TOF-SIMS Characterization of In Vivo and Transdermally Treated Mouse Skin

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Imaging mass spectrometry, using either the MALDI or the TOF-SIMS technique, is rapidly gaining acceptance for the characterization of molecular structures in the studies of plants and animals. To date, cross-sectioned specimens provide the most convenient sample preparation approach for imaging mass spectrometry to visualize specific molecular structures and localizations of disease markers in these specimens. The molecular characterization of in vivo and treated tissues extends the analytical requirements for imaging mass spectrometry beyond the spatial resolution capabilities of MALDI. The use of a TOF-SIMS Bi_3^{2+} primary ion beam for sub-micron molecular imaging coupled with non-destructive molecular depth profiling using a Gas Cluster Ion Beam (GCIB) opens the possibility of 3D high-resolution imaging of the surface barrier layers and internal structures of mouse skin. The imaging of tissues with sub-micron spatial resolution can also be used to elucidate the transdermal penetration of topically applied drugs, which is thought to be controlled by the barrier layers of the skin.

Mouse tail cross sections were obtained from animals that were given general anesthesia before being sacrificed as well as from animals that were not anesthetized for a control. The freeze-dried samples were analyzed using mosaic TOF-SIMS imaging. The TOF-SIMS spectra from the muscle tissues with and without exposure to the general anesthesia confirm the action of the anesthesia as an acetylcholine inhibitor and its interaction with the ligand gated sodium channels in the cell membrane. Imaging of the outermost surface regions of the mice skin confirms molecular signatures of the ceramide and other constituents in the barrier layers of skin that are important for the transepidermal penetration. Both the line-scan analysis of the cross-sectioned sample as well as the GCIB depth profiling of the outer surface of the skin showed that there exist distinct layers having different molecular profiles in the barrier layer of the skin. These results suggest that TOF-SIMS measurement with GCIB depth profiling provides a novel analytical method to investigate transepidermal penetration of various molecules into the barrier layer of the skin.