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MEDIA ADVISORY

LA JOLLA RESEARCHERS ARE FIRST TO ACHIEVE TOTAL SYNTHESIS OF NATURAL FORM OF COMPLEX CALICHEAMICIN MOLECULE

Implications for Future Anti-Cancer Agent

WHAT: A team of researchers led by K.C. Nicolaou, Ph.D. has reported in this week's issue of the Journal of the American Chemical Society (JACS) the first total synthesis of calicheamicin in its naturally occurring form. The work is a major accomplishment; for years, the nation's top synthetic organic chemists have attempted to synthesize this remarkably complex molecular structure.

WHO: Dr. Nicolaou is the Darlene Shiley Professor and chairman of the Department of Chemistry at The Scripps Research Institute; and a professor of chemistry in the Department of Chemistry, University of California, San Diego. Both institutions are located in La Jolla, California.

Additional authors of the journal article were UCSD graduate students C.W. Hummel and E.N. Puitsinos; and M. Nakada, A.L. Smith, K. Shibayama, and H. Saimoto, all postdocs at TSRI.

BACKGROUND: Calicheamicin is a member of the enediyne class of anti-cancer antibiotics which are produced by bacteria found in soil. Additional enediynes are dynemicin, the esperamicins, and neocarzinostatnin chromophore. Although enediynes have been studied since 1987 for their ability to cleave DNA and kill cancer cells, the naturally-occurring antibiotics are toxic to healthy cells as well.
In the May 22, 1992 issue of the journal Science, Nicolaou and his team announced that they had made a "mimic" of the enediyne dynemicin, which appeared to be able to take advantage of an enediyne's potent anticancer activity, while leaving healthy cells intact. The molecule they synthesized was a simpler version of the true, naturally-occurring dynemicin enediyne.

With the total synthesis of calicheamicin, Nicolaou notes that "we can now use the same methodology to make variations that may be simpler, even better than the naturally occurring substances."

FOR COMMENT ON THE SYNTHESIS OF CALICHEAMICIN:

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