

Ceramidy v kůži **a jejich využití v léčbě kožních onemocnění**

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*Univerzita Karlova,
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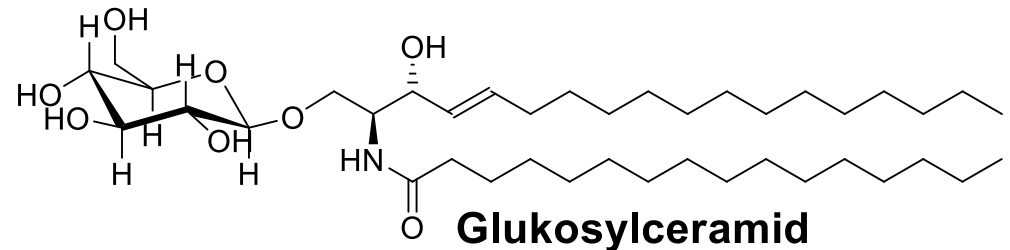
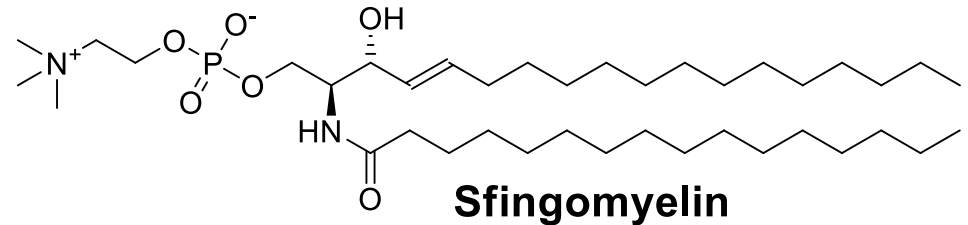
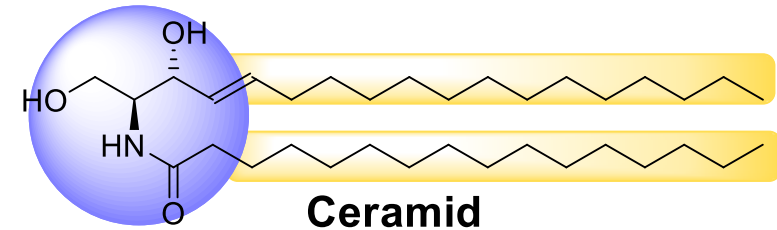
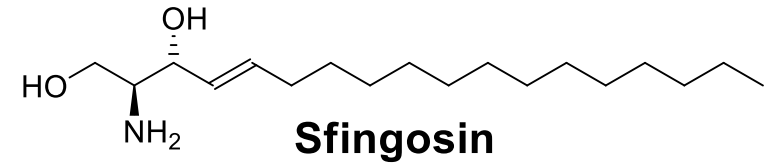


Ceramidy

- sfingolipidy (1884)
- polární „hlava“
a 2 hydrofobní řetězce

Výskyt ceramidů:

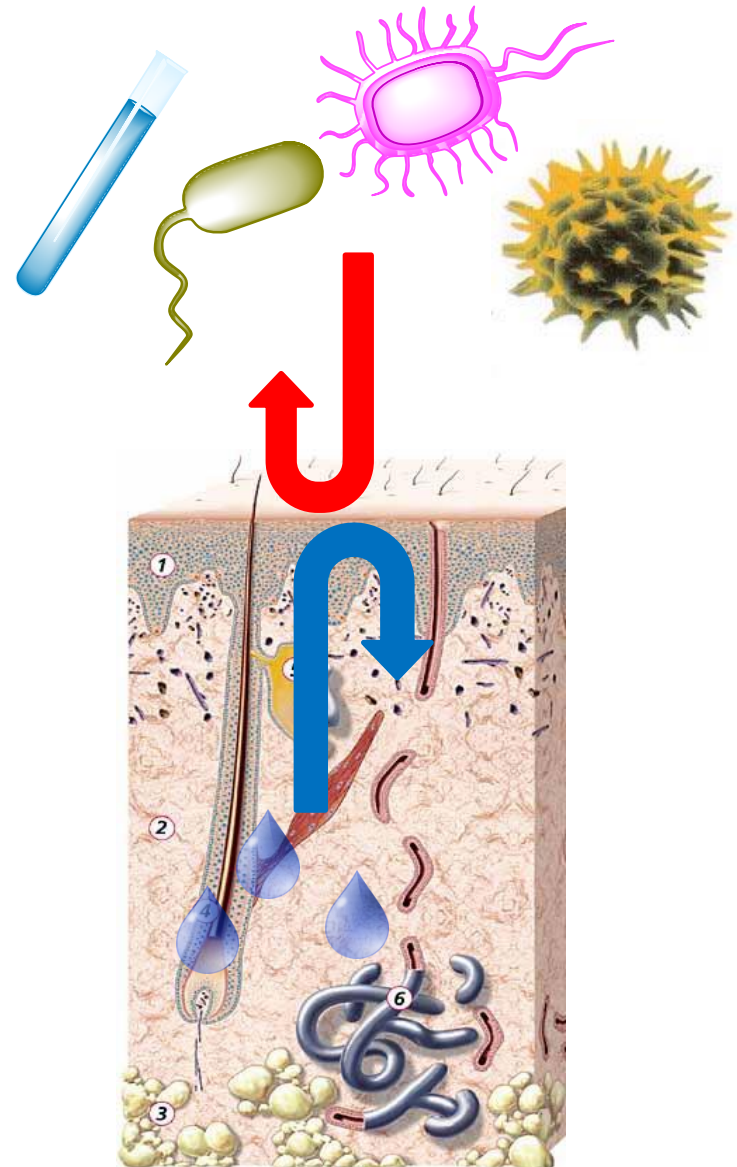
1. všechny buňky (nízké koncentrace)
- **buněčná signalizace**
2. mezi buňkami rohové vrstvy kůže
(vysoké koncentrace)
- **bariérová funkce kůže**



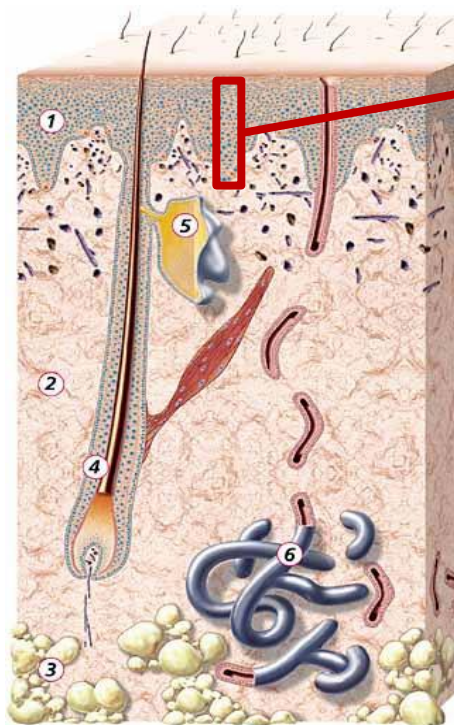
Weinberg, Prose, Kristal, Color Atlas of Pediatric Dermatology

Úloha ceramidů v kůži

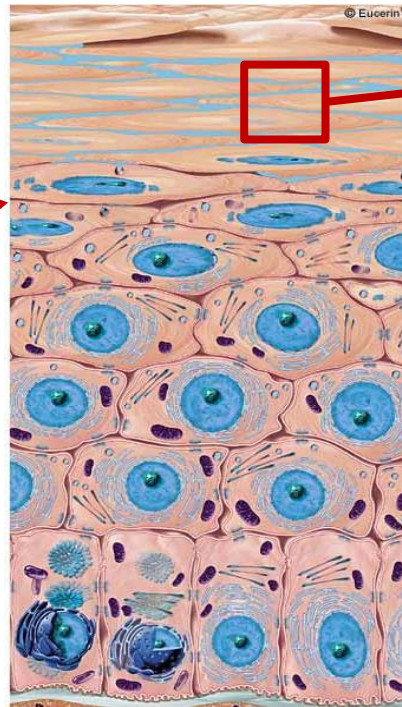
- zabránit **prostupu toxických látek**, alergenů a mikrobů do organismu
- zamezit nadměrné **ztrátě vody** a endogenních látek z organismu



