Researchers create first inhibitor for enzyme linked to cancers

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Recent studies showing acid ceramidase (AC) to be upregulated in melanoma, lung and prostate cancers have made the enzyme a desired target for novel synthetic inhibitor compounds. This week in *Angewandte Chemie*, a top journal in chemistry, UC Irvine and Italian Institute of Technology scientists describe the very first class of AC inhibitors that may aid in the efficacy of chemotherapies.

AC, which is encoded by the ASAH1 gene, plays an important role in the regulation of cell fate, setting the balance between pro-aging/death and pro-life signals. Mutations in the ASAH1 gene have been associated with a lysosomal storage disorder called Farber disease and with spinal muscular atrophy.

In their *Angewandte Chemie* study, Daniele Piomelli - the Louise Turner Arnold Chair in the Neurosciences at UCI - and colleagues present a potent and systematically active small-molecule inhibitor of intracellular AC. In in vivo studies, the team found that inhibiting AC with their novel compound tilts the balance between pro-aging/death and pro-life chemical signals, favoring the former at the expenses of the latter.

"We hope that AC inhibitors may be one day used as 'chemosensitizers' - drugs that enhance the cancer-killing power of anti-tumoral drugs," said Piomelli, who is also affiliated with UCI's Chao Family Comprehensive Cancer Center. "The new chemical scaffold we published is a promising starting point for the development of novel therapeutic agents, and we aim to pursue its further pharmaceutical development."

Provided by University of California, Irvine