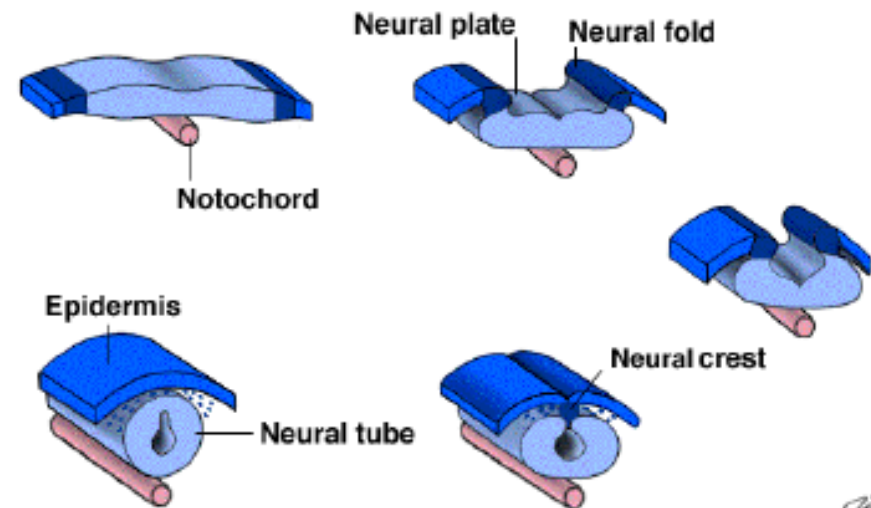
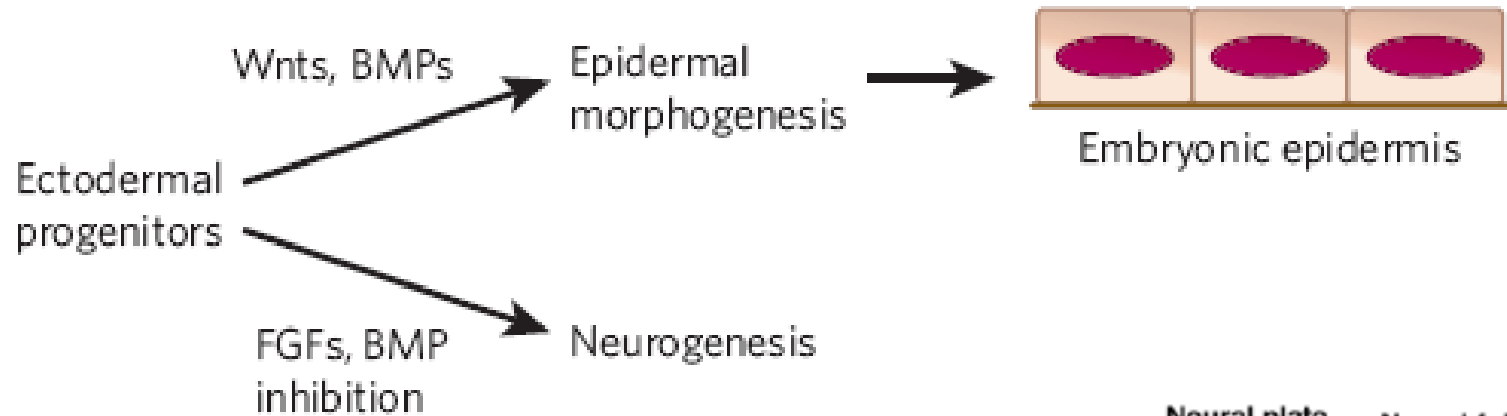


# A felszíni ektoderma differenciációja

- elkülönülése
- kialakulása az egyedfejlődés során
- szerkezete és a felnőttkori őssejtek
  - interfollikuláris epidermis
  - szőrtüsző
  - faggyúmirigy
- a bőrpótlás (klinikai) lehetőségei

# Az ektoderma specializációja

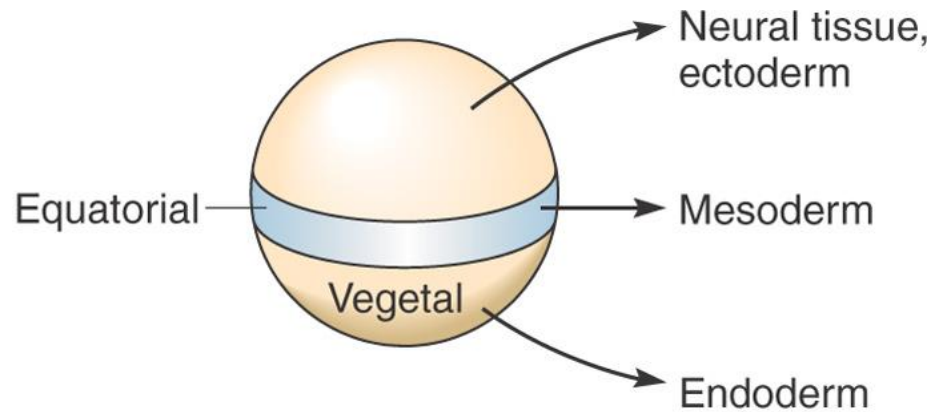
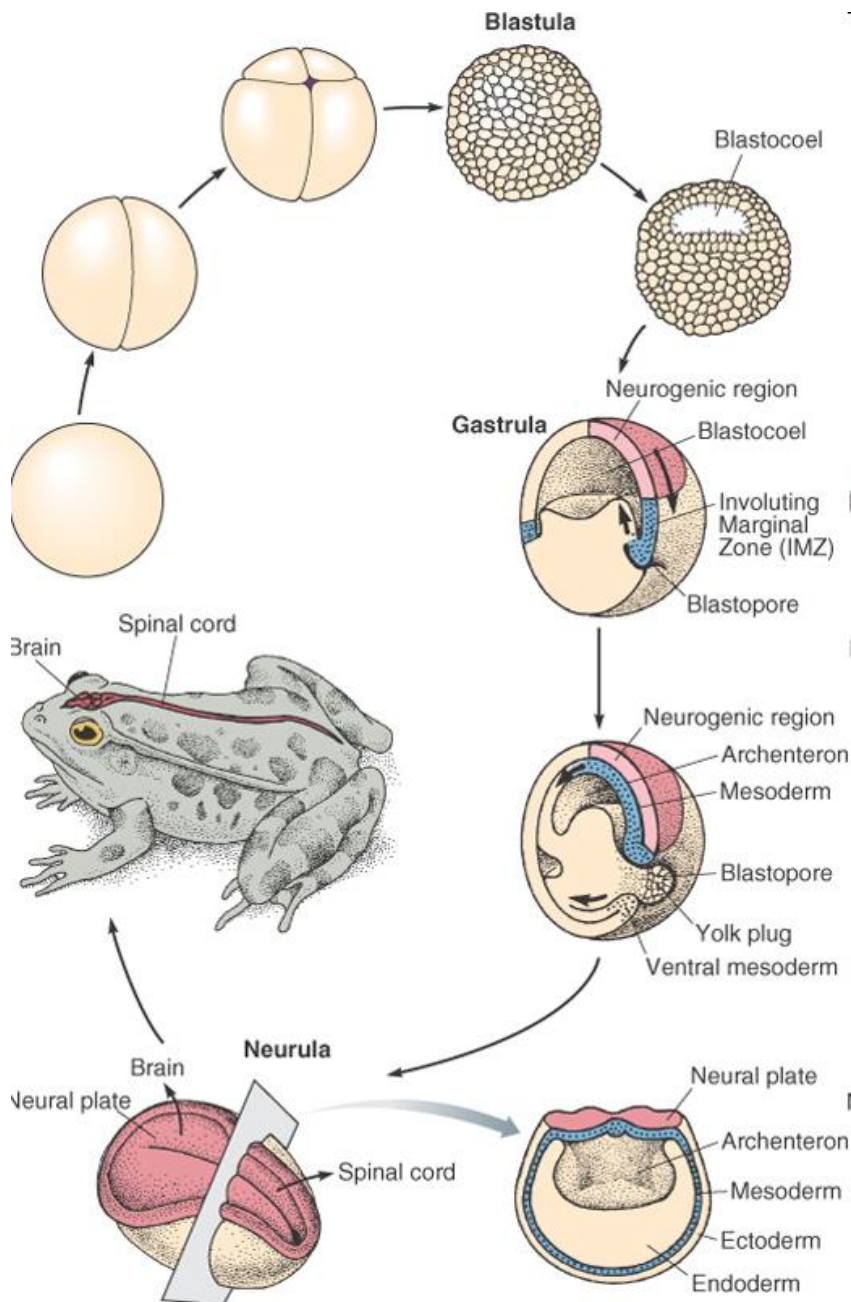


- **Wnt / BMP hatás:** epidermis

- **FGF hatás / BMP hatás gátlása:** neuroektoderma

# A kétéltűek embrionális fejlődése - az ektoderma elkülönülése

a [neuro]ektoderma az animális pólusból (animal cap) fejlődik ki



# A "klasszikus" kísérletek

- Spemann és Mangold: a dorzális ajak mint (neurális) organizátor

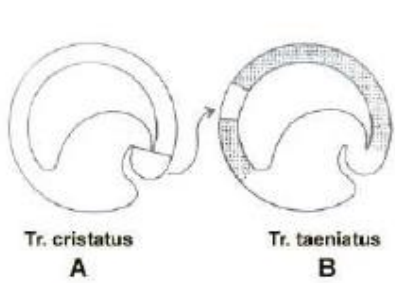
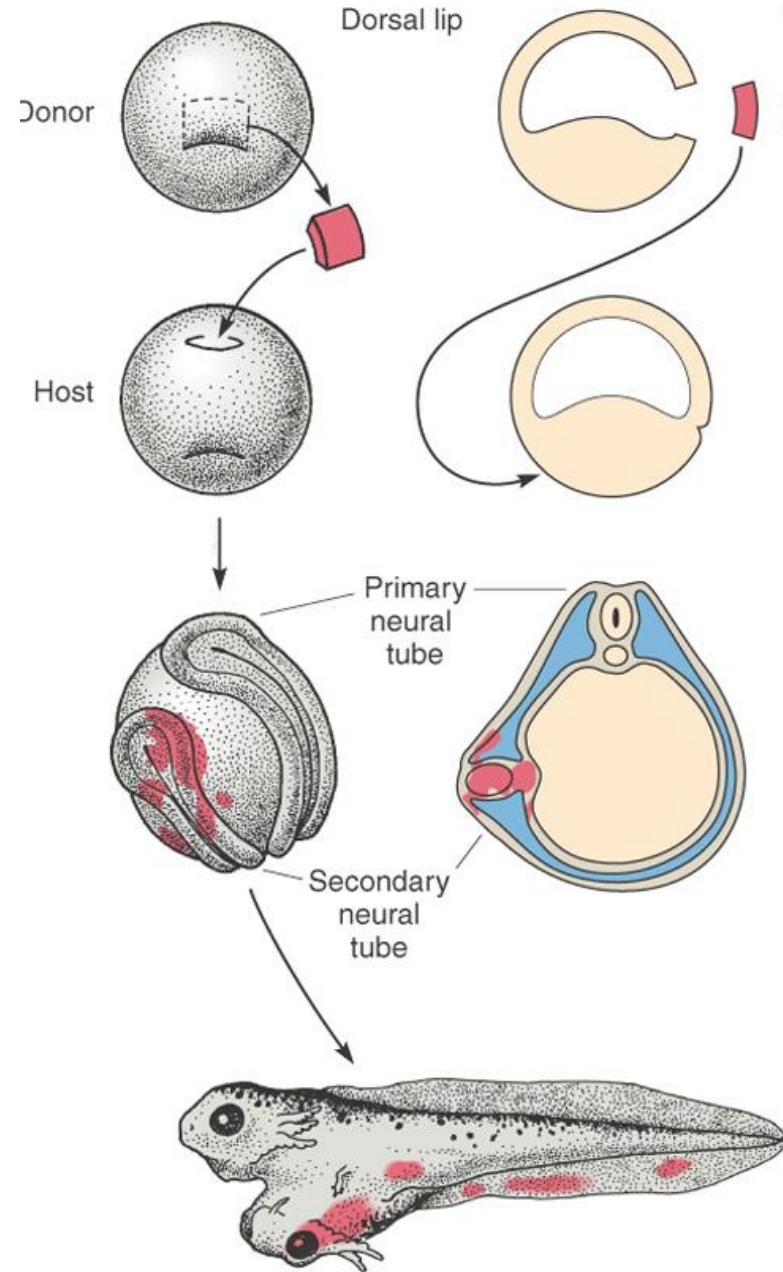


Fig. 19 (left) and 20. Um 132. The taeniatus stage of the newt larva stage; the secondary neural folds are viewed from the right side (Fig. 19), and from above (Fig. 20). 20X.



Fig. 21. Um 132b. The taeniatus embryo shown in Figs. 19 and 20, opened further, viewed from the left side. Surface view of the secondary neural folds, with dorsal neural tube somites, and notochord. 20X.

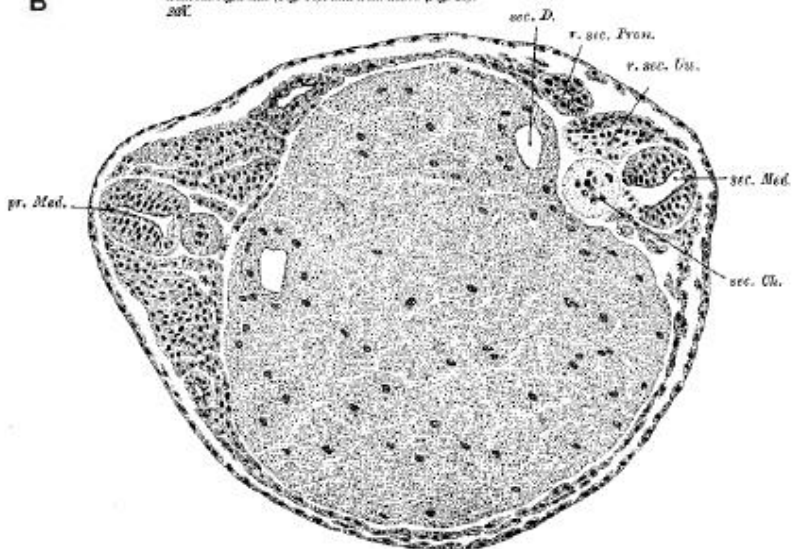
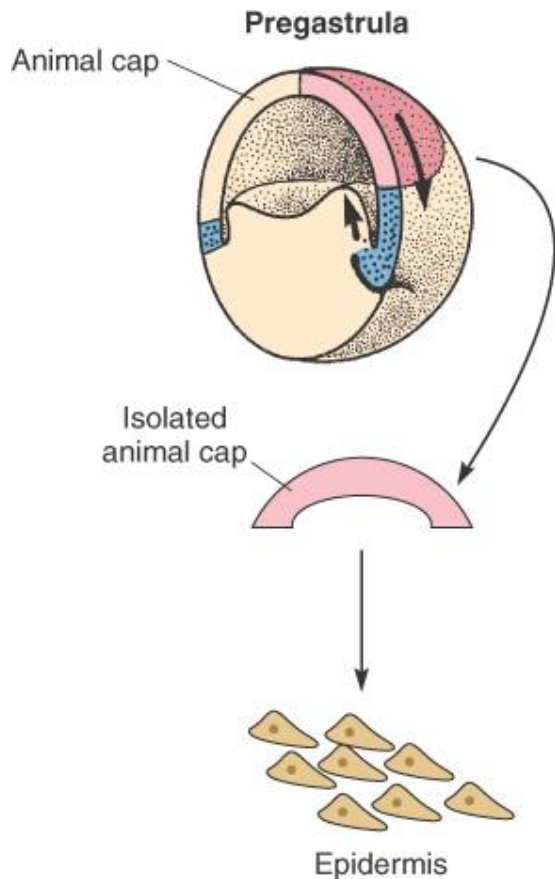


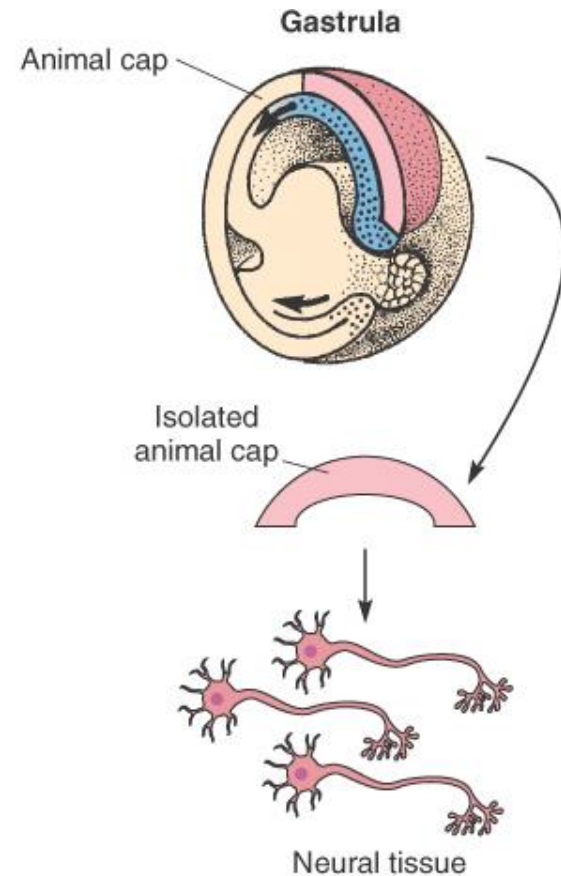
Fig. 24. Um 132b. Cross section through the middle of the embryo (cf. Fig. 21). The primary axial organs are to the figure and the secondary axial organs to the right. r. sec. Pron., right secondary pronephric duct. The implant formed notochord and part of the right secondary somite. 100X.

