

Advances in Drug Screening: Building a Better Haystack for the Needles of Tomorrow

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SAN FRANCISCO - With the discovery of suitable molecular targets - cellular molecules along pathways crucial for sustaining the life of cancer cells - comes the perplexing dilemma of where to find the next therapeutics that will bind to and disable those targets. While the possibilities for drug designs are near-limitless, the methods to screen drug databases and repositories are often problematic or ill-suited for the particular needs of researchers.

Today at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, researchers report new means of delving into vast stores of data in search of potential therapies, whether to find the next natural cancer fighter or to discover new classes of therapeutics.

[Targeting neuroblastoma tumor-initiating cells: High-throughput screening strategies to identify novel chemotherapeutics: Abstract A 205.](#)

While research has yielded exceptional advances in treatment and therapeutics for most adult cancers, there has been little improvement in survival rates for patients with the deadly childhood cancer neuroblastoma for the past 30 years. Armed with advances in stem cell knowledge, researchers at The Hospital for Sick Children in Toronto, Canada, are screening currently approved drugs for new neuroblastoma therapies that kill cancer while sparing children exposure to excessive amounts of toxic therapeutics.

Using their screening process, the researchers searched more than 5,000 drugs and uncovered 47 candidates that show good potential against neuroblastoma, including rapamycin, on which the researchers are currently focusing.

"Neuroblastoma is particularly difficult to treat without aggressive chemotherapy and, even when treated successfully, the chemotherapies currently in use frequently have side effects that can have devastating repercussions later in life," said Kristen Smith, Ph.D., a postdoctoral fellow at The Hospital for Sick Children. "We have developed an efficient screening process based on stem cells present in the growing bodies of children, cells that might be susceptible to harm from the necessary blunt force use of therapeutics."

Smith and her colleagues used a cell-based assay program that pits chemotherapeutics against neuroblastoma tumor-initiating cells (TICs) and skin-derived precursors (SKPs). As their full-name suggests, TICs are cancer stem cells developed from tumor samples removed from children. SKPs, however, are normal non-cancerous stem cells found in the skin. Both varieties of stem cells originate from the neural crest, the portion of a developing embryo that eventually comprises the peripheral nervous system.

"The idea is to find a drug that can kill a neuroblastoma TIC without harming an SKP," Smith said. "We reasoned that if the drug is potent enough to kill a tumor stem cell - without damaging a normal stem cell - then we may lessen the risk of SKPs or other stem cells becoming cancerous later in life."

According to Smith, 40 of the 47 drugs that were recognized in the screening have never been used to treat neuroblastoma. The researchers are currently studying the highlighted drugs in TICs from multiple neuroblastoma patients. One drug in particular, rapamycin, has already been studied in an animal model of neuroblastoma, with promising results and is in clinical studies, Smith says.

The work was performed in collaboration with clinicians at The Hospital for Sick Children, Alessandro Datti, Ph.D., at the Mt. Sinai Robotics Facility, and Herman Yeger, Ph.D. and Sylvain Baruchel, M.D. at the Hospital for Sick Children.

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