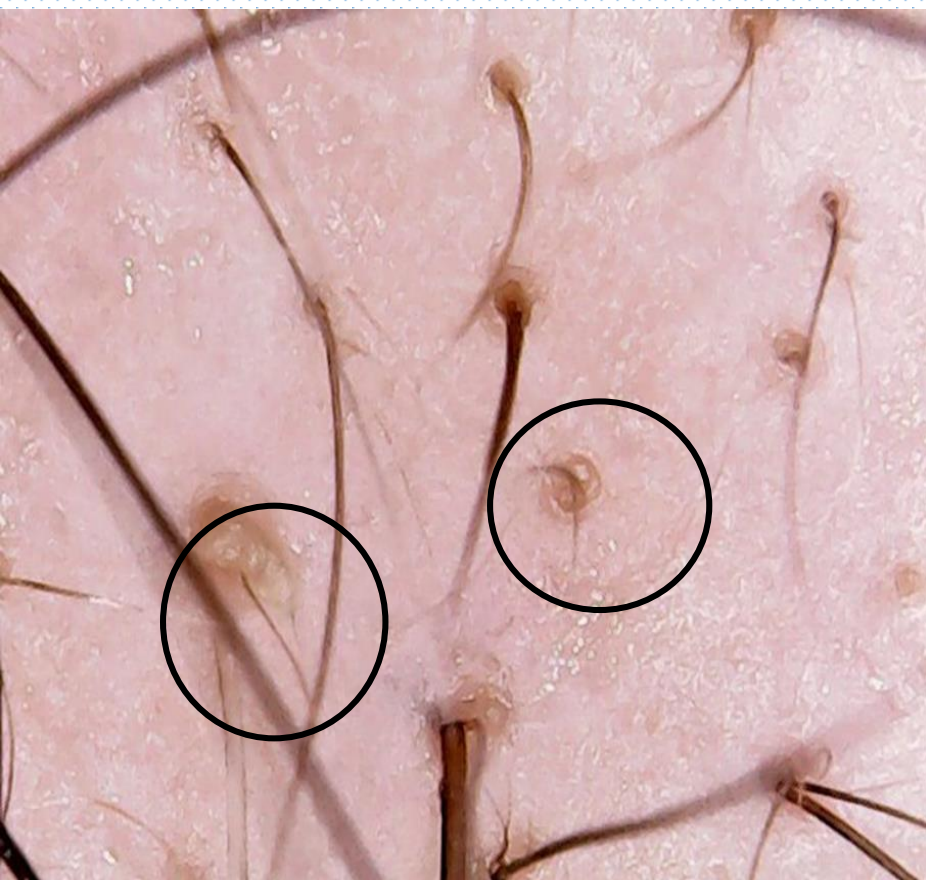


Foto al dermoscopio dopo 30 giorni di trattamento che evidenzia la nascita di nuovi capelli



T0



30gg



60gg



180gg



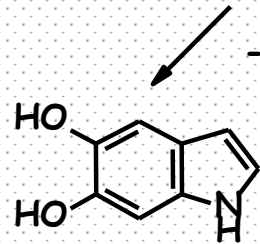
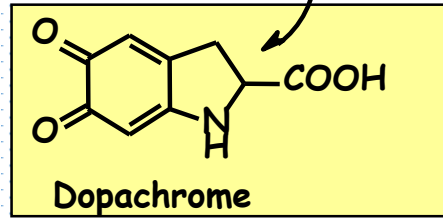
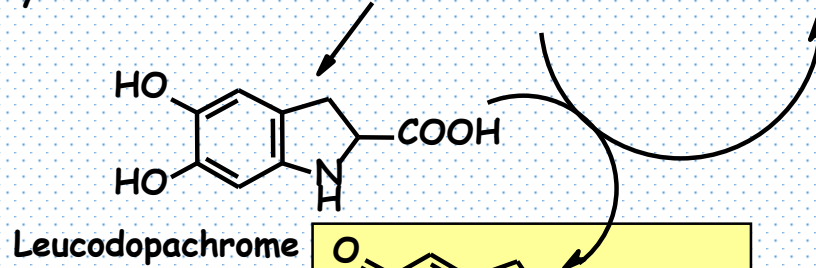
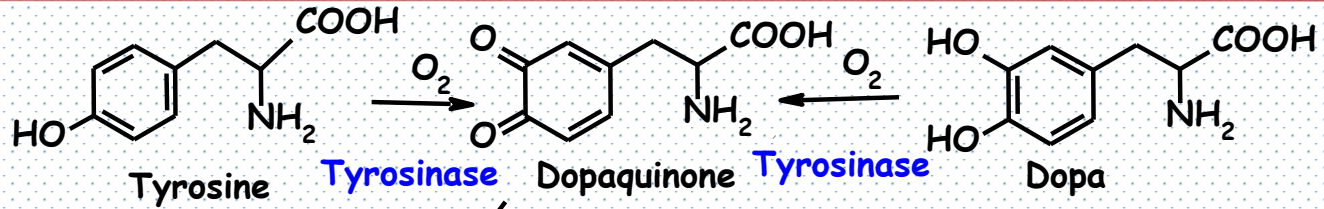
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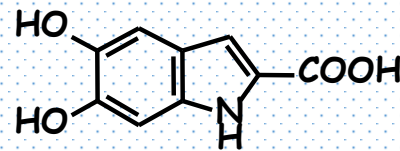
T180



