Drebrin Depletion Causes Abnormal Morphology in Mouse Skin

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Drebrin (Dbn) is an actin-associated protein [1]. A decrease in the amount of this protein in the brain has been implicated as a possible contributing factor in the pathogenesis of memory disturbance in Alzheimer's disease. Isoform E2 of Dbn has been identified in diverse non-neuronal cells, mostly in association with cell processes and intercellular junctions. It was reported Dbn is expressed in normal human skin, epithelial skin cancers, and cultured keratinocytes. Keratinocytes of normal epidermis contain almost no Dbn but the protein is readily seen in hair follicles [2].

We have previously reported that Dbn⁻/⁻ mice exhibited normal morphology and distribution, but a reduction in the number of skin mast cells, with reduced IgE-mediated histamine release and passive systemic anaphylaxis, because these mast cells had defects in FceRI-mediated degranulation. Specifically, the defects of mast cells were in actin cytoskeleton organization and calcium responses downstream of the FceRI, and agents that relieve actin reorganization rescued mast cell FceRI-induced degranulation. Our results indicated that Dbn regulates the actin cytoskeleton and calcium responses in mast cells, thus regulating mast cell function in vivo [3]. Using the same skin tissue materials, we further analyzed other morphological alterations of Dbn⁻/⁻ mice in this study.

Dbn⁻/⁻ mice and their wild-type (WT) littermates (6-8 weeks old) were generated as previously described [3]. The skin tissue of Dbn⁻/⁻ mice had normal architecture, showing distinct epidermis and dermis with easily recognizable layers of epithelia, dense connective tissue, fat layer, and muscles (Figure 1). While there was no significant difference in thickness of epidermis, the tissue showed a notably translucent appearance and a thicker dermic fat layer (Dbn⁻/⁻, 0.34±.12 mm vs. WT, 0.22±.02 mm) in toluidine blue stained 0.5 µm-thick sections and low magnification TEM images. Comparing with WT mice, tissue separation was observed in multiple places of fat layer in Dbn⁻/⁻, which presumably happened during tissue processing due to the weakness of fat layer in mutants. The adipocytes appeared larger in size and rigid in shape, likely indicating a lower tensile strength of the cell. Although these mice had intact basal lamina, with clearly recognizable structure and distribution of hemidesmosomes and microfilaments which defined the border of the epidermis and dermis, there was a remarkably reduced electron density of hemidesmosome and its associated microfilaments (Figure 2). It was noted that there were much fewer vesicle invaginations in Dbn⁻/⁻ basal lamina while caveolae-mediated pinocytotic pits were easily found in the Dbn⁻/⁻ endothelia and adipocytes, but they appeared to have a wider opening. Abnormalities were also founded in hair follicles, muscles, and nerves.

The current study suggests that Dbn depletion causes skin tissue abnormality, and that Dbn may play an important role in maintaining integrity of tissue, epithelial junctions and basal lamina, shape of adipocytes, and tensile strength of cell membranous structures.
References:
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\[\text{Figure 1. Dbn}^{-/-}\text{ skin shows remarkably thickening due to a thick layer of fat (double arrow). The tissue looks transparent and loose with tearing in some places. Adipocytes are larger and in rigid shape. Toluidine blue stained epon-embedded mouse skin, 0.5 \text{ \textmu m}-thick sections. M, muscle layer.}\]

\[\text{Figure 2. TEM micrographs of mouse skin showing basal lamina. Dbn}^{-/-}\text{ tissue appears in low electron density with a clearly defined lamina and normal structure of hemidesmosomes, but exhibits a lighter appearance with fewer microfilaments. Flask-shaped membrane invaginations (arrow) are often observed in WT but rare in Dbn}^{-/-}\text{ mutant. BL, basal lamina.}\]