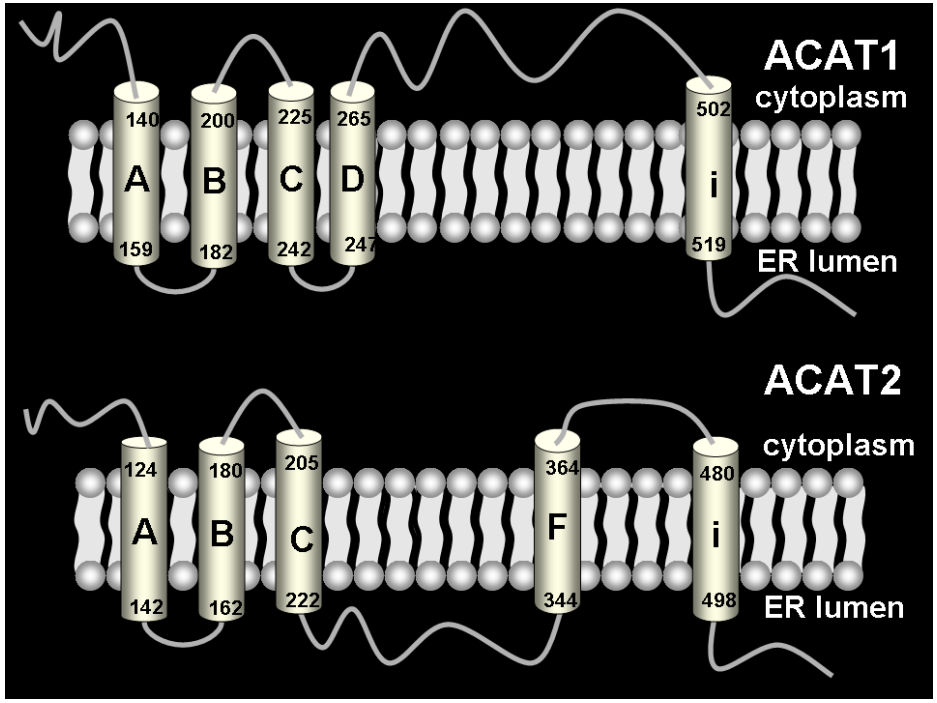
Supplemental figure A: *Topology model of ACAT isozymes from Ref. 19:* The model was based on a computer predicted topology map of ACAT enzymes, and truncated mutants were made, where, after each computer predicted transmembrane domain, a glycosylation reporter site was added. Based on utilization of the glycosylation site and accessibility by the exogenous proteases, the topology maps of both ACAT enzymes were determined in parallel. Both the enzymes have N_{cyto} C_{exo} orientation with five potential transmembrane domains. Interestingly, transmembrane domain D is not utilized and domain F is utilized in ACAT2, whereas the opposite is true for ACAT1. Computer predicted domains E, G, and H are not utilized in either of the enzymes.

Supplemental figure B: Chemical structure of PPPA molecule.

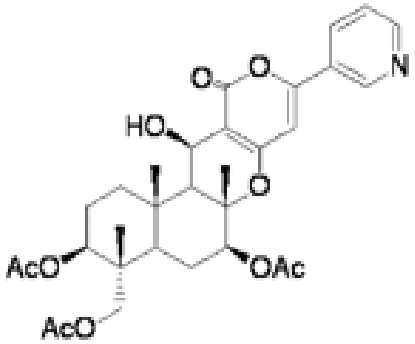
Supplemental figure C: Sequence similarity within the putative active site domain of the ACAT enzymes across the species. AGM ACAT1 and ACAT2 have 56% over all sequence similarity after first 100 amino acids where the sequence similarity is only 2%. The area of highest sequence similarity (83%) among these proteins is toward the C-terminus including amino acids 386-462 of ACAT1 and 364-440 of ACAT2. Due to high sequence conservation from yeast to humans, we defined this region as the putative active site domain of the ACAT enzymes. Two conserved motifs FYXDWWN and HEY within this region are represented by two boxes. ARE1 and ARE2 are the yeast homologs of ACAT enzymes; AGM represents African green monkey.

Supplementary figures

A



B



Pyripyropene A

C

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Human A1 386 HCWLNAFAEMLRFGDRMFYKDWWNSTSYSNYYRTWNVVVHDWLYYYAYKDFLWFFSKRFKSAAMLAVFAVSAVVHEY 462
AGM A1 386   HCWLNAFAEMLRFGDRMFYKDWWNSTSYSNYYRTWNVVVHDWLYYYAYKDFLWFFSKRFKSAAMLAVFAVSAVVHEY 462
Mouse A1 376 HCWLNAFAEMLRFGDRMFYKDWWNSTSYSNYYRTWNVVVHDWLYYYVYKDLLWFFSKRFKSAAMLAVFALSAVVHEY 452
AGM A2 364   HCWLNAFAEMLRFGDRMFYRDWWNSTSFSNYYRTWNVVVHDWLYSYVYQDGLWLLGAQARGVAMLGVFLVSAVAHEY 440
Human A2 360 HCWLNAFAEMLRFGDRMFYRDWWNSTSFSNYYRTWNVVVHDWLYSYVYQDGLRLLGARARGVAMLGVFLVSAVAHEY 436
Mouse A2 363 HCWLNAFAEMLRFGDRMFYRDWWNSTSFSNYYRTWNVVVHDWLYSYVYQDGLWLLGRRARGVAMLGVFLVSAVVHEY 439
ARE1 487     DALLNCVAELTRFADRYFYGDWWNCVSFEEFSRIWNVPVHKFLLRHVYHSSMGALHFS-KAQATLFTFLLSAVFHEI 562
ARE2 523     DAILNCIAELTCFADRYFYGDWWNCVSWEEFSRLWNVPVHKFLLRHVYHSSISFLQLN-KAQATIATFFISSVVHEL 523
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