Melanins: what's in a name?



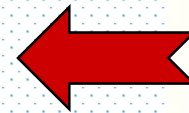
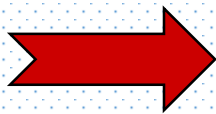
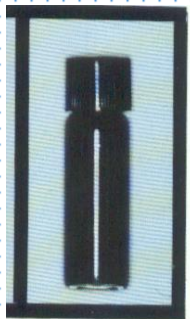
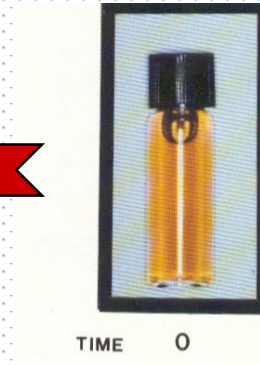
5,6-Dihydroxyindole (DHI)



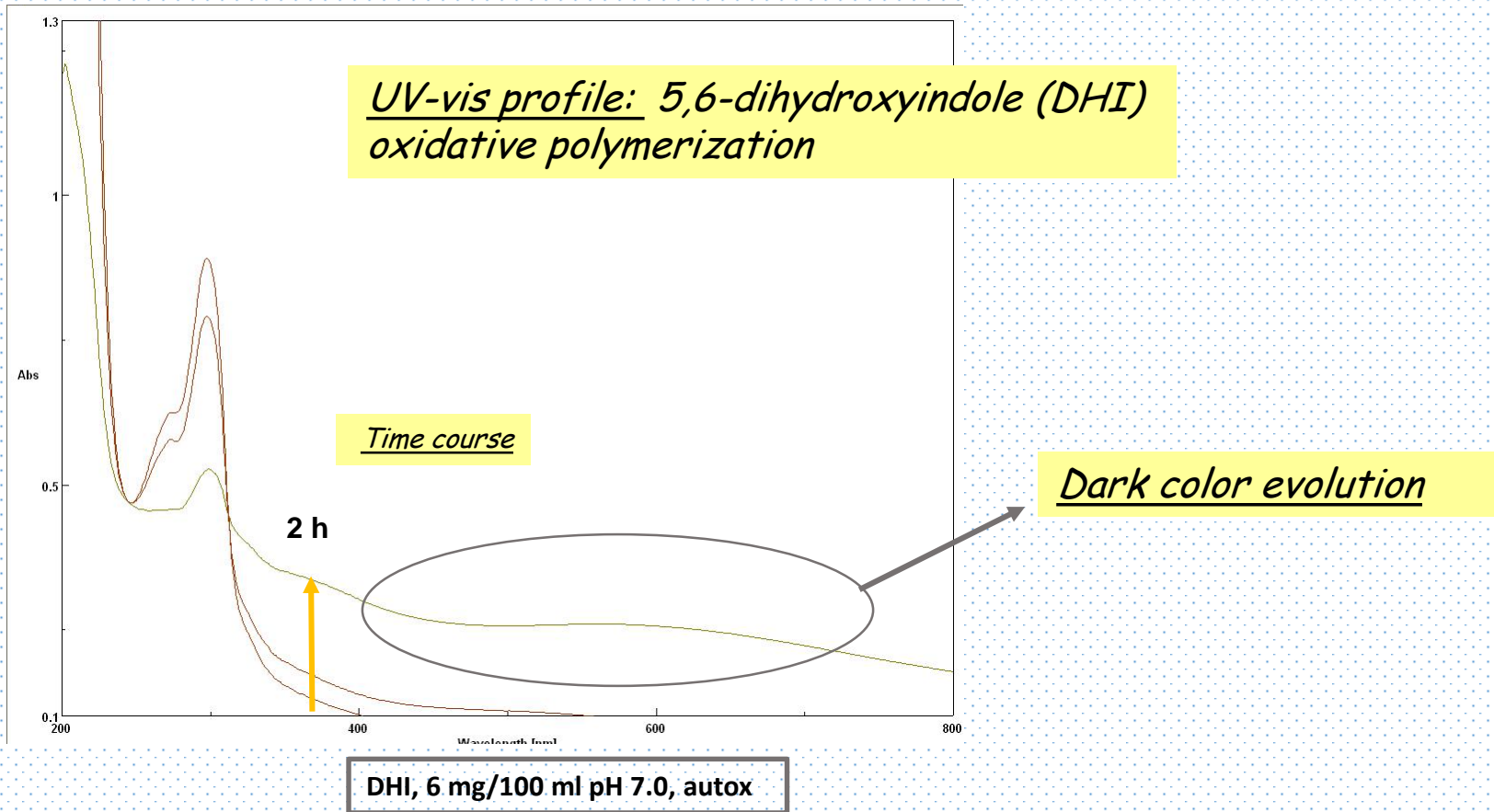
5,6-Dihydroxyindole-2-carboxylic acid (DHICA)