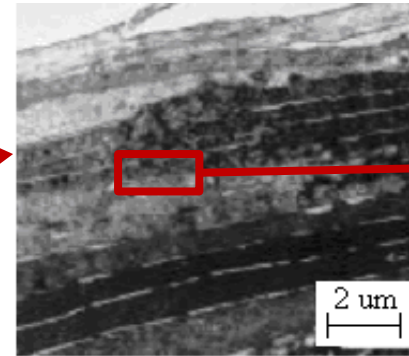
Kožní bariéra



kůž



epidermis

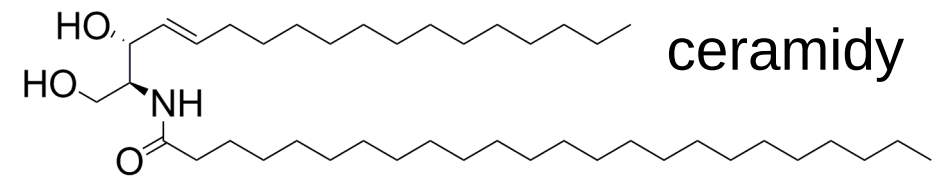


stratum corneum

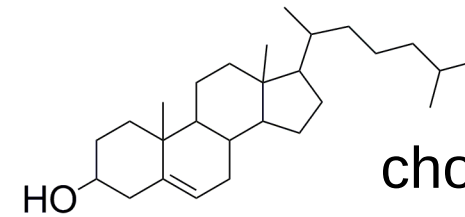


mezibuněčné lipidy

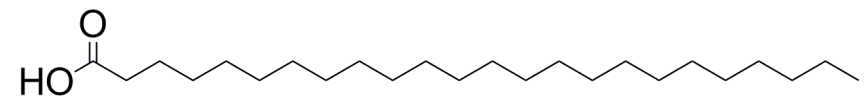
korneocyt



ceramidy



cholesterol



mastné kyseliny

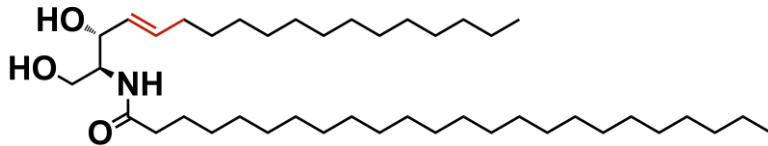
Struktura ceramidů v kůži

1) Volné ceramidy

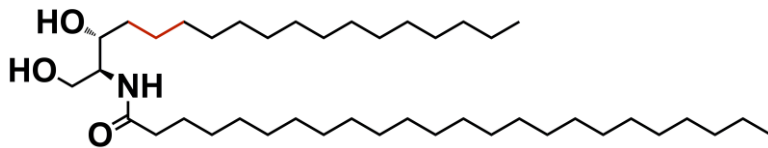
15 podtříd

> 400 chemicky různých struktur

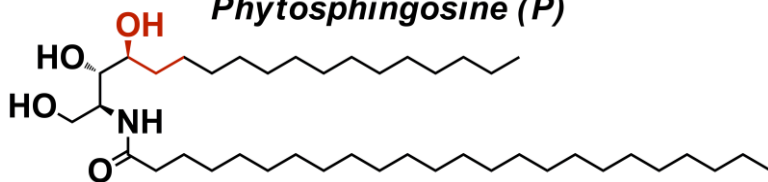
Sphingosine (S)



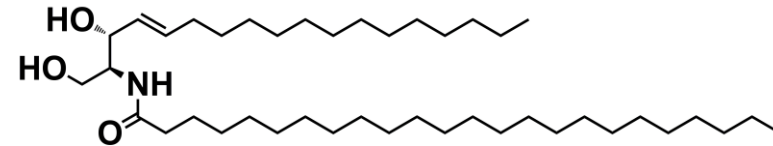
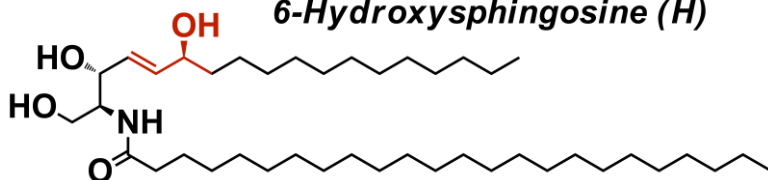
Dihydrosphingosine (DS)



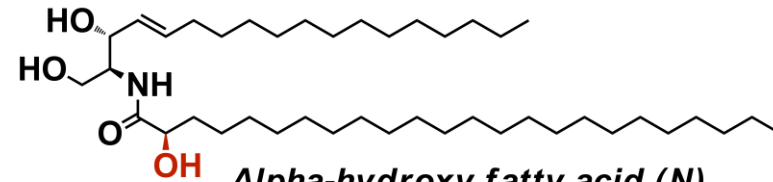
Phytosphingosine (P)



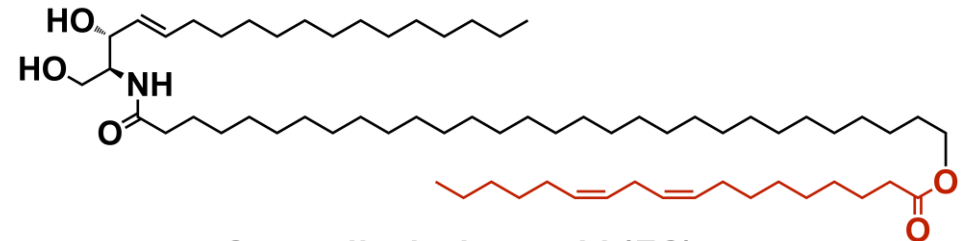
6-Hydroxysphingosine (H)



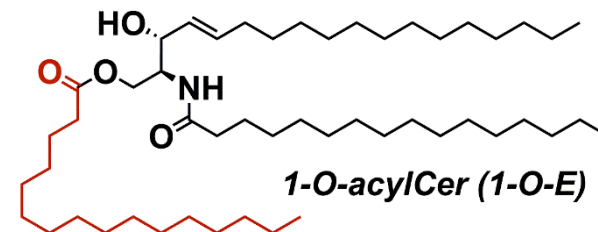
Non-hydroxy fatty acid (N)



Alpha-hydroxy fatty acid (N)



Omega-linoleyloxy acid (EO)



1-O-acylCer (1-O-E)

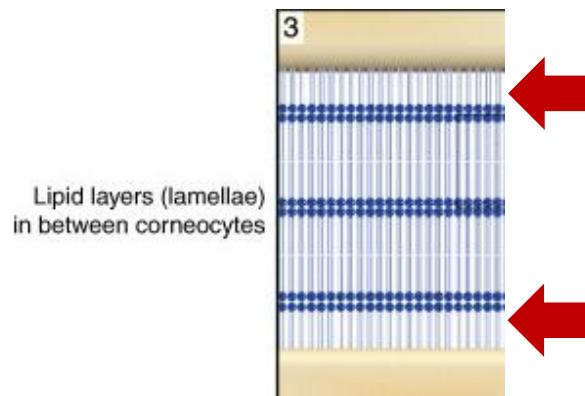
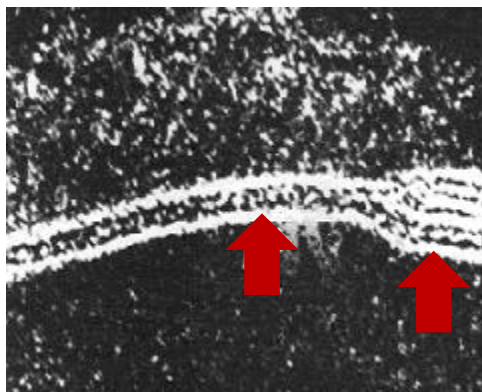
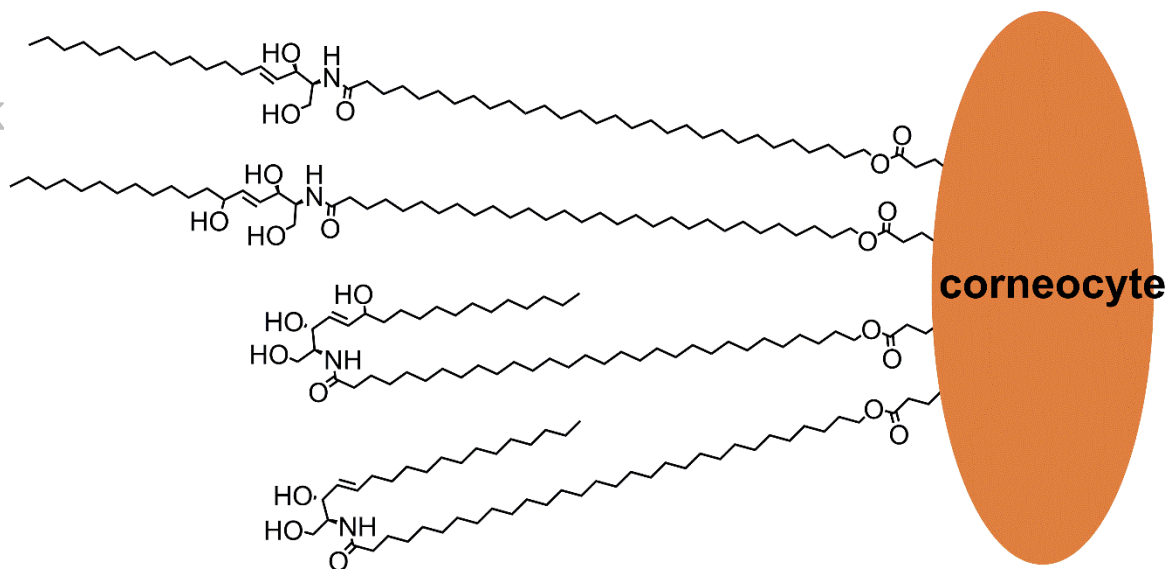
Struktura ceramidů v kůži