# A "klasszikus" kísérletek

- gasztruláció előtt izolálva az intakt animális pólus (animal cap) sejtek epidermisszé differenciálódnak



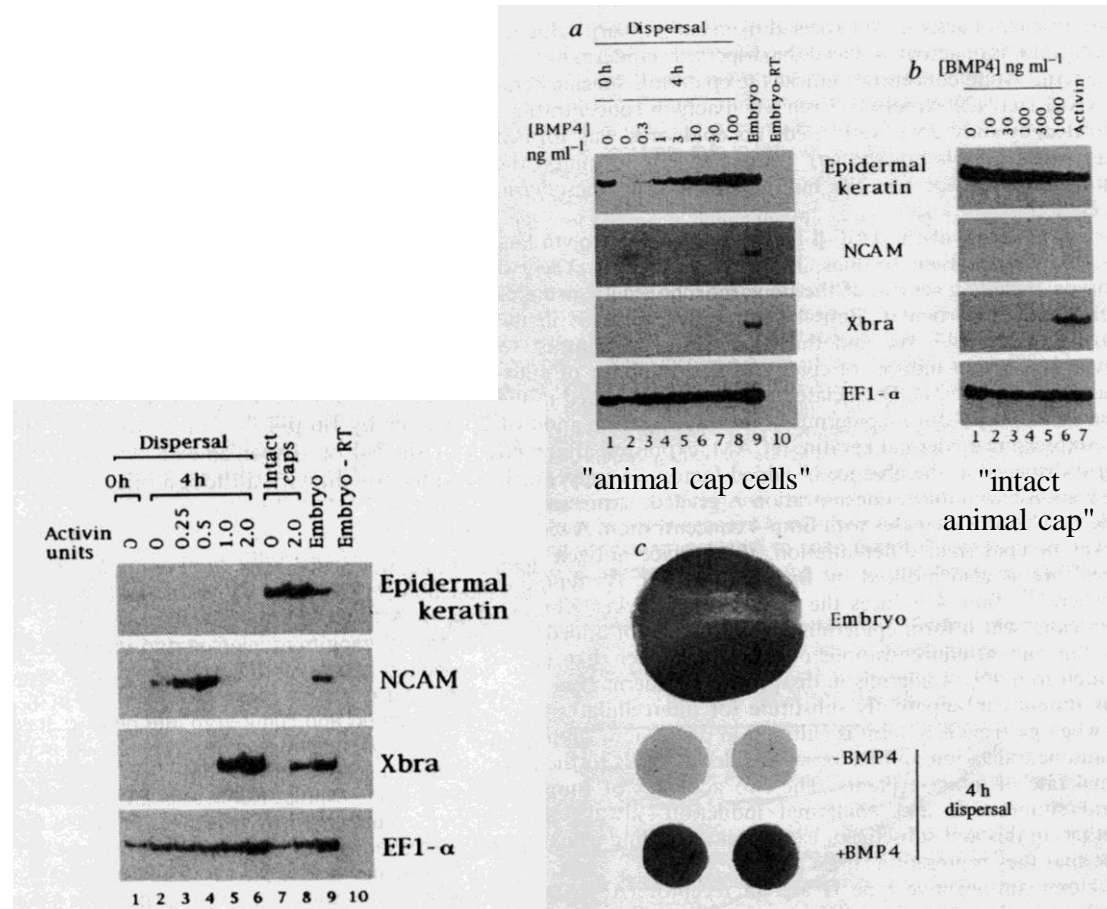
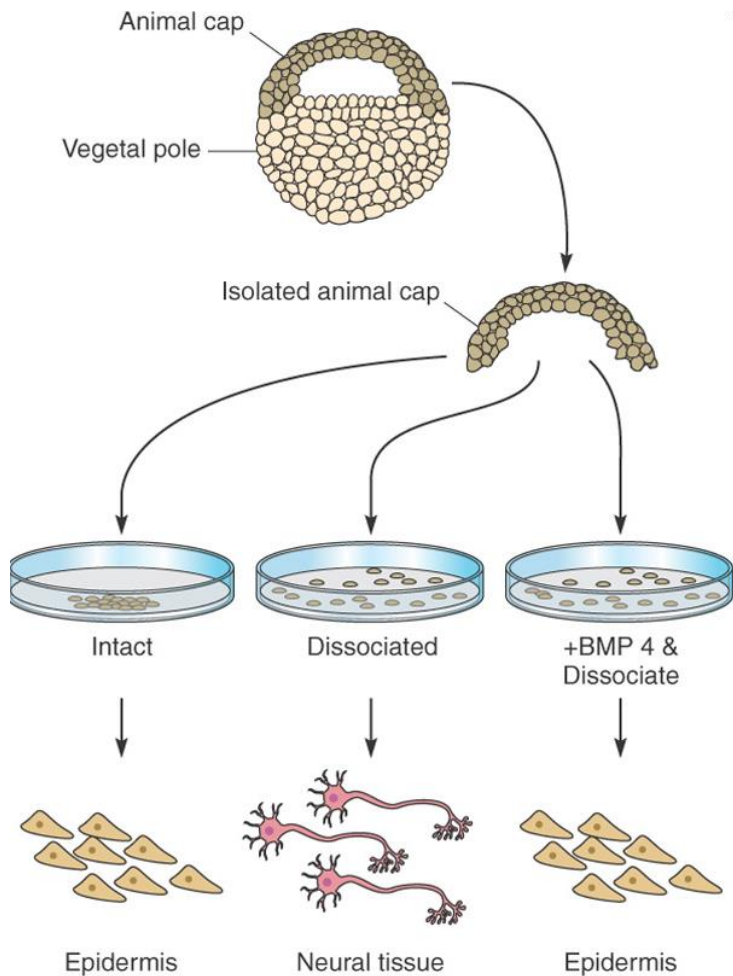
- gasztruláció után (ha a mezoderma már kialakult) izolálva, a disszociáltatott sejtekből már neuroektoderma fejlődik



- **chordin** / **noggin** / **follicistatin**: neuronális induktorok - a neuronális sorsot gátló inhibitor (Bmp) gátolják (ld. idegrendszer kialakulása)

# Az "úttörő" kísérletek: Bmp-4 és epidermis

- a disszociáltatott animális sejtek epidermis helyett neuroektodermát alakítanak ki
- BMP4 (bone morphogenetic protein) a neuronális sorsválasztást meggátolja és epidermis képződéséhez vezet

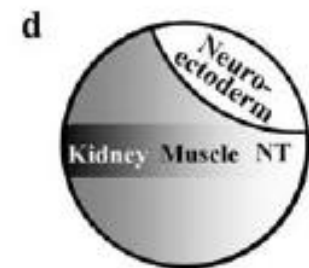
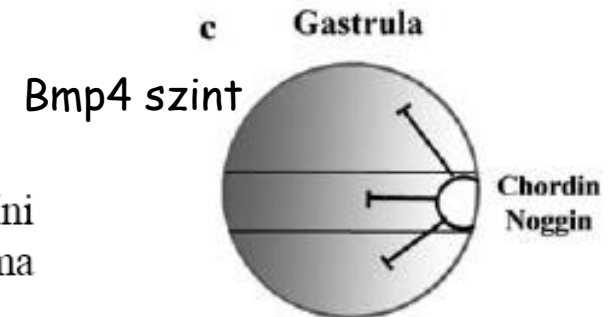
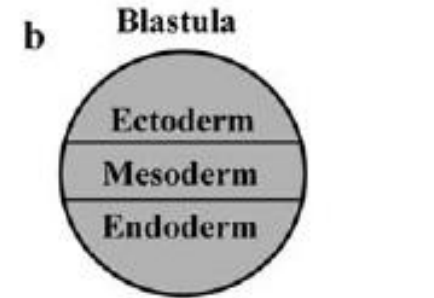
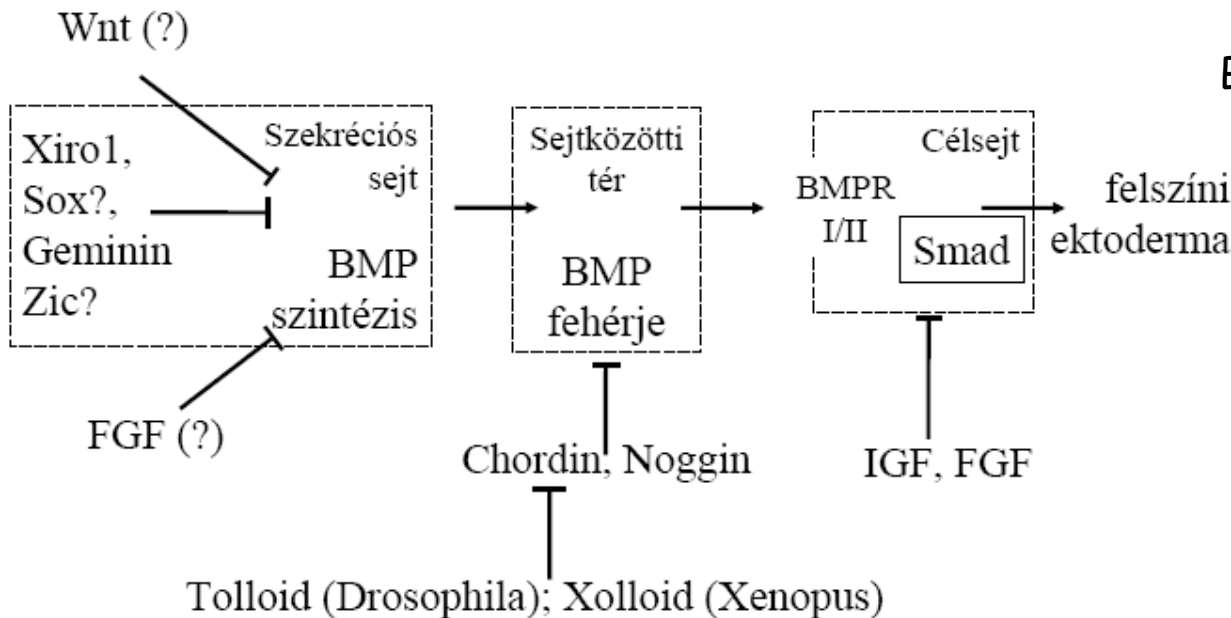


**Induction of epidermis and inhibition of neural fate by Bmp-4.**

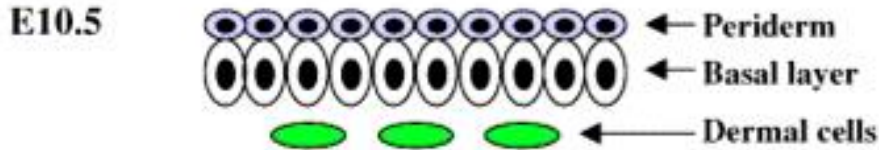
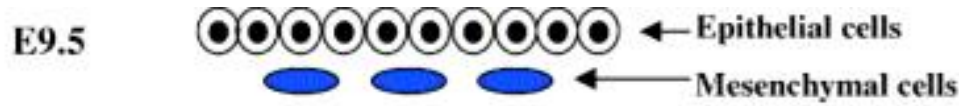
(Wilson PA, Hemmati-Brivanlou A. Nature. 1995 Jul 27;376 )

# A Bmp-4 és az epidermis kialakulása

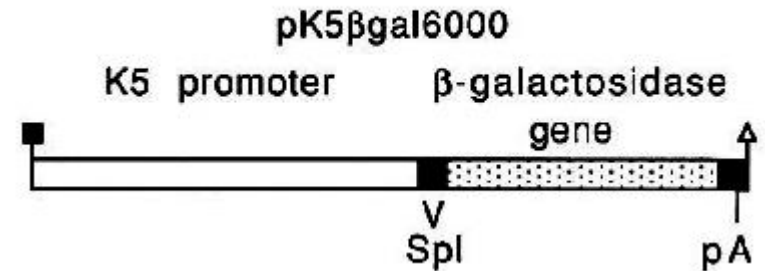
- a szekretált Bmp4 epidermis kialakulását indukálja
- a Bmp4 hatás antagonizálása neuroektodermális differenciációhoz vezet:
  - **Wnt**: Bmp4 szintézis gátlása
  - **chordin / noggin**: Bmp4 fehérje megkötése
  - **follistatin**: Bmp7 / activin fehérje megkötése
  - **FGF**: BmpR szignálút vonal (Smad) antagonizálása



# Egér embrió felszíni hámszövetének fejlődése



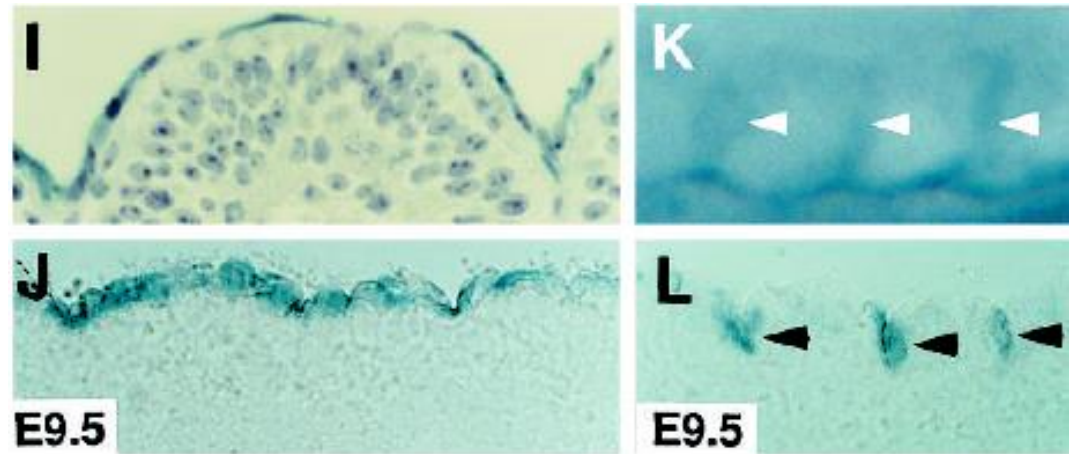
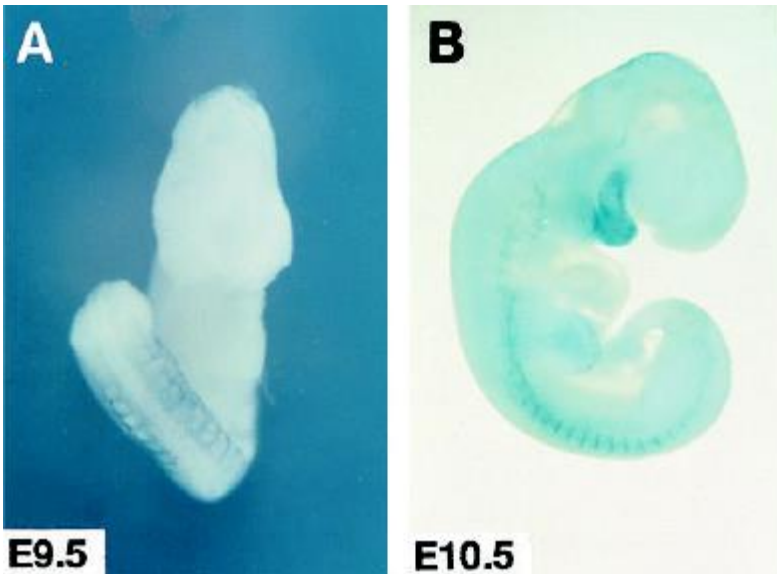
Epitélium elköteleződése:  
Keratin 5, 8, 14, 18



Allen G. Li, et al. Cytokine & Growth Factor Reviews 14 (2003) 99–111  
Roles of TGFβ signaling in epidermal/appendage development

Allen G. Li<sup>a</sup>, Maranke I. Koster<sup>b,c</sup>, Xiao-Jing Wang<sup>a,b,\*</sup>

K5-βGal



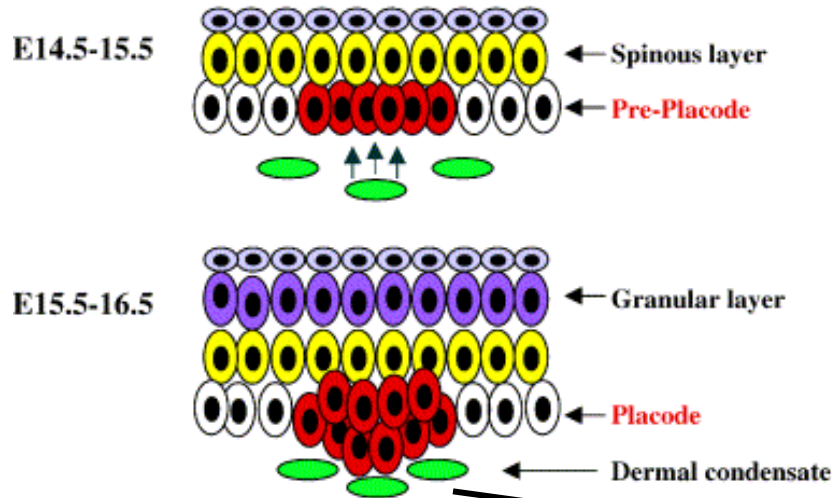
Byrne et al Development 120, 2369-2383 (1994)

Programming gene expression in developing epidermis

Carolyn Byrne<sup>1</sup>, Michael Tainsky<sup>2</sup> and Elaine Fuchs<sup>1,\*</sup>



