SPHINGOLIPID SIGNALING PATHWAY Endoplasmic reticulum Golgi Palmitoyl CoA SM0-Cer dhCer dhSph Õ DEGS CerS Serine Sphingolipid metabolism ► N-SIMase TNFα TNFR FAN Ionizing radiation **→**♀ SM A-SIMace SMS TRADD 0-O Cer Lysosome ROS Lysosome 0 ► FceRI TRAF2 Ag ► Cathepsin Cer O BID BAX Gab2 JNK ASK1 BAX Apoptosis PI3K CDase CerS p38 Adenosine OPIP3 Ο. Sph O PKCζ AKT ► BCL-2 ВΚ Gi PLD -p p53 SPHK SPPase 0 PLC PP2A Opioids PKCε ERK1/2 S1Plyase ABCC1 0 **→** ○ MAPK signaling pathway Phospho-S1P ethanolamine ^{+p}► ERK1/2 Cell survival S1Pı Raf Proliferation Gi PIP3 ►O ► PDK1 Vasodilatation ₱13K S1P₂Cardioprotection NO PI3K-Akt signaling pathway Migration and other Rac cytoskeletal events S1P3 Gq Secretion IP3 PKC S1P4 DG PTEN Stress-fiber ► G12/13 S1Ps Rho ROCK formation ▲ NF-ĸB

04071 2/1/19

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