1) Volné ceramidy

15 podtříd

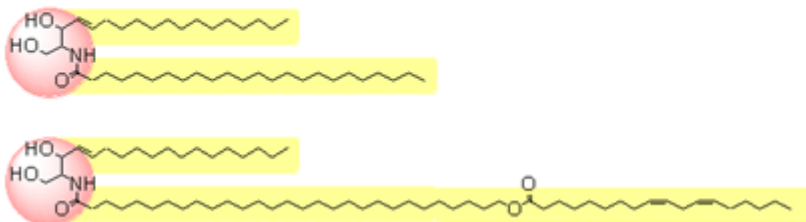
> 400 chemicky různých struk

2) Ceramidy vázané na bílkoviny (korneocytální lipidová obálka)

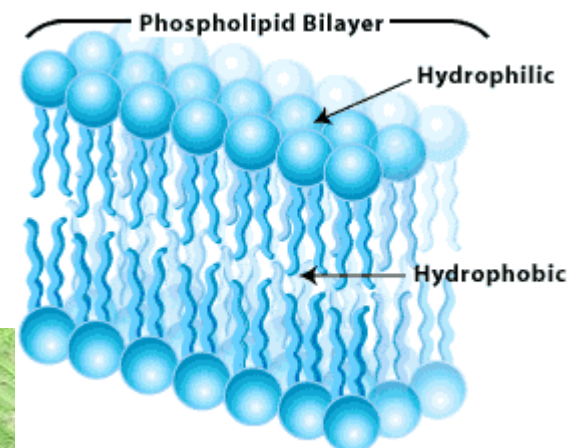
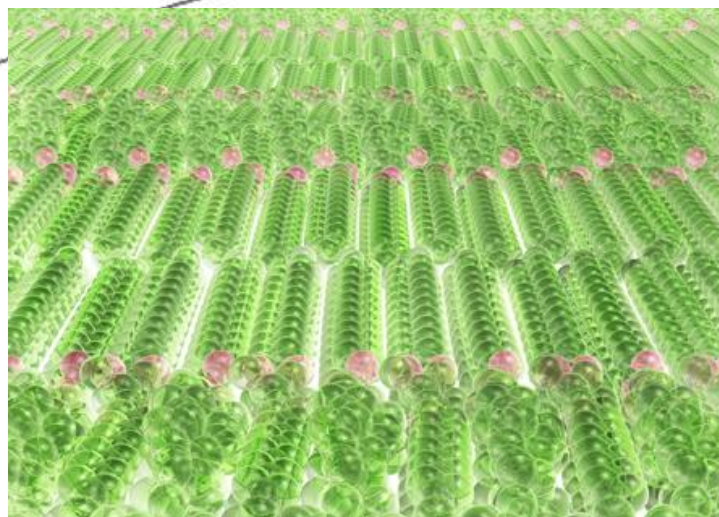
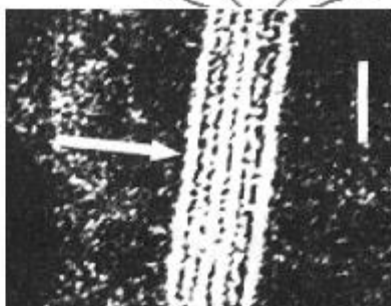
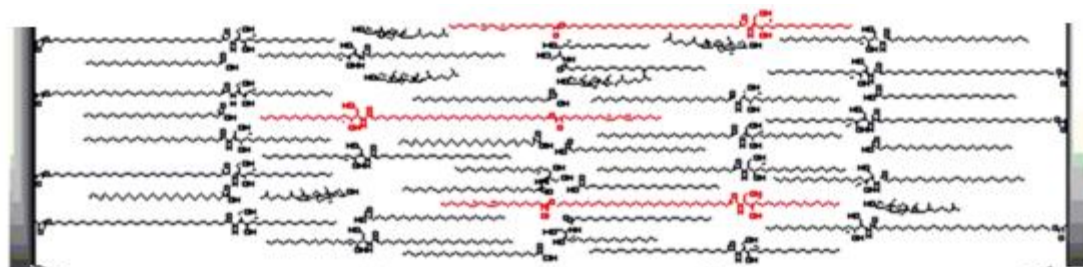
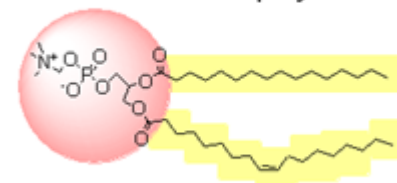


