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Glyco-markers in personalized cancer chemotherapy with platinum-drugs

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Personalized chemotherapy is an unmet need in cancer treatments. A molecular test that can accurately predict the drug efficacy on a patient would be invaluable in selecting effective treatment strategy.

We have identified two glycan structures, namely Glycomarker-1 and Glycomarker-2, whose expression levels on the cancer cell surface are associated with responses to chemotherapy with platinum drugs (US patent #7585503, and International pending patent). This finding introduces a new concept, linking glycan cell surface expressions with drug reactivity, and proposes a glycan-mediated mechanism for drug uptake.

Our initial studies profiling the cell surface glycans, using Flow Cytometry with specific glycan-binding lectins, on three isogenic pairs of ovarian carcinoma cell-lines, consisting of chemosensitive and acquired chemoresistant phenotypes, revealed at least a ten-fold decrease in alpha2-6Sialyl-R motif (Glycomarker-1) on resistant phenotypes compared to sensitive cells. Further studies by fluorescent confocal microscopy, colony forming assay, sialidase treatments, and mass-spectrometry confirmed the association of Glycomarker-1 with drug uptake.

Using Lectin histochemistry (LHC) on clinical samples proved a feasible assay for Glycomarker-1, tested on 64 human ovarian normal and cancerous tissue sections. The LHC on retrospective ovarian cancer specimens, with a known history of drug-response, correctly predicted drug-responses in 22 out of 27 (81.4%) patients.

During the studies on the mechanism for drug response, another glycan structure, Glycomarker 2, was identified demonstrating a similar expression pattern to Glycomarker 1. Further studies on Glycomarker-2 suggest an association of the two glycomarkers that would put forward a glycan-mediated mechanism for platinum-drug uptake by cancer cells.

Biography

Razi is the founder of AccuDava Inc., a biomedical company for personalized cancer chemotherapy (<http://www.accudava.com>), based on the discovery of two Glycomarkers. Razi received her PhD in Medical Sciences from Uppsala University-Sweden, in 1995. In her post-doctoral program, at the University of California-San Diego, she discovered a novel glycan-mediated lymphocytes activation mechanism in the immune system. She then joined the Consortium for Functional Glycomics (CFG), at The-Scripps-Research-Institute, where her team successfully developed and launched the world's largest mammalian glycan microarray in 2011. This unique platform that displays 611 defined glycans has since become available globally for studying glycan-mediated interactions.

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