CARB 112: Short carbohydrate amphiphiles as smart therapeutics targeting cancer

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Body

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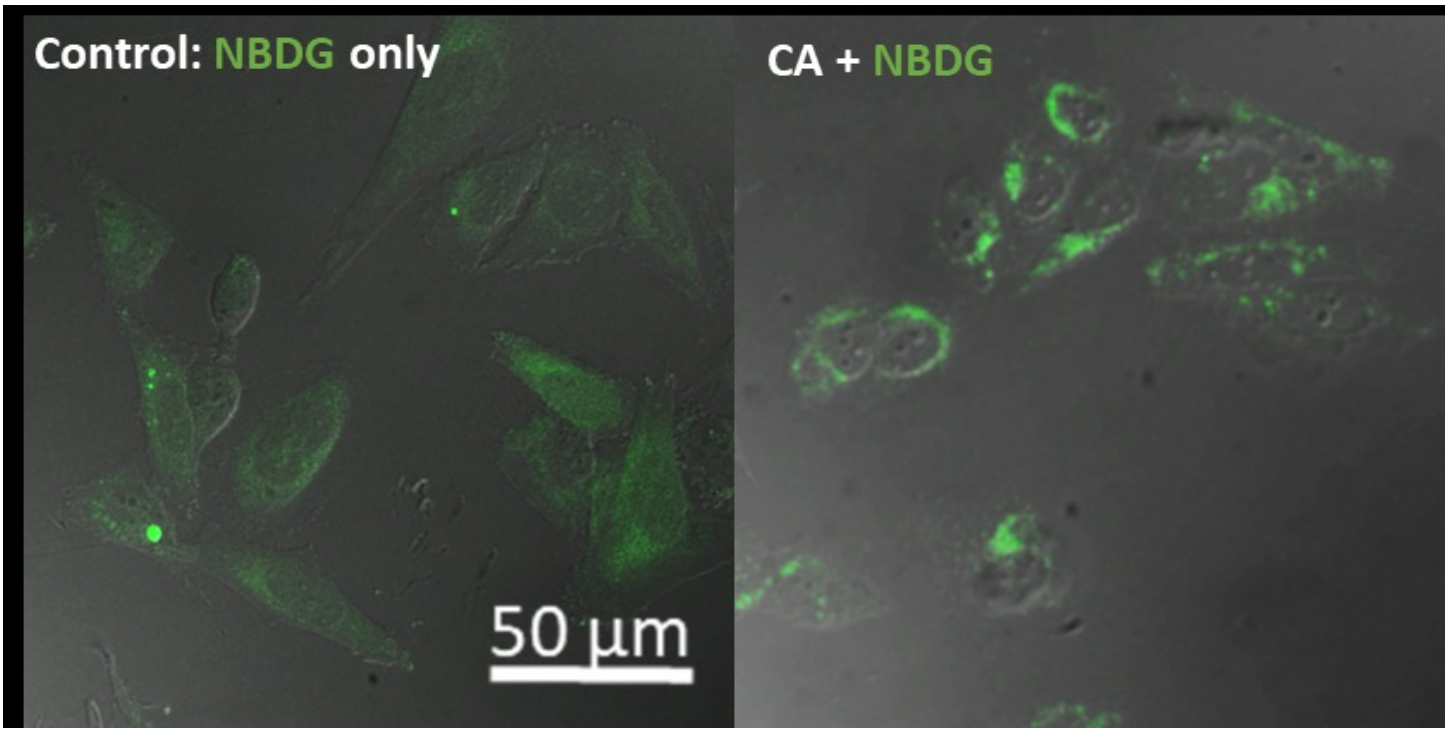
Biocatalytic self-assembly (BSA) emerged as selective and effective approach for cancer therapy. BSA makes use of enzyme-sensitive moiety that is incorporated in an amphiphilic molecule (usually peptide amphiphile, PA). This unit is transfomred/removed upon enzymatic action causing rebalance of the molecule's amphiphilicity and self-assembling ability. Among different enzymes, phosphatases (e.g. alkaline phosphatase, ALP) are the best studied ones for BSA targeting cancer. Recently, we describe a simple carbohydrate amphiphile (CA) as an alternative of PA and demonstrated its potential for treatment of osteosarcoma using BSA. Herein, we discuss another advantage of CAs in cancer therapy: they can act as antagonists of the glucose transporters (GLUTs) due to their structural similarity with glucose. Cancer cells have an accelerated metabolism, which requires high consumption of glucose. As a result, they overexpressed GLUTs, particularly GLUT1 and GLUT3. We studied several cancer cell lines overexpressing GLUTs and demonstrate that indeed the presence of CAs alter the glucose transport: a competitive assay showed that CAs reduced significantly the uptake of glucose, suggesting a possible blocking of GLUTs and glycolysis. Cancer cells cultured in the presence of CAs also showed a decrease in cell proliferation, metabolic activity and activation of an apoptotic pathway, that ultimately led to cell death. We conclude that the selective apoptosis of cancer cells is based on two synergistic mechanisms: formation of pericellular net that traps selectively the phosphatase overexpressing cells and blockage of glucose transport in these cells.



Glucose uptake blocked in the presence of the CA in the cancer cell line SaOs2. CA: Cabrohydrate amphiphile; NBDG: Fluorescent labeled Glucose

Presentation Details

CARB 112: Short carbohydrate amphiphiles as smart therapeutics targeting cancer
Tuesday, Aug 21 3:50 PM
Summer 1, Aloft Boston Seaport
(/acsboston18/event/f4d5b151f6cf911ef18f3d35f186ff12)