Uspořádání kožních lipidů

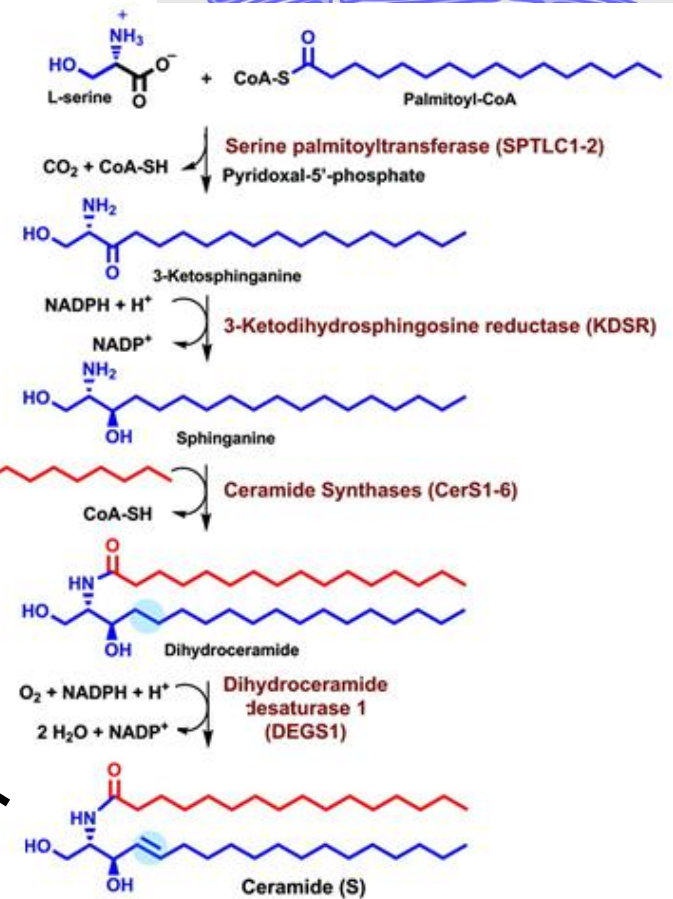
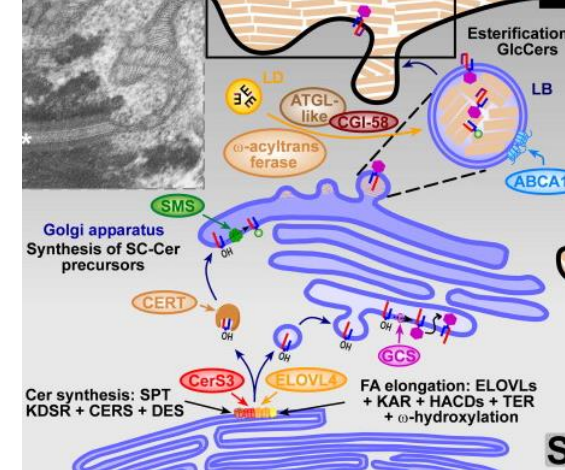
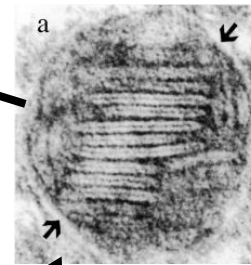
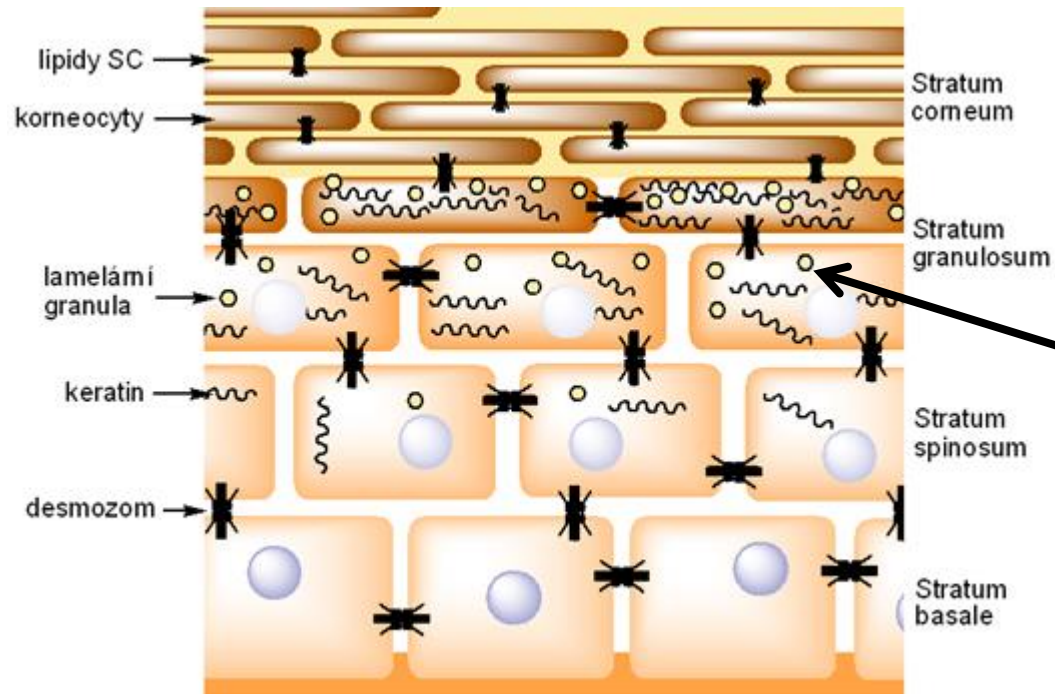
Ceramidy

