Development of the skin and its derivatives

Resources:
http://php.med.unsw.edu.au/embryology/
Larsen’s Human Embryology – Chapter 7
The Developing Human: Clinically Oriented Embryology

Dr Annemiek Beverdam – School of Medical Sciences, UNSW
Wallace Wurth Building Room 234 – A.Beverdam@unsw.edu.au
Lecture overview

Skin function and anatomy

Skin origins

Development of the overlying epidermis

Development of epidermal appendages:
  * Hair follicles
  * Glands
  * Nails
  * Teeth

Development of melanocytes

Development of the Dermis

Resources:
http://php.med.unsw.edu.au/embryology/
Larsen’s Human Embryology – Chapter 7
The Developing Human: Clinically Oriented Embryology
Skin Function and Anatomy

Largest organ of our body
Protects inner body from outside world (pathogens, water, sun)
Thermoregulation
Diverse: thick vs thin skin, scalp skin vs face skin, etc

Consists of:
- Overlying epidermis
- Epidermal appendages:
  - Hair follicles,
  - Glands: sebaceous, sweat, apocrine, mammary
  - Nails
  - Teeth
- Melanocytes
- (Merkel Cells
- Langerhans cells)
- Dermis
- Hypodermis
Skin origins

Trilaminar embryo

**Ectoderm (Neural crest)**
- brain, spinal cord, eyes, peripheral nervous system
- epidermis of skin and associated structures,
- melanocytes, cranial connective tissues (dermis)

**Mesoderm**
- musculo-skeletal system, limbs
- connective tissue of skin and organs
- urogenital system, heart, blood cells

**Endoderm**
- epithelial linings of gastrointestinal and respiratory tracts
Ectoderm
Overlying epidermis, epidermal appendages, nerve endings
Neural Crest
Melanocytes + Cranial Connective Tissue
Mesoderm
Dermis, Hypodermis

Somitic mesoderm (yellow): dermomyotome -> dorsal dermis
Somatic lateral plate mesoderm (purple) -> ventral dermis
Embryonic development:

*Chart indicates origin of epithelial part of organ only. These organs all have secondary supporting investments of mesodermal origin.
Epidermal development
Surface ectoderm

Skin/Interfollicular epidermis: stratified squamous epithelium
Appendages:
  - Hair follicles
  - Glands (sebaceous, sweat, apocrine, mammary, lacrimal, salivary)
  - Nails
  - Teeth
Development of Skin/interfollicular epidermis (IFE)

Week 4

Week 11

Week 24

Onset of stratification
Development of Skin/interfollicular epidermis (IFE)

Periderm formation: 4 weeks

Basement membrane

Basal layer

Periderm
Development of Skin/interfollicular epidermis (IFE) Stratification

Week 11: intermediate layer

Intermediate layer

24 weeks

Adult

11 weeks

17 weeks

Schoenwolf et al: Larsen's Human Embryology, 4th Edition. Copyright © 2008 by Churchill Livingstone, an imprint of Elsevier, Inc. All rights reserved
Stratified skin/IFE

Envelope proteins

- Loricrin
- Involucrin
- Filagrin

Keratin 1/10

Keratin 5/14

Junctions:

- Adherens junction
- Hemidesmosome
- Desmosome
- Focal contacts

Regeneration, skin types
Stratified skin/IFE

Thick skin

Thin skin
Epidermal Appendages
Surface ectoderm

- Hair follicles,
- Glands: sebaceous, sweat, apocrine, mammary, salivary, lacrimal
- Nails
- Teeth

Share common developmental mechanisms:
Epithelial to mesenchymal signaling inducing formation of placode and mesenchymal condensations, invagination of epidermis into dermis.
Hair follicle development and cycling

Epidermal appendage

Involved in thermoregulation/sun protection

Month 2-4: Onset hair follicle development
Hair follicles develop first in cranial region
Month 5: most hair follicles present ≈ 5,000,000 hair follicles

Anatomy
Hair follicle development

Month 2

Birth: 5000,000

(i) UNDIFFERENTIATED EPITHELIUM
(ii) PLACODE
(iii) GERM
(iv) PEG
(v) BULBOUS PEG

Signaling events

Mesenchymal condensate
Dermal papilla
Hair follicle development

- Hair germ
- Hair peg
- Bulbous hair peg
- Invasion of dermal cells
Hair follicle development

Formation of:
- Arrector pili muscle
- Hair follicle bulge
- Germinal matrix
- Inner and outer root sheaths

Babies are born with first generation of fine un-pigmented hairs: lanugo

Postnatal regeneration:
Hair follicle cycling
Postnatal hair follicle cycling

- **Telogen**: rest
- **Anagen**: growth
- **Catagen**: regression

**Ageing**

germ       peg       bulbous peg

**Diagram**

- **Initiation of follicular cycling**
- **Follicular morphogenesis**
- **Epidermis Placode**
- **Dermal papilla**
- **Sebaceous gland**
- **Arrector pili muscle**
- **Hair shaft**
- **Melanocytes**
- **Regressing epithelial column**
- **New hair germ**
- **Dermal papilla**
- **New hair**
Epidermal gland development