oxidative polymerization

EUMELANIN



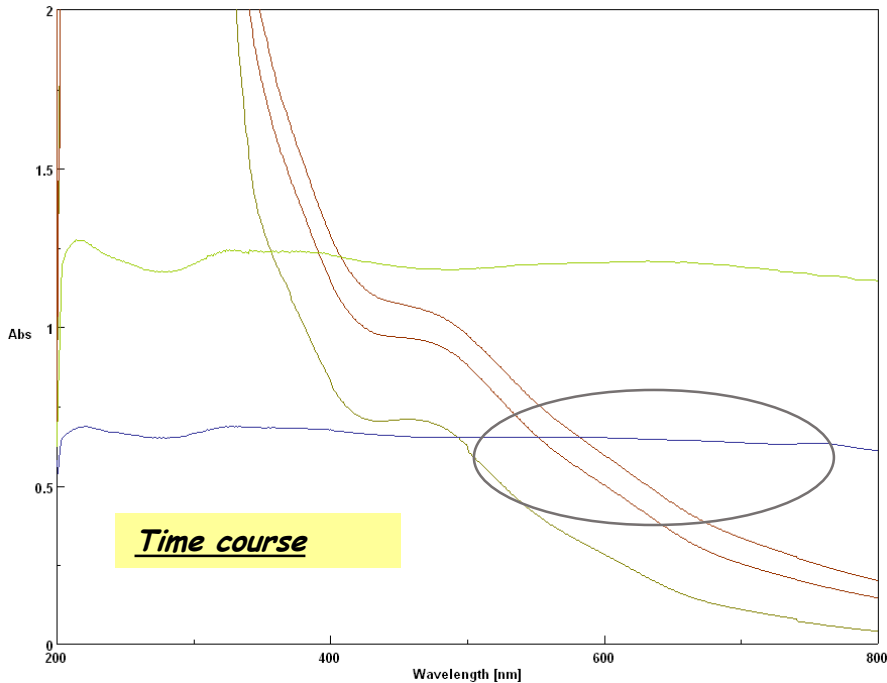
Melanins: the oxidation of DHI



Under standard condition: *DHI spontaneously oxidizes producing the emergence of a dark phase whose intensity is proportional to the progress of the oxidation and inversely proportional to the melanin particle size*