# Egér embrió felszíni hámszövetének fejlődése



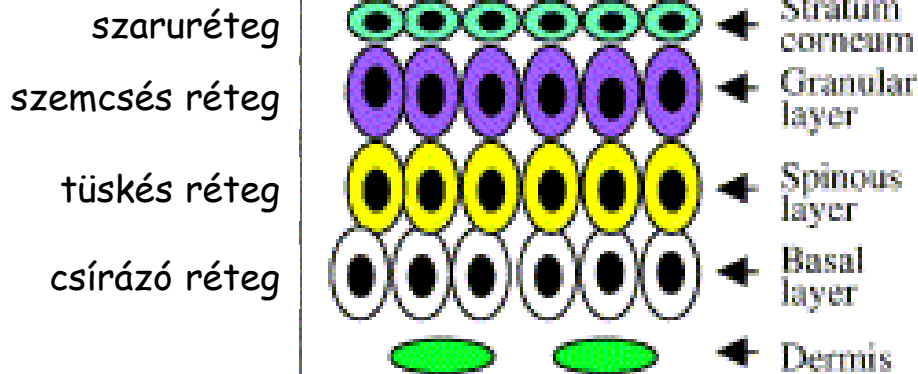
- fő sejttípusok elköteleződése; keratin 17
- elsődleges szőrtüszők indukciója
- fő sejttípusok differenciációja; Keratin 1, 10, 6; Smad4
- >E16: másodlagos szőrtüszők indukciója

Roles of TGFβ signaling in epidermal/appendage development

Allen G. Li<sup>a</sup>, Maranke I. Koster<sup>b,c</sup>, Xiao-Jing Wang<sup>a,b,\*</sup>

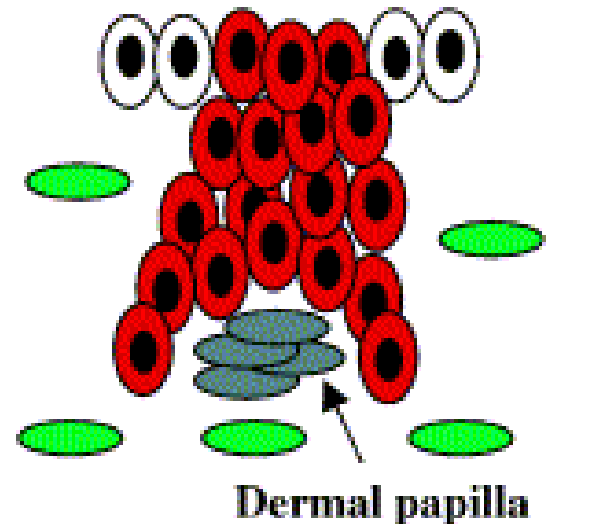
**E18.5**

interfollikuláris epidermis

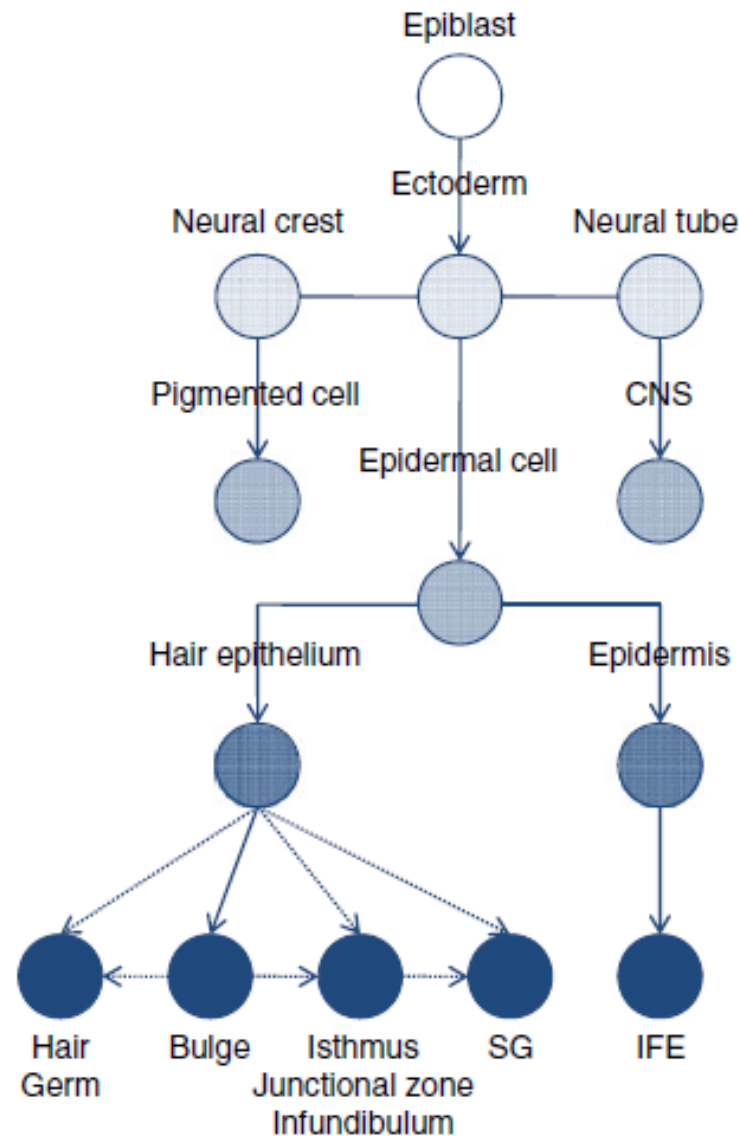


**E16.5-17.5**

szőrtüsző

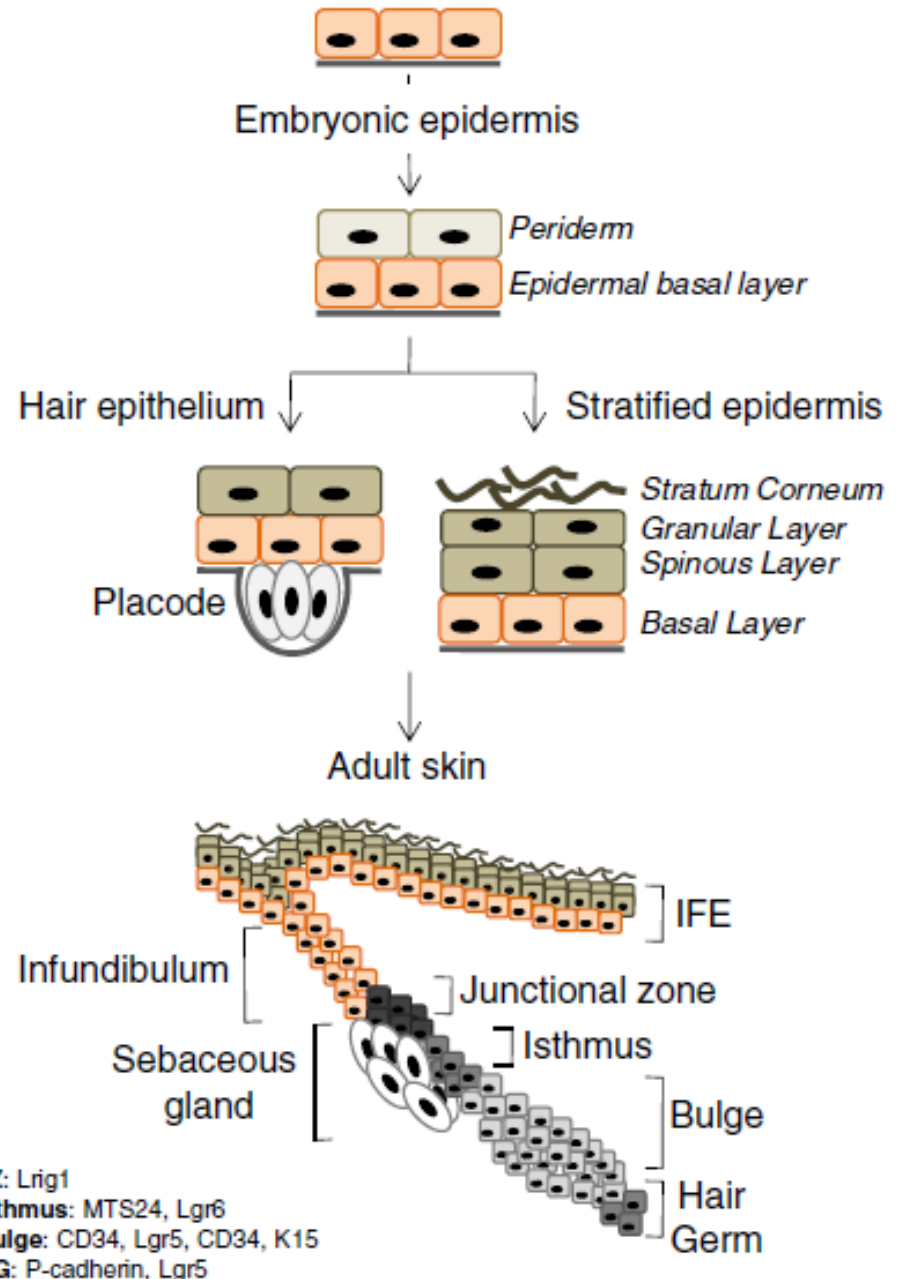


# Az epidermis specializációja



**Fig. 1** The developmental hierarchy for epidermal stem cell populations. The *dotted lines* indicate a putative relation between the populations. *CNS* central nervous system, *SG* sebaceous gland, *IFE* interfollicular epidermis

# Az epidermis specializációja



- B: „bulge” sejtek;
- HF: szőr folliculus;
- IFE: interfollikuláris epidermis;
- SG: sebaceous gland (faggyúmirigy)

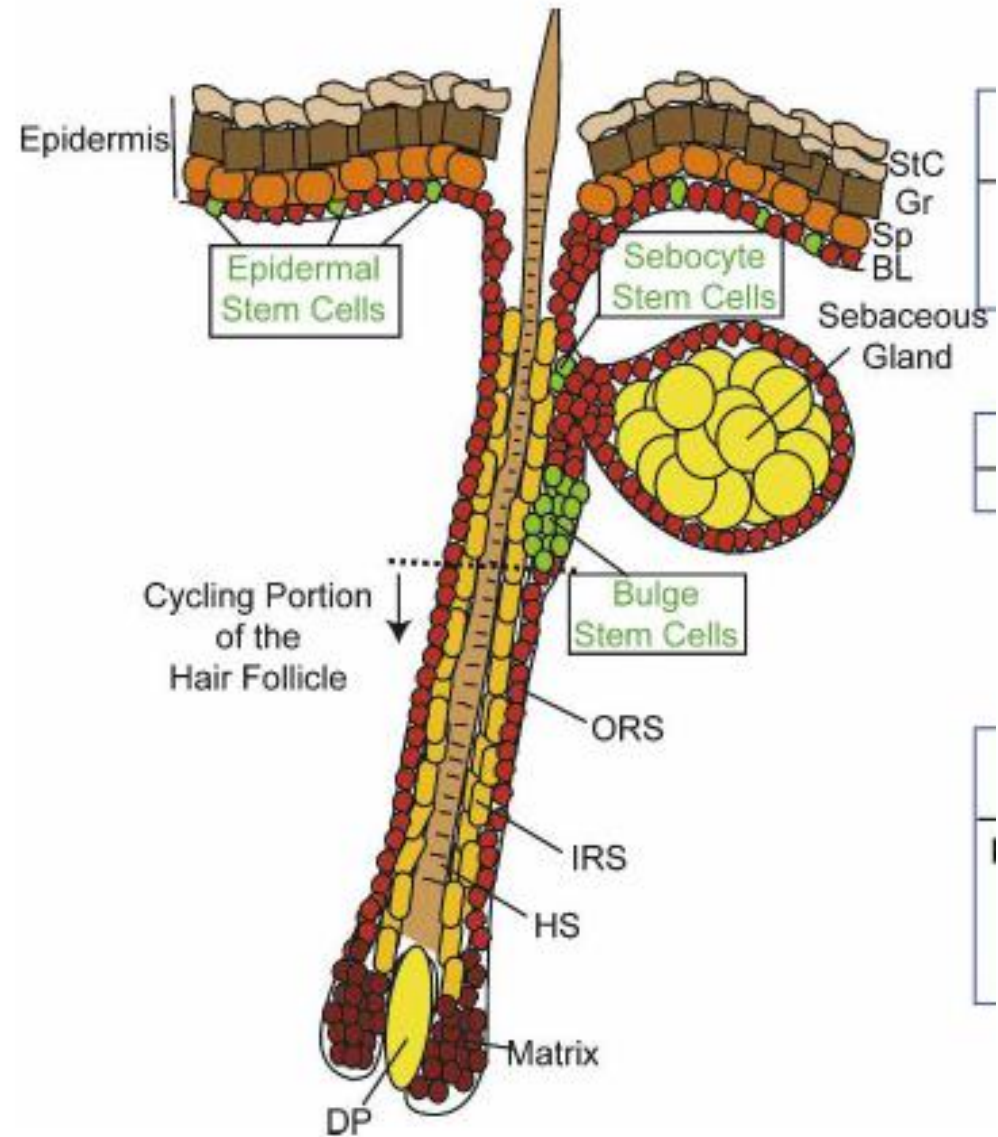
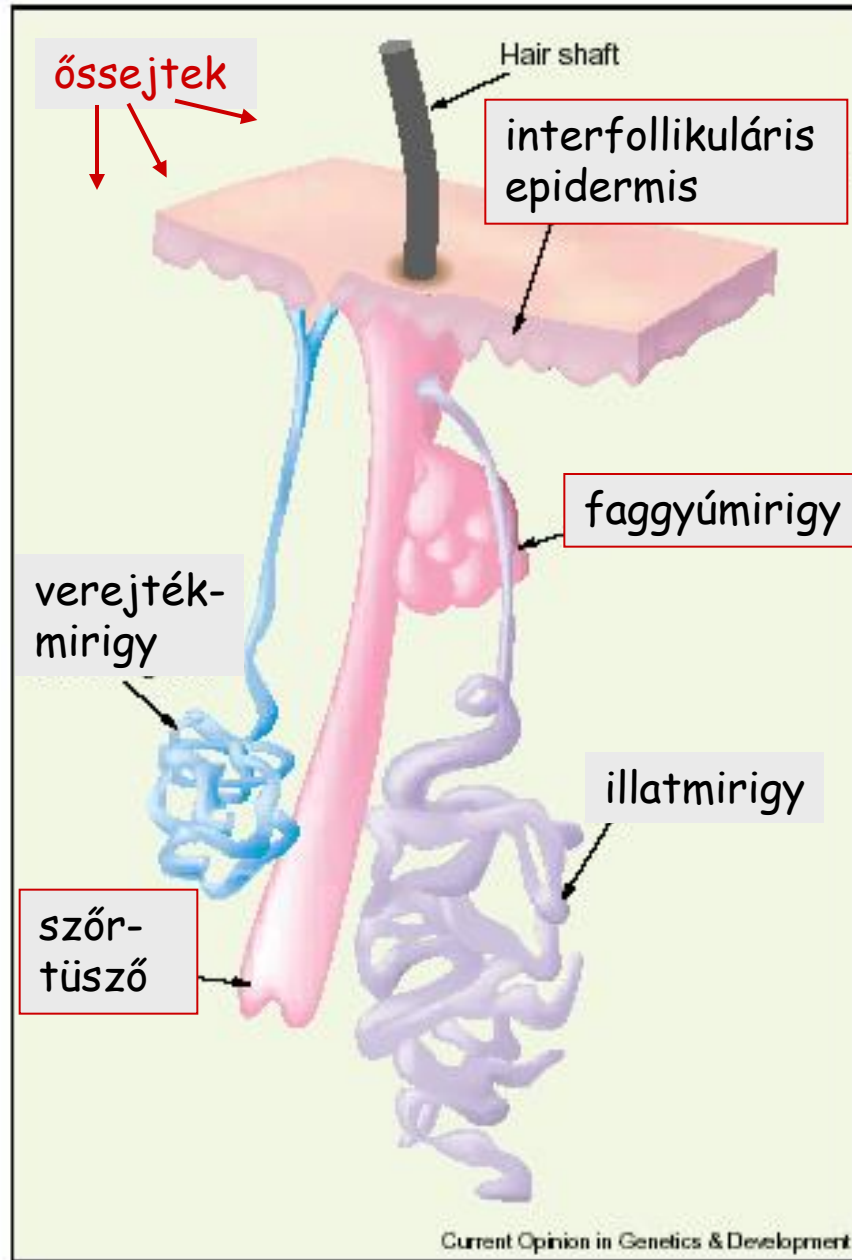
**Fig. 2** Epidermal structures formed during development until adulthood. The stratified epidermis is formed by E18.5 and gives rise to the interfollicular epidermis (IFE) and infundibulum in adult skin. The hair epithelium is initiated at around E14.5 by the placode or composed of bulge hair germ (HG), isthmus and junctional zone in adult skin. *Markers* for the respective epidermal compartments are indicated in the *left hand corner*

# Őssejtek a hámszövetben

More than one way to skin . . .

