NATIONAL DERMATOLOGY RESIDENT LECTURE SERIES SUMMARY

Lecture: Cornification and Disorders of Cornification by Dr. Aaron Wong
Date: April 14, 2020 via Zoom
Compiled by: Danny Mansour, PG2, University of British Columbia

Epidermal Growth and Differentiation

Zones of Epidermis*	Key Features	Clinical Correlate
Stratum Corneum	• Nucleus and organelles lost result → lipid-depleted corneocyte (keratins and filaggrin rich matrix) with a corneocyte-bound protein envelope and another corneocyte-bound lipid envelope in a lipid-rich extracellular matrix with lipid bilayers • Filaggrin → urocanic acid which blocks UV and forms natural moisturization factor	
Stratum Lucidum	• Dead cells containing dispersed keratohyaline • Not present in non-palmoplantar skin	
Stratum Granulosum	• Keratohyaline granules form ○ Basophilic due to PROTEINS (loricrin, involucrin, filaggrin, profilaggrin, keratin intermediate filaments, etc.) • Cornified lipid envelop (CLE) mainly formed • Keratin 2/11 formed here	• Defects in filaggrin → ichthyosis vulgaris • Defects in loricrin → Vohnwinkel syndrome without deafness (mutilating keratoderma with ichthyosis) or progressive symmetric erythrokeratodermia
Stratum Spinosum	• Contains lamellar granules (Odland bodies) – think LIPID (ceramides, glycoproteins, glycolipids, phospholipids, glucosyl ceramides, sterols, etc.), hydrolytic enzymes (steroid sulfatase and others), and proteins • K5/14 transitions here and forms K1/10 in non-acral skin and K1/9 in acral	• Mutation in K1/10 → bullous congenital ichthyosiform erythroderma • Reduction or absence of lamellar granules → Flegel disease and Harlequin ichthyosis • Absent steroid sulfatase → X-linked ichthyosis
Stratum Basale	• Stem cells form 10% of this layer • Give rise to transit amplifying cell (TAC) and epidermal proliferation unit (EPU) • Ornithine decarboxylase (ODC) – marker of proliferation • K5/14 synthesis → inserted into desmosome and hemidesmosome	• Mutation in K5/14 gene → epidermolysis bullosa simplex

*in palmoplantar skin

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Cornified Lipid Envelope

Function	Components	
	Protein (Keratohyaline Granules)	**Lipid (Lamellar Granules)**

• Water loss protection by reducing transepideraml water loss (TEWL)
• Protects from:
  ○ UV,
  ○ Temperature fluctuations
  ○ Mechanical insults
  ○ Microbes
  ○ chemicals
• Calcium plays an important role in barrier repair, regulates TGM1, and stimulates epidermal repair and growth
• [Ca] gradient granular > basal > spinosum >>> corneum). Disruption in barrier → influx of water → [Ca] gradient change → stimulate repair to restore gradient
	▪ Loricrin → #1 protein component of CLE = bulk weight, crosslinking to involucrin
	▪ Transglutaminase 1, 3, 5 → crosslinking and N(ε)-(γ-glutamyl) lysine isopeptide bonds
	  ○ 1 and 5 crosslink evoplakin, periplakin, and involucrin
	  ○ 3 and 1 crosslink loricrin to SPR
	  ○ TG1 defect → lamellar icthyosis
	  ○ TG3 → antigenic target of dermatitis herpetiformis
	  ○ TG5 defect → peeling skin syndrome, type A acral variant
	▪ Involucrin → scaffold (binds keratin, filaggrin, and loricrin) and substrate for transglutaminase
	• Profilaggrin → filaggrin (FILament AGGregating proteIN) binds intermediate filaments organizing them into fibrils
	  ○ Encoded by FLG gene
	▪ Small-protein rich residues (SPR)
	▪ Keratin 1/10, 5/14, 2/10
	▪ Skin-derived anti-leukoproteinase (SKALP, serine proteinase inhibitor) → structural integrity
	• Envoplakin and periplakin → forms part of scaffold as well and antigenic targets in paraneoplastic pemphigus (as well as others)
		• Free fatty acids
		• Cholesterol
		• Ceramides (omega-hydroxyl-ceramides and glucosyl ceramide)
		• Some cholesterol and cholesterol sulfate
		• Steroid sulfatase
		• Phospholipids
		• ABCA12 (lipid transporter, structural component of granules) – defect results in Harlequin ichthyosis

Keratin

- Humane genome has at least 54 keratin genes
- Skin:
  - Type 1 (acidic, low molecular weight): keratin 9-28 by chromosome 17
  - Type 2 (basic): keratins 1-8 by chromosome 12
- Hair:
  - Type 1 (acidic): hair keratin 31-40
  - Type 2 (basic): hair keratin 81-86