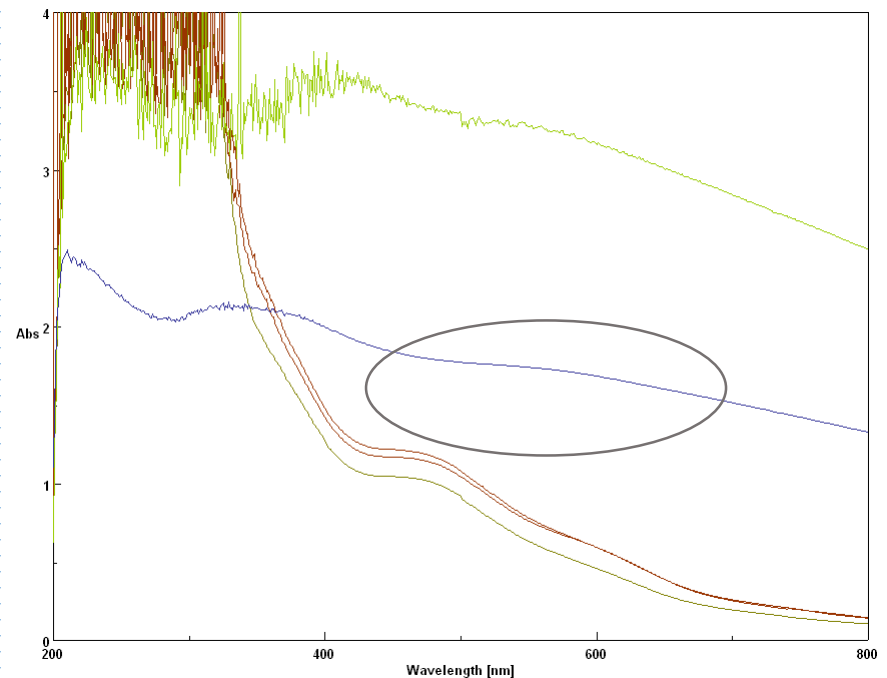
Melanins: the impact of apple extract

Dark color evolution



DHI, 6 mg/100 ml pH 7.0, autotox

After one day of reaction progress :
DHI (on the right) presents an average A in the UV-vis region of ca. 0,7.



DHI, 6 mg/100 ml pH 7.0, AMS12 mg/100 ml , autotox

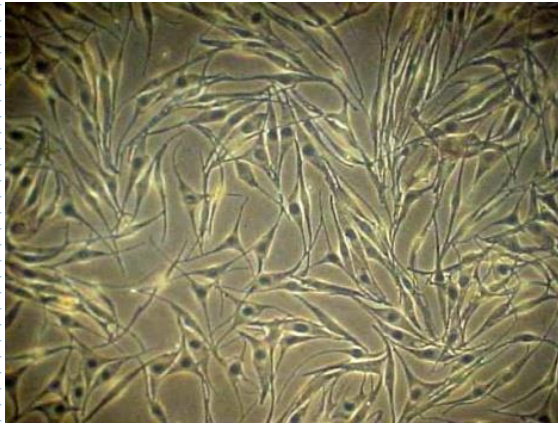
After one day of reaction progress:
5,6-dihydroxyindole (DHI) oxidative polymerization in presence of apple extract increases A in the UV-vis region over 2 .