Epidermal appendages: outgrowths from IFE or HF

- Sebaceous glands: sebum/vernix
- Sweat glands
- Apocrine glands (pheromones)
- Mammary glands
- Salivary glands
- Lacrimal glands
Epidermal gland development
Epidermal appendages

Sebaceous glands: develop from hair follicle (4 weeks+)
Sweat glands: develop from basal layer IFE (20 weeks+)
Apocrine glands: develop in association with HFs, most lost late in fetal dev.
Mammary gland development
Epidermal appendage

4 weeks:

- Mammary ridges
- 6th week: Primary bud
- 7th week: Secondary buds
- 4th month: Lactiferous ducts
- 6th month: Mammary pit
- 8th month: Postnatal regenerative growth

*Schoenwolf et al: Larsen's Human Embryology, 4th Edition. Copyright © 2008 by Churchill Livingstone, an imprint of Elsevier, Inc. All rights reserved*
Teeth
Tooth development

Ectoderm/cranial neural crest derived mesenchyme

Week 6: dental lamina
U-shaped ridge

Week 7: Mesenchyme condensation

Week 8: Mesenchyme invades base tooth bud:
Dental papilla

Week 14: Epithelial cells:
Ameloblasts: enamel
Mesenchymal cells:
Odontoblasts: dentin

Tucker and Sharpe, Nature Genetics 2004
Tooth development

Week 6: dental lamina forms

Week 7-8: formation of tooth buds:
Bud stage

Week 8: formation of dental papilla:
Cap and Bell Stage
Tooth development

Primary teeth
10 + 10

Adult teeth
16 + 16
Nail development
Ectoderm

**Week 10:** epidermal thickening, nail field

**Week 11:** nail anlagen moves proximally, nail folds, proximal hair fold: formation of formative zone

Nail development

Ectoderm

Melanocytes
Melanocyte development
Neural crest

Week 6
E8.5-E10.5

Ernfors, Exp Cell Res 2010
Melanocyte development
Neural crest

Week 6/7
E9.5-E12.5
Active proliferation
Migration into epidermis
direction of melanoblast migration
dermis
epidermis

Week 10
E13
Migration into Hair Pegs
E14.5
E15.5
E17.5
Final destination:
Bulge
Matrix
Basal layer (Humans)

Millar, Plos Biology 2005
Melanocyte development
Neural crest

Before stratification
Onset stratification
Bulbous hair pegs
Anagen
Matrix
Hair follicle Bulge

Djian-Zaouche,
Pigment Cell Melanoma Res 2012
Dermis
Connective tissue with:
- Fibroblasts
- Blood vessels
- Nerve endings
- Sensory receptors
- Muscle bundles
Dermis development

Somitic mesoderm -> trunk
Somatic lateral plate mesoderm -> trunk, limbs
Cranial neural crest derived mesenchyme -> cranial region
Dermis development

3 Months: formation of papillary layer (dermal papillae and epidermal ridges)

Inner dermis: reticular layer
Lecture overview

Skin

Skin origins

Development of the overlying epidermis

Development of epidermal appendages:
- Hair follicles
- Glands
- Mammary glands
- Nails
- Teeth

Development of Melanocytes

Development of the Dermis

Resources:
http://php.med.unsw.edu.au/embryology/
Larsen’s Human Embryology – Chapter 7
The Developing Human: Clinically Oriented Embryology

Dr Annemiek Beverdam – School of Medical Sciences, UNSW
Wallace Wurth Building Room 234 – A.Beverdam@unsw.edu.au
1. Hair follicles develop from:

A – the epidermis
B – the dermis
C – the hypodermis
D – the melanocytes
1. Hair follicles develop from:

A – the epidermis
B – the dermis
C – the hypodermis
D – the melanocytes
2. Hair follicle development:

A – is controlled by signaling exclusively from the mesenchyme
B – is controlled by signaling exclusively from the surface ectoderm
C – is controlled by signaling from mesenchyme and surface ectoderm
D – is controlled by signaling from the melanocyte stem cells
2. Hair follicle development:

A – is controlled by signaling exclusively from the mesenchyme
B – is controlled by signaling exclusively from the surface ectoderm
C – is controlled by signaling from mesenchyme and surface ectoderm
D – is controlled by signaling from the melanocyte stem cells
3. The non-cranial dermis is derived from:

A – ectoderm
B – mesoderm
C – neurectoderm
D – endoderm
3. The non-cranial dermis is derived from:

A – ectoderm  
B – mesoderm  
C – neurectoderm  
D – endoderm
4. Human melanocytes:

A – are ectodermal in origin
B – initially populate the dermis
C – are eventually localized in the basal epidermal layer and hair follicle
D – all of the above
4. Human melanocytes:

A – are ectodermal in origin
B – initially populate the dermis
C – are eventually localized in the basal epidermal layer and hair follicle
D – all of the above
5. Epidermal appendages are:

A – nails
B – mammary glands
C – teeth
D – all of the above
5. Epidermal appendages are:

A – nails  
B – mammary glands  
C – teeth  
D – all of the above