KERATINOCYTE BIOLOGY & PATHOLOGY

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KERATINOCYTE BIOLOGY: SKIN

BILAYERED ORGAN
EPIDERMIS - CONTINUALLY RENEWING & RAPIDLY PROLIFERATING PROTECTIVE COAT
- READILY REPAIRED FROM EXTERNAL DAMAGE BARRIER

90-95% OF EPIDERMAL CELLS ARE KERATINOCYTES
KERATINOCYTES INTERACT WITH:
- EACH OTHER
- BASAL LAMINA AND DERMIS
- IMMIGRANT CELLS
  (MELANOCYTES, LANGERHANS CELLS, MERKEL CELLS)

OUTLINE
1) LIFE OF KERATINOCYTE AS IT MIGRATES THROUGH EACH LAYER OF THE EPIDERMIS

2) ASPECTS / MECHANISMS OF KERATINOCYTE BIOLOGY
   AND HOW DISRUPTION IN THESE ➔ PATHOLOGY
KERATINOCYTE BIOLOGY & PATHOLOGY

REFERENCES – RESOURCES

THE BIOLOGY OF THE SKIN
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THE MILTON OKIN DERMATOPATHOLOGY SLIDE COLLECTION
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GENETIC PATHWAYS IN DISORDERS OF EPIDERMAL DIFFERENTIATION

CELL DEATH BY CORNIFICATION
ECKHART L, LIPPENS S, TSCHACHLER E, DECKERCQ W. BIOCHIM BIOPHYS ACTA. 2013; DEC 1833(12):3471-80

CORNIFICATION OF THE SKIN: A NON-APOPTOTIC CELL DEATH MECHANISM

REGULATION OF KERATIN NETWORK ORGANIZATION
LOSCHKE F, SELTMANN K, BOUAMEUR J-E, MAGIN TM. CURRENT OPINION IN CELL BIOLOGY 2015, 32:56-65

KERATINS AND SKIN DISEASE
KNOBEL M, O’TOOLE EA, SMITH FJD. CELL TISSUE RES 2015, 360:583-589
KERATINOCYTE BIOLOGY

KERATINOCYTES ARISE FROM SUPERFICIAL ECTODERM DURING 1ST FEW WEEKS OF EMBRYONIC DEVELOPMENT

THE STRUCTURE OF EACH KERATINOCYTE DEPENDS ON ITS POSITION IN THE EPIDERMIS AND STATE OF DIFFERENTIATION (KERATINIZATION/CORNIFICATION)
LIFE OF THE KERATINOCYTE: KERATINIZATION/CORNIFICATION

LOSS OF ABILITY TO PROLIFERATE

▲ CELL SIZE; FLATTENING

FORMATION OF NEW ORGANELLES,
RE-ORGANIZATION OF EXISTING ORGANELLES,
THEN LOSS OF ORGANELLES

SYNTHESIS OF NEW PROTEINS & LIPIDS
CHANGES IN PLASMA MEMBRANE,
CELL SURFACE ANTIGENS & RECEPTORS

DEHYDRATION
▼
CORNEOCYTE
TERMINALLY DIFFERENTIATED – NON VIABLE BUT FUNCTIONAL CELL

Keri T. N. O’Cyte
LIFE OF THE KERATINOCYTE:
BASAL CELLS

LOWERMOST LAYER, COLUMNAR SHAPE

STEM CELLS [ACCUMULATE DELETERIOUS MUTATIONS; GENE THERAPY TARGET]

CYTOSKELETON: K5/K14 – DIVISION/MIGRATION

ATTACHED TO BASEMENT MEMBRANE VIA HEMIDESMOSOMES
LIFE OF THE KERATINOCYTE:
SPINOUS (PRICKLE) CELLS

SUPRABASILAR LOCATION

POLYHEDRAL SHAPE

LARGE NUMBER OF DESMOSOMES (SPINES) BETWEEN CELLS [SHRINKAGE ARTIFACT]

