

A new three-headed, long-tailed molecular beast eats cancer

We made and tested a series of new compounds containing three chemical rings and hooked them to long carbon tails. These new molecules killed a broad range of pediatric and adult cancer cells including neuroblastoma, osteosarcoma, malignant peripheral sheath nerve tumor, Ewing sarcoma, rhabdomyosarcoma, lymphoma, mammary carcinoma, colon carcinoma and lung carcinoma. The version with 16 carbons in the tail, which we call RC₁₆, was the best. Importantly, RC₁₆ was ten times less toxic to normal cells than to tumor cells.

RC₁₆ Intrinsic antitumor activity

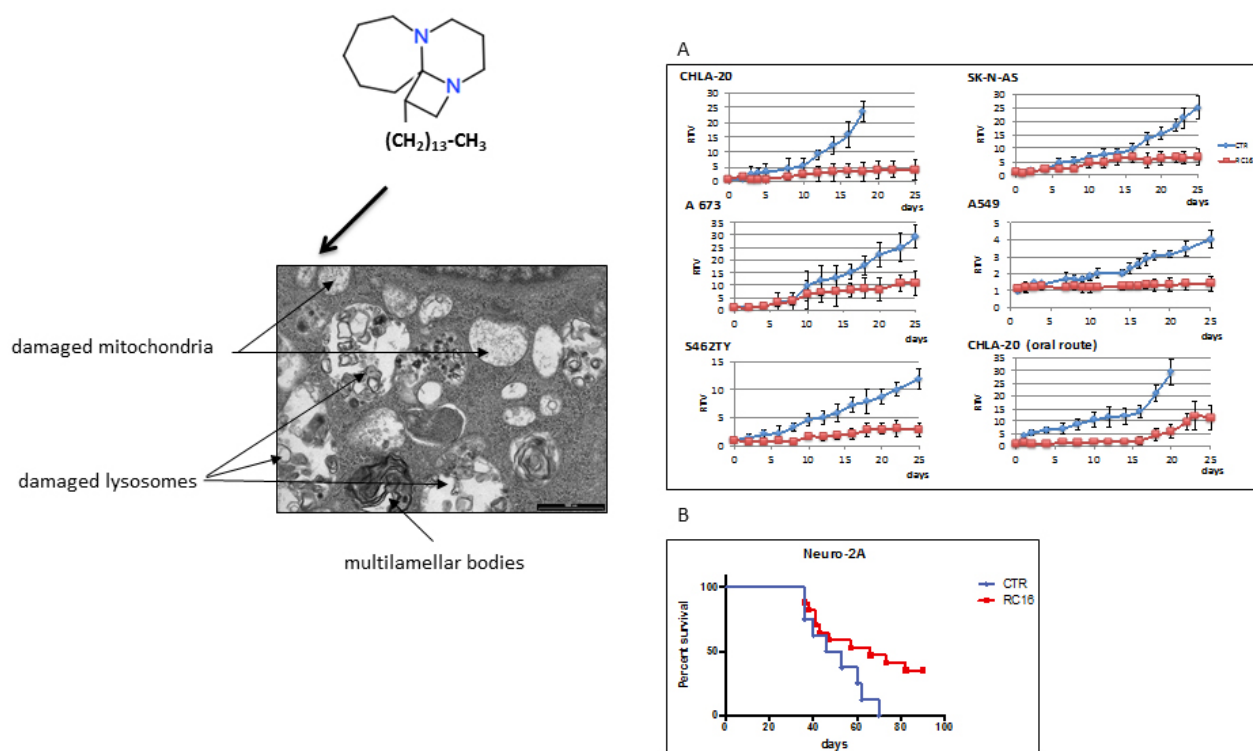


Fig. 1. A: RC16 inhibition of the tumor growth in tumor xenograft models (CHLA-20, SK-N-AS, A673, A549, S462TY) by intravenous administration and oral administration (CHLA-20). P-values less than 0.05

B: RC16 improvement of the survival after intravenous administration in a metastatic model of murine neuroblastoma (Neuro-2A). P-values less than 0.05

Our data suggests the three heads bind to acids on the surface of cancer cells then the tail, which chemically resembles the cell membrane, allows it to slip inside the cell. Once there, RC₁₆ cripples the cell by destroying its “batteries,” the mitochondria. When given by vein or by mouth to mice who had growing tumors, RC₁₆ suppressed tumor growth and improved animal survival as shown

in Figure 1. We also found the molecule could serve as a Trojan horse for other drugs. Because the head rings like water but the tail does not, when in solution the molecules circle up in a ball with the heads facing the outward and the tails inward. If added to the mixture, any drugs that also don't like water get protected inside the ball, making the ball a delivery vessel for the drug. Thus, we were able to package chemotherapy drugs such as Doxorubicin, Etoposide and Paclitaxel with RC₁₆ and improve their delivery to cells (Fig. 2).