Elaine Fuchs and Valerie Horsley

*Genes & Dev.* 2008 22: 976-985

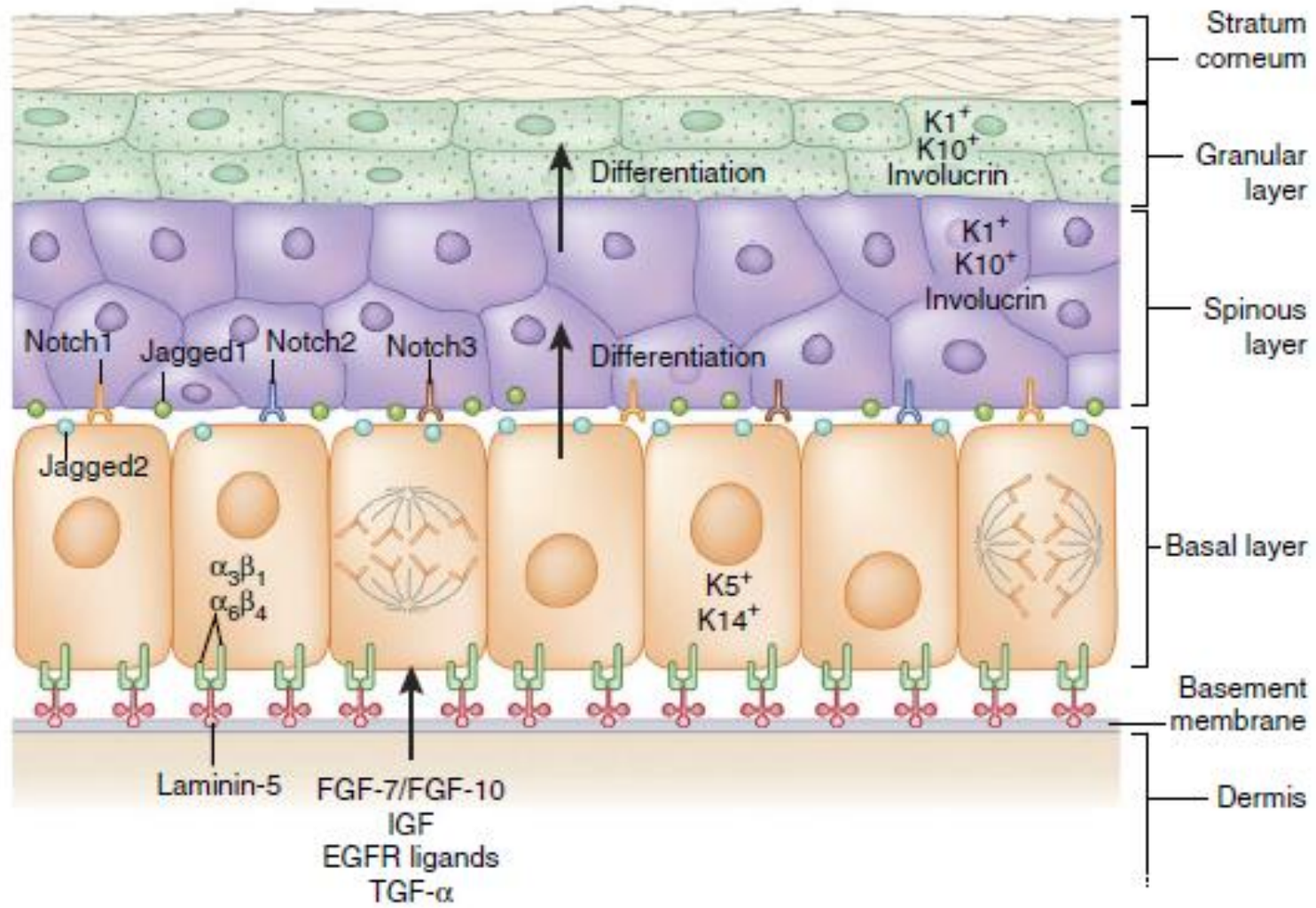


Stem cell fate and patterning in mammalian epidermis

Fiona M Watt

# Az interfollikuláris epidermis (IFE) kialakulása

- őssejt-fenntartás / proliferáció szabályozása : szekvenciális lépések



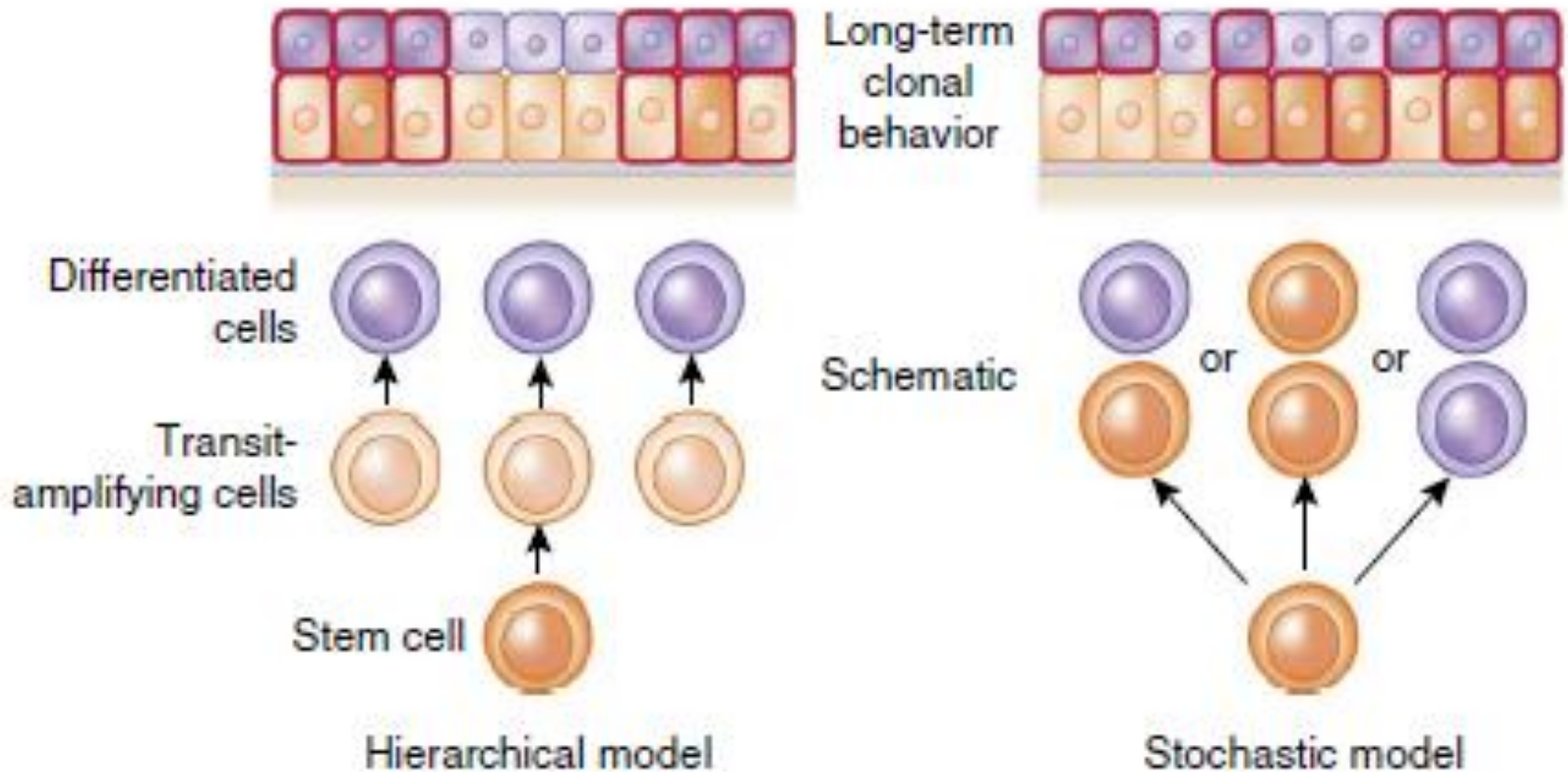
Emerging interactions between skin stem cells and their niches

Ya-Chieh Hsu<sup>1,2</sup>, Lishi Li<sup>1</sup> & Elaine Fuchs<sup>1</sup>

NATURE MEDICINE | VOLUME 20 | NUMBER 8 | AUGUST 2014

# Az interfollikuláris epidermis (IFE) kialakulása

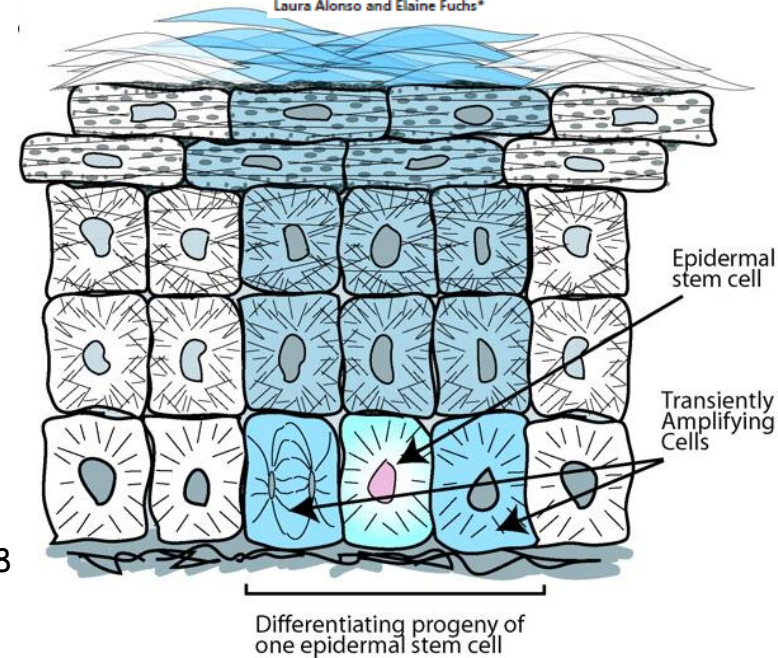
- hierarchikus vagy stochasztikus differenciációs lépések?



# Őssejtek az IFE-ben

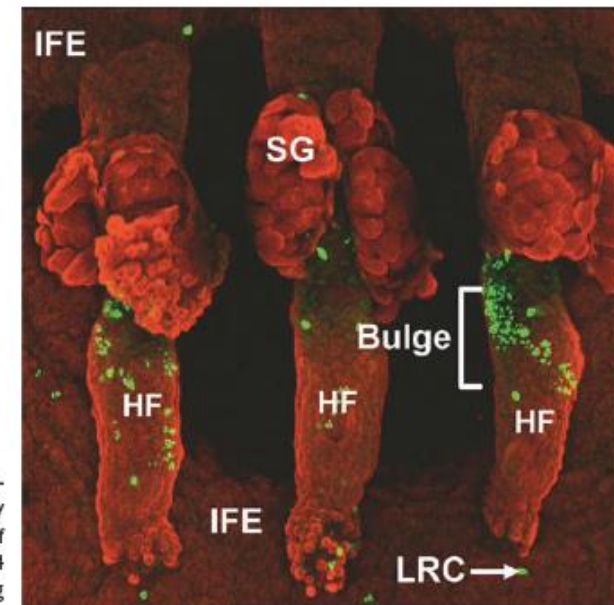
## Stem cells of the skin epithelium

Laura Alonso and Elaine Fuchs\*



- az emberi epidermisz ~2/4 hét alatt kicserélődik
- az őssejtek lassan osztódnak, 2-7 % (10-12% / <0.2%) a bazális réteg sejtjeinek
- köztes sokszorozó (transit amplifying) sejtek 3-6 alkalommal osztódnak (kolónia képző képesség)
- egy emberi epidermális őssejt in vitro  $\sim 1,7 \times 10^{38}$  sejt létrehozására is képes
- EPU (epithelial proliferating unit): kolónia képző képesség; hexagonális elrendezés
- LRCs (label retaining cells): BrdU pulzus jelölést hosszasan megtartó sejtek: a legtöbb a **bulge régióban**
  - lassan osztódó (ős?)sejtek
  - az "immortal DNA strand" szelektív megőrzése?

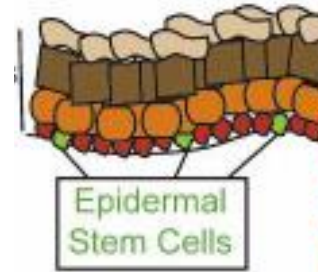
Fig. 2. BrdU label-retaining cells in a whole mount of mouse tail epidermis. A ten day-old mouse was injected with 50 mg BrdU/kg body weight every 12 h for a total of four injections. After a chase period of 10 wk, tissue was immunolabeled to detect BrdU (green) and Keratin 14 (red). HF, hair follicle; IFE, interfollicular epidermis; LRC, label-retaining cell; SG, sebaceous gland.



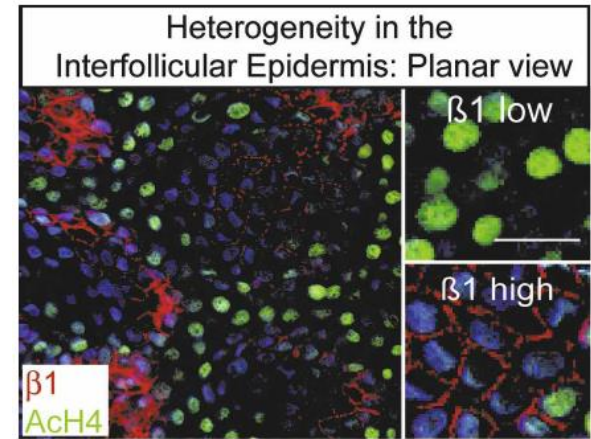
# Őssejtek az IFE-ben

- nincs igazán jó marker.....

Potential Markers of Interfollicular Epidermal Stem Cells
$\beta$ 1 integrin $\alpha$ 6 integrin p63



- a bazális réteg igen heterogén összetételű



- normál, felnőtt-kori sejtpótlás az embrionális lépésekhez hasonló

	Stem Cell	Proliferative Progeny	Differentiated Cells	Mechanisms of Stem Cell Regulation
Epidermis			<p>Spinous Cells Granular Cells Stratum Corneum</p>	<p><b>Proliferation</b></p> <p>c-Myc    <math>\beta</math>1 integrin                      p63     TGF<math>\alpha</math>                      TGF<math>\beta</math>(-)</p> <p><b>Differentiation</b></p> <p>Notch    C/EBP<math>\alpha/\beta</math>                      PPAR<math>\alpha</math> AP2<math>\alpha/\gamma</math></p>

More than one way to skin . . .

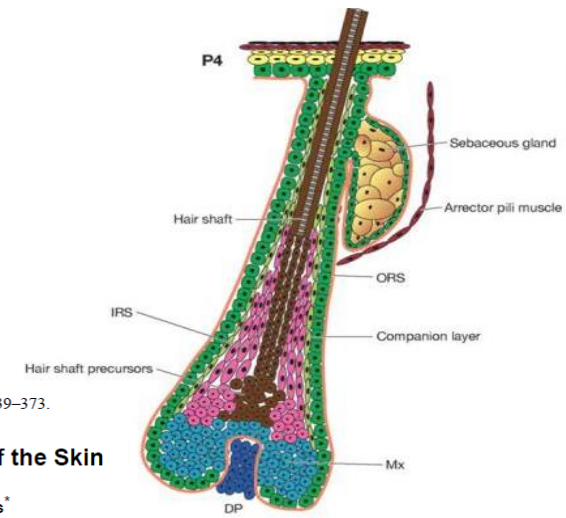
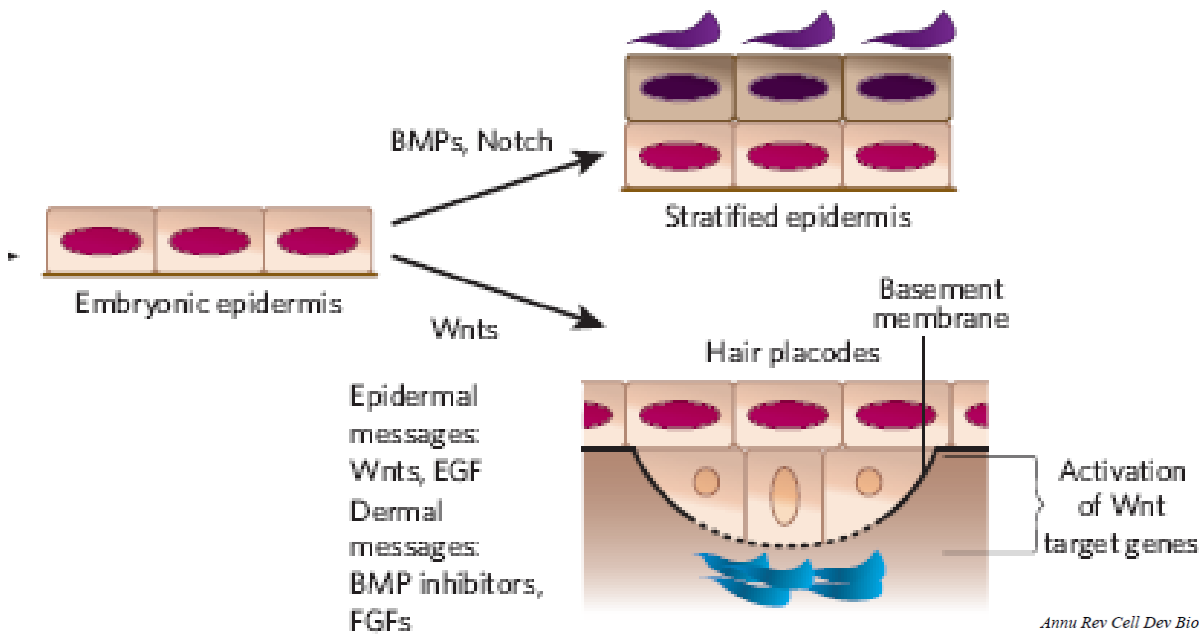
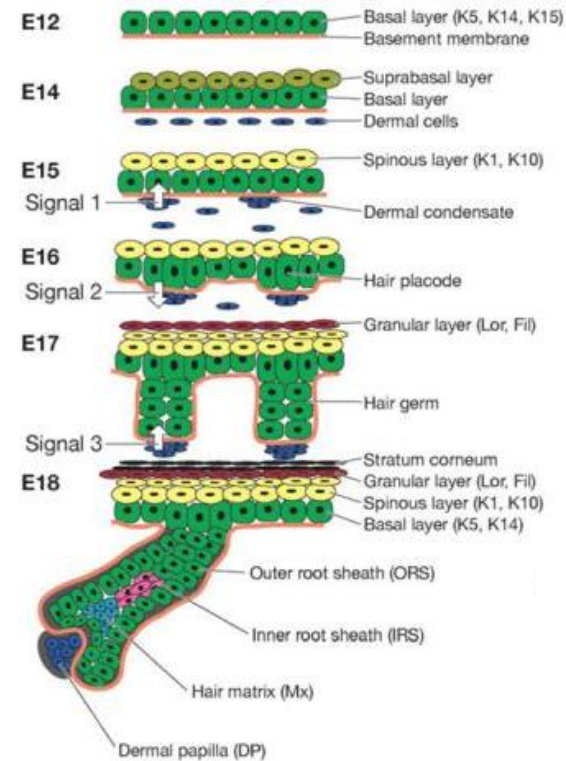
Elaine Fuchs and Valerie Horsley

Genes & Dev. 2008 22: 976-985



# A szőrtüsző kialakulása - embrionálisan

1. mesenchimából (dermis) induktív szignál
2. epidermális keratinociták aggregálnak, placod kialakítása (Wnt, EGF)
3. hajcsíra kialakítása: lefelé növekvő placod sejtek közé türemkednek a dermális sejtek (irhaszemölcs) (FGF, BMP inhibitorok)



*Annu Rev Cell Dev Biol.* 2006 ; 22: 339–373.