CONTAIN NEWLY SYNTHESIZED K1/K10

UPPERMOST ARE FLATTENED – LAMELLAR GRANULES
LIFE OF THE KERATINOCYTE:
GRANULAR CELLS

BELOW STRATUM CORNEUM

2-3 CELL LAYERS THICK

- KERATOHYALIN GRANULES
- BASOPHILIC GRANULES CONTAINING PROFILAGGRIN, LORICRIN

INVOLVED IN AGGREGATION (DISULFIDE BONDING) OF KERATIN FILAMENTS

- LAMELLAR GRANULES

MEMBRANE BOUND, SECRETORY ORGANELLES ORIGINATE IN GOLGI

TRANSPORT LIPIDS INTO INTERCELLULAR SPACE

AT THE TRANSITION TO THE STRATUM CORNEUM
LIFE OF THE KERATINOCYTE:
THE TRANSITION

GRANULAR CELL → ABRUPT → CORNEOCYTE

GRANULAR CELL SYNTHESIZES, MODIFIES AND CROSSLINKS THE PROTEINS INVOLVED IN ITS PROGRAMMED DEATH

(LORICRIN, INVOLUCRIN, KERATOLININ, SMALL PROLINE-RICH PROTEINS (CORNIFIN, SPR1, SPR2), ELATIN,
FILAGGRIN LINKER SEGMENT PEPTIDE, AND ENVOPLAKIN)

ARE CROSSLINKED BY TRANSGLUTAMINASE TO FORM A 7-15 NM THICK BORDER IN CORNEOCYTES (CORNIFIED ENVELOPE)

BETWEEN GRANULAR AND 1\textsuperscript{ST} CORNIFED LAYER THE CONTENTS OF LAMELLAR GRANULES RELEASED → INTERCELLULAR LAMELLAE

INVOLVES DESTRUCTION OF CELLULAR ORGANELLES INCLUDING NUCLEUS
LIFE OF THE KERATINOCYTE:
THE TRANSITION

**TRANSGLUTAMINASES (TGM)**

A GROUP OF ENZYMES THAT CATALYZE CALCIUM-DEPENDENT CROSS-LINKS BETWEEN PROTEINS

TGM 1, 3 & 5 ARE EXPRESSED IN KERATINOCYTES INVOLVED IN THE FORMATION OF THE CORNIFIED ENVELOPE OF THE EPIDERMIS WITH LORICRIN AND OTHER PROTEINS AS SUBSTRATES
Assembly of the Epidermal Cornified Cell Envelope
Andrey Kalin, Lyuben N. Marekov and Peter M. Steinert

MATURATION (TRANSITION) OF KERATINOCYTE INTO CORNEOCYTE

LIFE OF THE KERATINOCYTE: STRATUM CORNEUM

CORNEOCYTES - LARGEST OF THE KERATINOCYTES
FLATTENED, POLYHEDRAL SHAPE
PRIMARILY KERATIN EMBEDDED IN A FILAGGRIN RICH MATRIX
HAVE A PROTEIN REINFORCED PLASMA MEMBRANE
ASSOCIATED WITH SURFACE LIPIDS

VARIABLE THICKNESS (15 CELLS UPPER ARM, 100’S ON VOLAR SURFACES)

AS CORNEOCTYES MOVE TO SURFACE - [STRATUM COMPACTUM ➔ DYSJUNCTUM]
CHANGE STRUCTURE, COMPOSITION & FUNCTION
PROTEOLYTIC DEGRADATION OF DESMOSOMES [DISADHESION & SHEDDING]
LESS CAPACITY TO BIND WATER

MAJOR BARRIER (WATER LOSS, ABSORPTION OF ENVIRONMENTAL SUBSTANCES)
MECHANICAL PROTECTION

NON-VIABLE BUT FUNCTIONAL
IF DISTURBED (TAPE STRIPPING) ➔ ↑ PROLIFERATION - BASAL LAYER
LIFE OF THE KERATINOCYTE: CORNEOCYTES