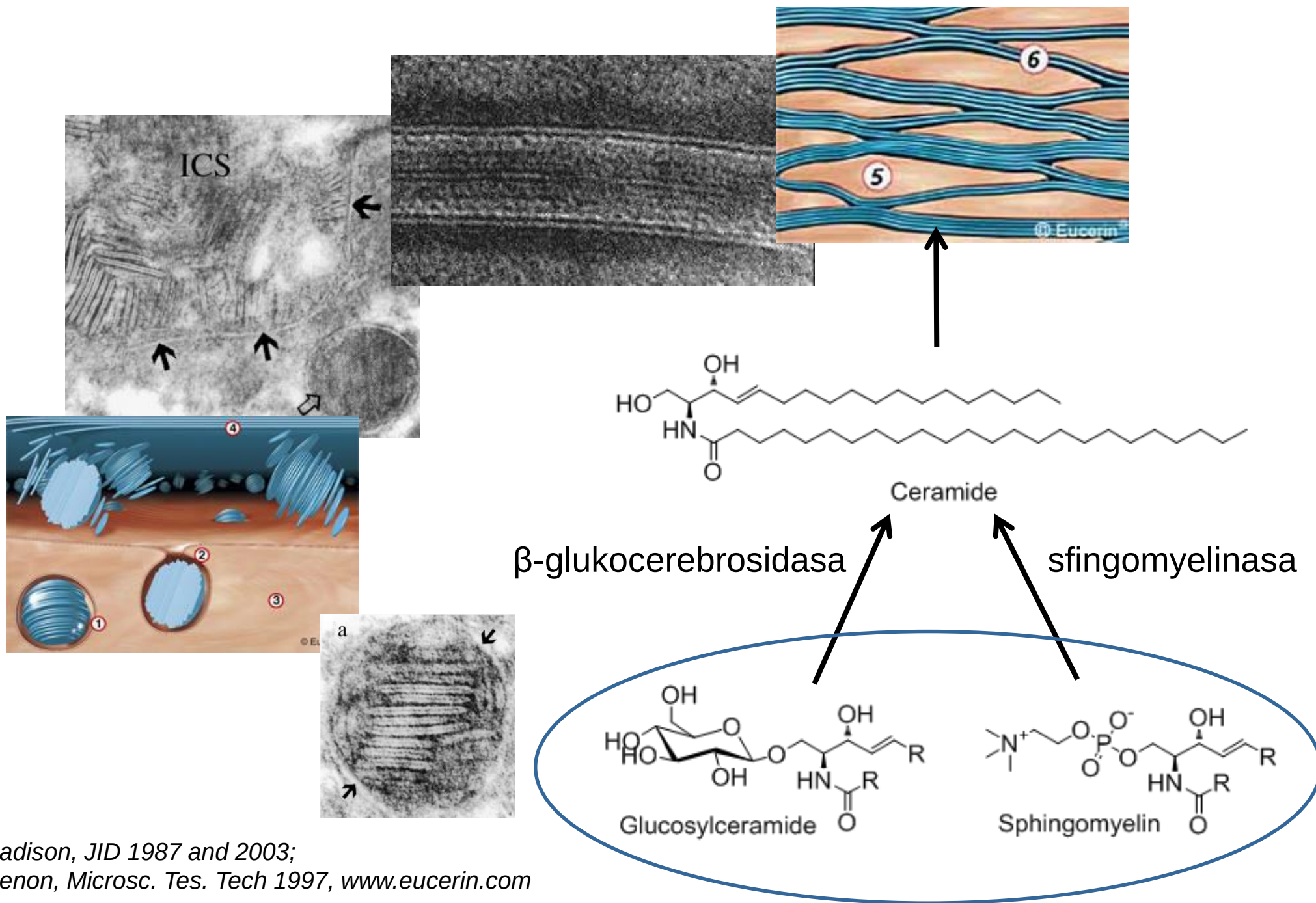


Fosfolipidy



Vznik kožní bariéry

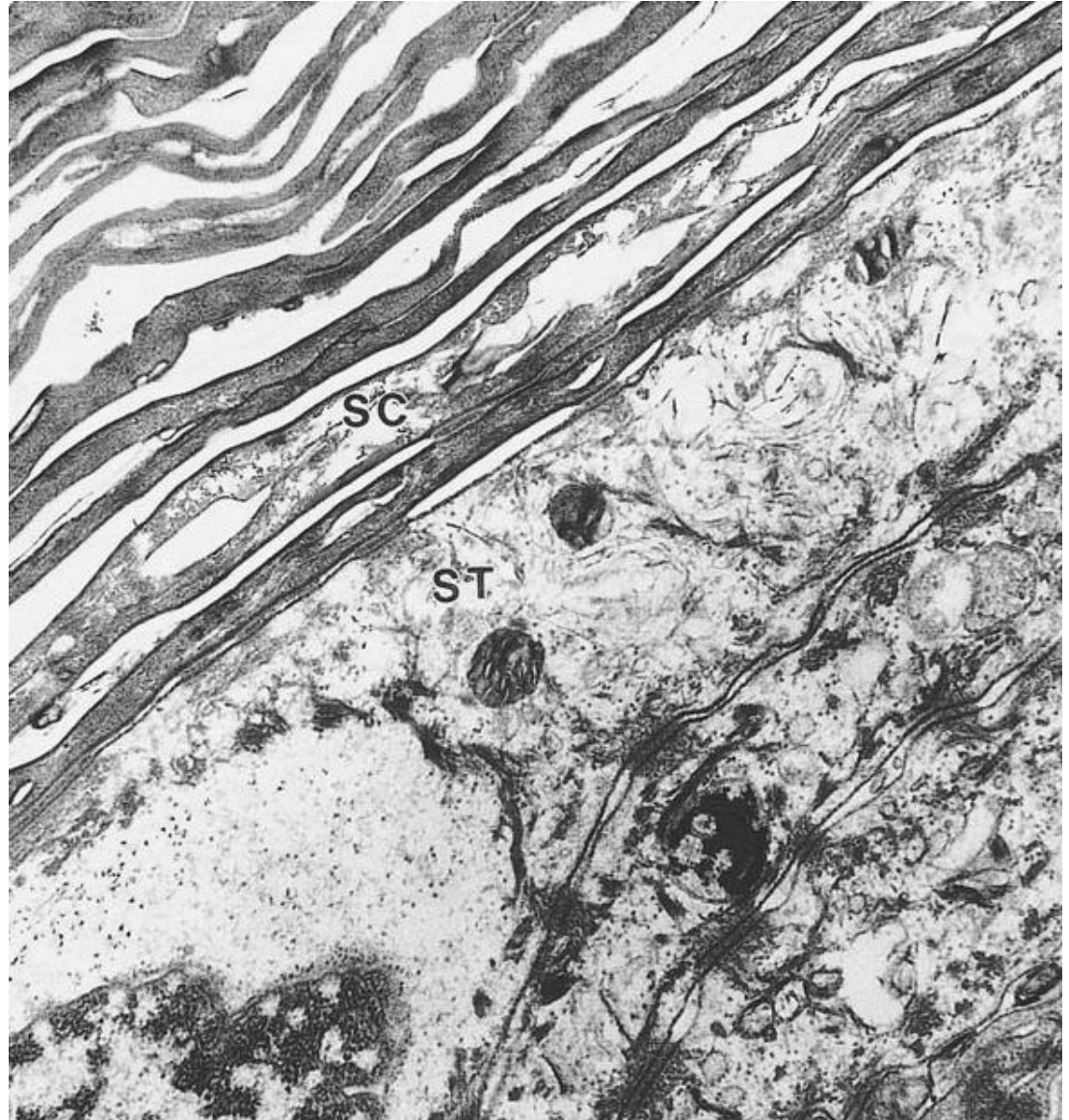
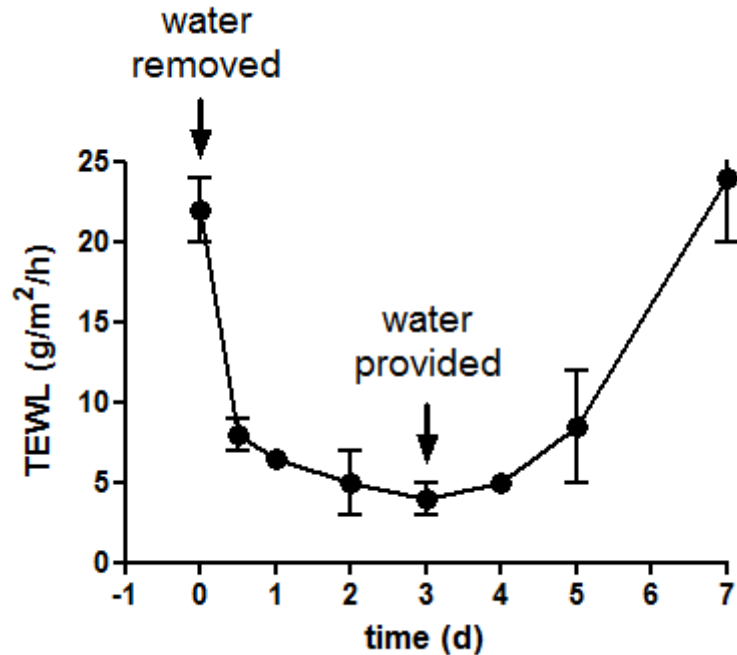




Adaptace kožní bariéry



www.sfu.ca

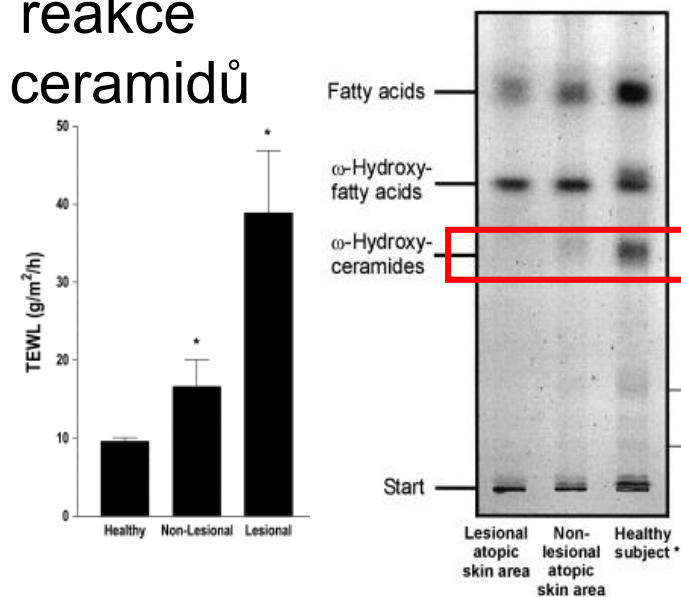
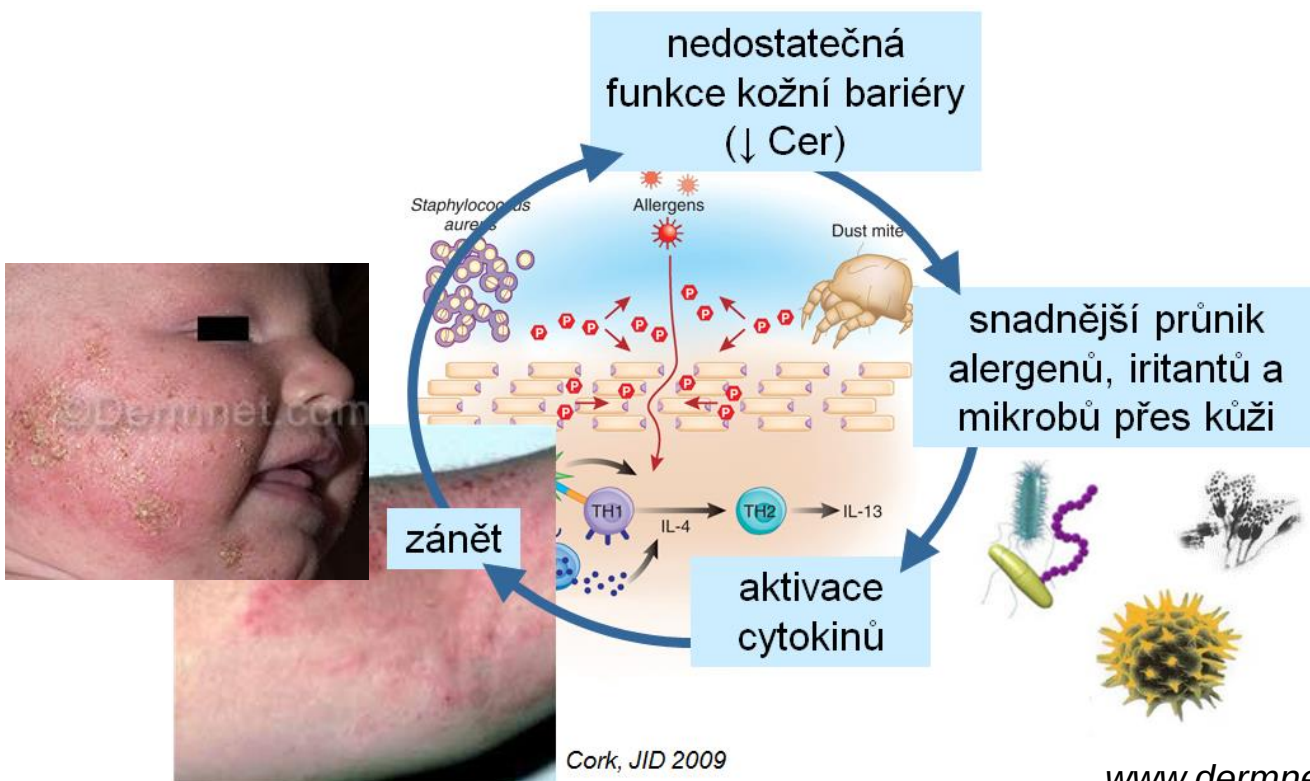


