caspases, serine proteases and cytochrome *c* release are blocked simultaneously and suggest c-*Myc* is essential to all pathways.

Future research will be needed to see if these findings can be extrapolated to other oncogenes and determine whether loss of functions will confer resistance to certain subsets of anticancer drugs. The current data have implications for the clinical setting and could change the choice of drugs for treatment of tumors driven by a MYC family member.

4 Grassilli, E. *et al*. (2004) Loss of Myc confers resistance to doxorubicin-induced apoptosis by preventing the activation of multiple serine protease-and caspase-mediated pathways. *J. Biol. Chem*. DOI 10.1074/jbc.M31353220, (E-pub ahead of print; http://www.jbc.org/)

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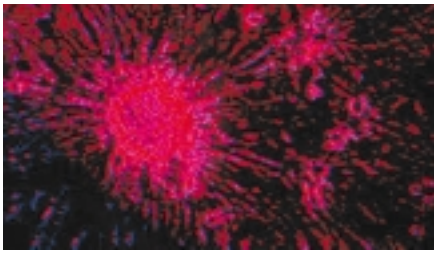
Lessening the resistance

Tumor cells can develop a very effective resistance mechanism to multiple antitumoral drugs, causing the failure of



cancer chemotherapy treatments. The multiple drug resistance (MDR) is due to either the cell-surface overexpression of transmembrane efflux pumps, P-glycoprotein (Pgp) or the constitutive expression of multidrug resistance-related proteins (MRPs) that are homologous to Pgp, and like Pgp are members of the ABC family. They transport a multitude of drugs outside of the cell and are not specific.

The most recent strategy in cancer treatment is the concomitant administration of antitumoral drugs with a MDR-modulator, which can cause tumor cell death. Therefore, many efforts are geared towards the synthesis and the study of MDR-modulators that specifically inhibit the transporter and allow the antitumor drug to stay inside the cell and provoke cell death.

Lee *et al*. [5] identified a series of dihydropyrroloquinolines derivatives that reverse Pgp-mediated MDR without antagonizing MRP. Among these derivatives, PGP-4008 was the most promising. PGP-4008 activity was characterized with different cell lines, and the authors showed that it potentiates the cytotoxicity of Pgp substrates only on cell lines that overexpress Pgp, and increases drug accumulation inside the cell. PGP-4008 has no effect on non-Pgp-overexpressing cells, nor does it affect the toxicity of non-Pgp substrates. PGP-4008 is specific to Pgp and does not antagonize MRP. *In vivo*, tumor growth was significantly slower when mice were treated with a combination of PGP-4008 and doxorubicin. Although more clinical studies are necessary to better characterize PGP-4008, it seems to be a promising drug because it specifically reverts Pgp-mediate MDR.

5 Lee, B.D. *et al*. (2004) Synthesis and evaluation of dihydropyrroloquinolines that selectively antagonize p-glycoprotein. *J. Med. Chem*. 47, 1413–1422

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Business

Collaboration

Partnership for cutting-edge genomics research

Children's Memorial Institute for Education and Research (http://www.childrensmemorial.org; CMIER, http://www.cmier.org) and The Translational Genomics Research Institute (TGen; http://www.tgen.org) have announced a partnership to conduct genomic research into childhood illnesses and help better define their relationship to adult disease.

Mary J.C. Hendrix, President and Scientific Director of the Chicago-based CMIER and Professor of Paediatrics at Northwestern University's Feinberg School of Medicine, said: 'This partnership will enable us to build a world-class genomics program that will profoundly impact human health and accelerate the rate of discovery into the molecular components of childhood diseases.'

The two institutes will conduct research on a broad spectrum of problems, including brain disorders such as schizophrenia, behavioural disorders, multiple sclerosis, cancer and autoimmune diseases. The research will focus on detecting genetic markers, using the latest DNA microarray technology, and finding faster ways of moving discoveries from the laboratory into the clinical setting.

TGen's President and Scientific Director, Jeffrey Trent, commented: 'Our collaboration with Children's Memorial further strengthens TGen's mission to advance research in an expedited manner. The sequence of the human genome has fuelled a rapid increase in gene discovery and analysis and our work with Children's Memorial will hopefully answer a number of questions surrounding childhood disease.'

Business was written by
Joanne Clough

People

Appointments

Dynavax names VP and Chief Business Officer

Dynavax Technologies (http://www.dynavax.com) has announced the appointment of D. Kevin Kwok as Vice President and Chief Business Officer.

Kwok was most recently VP for the transaction advisory group Clearview Projects, where he was responsible for the start-up and client management of the San Francisco practice. He brings more than 18 years worth of diverse industry experience with both pharmaceutical and biotech companies in various commercial areas.

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