RC₁₆ self-assembling ability and complexation of drugs

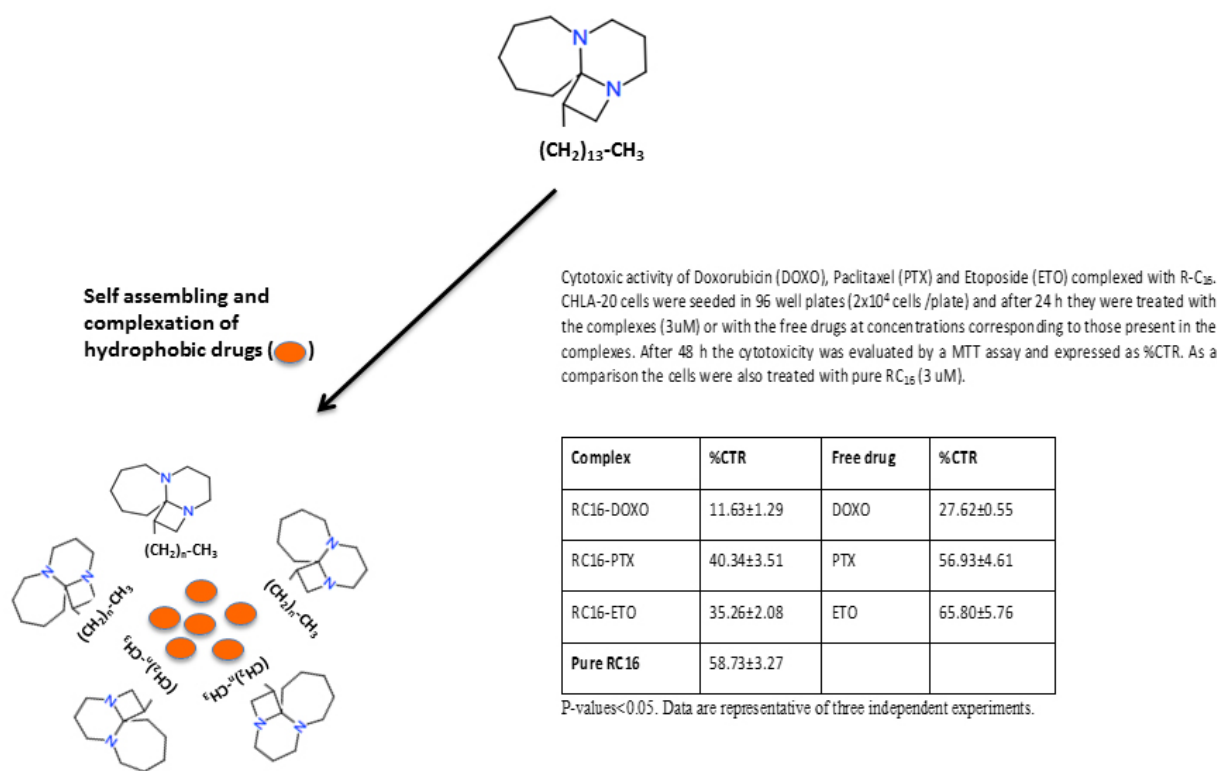


Fig. 2.

In particular this “micellar complexation” of Paclitaxel and Etoposide is advantageous because the very low water solubility of these drugs strongly limits their therapeutic use. The currently used solvents on the market such as Cremophor EL, benzyl alcohol and ethanol often cause serious adverse reactions especially after repeated administration. Packaging Doxorubicin is also encouraging because this approach might reduce its side effects on the heart.

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Publication

[Preparation and Evaluation of a Novel Class of Amphiphilic Amines as Antitumor Agents and Nanocarriers for Bioactive Molecules.](#)

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