Role of acid ceramidase in the degradation of *N*-acylethanolamines, a group of anti-inflammatory and anorexic lipid mediators

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N-Acylethanolamines (NAEs) constitute a class of lipid mediators and include palmitoylethanolamide, oleoylethanolamide and anandamide, which show anti-inflammatory/analgesic, anorexic and cannabimimetic actions, respectively. Acid ceramidase (AC) is a well-known lysosomal enzyme degrading ceramide (*N*-acylsphingosine). Our earlier study showed that recombinant AC hydrolyzes not only ceramide but also NAEs in the cell-free assay system. Here, we examined the biological significance of this NAE-hydrolyzing activity at cell and tissue levels. When HEK293 cells were metabolically labeled with [^{14}C]ethanolamine, overexpression of AC lowered the ^{14}C-labeled NAE level. LC-MS/MS analysis showed that the AC overexpression decreased the amounts of quantitatively major NAE species. Furthermore, the knockdown of endogenous AC in LNCaP prostate cells increased the levels of NAE species. Since saposin D is presumed to be an activator protein of AC, we compared AC activities between wild-type and saposin D-deficient mice. The brain homogenate from the mutant mice showed much less hydrolysis rate for NAE as well as ceramide. These results suggest a role of AC in the degradation of NAEs in cells and tissues.