The Editor's Choice

Abe R

JOURNAL OF
Dermatological Science

VOLUME 94 NUMBER 2

Classification of 3097 patients from the Japanese melanoma study database using the American joint committee on cancer eighth edition cancer staging system

The American Joint Committee on Cancer (AJCC) 8th Edition Cancer Staging System was implemented in 2018; however, it has not been validated in an Asian melanoma population. Fujisawa Y et al validated the new system using a cohort of Japanese melanoma patients. In total, data for 3097 patients were analyzed. The 5-year disease-specific survival according to the 7th and 8th Edition staging system were as follows: IA = 98.5%/97.9%; IB = 95.4%/96.2%; IIA = 94.2%/94.1%; IIB = 84.6%/84.4%; IIC = 72.2%/72.2%; IIIA = 76.2%/87.5%; IIIB = 60.7%/72.6%; IIIC = 42.0%/55.3% and IIID = none/26.0%. The results show that new staging system could efficiently classify our Japanese melanoma cohort. These results indicate that adjuvant therapies for Stage IIB and IIC should be developed, since the relapse-free survival for these stages were equivalent to Stage IIIA and IIIB, respectively.

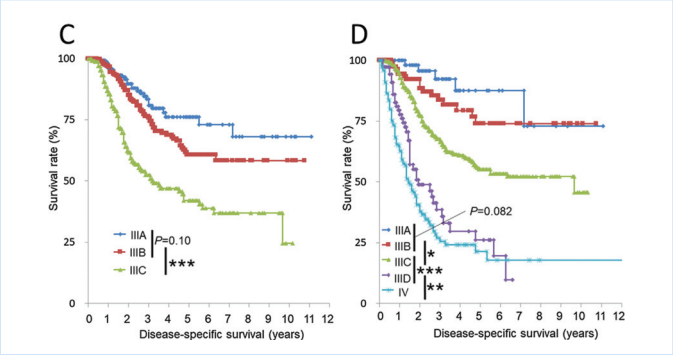

Fig. 2. Disease-specific survival curves for Stage I-III disease.
C) Stage III by AJCC 7th Edition staging.
D) Stage III by AJCC 8th Edition staging.
*: P < 0.05, **: P < 0.01, ***: P < 0.001.
338 × 381 mm (96 × 96 DPI).

IGF-1R deficiency in human keratinocytes disrupts epidermal homeostasis and stem cell maintenance

Epidermal stem cells (ESCs) are keratinocytes that reside in the basal layer of the epidermis and mediate epidermal homeostasis. Insulin-like growth factor 1 (IGF-1) signaling through its receptor (IGF-1R) has been identified as an important regulator in rodent skin development and differentiation. However, the role of IGF-1/IGF-1R signaling in human keratinocytes is not yet well understood. Muraguchi T et al aimed to clarify the role of IGF-1/IGF-1R signaling in human epidermal homeostasis. IGF-1R KO HaCaT keratinocytes were successfully established and produced thin epidermis in three-dimensional culture models. Keratin10-positive cells were frequently found in the basal layer of the reconstructed epidermis. IGF-1/IGF-1R signaling was demonstrated to play a key role in maintaining human epidermal homeostasis. This method provides a new framework to investigate gene function in human epidermal homeostasis.

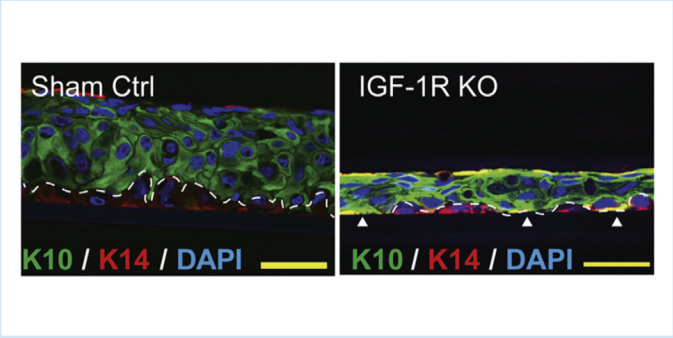

Fig. 4. IGF-1R deficiency in human keratinocytes causes epidermal hypoplasia.
C: Representative images of immunohistochemistry for keratin 14 (K14) and keratin 10 (K10) in the epidermal layer of control RE (left) and those produced using KO cells (right). Arrowheads indicate epidermal differentiation marker K10-positive basal cells.

Toll-like receptor 2 utilizes RAB11A for melanosome transfer from melanocytes to keratinocytes

Epidermal cells express TLRs to sense the signals from the outer world and induce cytokines and antimicrobial peptides to protect the human body. TLR2, which recognizes bacterial lipoprotein, enhances melanogenesis in melanocytes and melanosome transfer to keratinocytes. Koike S et al sought whether recycling endosome-associated RABs are involved in TLR2-dependent melanosome transfer. TLR2 stimuli augment RAB11A expression in human epidermal melanocytes and facilitate melanosome transfer to neighboring keratinocytes through RAB11A-associated melanosome transportation. TLR2 agonist HKLM induces de-novo melanin synthesis by increasing melanogenic genes TYR and dopachrome tautomerase expression and melanosome maturation. Because the membrane trafficking and vesicular transformation are the fundamental of melanosome maturation and transportation, our studies indicate molecular mechanisms how microenvironment including microbiota in epidermis would affect pigmentation process and postinflammatory pigmentation through innate immune receptor TLRs.

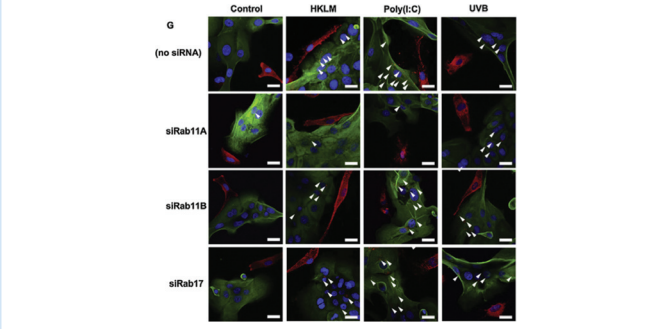

Fig. 2. Knockdown of RAB11A decreases melanosome transfer by HKLM and Poly(I:C).
(G) Melanocytes treated with siRNA of RAB11A, RAB11B, RAB17 for 24 h were co-cultured with keratinocytes, and stimulated by HKLM (10^8 cells ml^{-1}), Poly(I:C) (1 μg ml^{-1}) or UVB irradiation (15 mJ cm^{-2}). After 24 h incubation, PMEL/Gp100 (red), keratin (green) and nuclei (DAPI, blue) were visualized by immunofluorescence staining. The arrowheads indicate melanosomes transferred to keratinocytes. Scale bars = 50 μm.