Poškození kožní bariéry se sníženým obsahem ceramidů

- Atopická dermatitida**

zánětlivé kožní onemocnění, atypická imunitní reakce

↑ propustnost kůže pro vodu, ↓ celkový obsah ceramidů



Poškození kožní bariéry se sníženým obsahem ceramidů

- Atopická dermatitida

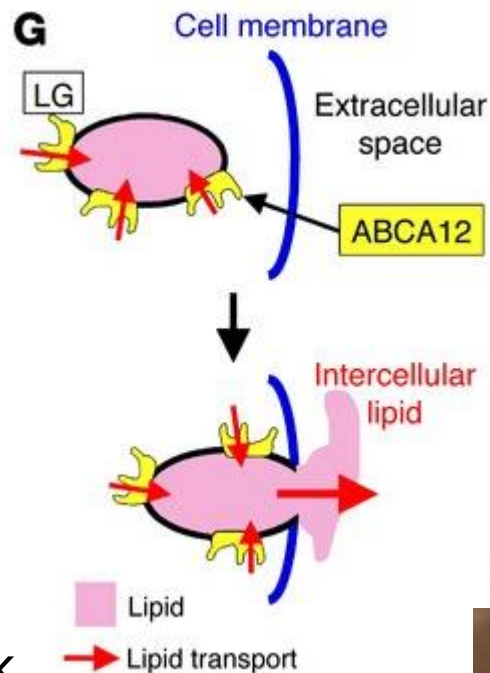
- **Psoriáza**

↓ množství prosaposinu → nedostatečná aktivace
enzymů uvolňujících ceramidy



Poškození kožní bariéry se sníženým obsahem ceramidů

- Atopická dermatitida
- Psoriáza
- **Ichtyózy**
např. harlekýnská ichthyóza
- mutace genu pro transportér *ABCA12* → neschopnost transportovat GlcCer do lamelárních granul → nedostatek ceramidů ve stratum corneum



Poškození kožní bariéry se sníženým obsahem ceramidů

- Atopická dermatitida
- Psoriáza
- Ichtyózy
- Stárnoucí kůže

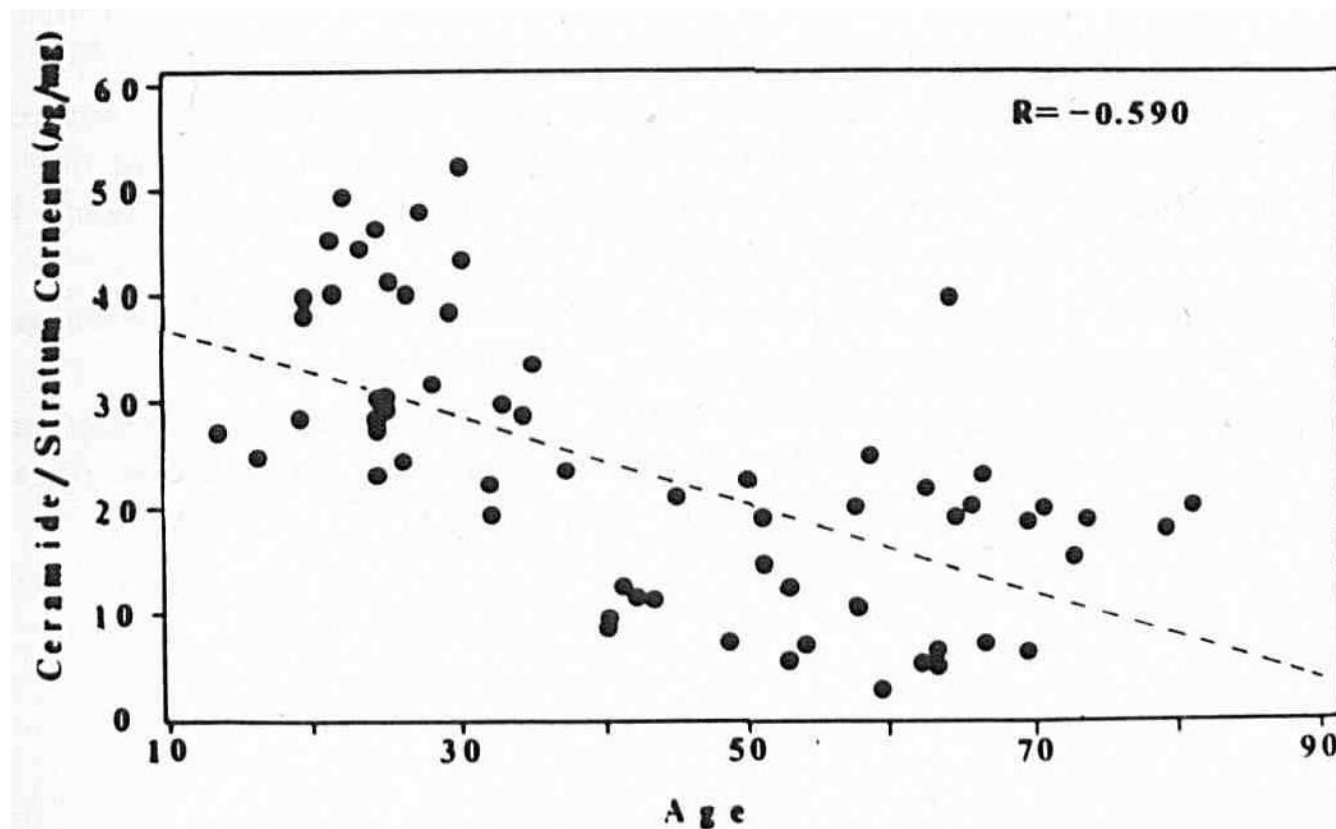
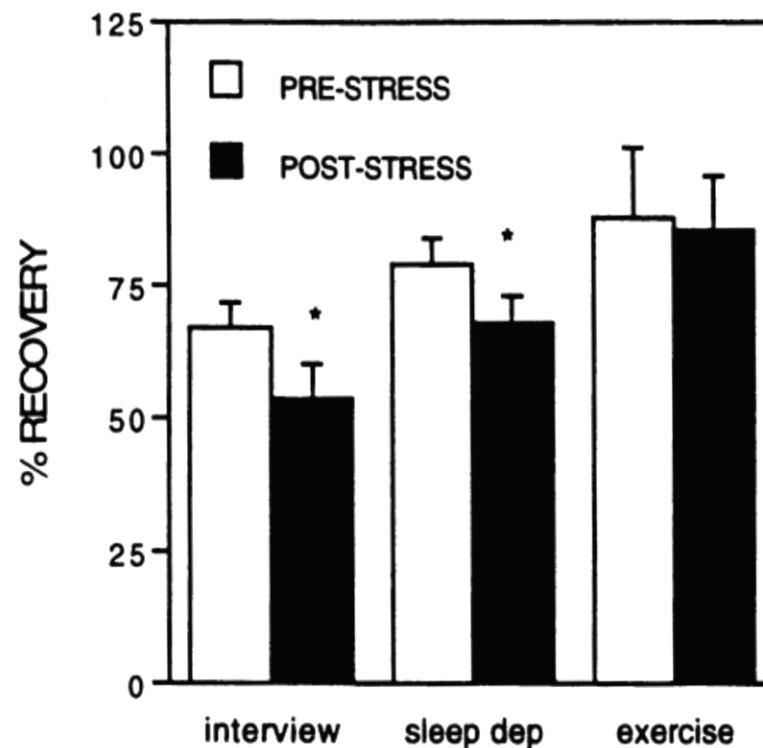


Figure 5. Total ceramide content (μg) per mg stratum corneum as a function of age in healthy subjects ($n = 65$), $r = -0.59$, $p < 0.01$.