## Epidermal Stem Cells of the Skin

Cédric Blanpain and Elaine Fuchs\*

Scratching the surface of skin development

Elaine Fuchs<sup>1</sup>

NATURE|Vol 445|22 February 2007|doi:10.1038/nature05659

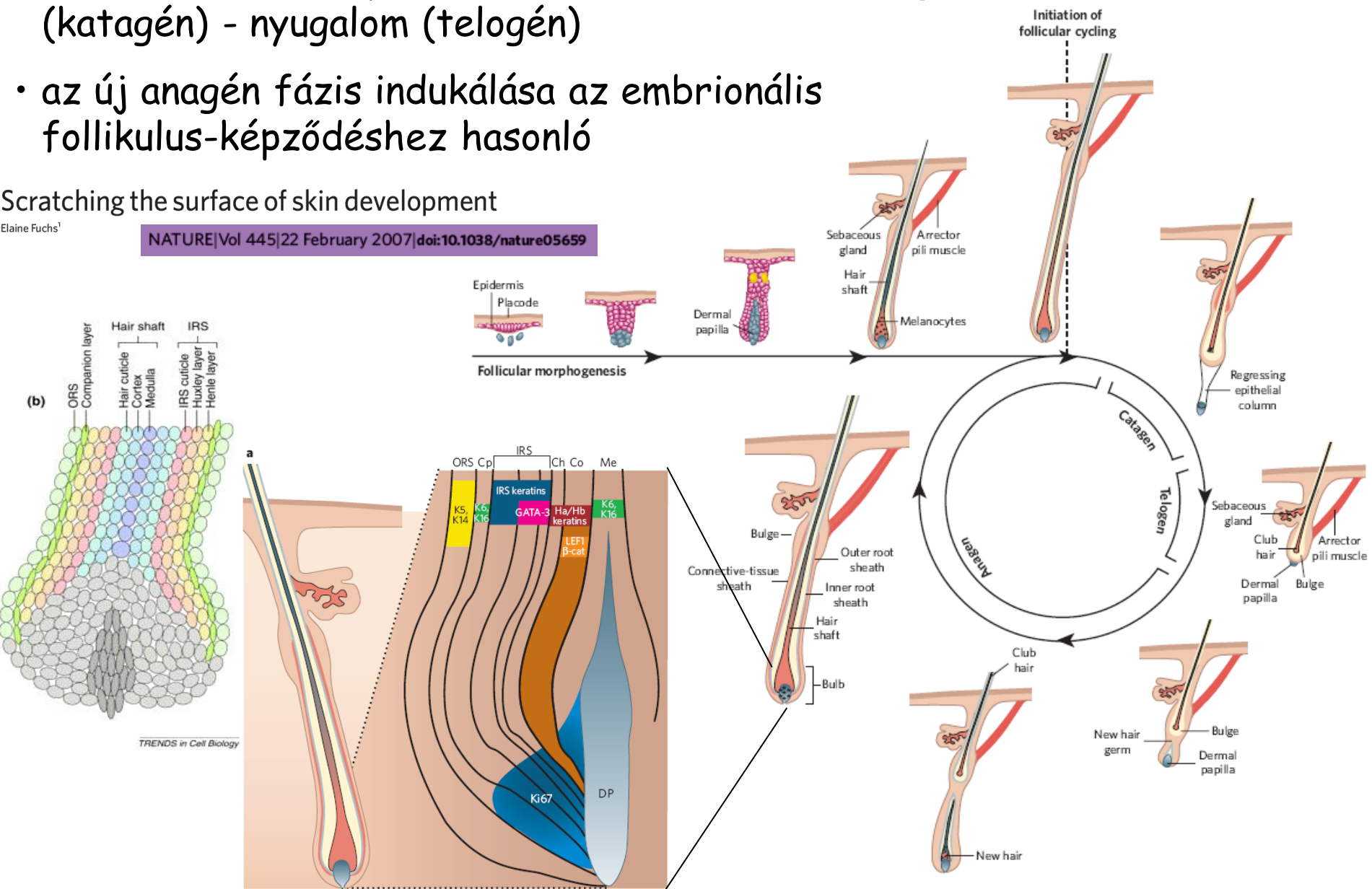
# A felnőtt kori szőrképzés

- felnőtt korban folyamatos ciklus: növekedés (anagén) - visszahúzódás (katagén) - nyugalom (telogén)
- az új anagén fázis indukálása az embrionális follikulum-képződéshez hasonló

Scratching the surface of skin development

Elaine Fuchs<sup>1</sup>

NATURE | Vol 445 | 22 February 2007 | doi:10.1038/nature05659



TRENDS in Cell Biology

**Abbreviations**

<b>BMP</b>	Bone morphogenetic protein
<b>CCL</b>	Companion cell layer
<b>DP</b>	Dermal papilla
<b>EGF</b>	Epidermal growth factor
<b>FGF</b>	Fibroblast growth factor
<b>HS</b>	Hair shaft
<b>IRS</b>	Inner root sheath
<b>ORS</b>	Outer root sheath
<b>SGK3</b>	Serum and glucocorticoid responsive kinase 3
<b>Shh</b>	Sonic hedgehog
<b>TGFβ</b>	Transforming growth factor β
<b>Wnt</b>	Wingless/MTV Integration site factor

**Anagen-to-catagen transition**

Proliferation ceases  
Apoptosis begins in bulb/ORS  
Differentiation slows

**Catagen**

Regression phase  
Extensive apoptosis  
Differentiation ceases  
Hair club formed  
DP remains in contact with epithelium

**Catagen-to-telogen transition**

Club hair anchored  
Apoptosis ceases  
DP reaches stem cell niche  
Follicle becomes quiescent

**Telogen**

Resting phase  
No significant proliferation, apoptosis or differentiation  
DP near stem cells

**Exogen**

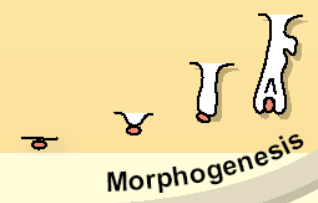
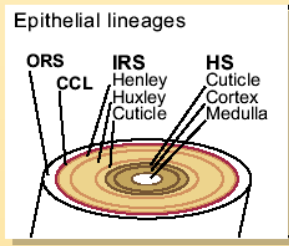
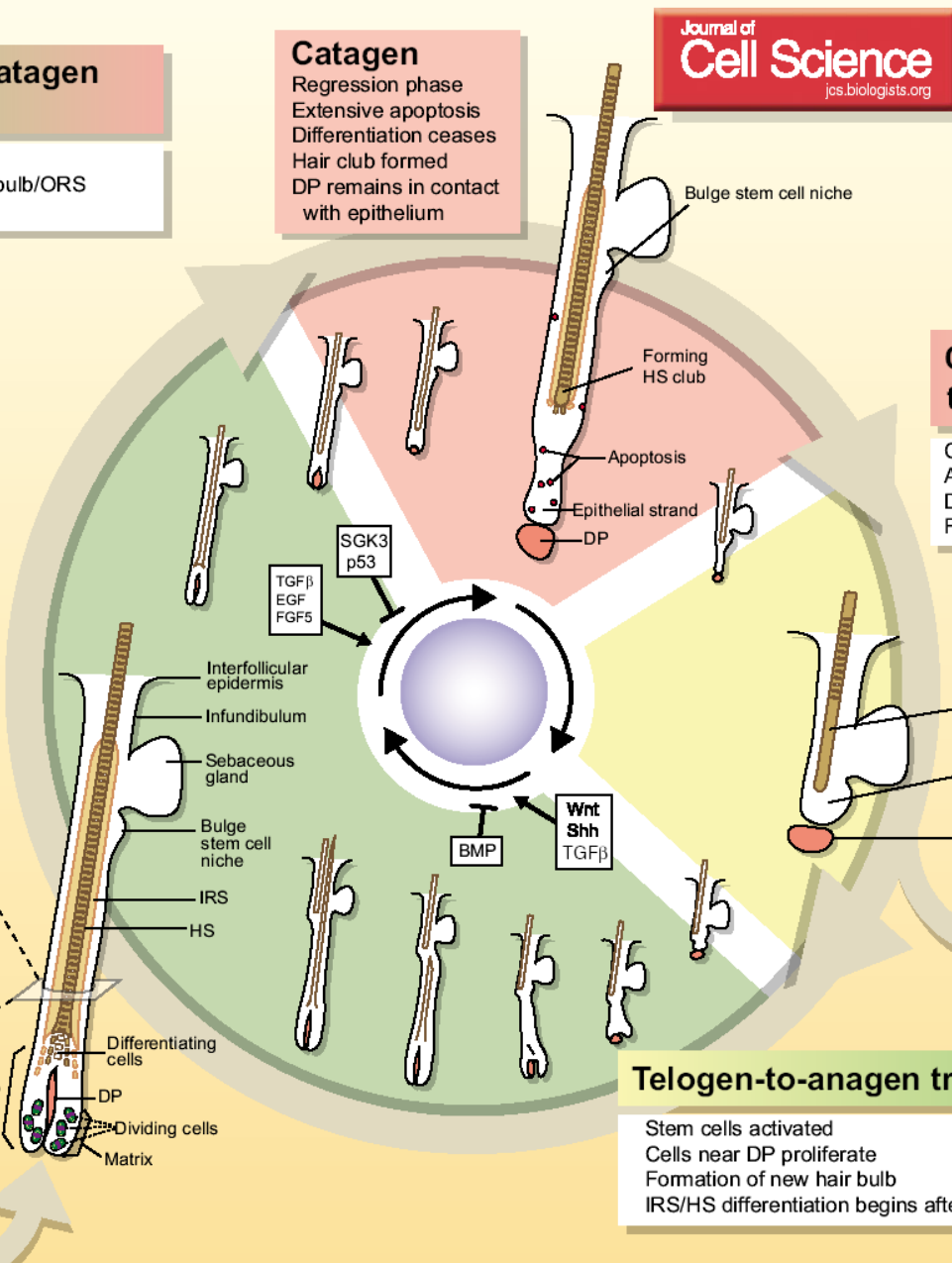
Club hair loss  
(may not occur each hair cycle)

**Telogen-to-anagen transition**

Stem cells activated  
Cells near DP proliferate  
Formation of new hair bulb  
IRS/HS differentiation begins after bulb formed

**Anagen**

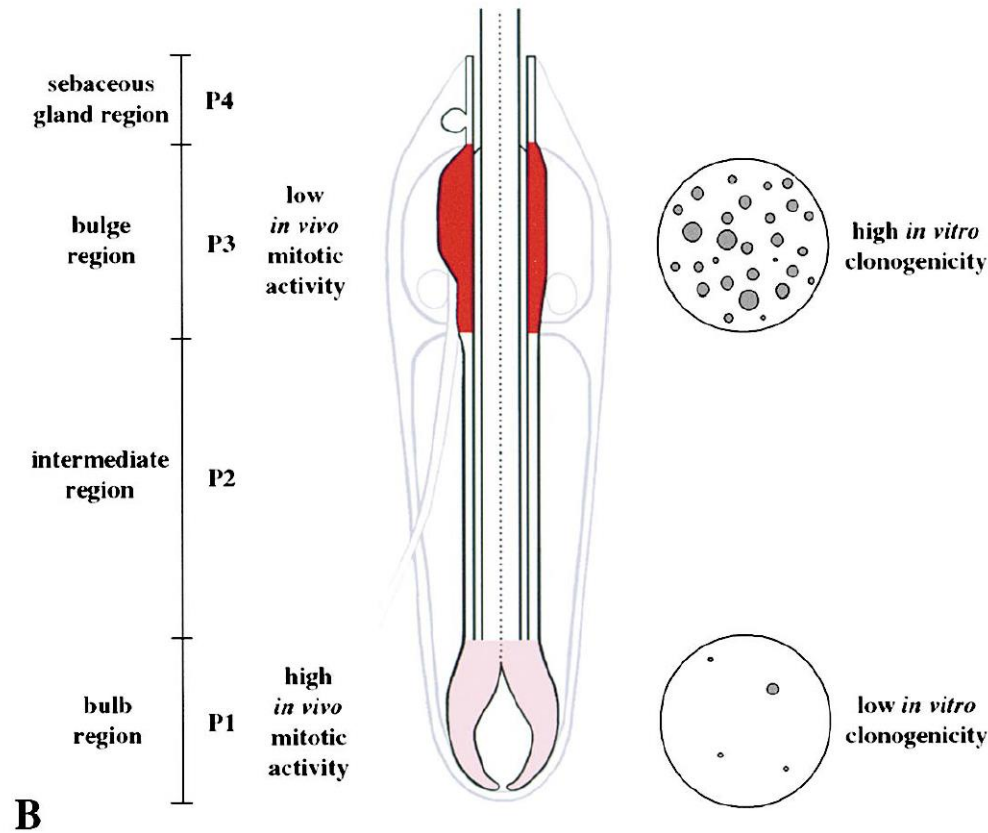
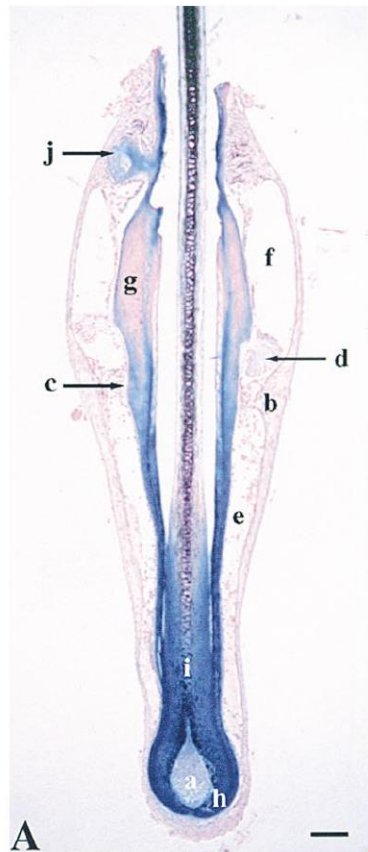
HS growth phase  
Rapid proliferation in bulb  
HS/IRS differentiation  
IRS degrades in infundibulum  
Duration of anagen determines length of HS  
Sensitive to chemotherapy



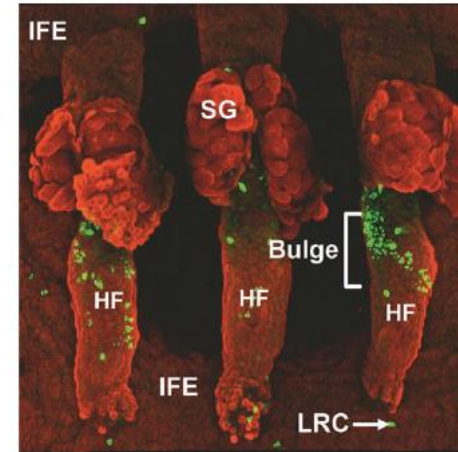
# The Hair Cycle

Laura Alonso and Elaine Fuchs

# A szőrtüsző őssejtjei: bulge sejtek



## LRCs (label retaining cells)



Distinct Epidermal Stem Cell Compartments are Maintained by Independent Niche Microenvironments

Kristin M. Braun and David M. Prowe\*

*Stem Cell Reviews*

Location of Proliferative Cells in a Vibrissal Follicle (A) b-galactosidase staining of a longitudinal section of a vibrissal follicle obtained from a Rosa 26 heterozygous mouse. a: follicular papilla, b: capsula, c: dermal sheath, d: ringwulst, e: lower vascular sinus, f: upper vascular sinus, g: bulge region, h: matrix, i: hair, j: sebaceous gland. Movement of the whisker results from the contraction of the bundles of the striated muscle fibers that envelop the follicle capsula (not shown on this section). (B) Main locations of the clonogenic keratinocytes in an anagen vibrissal follicle. Note the inverse relation between mitotic activity in vivo and clonogenicity in vitro. Bar: 100  $\mu$ m.