Dark color evolution



DHI, 6 mg/100 ml pH 7.0, auttox

DHI, 6 mg/100 ml pH 7.0, AMS12 mg/100 ml , auttox



Valutazione degli effetti di AMS in melanociti umani

AMS *in vitro*

concentrazione 0.5 ÷ 1 mg/ml

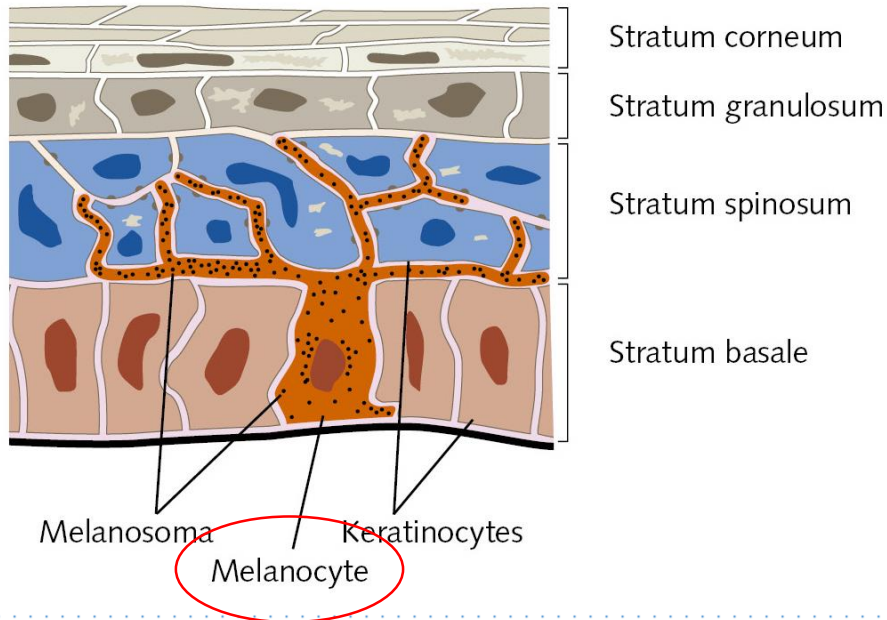
Tempo 48 ÷ 96 h

ATCC® PCS-200-013 Batch 63285932

Human scalp Gender: Female

Age: 40 years old

Race: caucasian



Effetto di AMS sulla pigmentazione di cute e capelli

- Colture primarie umane di melanociti

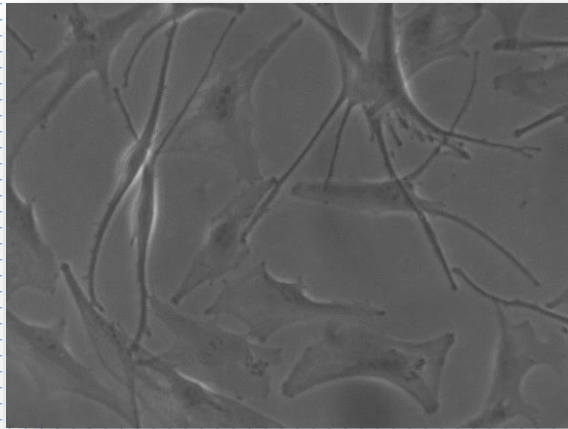
Stimolazione e vitalità dei melanociti

- Test in vitro e microarray per profili di espressione genica

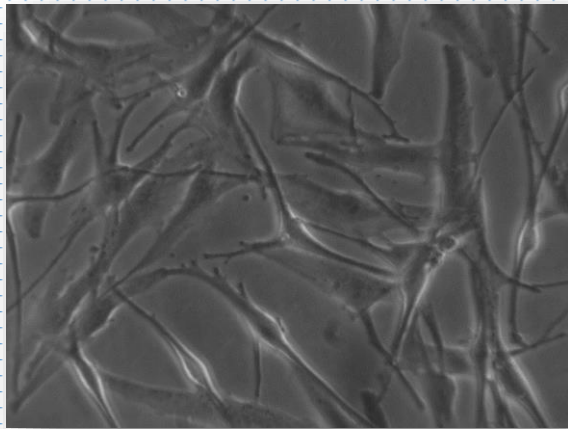
Sintesi, espressione ed accumulo delle melanine

- Attività dei principali enzimi del pathway biosintetico e dosaggio cellulare delle melanine