STRATUM CORNEUM BARRIER: BRICK & MORTAR MODEL

LIPID-DEPLETED, PROTEIN-RICH CORNEOCYTE

CONTINUOUS, EXTRACELLULAR LIPID MATRIX
LIFE OF THE KERATINOCYTE

IN HEALTH (BIOLOGY) AND DISEASE

BIRTH
GROWTH & DEVELOPMENT: KINETICS
PSORIASIS

PROLIFERATION & DIFFERENTIATION
DARIER’S DISEASE, HAILEY-HAILEY

STRUCTURE
CYTOSKELETON - KERATIN INTERMEDIATE FILAMENTS
EPIDERMOLYSIS BULLOSA SIMPLEX; EPIDERMOLYTIC HYPERKERATOSIS, ETC

DIFFERENTIATION-THE ROAD TO MATURITY
STRATUM CORNEUM FORMATION
ICHTHYOSSES

REPAIR: DNA REPAIR
XERODERMA PIGMENTOSUM

DEATH: HALLMARK OF CORNEOCYTE FUNCTION
SKIN CANCER
KERATINOCYTE BIOLOGY: BIRTH AND GROWTH

<<10% STEM CELLS
LONG-LIVED SLOW CYCLING HI β-INTEGRIN
H³THYMIDINE-LABEL RETAINING

~50% TRANSIT AMPLIFYING CELLS
CAN UNDERGO LIMITED # DIVISIONS IN 1ST 2 LAYERS

~40% DIFFERENTIATING CELLS
COMMITTED TO TERMINAL DIFFERENTIATION

UNLIMITED # DIVISIONS
COMMITTED PROGENITOR CELLS

1ST 2 LAYERS
KERATINOCYTE BIOLOGY: PROLIFERATION AND DIFFERENTIATION

REGULATED BY A SPECTRUM OF GROWTH FACTORS & OTHER FACTORS

MITOGENS

- EGF (EPIDERMAL GROWTH FACTOR)
- TGF-α (TRANSFORMING GROWTH FACTOR)
- KGF (KERATINOCYTE GROWTH FACTOR)

TGF-β - SUPPRESSES DNA SYNTHESIS & MITOSIS
- PROMOTES DIFFERENTIATION

KERATINOCYTE DERIVED CYTOKINES: IL-1, IL-6, IL-7, IL-8, IL10, IL-12, IL-15, IL-18, IL-20, IL-22, IL-24, GM-CSF, etc.

RETINOIC ACID RECEPTORS (RAR), RETINOID X RECEPTORS (RXR)

VITAMIN D RECEPTORS (VDR)

etc...
KERATINOCYTE BIOLOGY: KINETICS

EPIDERMIS - A CONTINUOUSLY RENEWING POPULATION: RENEWAL = 28 DAYS

TIME SPENT IN STRATUM CORNEUM 14 DAYS

TRANSIT TIME: TIME TO MOVE THRU VISIBLE EPIDERMIS (BASAL CELL → UPPERMOST GRANULAR LAYER) = 14 DAYS

RATE OF RENEWAL CAN BE ALTERED IN RESPONSE TO STIMULI, IN WOUND HEALING, PSORIASIS, ETC. E.G., PSORIASIS-TRANSIT TIME REDUCED TO 4 DAYS
KERATINOCYTE PATHOLOGY: PSORIASIS

INFLAMMATION - MANY ACTIVATED T CELLS IN EPIDERMIS

KERATINOCYTE HYPERPROLIFERATION
8 X SHORTENING OF CELL CYCLE (FROM 311 H TO 36 H)
2 X INCREASE IN PROLIFERATIVE CELL POPULATION

HYPERKERATOSIS, ACANTHOSIS

PARAKERATOSIS [NUCLEI RETAINED – INCOMPLETE CORNEOCYTE DIFFERENTIATION]
IMPAIRED BARRIER FUNCTION
KERATINOCYTE BIOLOGY:
PROLIFERATION AND DIFFERENTIATION

REGULATED BY A SPECTRUM OF GROWTH FACTORS & OTHER FACTORS

CALCIUM

EPIDERMAL CALCIUM GRADIENT IN VIVO
INCREASES FROM BASAL TO GRANULAR LAYER
IN VITRO, ↑ CALCIUM TRIGGERS DIFFERENTIATION
MUTATIONS IN ATP2A2 - ENCODES SERCA2 (SARCO/ENDOPLASMIC RETICULUM Ca\(^{++}\)ATPase PUMP) (ENDOPLASMIC RETICULUM)

ABNORMAL INTRACELLULAR Ca\(^{++}\) HOMEOSTASIS $\rightarrow$ INTERFERENCE WITH:
- DIFFERENTIATION (HYPERKERATOSIS, DYSKERATOSIS, PAPILLOMATOSIS)
- CELL-CELL ADHESION (ACANTHOLYSIS)

AUTOSOMAL DOMINANT
(KERATOSIS FOLLICULARIS)

HYPERKERATOTIC
FOLLICULAR PAPULES WHICH
COALESE INTO PLAQUES

GRAINS
CORPS RONDS
ACANTHOLYSIS
ABNORMAL CALCIUM SIGNALING IN KERATINOCYTES LEADS TO ACANTHOLYSIS

AUTOSOMAL DOMINANT (CHRONIC BENIGN FAMILIAL PEMPHIGUS)