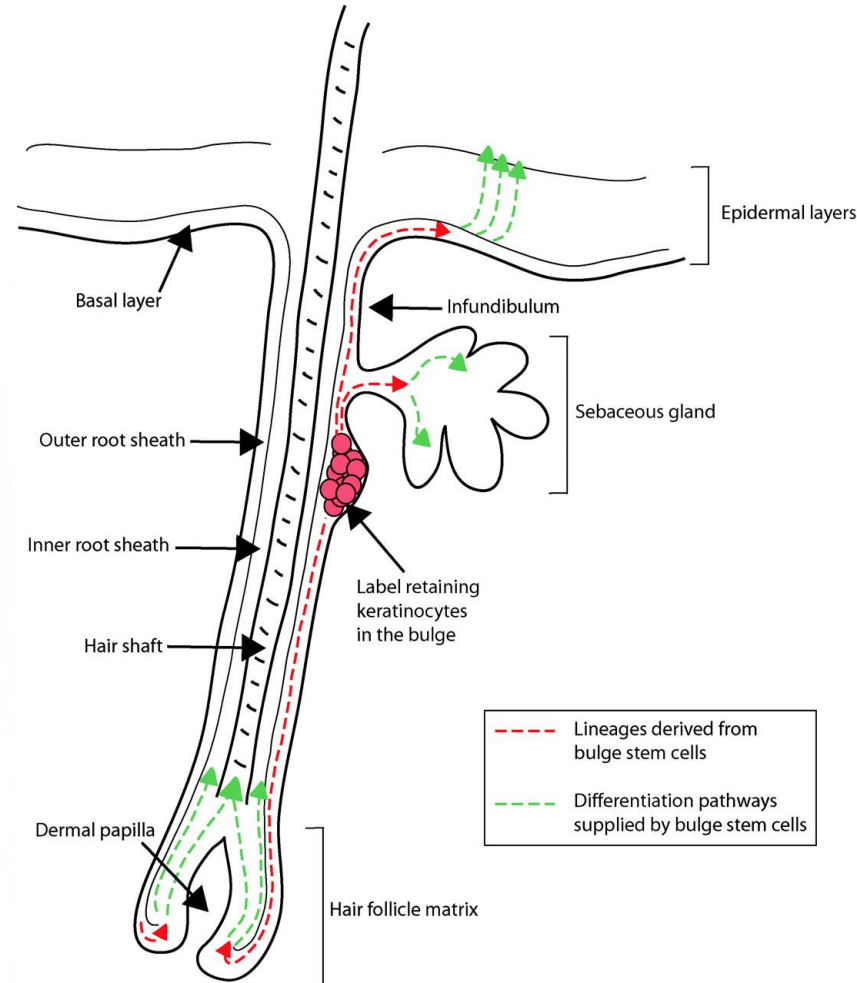
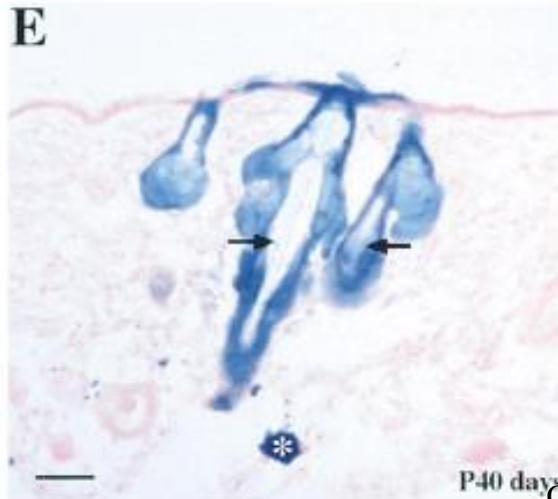
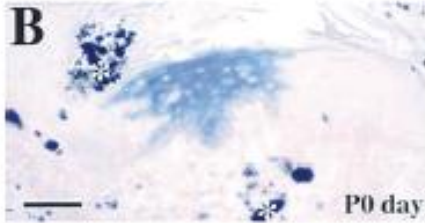
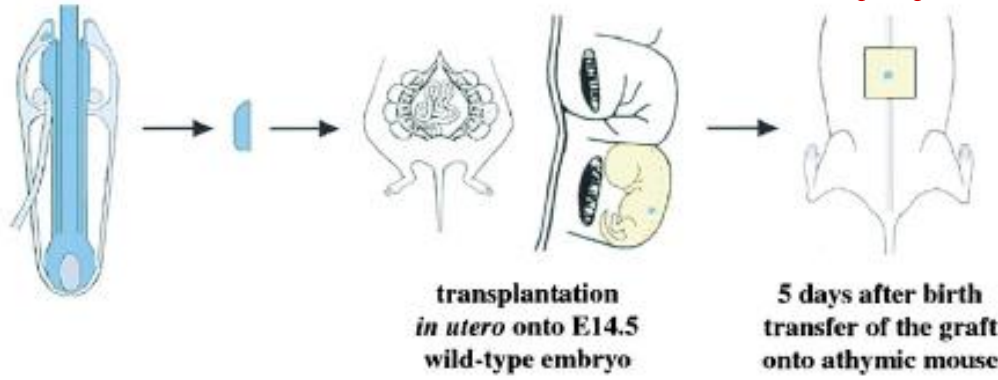
Cell, Vol. 104, 233–245, January 26, 2001, Copyright ©2001 by Cell Press

**Morphogenesis and Renewal of Hair Follicles from Adult Multipotent Stem Cells**

Oshima et al., Cell, Vol. 104, 233–245, January 26, 2001,

# A szőrtüsző őssejtjei: a bulge sejtek

**A**



## Stem cells of the skin epithelium

Laura Alonso and Elaine Fuchs\*

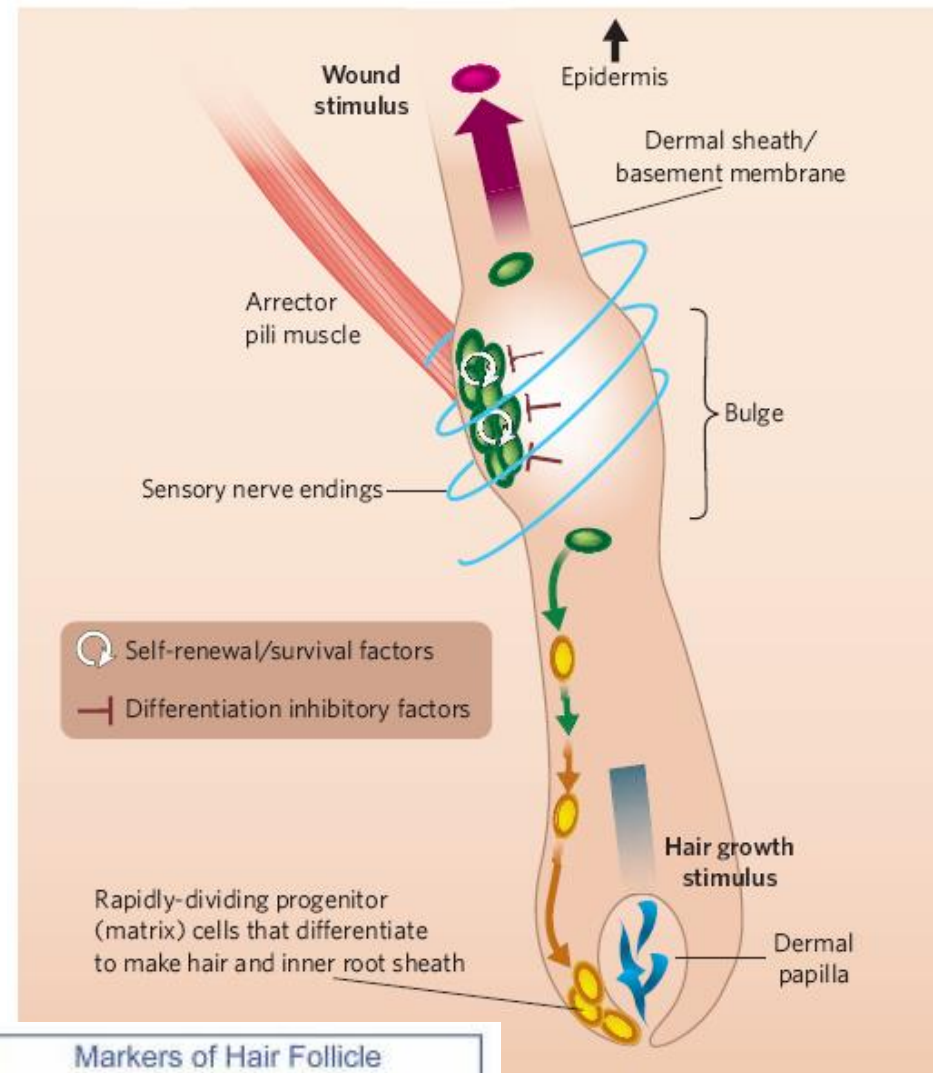
PNAS | September 30, 2003 | vol. 100 | suppl. 1 | 1

## Morphogenesis and Renewal of Hair Follicles from Adult Multipotent Stem Cells

Oshima et al., Cell, Vol. 104, 233–245, January 26, 2001,

# A szőrtüsző őssejtjei: bulge sejtek

- ritka osztódás; anagén fázisban aktiváció, HF kialakítás
- aktiváció csak az alsó bulge régió néhány sejtjét érinti; ezek lefelé (dermal papilla; DP) vándorolnak
- Wnt érzékeny sejtek (Frz, TCF3), de Wnt gátló molekulákat (BMP) is szekretálnak - differenciálatlan állapot fenntartása
- aktiváció -> anagén alatt a folliculus alján  $\beta$ -catenin/LEF1/TCF3 aktiválás (noggin) -> DP: induktív szignálok, elköteleződés irányítása, HF lefelé növése -> bulge sejtek újra nyugalmi állapotba térnek
- normálisan csak HF-et alakít ki, de sérülés esetén mind IFE, mind SG képzésre is képes



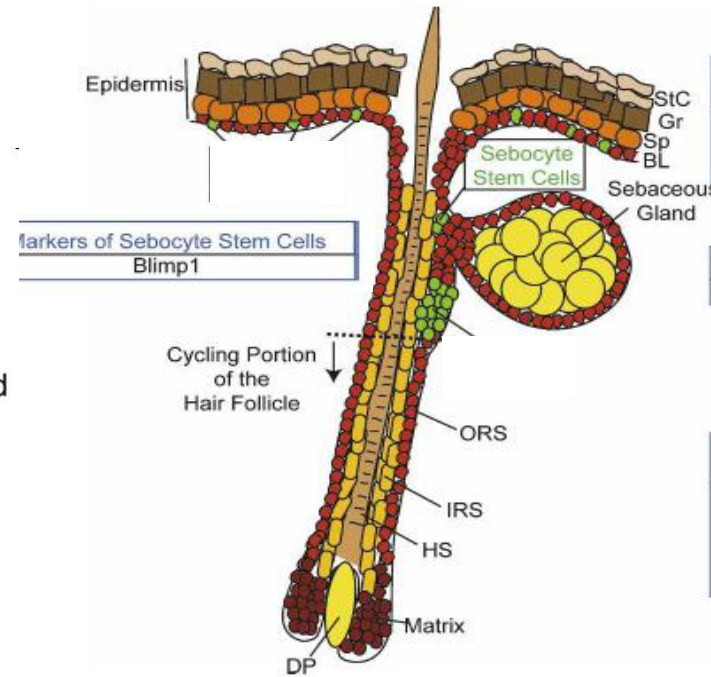
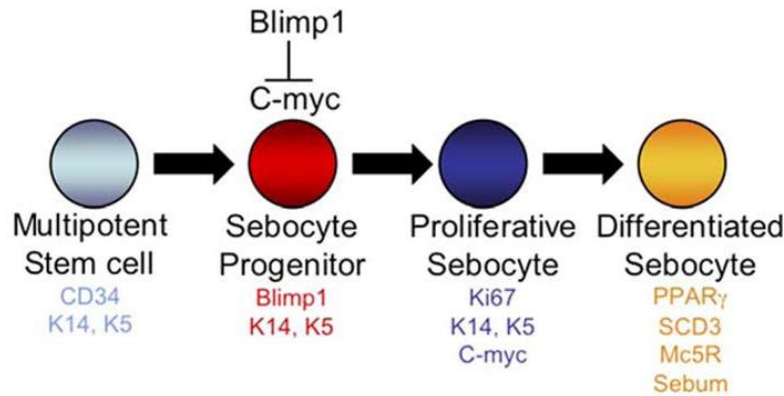
Markers of Hair Follicle Bulge Stem Cells	
DNA label retention	TCF3
CD34	Sox9
NFATc1	Lhx2
Vitamin D receptor	

Scratching the surface of skin development

Elaine Fuchs<sup>1</sup>

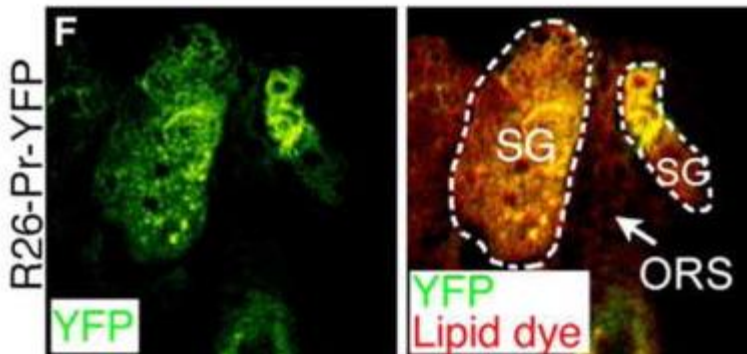
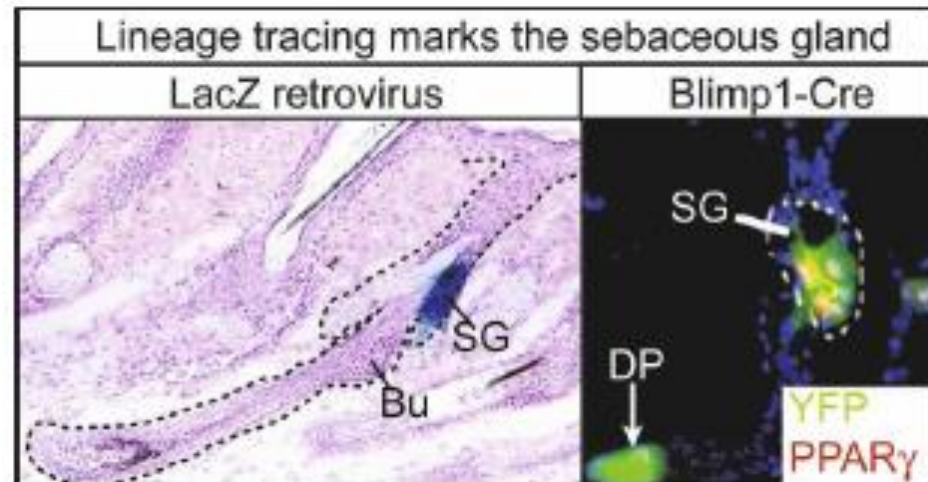
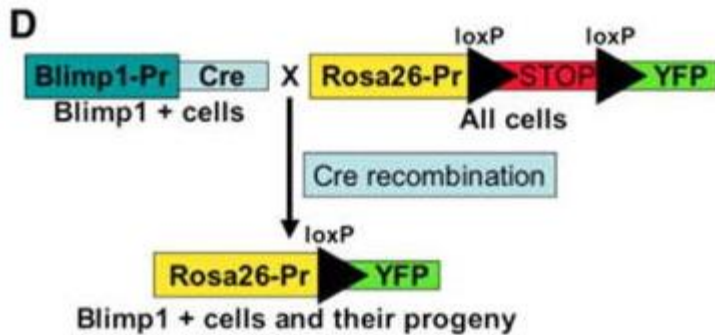
# Bulge régió - lokális őssejt niche (faggyúmirigy)

- Blimp1 transzkripció represszor: SG marker?



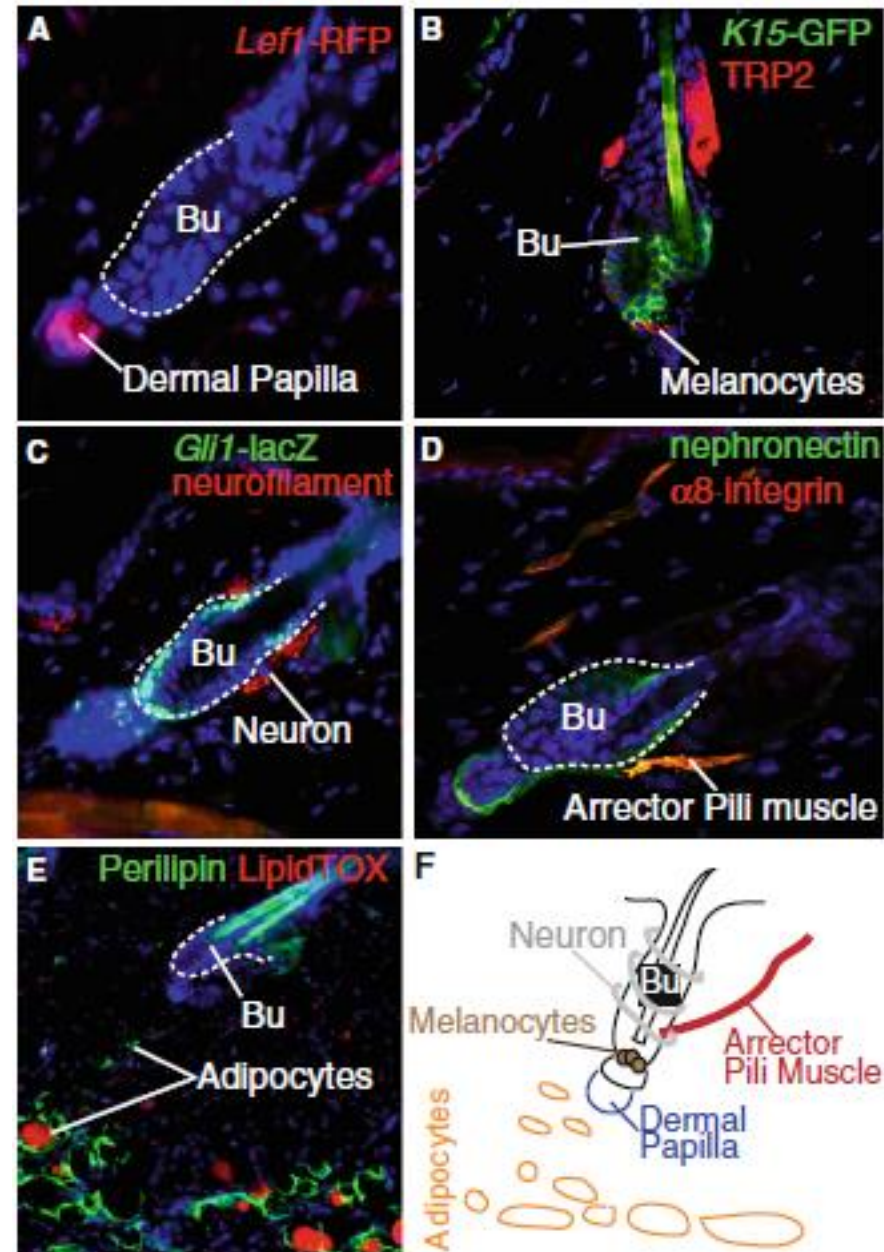
More than one way to skin . . .