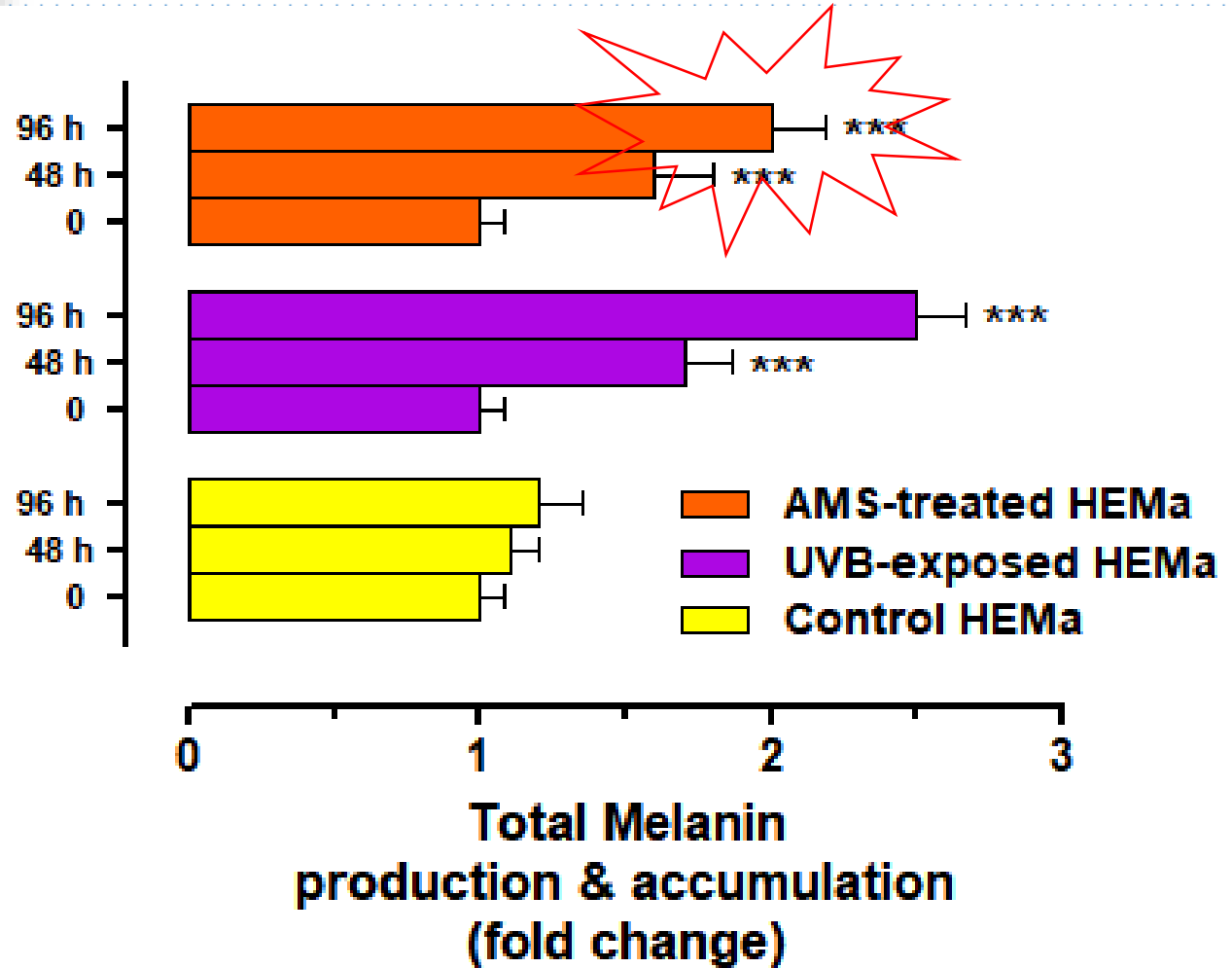
Effetto di AMS sulla produzione di melanine in melanociti primari umani