CRUSTING, OOZING, SCALING INTERTRIGINOUS PLAQUES

MUTATIONS IN ATP2C1 - ENCODES Ca^{++}ATPase PUMP SECRETORY PATHWAY CALCIUM / MANGANESE ATPASE (SPCA1) (GOLGI APPARATUS)

ACANTHOLYSIS DILAPIDATED BRICK WALL APPEARANCE

KERATINOCYTE PATHOLOGY: HAILEY-HAILEY DISEASE
KERATINOCYTE BIOLOGY: STRUCTURE

KERATIN INTERMEDIATE FILAMENTS (KIF) ➔ CYTOSKELETON

8-10 NM THICK
INTERMEDIATE BETWEEN 6NM ACTIN MICROFILAMENTS
AND 23 NM MICROTUBULES

ORGANIZED IN BUNDLES

EXTEND THRU CYTOPLASM FROM NUCLEAR ENVELOPE TO
HEMIDESMOSOMES AT PLASMA MEMBRANE
KERATINOCYTE BIOLOGY: STRUCTURE

~54 KERATINS

2 FAMILIES

ACIDIC, TYPE I (K9-28, K31-40) CHROMOSOME 17q

NEUTRAL-BASIC, TYPE II (K1-8, K71-80, 81-86) CHROMOSOME 12q

PAIR

HETERODIMERS
FOUR STRANDS ➔ PROTOFIBRIL
FOUR PROTOFIBRILS ➔ FILAMENT (KIF)

POSSIBLE STRUCTURE OF A FILAMENT

TWO CHAIN COILED COIL MOLECULAR STRAND

FOUR MOLECULAR STRANDS FORM ONE PROTOFIBRIL

FOUR PROTOFIBRILS FORM A FILAMENT
(1) GROWTH FACTOR SIGNALING & FORCE ARE SENSED & TRANSMITTED AT DESMOSOMES & HEMIDESMOSOMES → ORGANIZATION OF NETWORK (2).

(3) KERATIN BUNDLING CAN RESULT FROM INTRINSIC KERATIN PROPERTIES (DISULFIDE BONDING, CYTOLINKERS, ETC) → MAY CONTRIBUTE TO CELL STIFFNESS & PROTECTION OF THE NUCLEUS.

(4) KERATINS REGULATE MAINTENANCE OF HEMIDESMOSOMES & DESOMSOMES THROUGH SEQUESTRATION OF KINASES (Src, Akt, PKCa and CK1α [GREEN CIRCLES]) & DIRECT INTERACTIONS.

(5) POSTTRANSLATIONAL MODIFICATIONS (PTMs, ORANGE CIRCLES & BLACK TRIANGLES) OF KERATINS CAN ↑ NETWORK DYNAMICS & NON-POLYMERIC KERATIN STATE.

BOTH (4) AND (5) → WEAKER CELL ADHESION & ENHANCED CELL MIGRATION.

(6) MUTATIONS IN KERATIN GENES → MISFOLDING & FORMATION OF AGGREGATES → WEAKEN CELL ADHESION → TISSUE FRAGILITY.
KRT9 EXPRESSED ONLY IN Volar SKIN

ABNORMAL CONDITIONS, E.G. STRESS ➔ KRT6 & 16
KERATINOCYTE PATHOLOGY

STRUCTURE - KERATINS

EPIDERMOLYTIC ICHTHYOSES

EPIDERMOLYSIS BULLOSA SIMPLEX
EPIDERMOLYTIC HYPERKERATOSIS
EPIDERMOLYTIC PALMOPLANTAR KERATODERMA
ICHTHYOSIS BULLOSA OF SIEMENS
KERATINOCYTE PATHOLOGY: EPIDERMOLYSIS BULLOSA SIMPLEX

AUTOSOMAL DOMINANT
DIFFERENT DEGREES OF SEVERITY:
DOWLING MEARA > WEBER-COCKAYNE > KOEBNER
DOWLING MEARA OFTEN LETHAL IN INFANCY
BLISTERS WHICH HEAL WITHOUT SCARRING

LYSIS OF CELLS IN BASAL LAYER

CLUMPING OF KIF IN BASAL CELLS ON EM

MUTATIONS IN KRT5 OR KRT14 (ENCODE KERATIN 5 OR 14)
GENES EXPRESSED IN THE BASAL CELL LAYER

KIF FORM CYTOSKELETON

CYTOSKELETON FAILURE ➔ KERATINOCYTE FRAGILITY AND BLISTERING LIMITED TO BASAL LAYER
LOCATION OF MUTANT GENE EXPRESSION (BASAL CELL LAYER) ↔ PATHOLOGY
KERATINOCYTE PATHOLOGY: EPIDERMOLYTIC HYPERKERATOSIS