Poškození kožní bariéry se sníženým obsahem ceramidů

- Atopická dermatitida
- Psoriáza
- Ichtyózy
- Suchá a stárnoucí kůže
- Psychologický stres

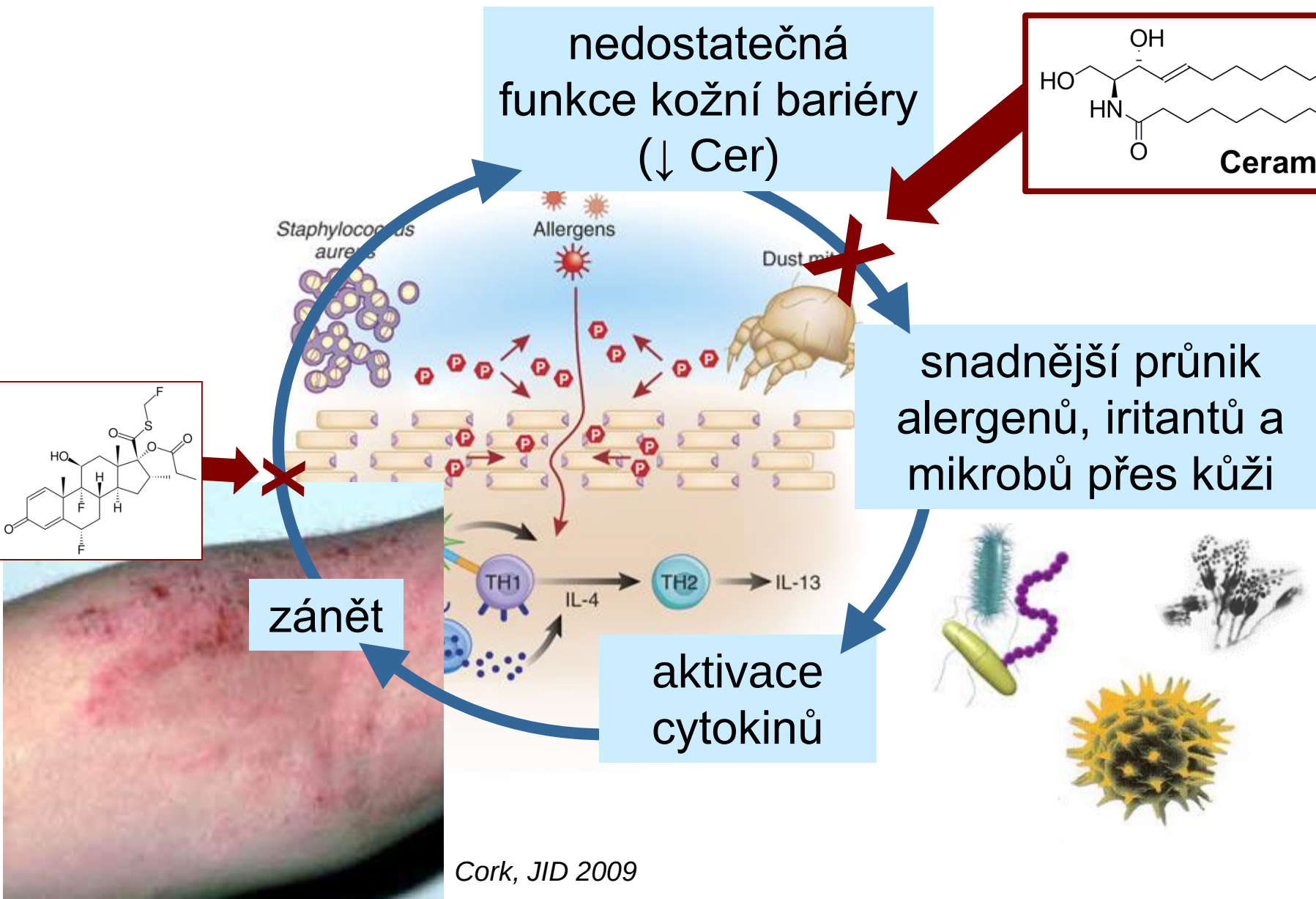
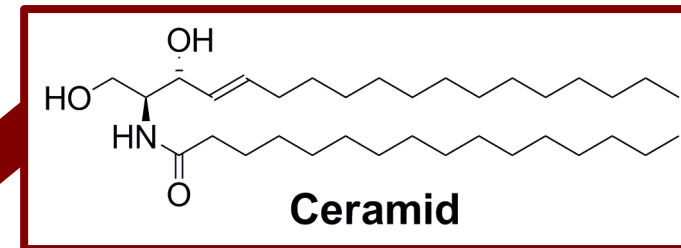


Ženy, schopnost regenerace kožní bariéry:

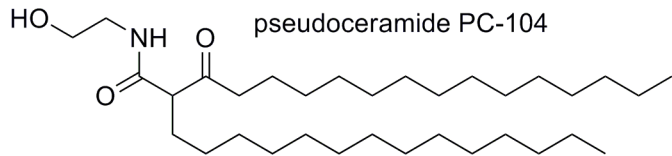
- a) pracovní pohovor 5 min
- b) 42 h spánková deprivace
- c) 3 dny 1-h cvičení na rotopedu

(Altemus JID 2001)

Využití (pseudo)ceramidů v terapii



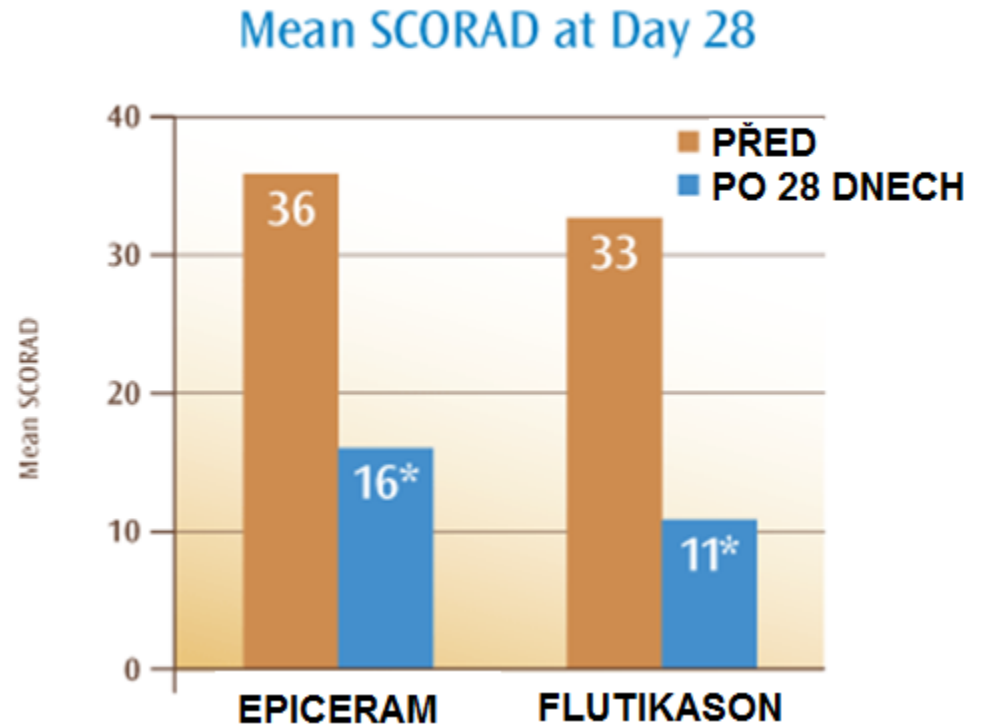
Využití pseudoceramidů v terapii?

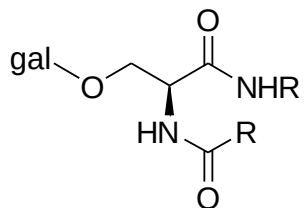


před

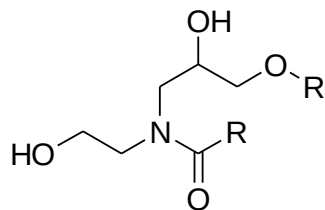


po 12 týdnech

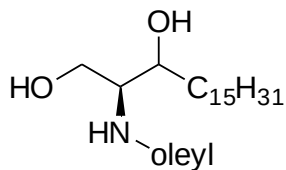




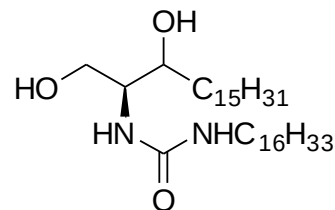
Fukunaga,
BMCL 2003



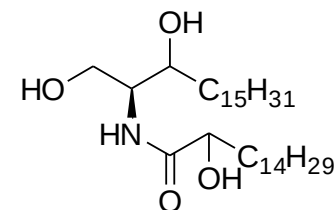
Imokawa, JID 1997



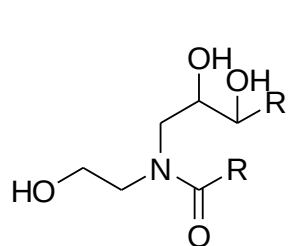
L'Oreal
"Ceramide R"



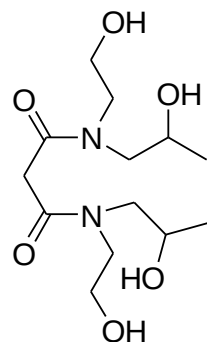
L'Oreal
US 6203808, 2001



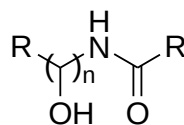
L'Oreal
US 6497888, 2002



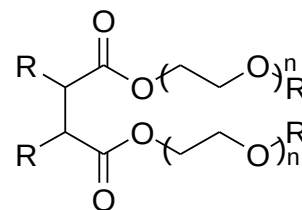
Elizabeth Arden
US 5206020, 1993



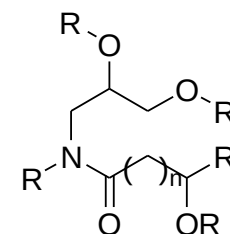
Quest
US 5656668, 1997



Henkel
WO 9924535, 1999



Henkel
WO 9535088, 1995



Unilever
EP 0495624, 1992

BUILD AND RENEW.