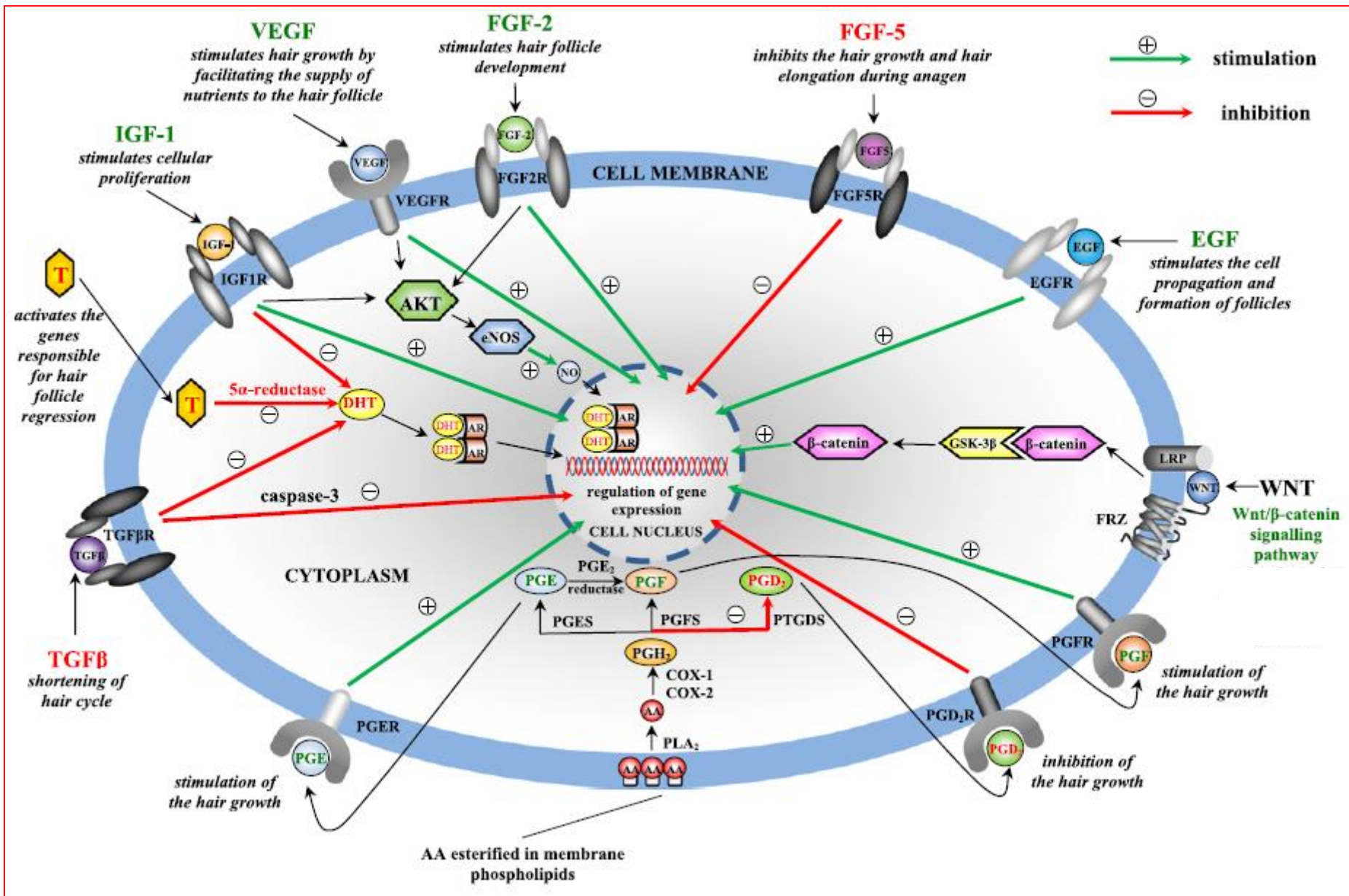


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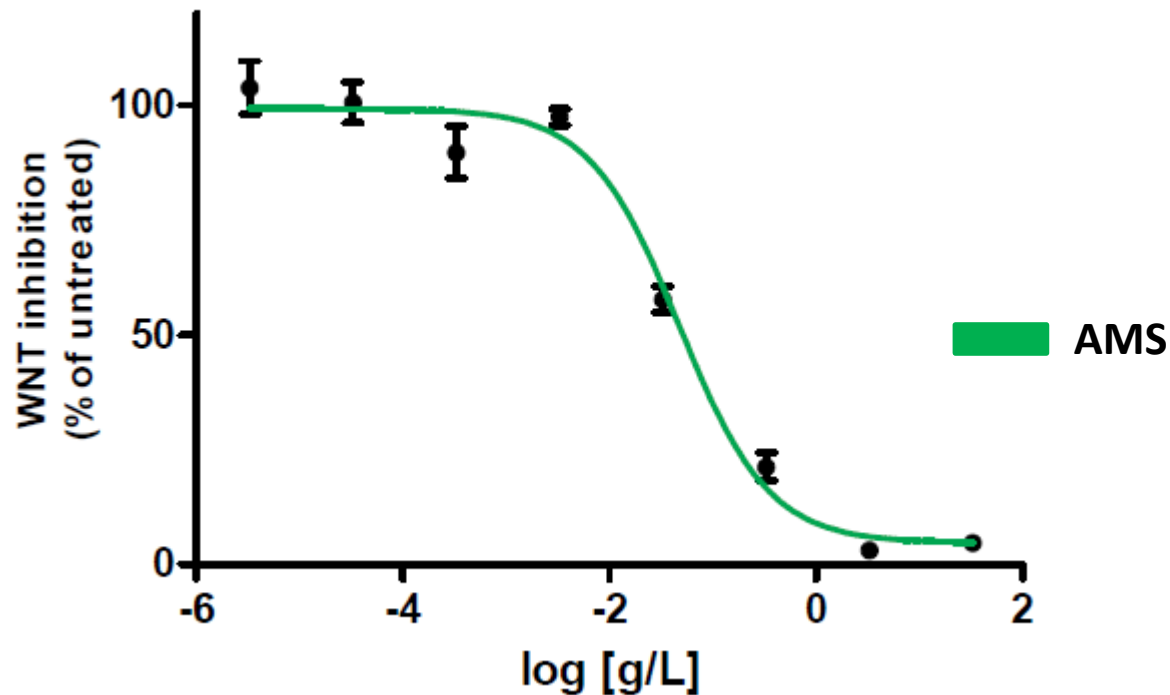