AUTOSOMAL DOMINANT
1 IN 200,000 – 300,000
HYPERKERATOSIS - ACCENTUATED OVER JOINTS
BLISTERING

HYPERKERATOSIS - VACUOLAR DEGENERATION
EPIDERMOLYSIS ABOVE BASAL CELL LAYER

MUTATIONS IN KRT1 OR KRT10 (ENCODE KERATIN 1 OR 10)
GENES EXPRESSED ABOVE THE BASAL CELL LAYER

KIF FORM CYTOSKELETON

CYTOSKELETON FAILURE ➔ KERATINOCYTE FRAGILITY, HYPERKERATOSIS, BLISTERING, ↑ PROLIFERATION
LOCATION OF MUTANT GENE EXPRESSION (SUPRABASALAR) ↔ PATHOLOGY
KERATINOCYTE PATHOLOGY: PALMOPLANTAR EPIDERMOLYTIC HYPERKERATOSIS (VÖRNER)

AUTOSOMAL DOMINANT
HYPERKERATOSIS PALMS & SOLES

MUTATIONS IN $KRT9$ – (ENCODES KERATIN 9)
$KRT9$ EXPRESSED ONLY IN PALMS AND SOLES
DISEASE CONFINED TO PALMS AND SOLES

CYTOSKELETON FAILURE $\Rightarrow$ KERATINOCYTE FRAGILITY, HYPERKERATOSIS, BLISTERING, ↑ PROLIFERATION

LOCATION OF MUTANT GENE EXPRESSION (VOLAR SKIN) $\leftrightarrow$ PATHOLOGY
MUTATIONS IN KRT2 – (ENCODES KERATIN 2)
KRT2 EXPRESSED IN SUPERFICIAL EPIDERMIS
KERATINOCYTE FRAGILITY AT GRANULAR LAYER

MOLTING (MAUSERUNG)
LOSS OF SUPERFICIAL EPIDERMIS

LOCATION OF MUTANT GENE EXPRESSION ↔ PATHOLOGY

KERATINOCYTE PATHOLOGY: ICHTHYOSIS BULLOSA OF SEIMENS

AUTOSOMAL DOMINANT HYPERKERATOSIS & PEELING

TRAUPE H. THE ICHTHYOSSES. SPRINGER-VERLAG 1989
STRATUM CORNEUM BARRIER

LIPID-DEPLETED, PROTEIN-RICH CORNEOCYTE

CONTINUOUS, EXTRACELLULAR LIPID MATRIX

KERATINOCYTE BIOLOGY CORNIFICATION - BRICKS

KERATINOCYTE PATHOLOGY

LAMELLAR ICHTHYOSIS

ICHTHYOSIS VULGARIS
KERATINOCYTE PATHOLOGY: LAMELLAR ICHTHYOSIS

AUTOSOMAL RECESSIVE
1 IN 200,000 – 300,000
COLLODIAN PRESENTATION
LARGE PLATE-LIKE SCALE
ECTROPION, ECLABIUM, ALOPECIA

HYPERGRANULOSIS
COMPACT HYPERKERATOSIS

IN SOME FAMILIES – MUTATIONS IN TGM1 (TRANSGLUTAMINASE 1)

TRANSGLUTAMINASE CROSSLINKS PROTEINS TO FORM CORNIFIED ENVELOPE OF THE STRATUM CORNEUM

ABNORMAL PROTEIN CROSSLINKING IN THE KERATINOCYTE ➔ SCALING, ABNORMAL BARRIER FUNCTION
AUTOSOMAL SEMIDOMINANT INHERITANCE
COMMON: 1 IN 300
FINE, WHITE SCALE, WORSE ON LEGS/HEELS
HYPERLINEAR PALMS, KERATOSIS PILARIS, ATOPY
MUTATIONS IN FLG ENCODES FILAGGRIN

PROFILAGGRIN IS THE MAJOR PROTEIN OF KERATOHYALIN GRANULES
WHEN CLEAVED INTO MULTIPLE FILAGGRIN PEPTIDES, THE FILAGGRIN PEPTIDES
AGGREGATE KERATIN FILAMENTS DURING THE FORMATION OF THE CORNIFED ENVELOPE

