Accepted Manuscript

Structure-activity relationship study of leucinostatin A, a modulator of tumor−stroma interaction

Hikaru Abe, Manabu Kawada, Chiharu Sakashita, Takumi Watanabe, Masakatsu Shibasaki

PII: S0040-4020(18)30612-4

DOI: 10.1016/j.tet.2018.05.064

Reference: TET 29571

To appear in: *Tetrahedron*

Received Date: 11 April 2018

Revised Date: 18 May 2018

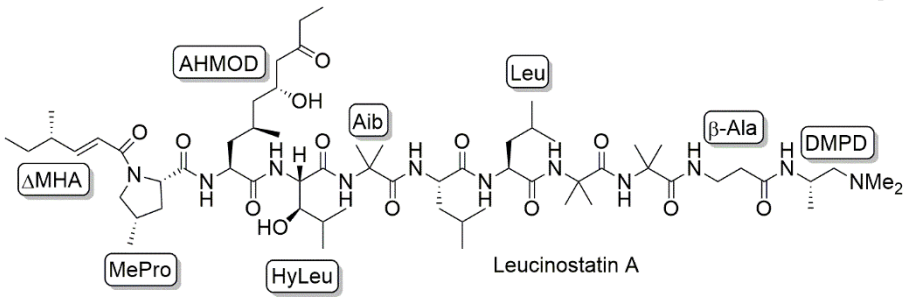
Accepted Date: 22 May 2018

Please cite this article as: Abe H, Kawada M, Sakashita C, Watanabe T, Shibasaki M, Structure-activity relationship study of leucinostatin A, a modulator of tumor−stroma interaction, *Tetrahedron* (2018), doi: 10.1016/j.tet.2018.05.064.

Structure-Activity Relationship Study of Leucinostatin A, a Modulator of Tumor−Stroma Interaction

Hikaru Abe, Manabu Kawada, Chiharu Sakashita, Takumi Watanabe*, Masakatsu Shibasaki*

Institute of Microbial Chemistry (BIKAKEN), Tokyo, 3-14-23 Kamiosaki, Shinagawa-ku, Tokyo 141-0021, Japan



(Graphical Abstract)

Keywords: Leucinostatin, Structure-Activity Relationship, Tumor−Stroma Interaction, Peptide, Anticancer agent

ABSTRACT:. Structure-activity relationship studies of leucinostatin A, a natural nonapeptide, were performed to gain insight into the structural requirements for leucinostatin A to exhibit antiproliferative activity against DU-145 prostate cancer cells under cocultured conditions with the corresponding stromal cells. Twenty truncated peptide analogs of leucinostatin A revealed that the nonapeptide structure as a whole is essential for the biological activity. Alanine scanning demonstrated the importance of some of the amino acid components, including hydroxyleucine and