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Chemical and Microbial Modifications of Annonalide: Antiproliferative Activities and Studies of Annolalide-DNA Interactions

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Natural products and their semisynthetic derivatives have been extensively investigated as sources of new drug candidates with a variety of pharmacological activities (Newman &Cragg, 2016; Barnes et al., 2016). The increasing number of natural product derivatives reported in the literaturecorroborates the semi-synthesis as an important tool for improving the biological activity of starting natural products, not to mention improvements in other important parameters like toxicity, selectivity, lipophilicity and bioavailability. Enhancing lipophilicity and introducing halogen atoms in the natural products are examples of modifications that improved the biological activity (Barnes, et al., 2016).

Annonalide(**1**) is a highly oxygenated pimaranediterpene, first isolated from *Annona coriacea* (Annonaceae) (Mussini, et al, 1973; Orsini, et al, 1977) and subsequently from *Casimirellaampla* (formerly *Humiriantheraampla*) (Graebner, et al, 2000; Graebner, et al, 2002; Adou, et al, 2005). This natural product has previously been reported aspromisingantitumor compound (Graebner, et al, 2002).

In this short lecture, I willpresentchemical and microbial modifications of annonalide to yield novel derivatives which were tested against five human tumor cell lines (HL-60, PC-3, HepG2, SF-295 and HCT-116). Additionally, studies of the interaction of annonalide with ctDNAwill also be discussed.

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