Elaine Fuchs and Valerie Horsley  
*Genes & Dev.* 2008 22: 976-985



# Bulge régió - lokális őssejt niche (zsírsejtek)

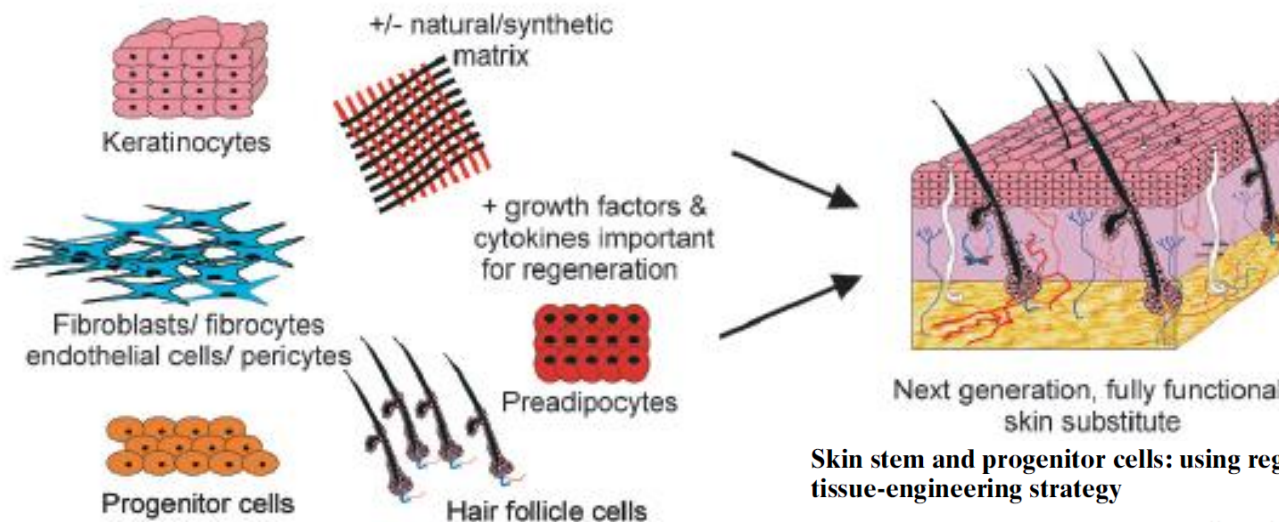
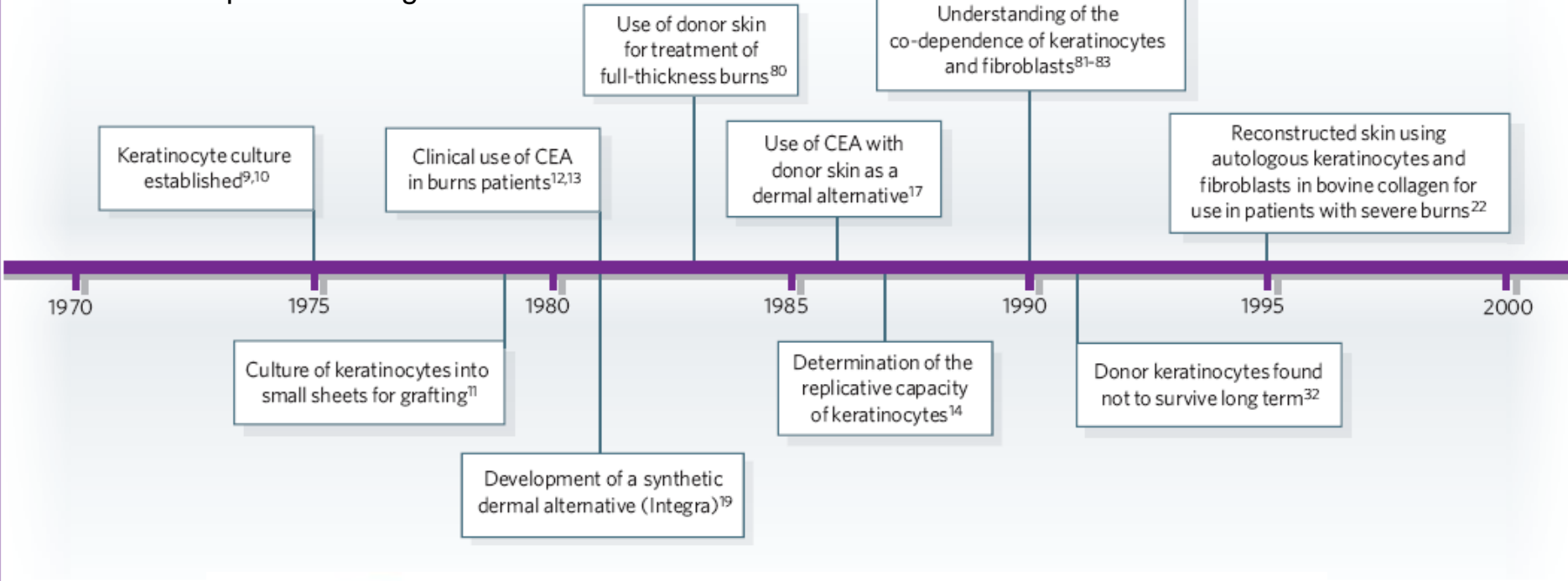
- a haj-ciklussal együtt változik az intradermális adipociták mennyisége: folliculáris növekedés során a legnagyobb mennyiségben
  - éretlen adipocita: telogén-anagén átmenet, folliculáris növekedés serkentés
  - érett adipocita: BMP2 termelés -> telogén fázis fenntartása
- hőmérséklet-szabályozás, mechanikai védelem -> ha kevés az adipocita, nem indul be az anagén fázis (?)





## Timeline

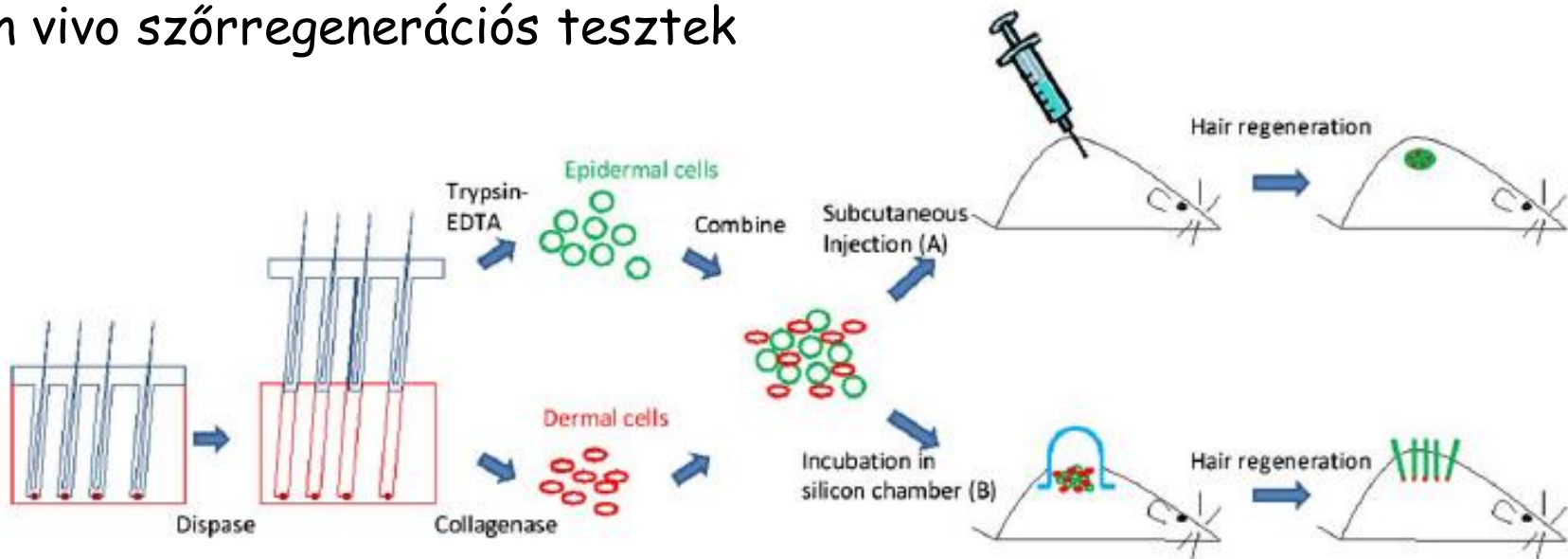
### CEA: cultured epithelial autografts



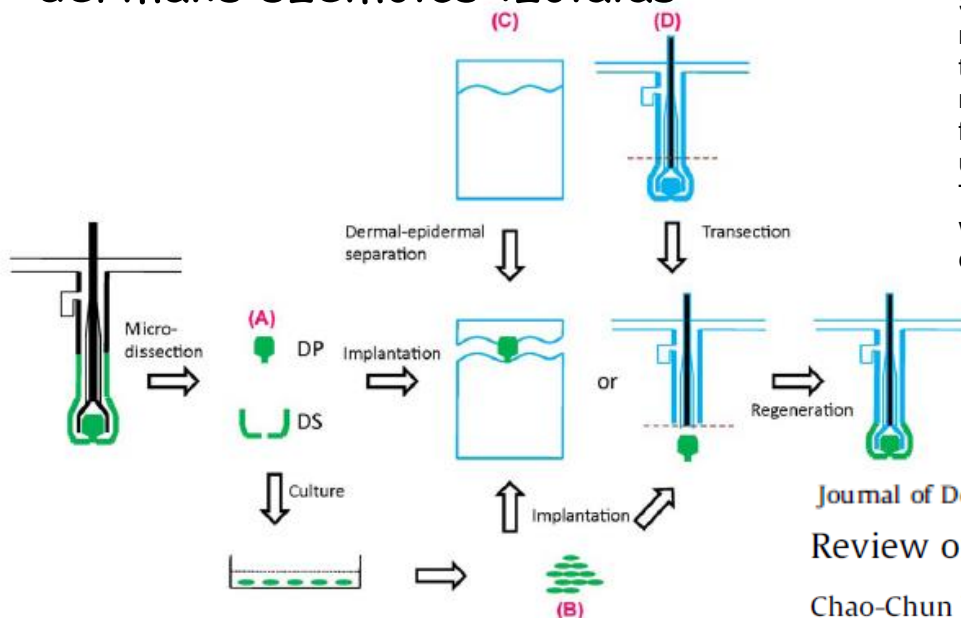
**Skin stem and progenitor cells: using regeneration as a tissue-engineering strategy**

# Bőrpótlási lehetőségek

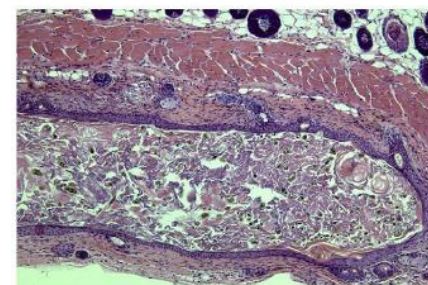
- in vivo szőrregenerációs tesztek



- dermális szemölcs izolálás



Subcutaneous injection of dissociated murine epidermal and dermal cells into the back skin of a nude mouse. (a) A nodule or "patch" with regenerated hair follicles can be observed from the undersurface of the skin in 2 weeks. (b) The histology shows formation of a cyst with hair follicles coming out from the cyst wall.



Journal of Dermatological Science 57 (2010) 2–11

Review of hair follicle dermal cells

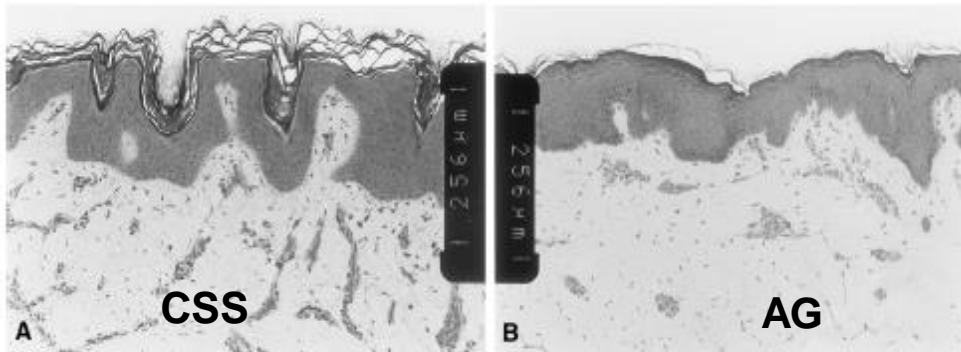
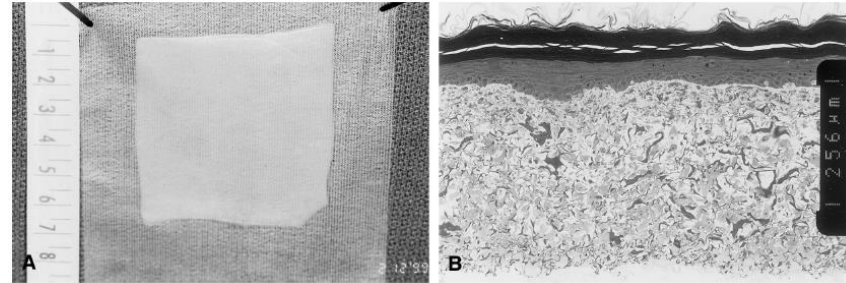
Chao-Chun Yang<sup>a,b,c</sup>, George Cotsarelis<sup>a,\*</sup>

# Bőrpótlási lehetőségek

- IFE őssejtek
  - megégett betegek keratinocitáinak in vitro tenyésztése; re-epitelializáció
    - "holoclones": "igazi" ESCs izolálás; nagy proliferációs képesség, kis sejtek, funkcionális epidermis kialakítása
    - "paraclones": kevés, nagy, lapos sejt (végdifferenciált)
    - "meroclones": elég kicsi, heterogén populáció, limitált osztódás (transit amplifying sejtek?)
  - nincs szőrtüsző / faggyúmirigy pótlás
  - sérülés esetén ált. bulge sejtekből, nem az IFE őssejtekből történik a kolonizáció
  - teljes regenerációhoz az epidermis izolálása ált. nem elég - mély sérülés, káros hatások autológ transzplantáció esetén (allogén transzplantáció - kilökődés; nem humán sejtek/anyagok - kilökődés, biztonság)

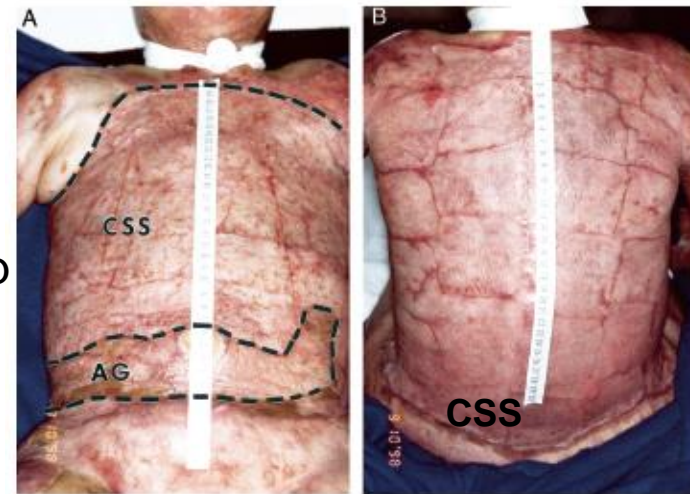
# Bőrpótlási lehetőségek

- mesterséges szubsztrátok
  - hordozó mátrix: pl. *GAG* (glükóz-aminoglikán)
  - fokozatos sejt"ráépítés"
    - keratinocita
    - fibroblaszt
    - endotél
    - melanocita
    - Langerhans sejtek??
  - növekedési faktorok „enkapszulációja” (tumorképzés!!)