T 96





AMS down-regola il pathway di WNT



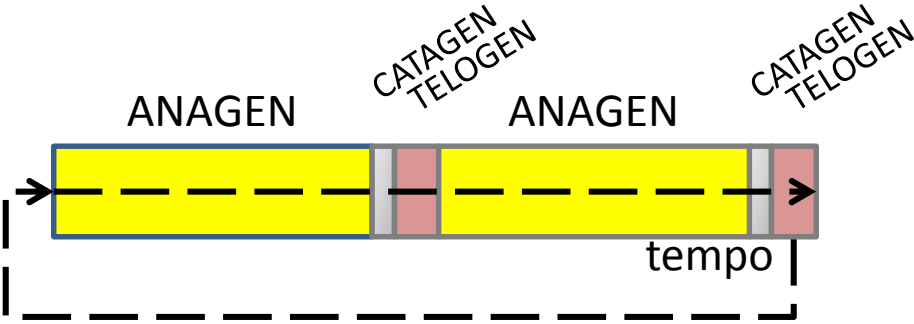
nutrients



WNT Inhibitory Activity of *Malus Pumila miller cv Annurca* and *Malus domestica cv Limoncella* Apple Extracts on Human Colon-Rectal Cells Carrying Familial Adenomatous Polyposis Mutations

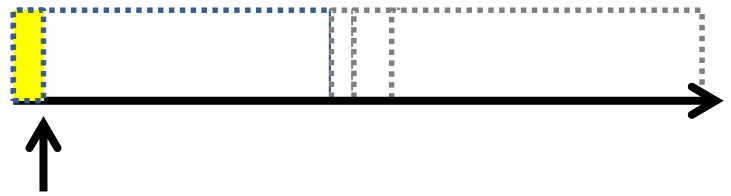
Riccio, G., Mastro, M., Bottone, S., Badolati, N., Rossi, G. B., Tenore, G. C., ... **Novellino, E.** (2017). *Nutrients*, 9(11), 1262.

I bulbi del capello spendono la maggior parte del loro tempo in fasi **ANAGEN** di crescita, intervallate da brevi fasi **CATAGEN** di regressione e **TELOGEN** di quiescenza e ricambio



Su bulbi murini in fase ANAGEN

Annurtricomplex....



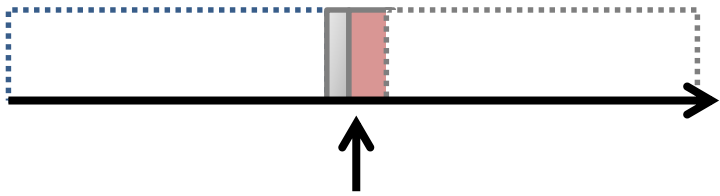
.....estende la fase ANAGEN



Estendendo la fase ANAGEN si promuove crescita, allungamento e trofismo dei peli

Su bulbi murini in fase TELOGEN

Annurtricomplex....



..... rallenta la transizione TELOGEN-ANAGEN



Estendendo la fase TELOGEN si favorisce il rinfoltimento dei peli

IL MATTINO

3 marzo 2018
Sabato

Fondato nel 1892

la  osca

La rivincita della mela annurca

Pietro Treccagnoli

È la rivincita della mela povera, la mela annurca, frutto antico che compare anche nei dipinti rinvenuti negli Scavi di Pompei, prodotto campano per eccellenza che in origine era intensivamente coltivato quasi solo nel Giuglianese. Nei primi giorni d'autunno le campagne a nord di Napoli si trasformavano in una larga distesa sempre più rossa, per le mele messe a maturare sui lunghi tappeti di paglia. Frutto di nobiltà contadina, ma negletto per decenni. Poi la rivalutazione commerciale e la scoperta delle sue qualità farmacologiche.

Che aiutasse a combattere il colesterolo era noto. Per accaparrarsi i suoi estratti venduti come inte-



gratori in farmacia occorre prenotarsi con almeno due settimane d'anticipo. Ora, però, uno studio del Pascale e della Federico II ha scoperto che l'annurca può evitare la caduta dei capelli a chi si sottopone alle chemioterapie per combattere il cancro. Siamo agli inizi della sperimentazione che riguarda le pazienti colpite dal tumore al seno. Le donne non dovrebbero essere più costrette a usare cappelli e parucche per nascondere l'avvilente effetto collaterale delle cure. La mela che le mamme usavano come panacea ai nostri malanni d'infanzia non è più il frutto proibito che provocò la cacciata dal Paradiso terrestre, ma un alleato di Eva per evitare i danni di un infido serpente.

La procianidina B2 delle mele promuove la crescita dei capelli !



Ettore Novellino

Napoli, 15 aprile 2018