CERAMIDE CAPSULES

Daily Youth Restoring Serum

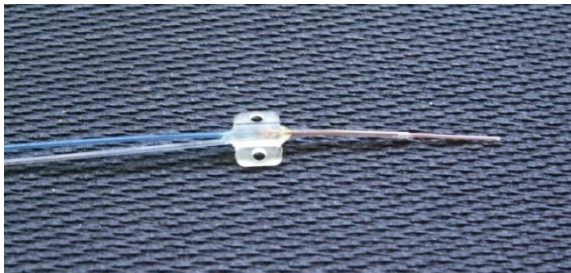
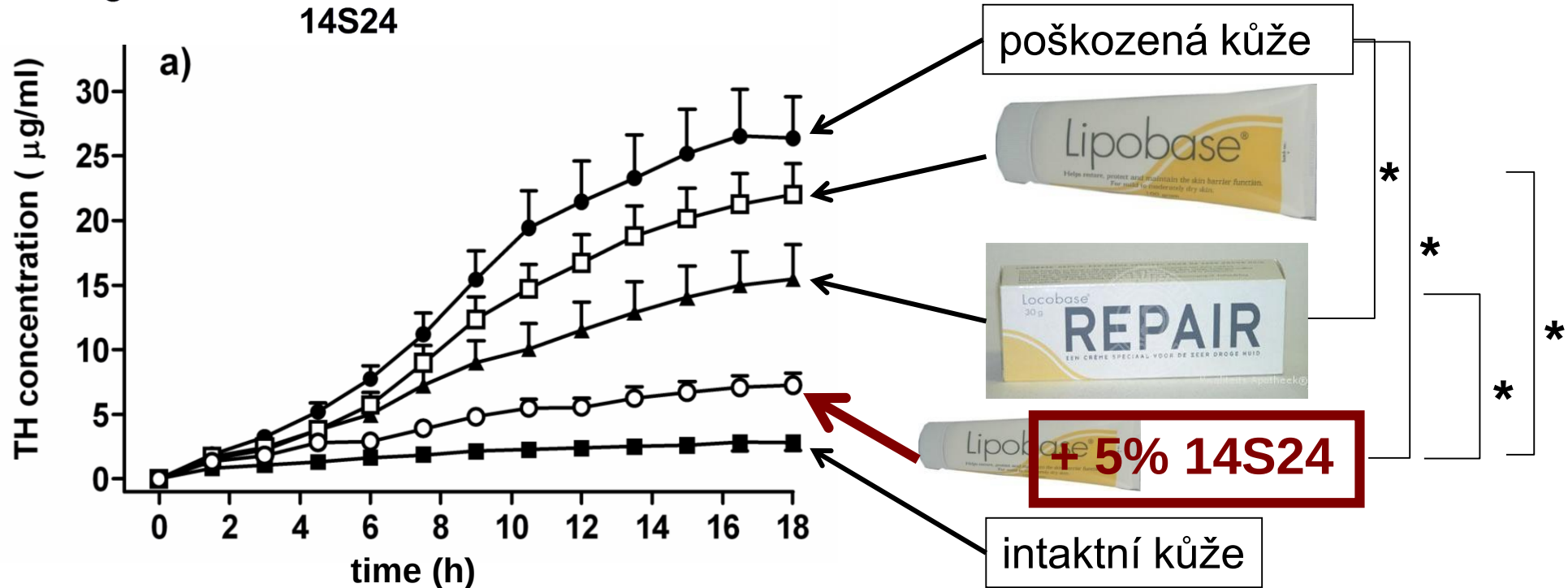
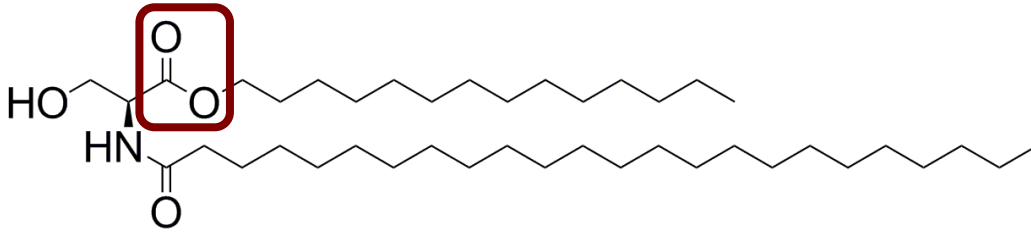
The power to restore youthful, more radiant-looking skin, right in the palm of your hand.

Developed by Arden Active Skincare, this anti-aging powerhouse visibly improves tone and clarity, and reduces the look of lines and wrinkles. Featuring Ceramide Lipid Complex, it helps strengthen skin's moisture barrier for firmer, smoother and more youthful-looking skin.

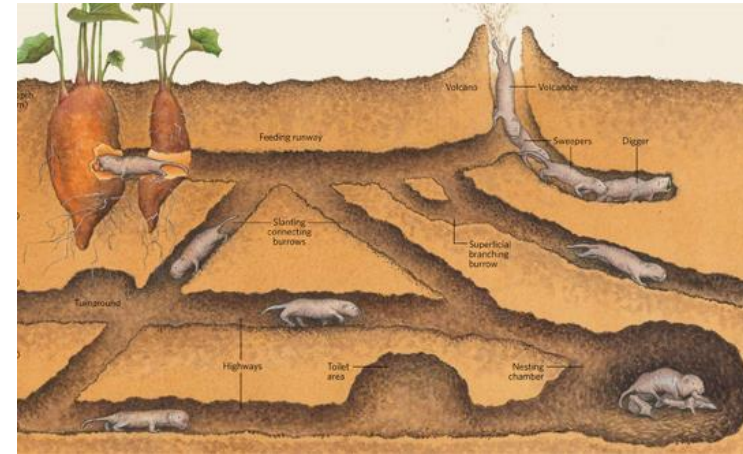
Proof... not Promises™
100% of women showed a noticeable improvement in their skin.*




Pseudoceramid 14S24



Adaptace kožní bariéry 2



<http://www.the-scientist.com/?articles.view/articleNo/32136/title/Underground-Supermodels/>

VERTEBRATE OF THE YEAR

Science, 2013

The Rat That Ages Beautifully

They will never win a beauty contest, but naked mole rats (*Heterocephalus glaber*) may hold a lesson or two for humans. Two studies this year, for instance, found clues to why these rodents can live 30 years, cancer-free. One secret may be a ribosome that excels at producing error-free proteins; misformed proteins can clog up the body's systems and accelerate aging. Another could be a supersized version of a complex sugar that seems to protect against cancer. Naked mole rats don't break this compound down as fast as other animals, so it builds up in the spaces between cells and may keep the cells from clumping together and forming tumors.



Rypoš lysý (naked mole rat)

- Eusociální savec
- Thermokonformer
- Extrémně dlouhověký
- Resistentní k nádorům
- Necítí bolest
- **Schopnost „zapnout a vypnout“ kožní bariéru**

Závěr

- kožní bariéra založená na **ceramidech ve stratum corneum** je **nutná pro přežití** člověka v suchozemském prostředí
- mnohá **kožní onemocnění** jsou spojena s nedostatkem ceramidů
- topická aplikace ceramidů/pseudoceramidů je **slibným přístupem v terapii/prevenci** těchto chorob
- porozumění adaptacím kožní bariéry u zvířat by mohlo pomoci odhalit **nové možnosti terapie** kožních onemocnění

Skin barrier research group

<http://portal.faf.cuni.cz/Groups/Skin-barrier-research-group>