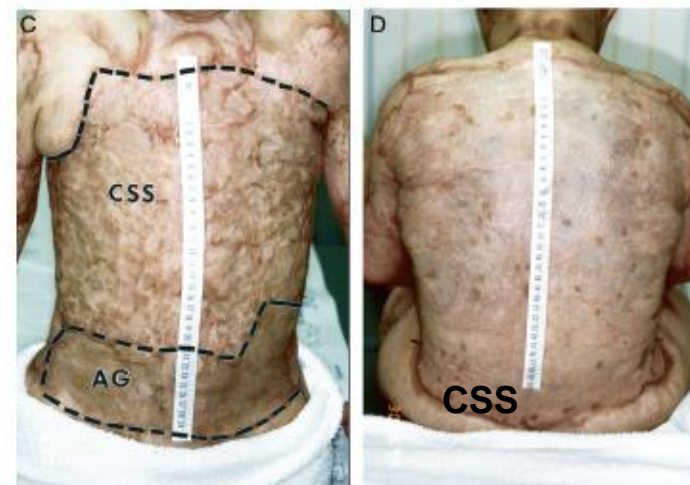


AG: autológ transzplantáció  
CSS: cultured skin substituents

~60 nap



1 év



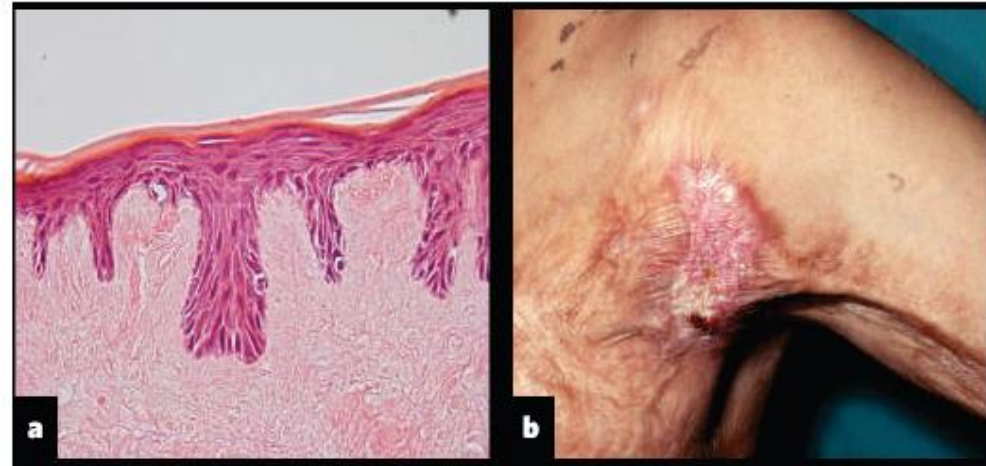
# Bőrpótlási lehetőségek

Progress and opportunities for  
tissue-engineered skin

Sheila MacNeil<sup>1</sup>

NATURE | Vol 445 | 22 February 2007 | doi:10.1038/nature05664

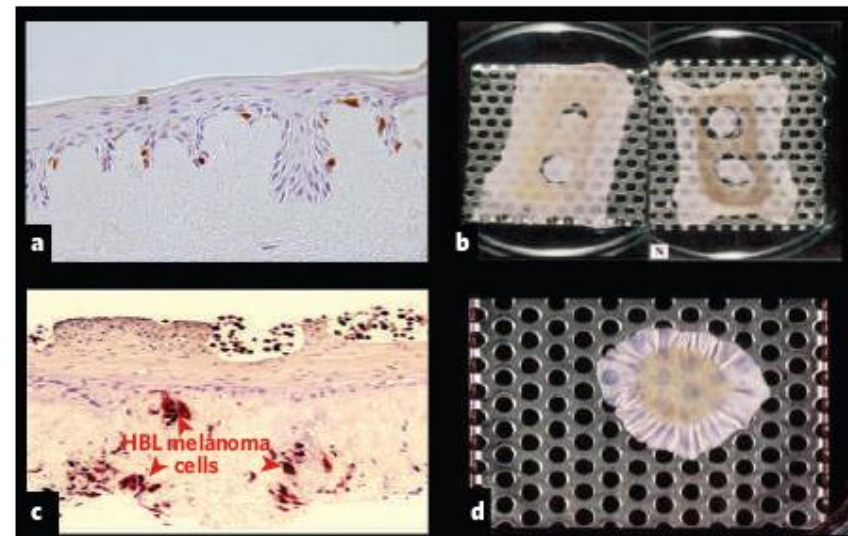
- mesterséges szubsztrátok
  - de-epidermized acellular donor dermis, mint megtapadási felület



**Figure 2 | An example of the clinical use of tissue-engineered skin.**

**a**, The appearance of reconstructed tissue-engineered human skin based on sterilized de-epidermized acellular donor dermis to which the patient's own laboratory-expanded keratinocytes and fibroblasts were added.  
**b**, The appearance of this reconstructed skin 2 months after its use in elective surgery to correct contraction in a patient who had suffered severe skin contractions as a result of earlier burns injuries. The tissue-engineered skin graft was placed in the axilla to allow the patient a more normal range of movement. (Images reproduced, with permission, from ref. 39.)

- Ingenta: szilikon membránon - ideiglenes barrier a dermis vaszkularizációjának elősegítésére



**Table 1. Characteristics of the ideal skin substitute**

	Derm oepidermal substitute (composite)			Dermal substitute				Epidermal substitute		Ref
	Cadaveric skin (nonprofit skin banks)	Koroskin*	Apigrat*	Alloderm*	SureDerm*	Integra*	Derma graft*	MySkin*	Cell Spray*	
Patient safety	Potential for viral transmission Immune rejection	Potential for viral transmission Immune rejection	Potential for viral transmission	Potential for viral transmission	Potential for viral transmission	n/a <sup>b</sup>	Potential for viral transmission	Autologous keratinocytes are cocultured with irradiated murine cells	n/a	[2]
Scaffold degradability	Rejection rather than degradation	Rejection rather than degradation	1–2 months	Incorporates into wound bed	Incorporates into wound bed	Half-life, 30 days	Degrades by hydrolysis	<29 days	n/f	[81]
Duration of cover	Temporary	Temporary	Temporary	Permanent	Permanent	Semi-permanent	Temporary	Permanent	Permanent	[4]
Neodermis formation	Dermis revascularises and integrates into the wound bed. The epidermis is rejected 3–4 weeks post-transplantation	Dermis revascularises and integrates into the wound bed. The epidermis is rejected 3–4 weeks post-transplantation	Delivers ECM components, cytokines and GF to the wound	Repopulated by host cells, i.e., incorporates into host tissue	Repopulated by host cells, i.e., incorporates into host tissue	Neodermis formation complete in 15–20 days	Scaffolds degrade over 20–30 days. Fibroblasts simultaneously produce ECM components and GF	Only applicable in partial-thickness and graft donor side wounds, but not in full-thickness wounds	Only applicable in partial-thickness and graft donor side wounds, but not in full-thickness wounds	[82–85]
Shelf life	7–10 days if fresh. Unlimited if lyophilised	Unlimited if lyophilised	5–10 days	2 years	Up to 2 years	2 years	Up to 6 months	3 days	n/f	[4]
Cost (/cm <sup>2</sup> ) (in 2007)	donated	£0.60	£14.20	£5.90	n/f	£3.32	£7.14	n/f	n/f	[2]
Mechanical stability	Lyophilisation improves mechanical stability significantly	Lyophilisation improves mechanical stability significantly	Requires delicate handling	Stable due to presence of basement membrane.	No adverse information regarding fragility and manual handling	Easy handling	Easy handling	Easy handling and application due to a silicone support layer	Very fragile and difficult to handle	[4,86]
Scaffold vascularisation (i.e., 'take')	Cadaveric allografts take initially, i.e., vascularisation is observed, however, subsequent graft rejection requires its eventual removal	Takes initially, i.e., vascularisation is observed, however, subsequent graft rejection requires its eventual removal	Take rates depend on the type of wound and are very variable ranging from 16 to 41%	Uncertain rates of vascularisation	No adverse information regarding delayed or failed graft take	Takes relatively long time for vascularisation (10–14 days)	Take is facilitated by fibrovascular in growth and re-epithelialisation and wound closure by keratinocytes migration from wound edges	Cannot be used for full-thickness wounds as dermal component missing	Uncertain rate of take as it depends on cell-cell and cell-ECM adhesion rather than vascularisation. Higher risk of bacterial contamination leading to graft loss	[75]
No. of stages necessary for completion	Multiple because cadaveric grafts require eventual replacement	Multiple because cadaveric grafts require eventual replacement	One-stage process but needs cografting with autologous epithelial cells in full-thickness burns	One-stage process (using ultrathin split-thickness graft)	Two-stage process (using split-thickness graft)	Two-stage process (using split-thickness graft)	Two-stage process if used in burn injuries (using split-thickness graft)	Up to 12 individual applications	One-stage process	[4]

\*Commercialised product

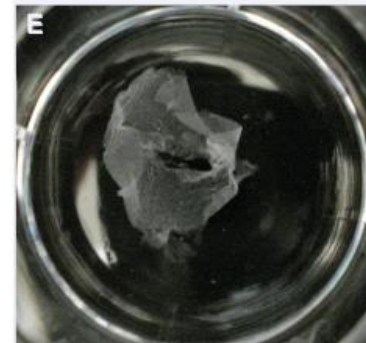
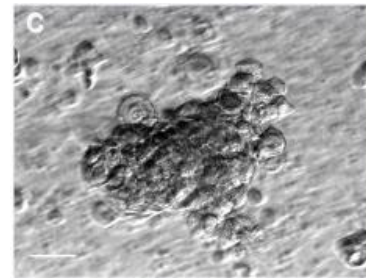
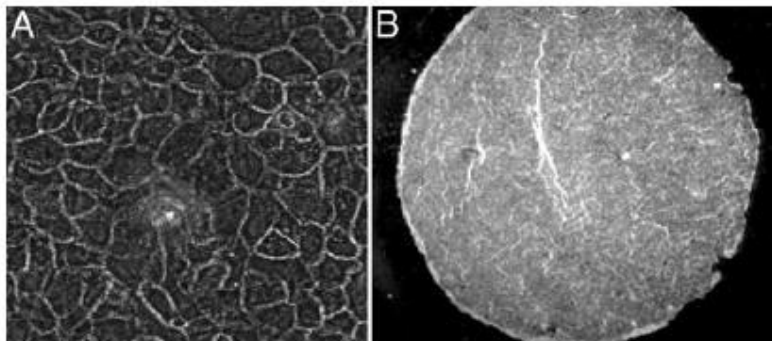
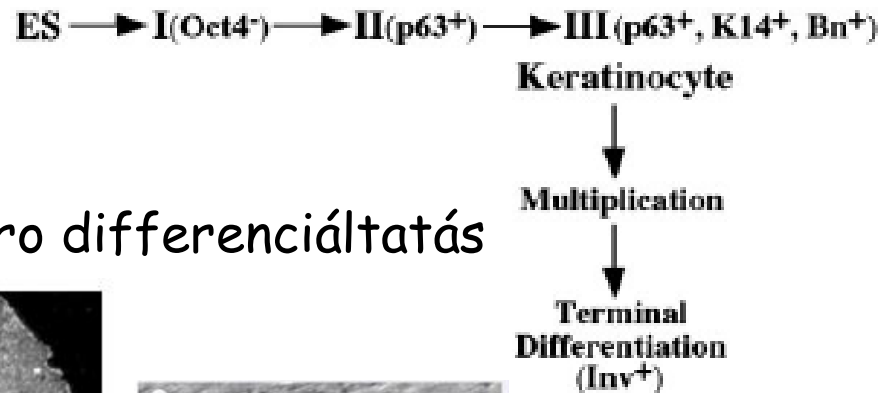
<sup>b</sup>n/a, not applicable; n/f, not found.

# Bőrpótlási lehetőségek

- hESCs (humán embrionális őssejt) differenciáltatás
  - embryoid body képzés ES sejtekből; scid egerekbe visszaültetés - visszaizolálható csomóban keratinocita progenitorok - in vitro differenciáltatás

- Oct4+ eltűnés, keratinocita markerek (p63, K14) megjelenés

- immortalizáció HPV vírussal - in vitro differenciáltatás



- kombinált RA és BMP4 kezelés: keratinocita sors (de BMP4 - trophoblast!)

*J. Cell. Mol. Med. Vol 12, No 3, 2008 pp. 709-729*

Engineering tissue from human embryonic stem cells

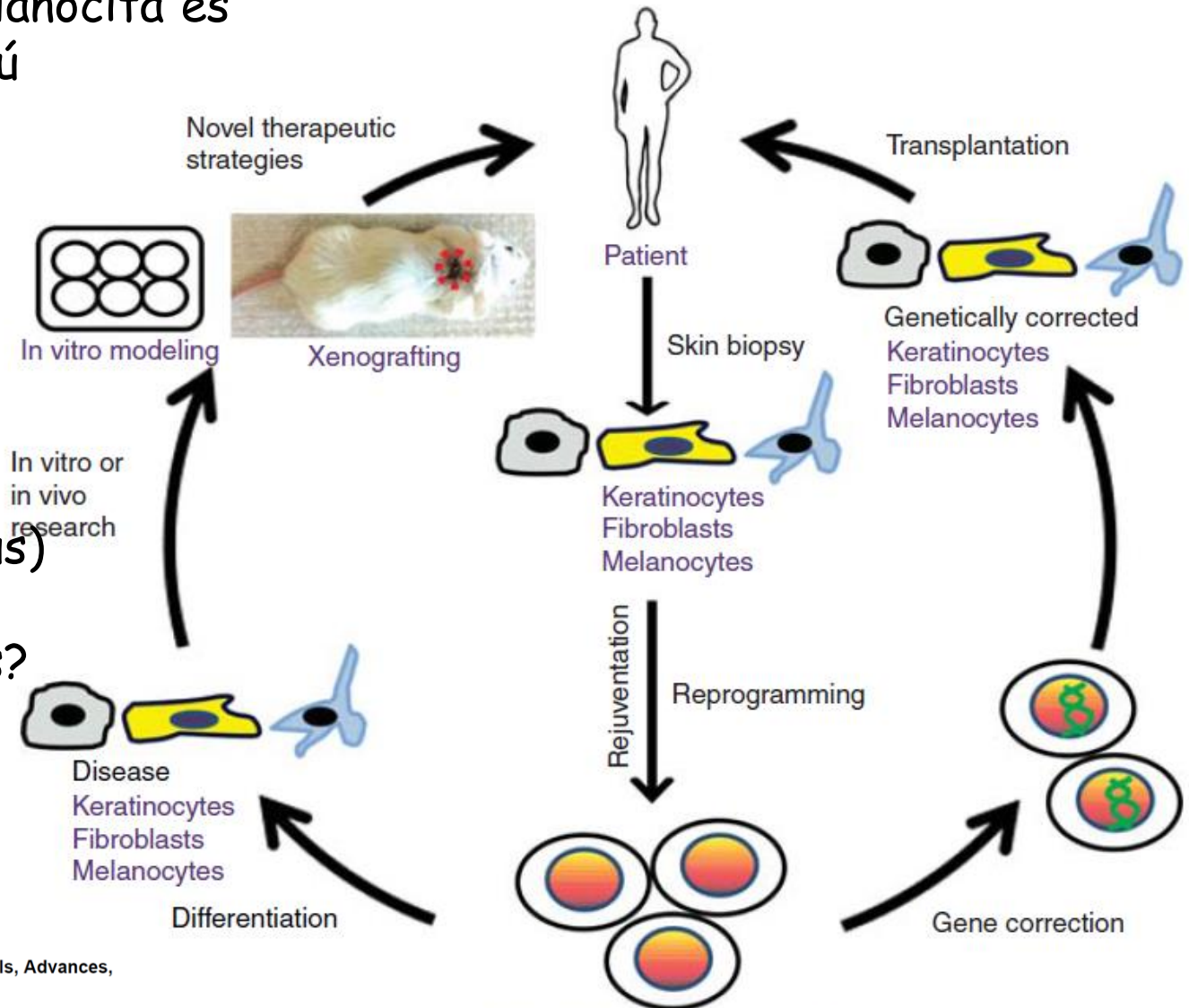
# Bőrpótlási lehetőségek

- iPSC differenciáltatás

- keratinocita, melanocita és fibroblaszt irányú differenciáltatás

- izolálás, differenciáltatás és géncorrekció biztonsága??

- saját (szingenikus) vagy allogén (humán) előállítás?





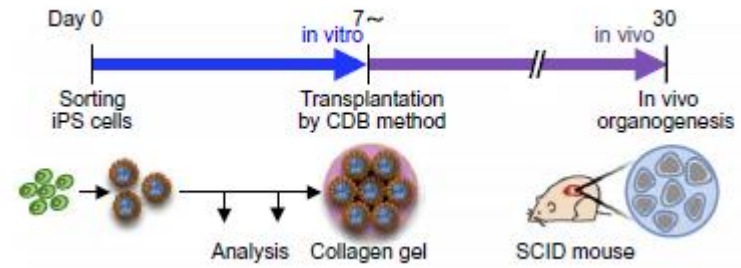
# Bioengineering a 3D integumentary organ system from iPS cells using an in vivo transplantation model

Ryoji Takagi,<sup>1\*</sup> Junko Ishimaru,<sup>1\*</sup> Ayaka Sugawara,<sup>1\*</sup> Koh-ei Toyoshima,<sup>2,3,4</sup> Kentaro Ishida,<sup>5</sup> Miho Ogawa,<sup>2,3,4</sup> Kei Sakakibara,<sup>1</sup> Kyosuke Asakawa,<sup>2</sup> Akitoshi Kashiwakura,<sup>1</sup> Masamitsu Oshima,<sup>5</sup> Ryohei Minamide,<sup>2</sup> Akio Sato,<sup>4</sup> Toshihiro Yoshitake,<sup>4</sup> Akira Takeda,<sup>4</sup> Hiroshi Egusa,<sup>6</sup> Takashi Tsuji<sup>2,3,5†</sup>

Sci. Adv. 2016;2:e1500887

1 April 2016

- CDB (clustering-dependent embryoid body) transzplantációs eljárás SCID egerekbe: iPS → aggregátumok (embryoid body, EB) → in vitro differenciáció → EB-k kollagénbe keverve a kötőszövetbe ültetve → nincs teratóma, csak epitél fejlődés



- Wnt10b: jelentősen fokozza a szőrfolikulus kialakulást

- Wnt10b: anagén - telogén átmenet, több ciklus is azonosítható; a m. arrector pili is megfelelően kötődik

- az XY iPS-ből kialakított HF-ek XX nude egérben is ciklusosan működtek

In vivo-organized integumentary organ system derived from male iPS cells (XY)

Intracutaneous transplantation

Orthotopic hair function