ABNORMAL
KERATIN INTERMEDIATE FILAMENT
AGGREGATION IN THE CORNEOCYTE

LIPID-DEPLETED, PROTEIN-RICH
CORNEOCYTE

CONTINUOUS, EXTRACELLULAR
LIPID MATRIX

SCALING, KERATOSIS PILARIS, ATOPY

KERATOHYALINE GRANULES ARE ABSENT IN HOMOZYGOTE

KERATOHYALINE GRANULES

LIPID  DEPLETED,  PROTEIN-RICH
CORNEOCYTE

CONTINUOUS, EXTRACELLULAR
LIPID MATRIX

SCALING, KERATOSIS PILARIS, ATOPY

HOMOZYGOTE
(2 MUTATIONS)

HETEROZYGOTE
(1 MUTATION)

CONTROL

LIGHT [microscopy] ELECTRON
KERATINOCYTE BIOLOGY CORNIFICATION – MORTAR

STRATUM CORNEUM BARRIER

LIPID-DEPLETED, PROTEIN-RICH CORNEOCYTE

CONTINUOUS, EXTRACELLULAR LIPID MATRIX

KERATINOCYTE PATHOLOGY

X-LINKED ICHTHYOSIS

CONGENITAL ICHTHYOSIFORM ERYTHRODERMA
KERATINOCYTE PATHOLOGY: X-LINKED ICHTHYOSIS

1 IN 6,000 MALES; ONSET: NEONATAL
SMALL, TIGHTLY ADHERENT SCALE
ADULT AFFECTED MALES & FEMALE CARRIERS:
COMMA-SHAPED CORNEAL OPACITIES (DO NOT AFFECT VISION)
ASSOCIATED CRYPTORCHIDISM, TESTICULAR CANCER
STEROID SULFATASE DEFICIENCY

LIPIDS (CHOLESTEROL SULFATE) → IN THE SUPERFICIAL STRATUM CORNEUM
MODIFIED BY STEROID SULFATASE → HYDRATION DESQUAMATION

LACK OF STEROID SULFATASE → ACCUMULATION OF CHOLESTEROL SULFATE IN CELLS & SERUM → LOSS OF INTERCELLULAR LAMELLAE DELAYED DESMOSOME DEGRADATION ABNORMAL CORNEOCYTE DYSADHESION RETENTION HYPERKERATOSIS

CONTINUOUS, EXTRACELLULAR LIPID MATRIX → LIPID-DEPLETED, PROTEIN-RICH CORNEOCYTE
KERATINOCYTE PATHOLOGY: CONGENITAL ICHTHYOSIFORM ERYTHRODERMA

AUTOSOMAL RECESSIVE
1 IN 200,000 – 300,000
COLLODIAN PRESENTATION, FINE, WHITE SCALE
OFTEN NONE TO MILD ECTROPION, ECLABIUM

IN SOME FAMILIES - MUTATIONS IN ALOXE3 OR ALOX12B
(ENCODE LIPOXYGENASES) \(\rightarrow\) CATALYZE FATTY ACID OXIDATION

STRATUM CORNEUM BARRIER

LIPID-DEPLETED, PROTEIN-RICH CORNEOCYTE

CONTINUOUS, EXTRACELLULAR LIPID MATRIX

ABNORMAL KERATINOCYTE LIPID METABOLISM

SCALING, ABNORMAL BARRIER FUNCTION, ERYTHEMA
KERATINOCYTE PATHOLOGY:
ICHTHYOSIS WITH CONFETTI

CONGENITAL ICHTHYOSIFORM ERYTHRODERMA
PROGRESSIVE DEVELOPMENT WHITE SPOTS
AUTOSOMAL DOMINANT
VERY RARE

KERATINOCYTES IN WHITE SPOTS = REVERTANTS TO WILD TYPE
LOSS OF DOMINANT MUTATIONS

HIGH FREQUENCY OF SKIN MOSAICISM

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KERATINOCYTE BIOLOGY & PATHOLOGY

KERATINOCYTES

PROVIDE OUR INTERFACE WITH THE WORLD

ESSENTIAL FOR HUMAN LIFE

SUFFER A BROAD RANGE OF PATHOLOGIC INSULTS

HAVE A WIDE RANGE OF MECHANISMS FOR COPING WITH INSULTS AND REPAIR OF DAMAGE

UNDERRATED AND UNDERVALUED

THANKS FOR LISTENING TO MY LIFE STORY

Keri T. N. O'Cyte