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

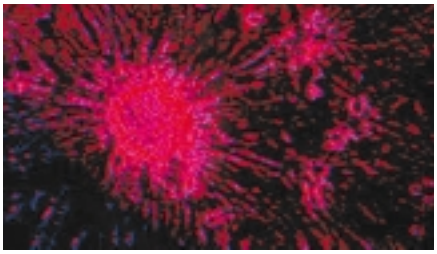
Future research will be needed to see if these findings can be extrapolated to other oncogenes and determine whether loss of functions will confer resistance to certain subsets of anticancer drugs. The current data have implications for the clinical setting and could change the choice of drugs for treatment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

Marieke Kruidering
kruidering@cmp.ucsf.edu

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

Muriel Laine
lainem@mail.rockefeller.edu

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.

1359-6446/04/$ – see front matter PII: S1359-6446(04)03079-X

Dino Dina, President and Chief Executive Officer of Dynavax, said: 'We are excited to have Kevin join our team. We expect him to play a key role in managing our existing relationships… while we continue to develop our strategy to secure the commercial success of the products under development.'

Dynavax discovers and develops innovative products to treat and prevent allergies, infectious diseases and chronic inflammatory diseases. The clinical development programs are based on immunostimulatory sequences.

Avigen appoints Kenneth Chahine as President and CEO

Avigen (http://www.avigen.com) have announced the promotion of Ken Chahine to President and Chief Executive Officer. Chahine, who was previously Avigen's Chief Operating Officer, replaces John Monahan, who has resigned to pursue other opportunities.

Philip Whitcome, Avigen's Chairman of the Board, commented: Ken Chahine has brought outstanding operational leadership to Avigen… His combination of technical, legal and business expertise make him well suited to lead Avigen forward in the commercialization of its products.'

Avigen focuses on the development of DNA-based drugs for serious chronic conditions. The company's proposed gene-delivery products are designed for direct administration to patients to achieve expression of therapeutic proteins within the body.

Pratik Multani appointed VP, Clinical Development at Salmedix

Pratik Multani has been appointed to the newly created position of Vice President, Clinical Development at Salmedix (http://www.salmedix.com). Multani, and oncologist, has a wealth of experience in the development of pharmaceutical products for cancer patients and will lead Salmedix's clinical development organization and clinical operations activities.

Multani was most recently Senior Director, Medical Research at Biogen Idec, prior to which he held academic and clinical positions at Harvard Medical School and Massachusetts General Hospital.

Andrew Morr, COO of Salmedix, said: Adding Dr Multani to Salmedix… is an important step in assuring the company's success with the development of our pipeline of cancer drugs.'

Salmedix is developing promising oncology drugs, with an initial commercial focus on haematologic cancers.

Synta appoint Matthew L. Sherman as Senior VP and CMO

Synta Pharmaceuticals (http://www.syntapharma.com) has appointed Matthew L. Sherman as Senior Vice President and Chief Medical Officer.

President and CEO of Synta, Safi Bahcall, commented: 'Our pipeline and company have developed at a remarkable pace. [Sherman] brings to Synta an outstanding track record in clinical development, FDA product approval experience, and demonstrated leader skills in building and managing major clinical development organizations.'

Sherman joins Synta from Wyeth where he most recently served as Assistant VP of Medical Research, Clinical Research, and Development and Therapeutic Area Director for Oncology at Wyeth Research. He began his career at Harvard Medical School, where he also held posts of Assistant Professor of Medicine and Assistant Clinical Professor of Medicine.

'Synta is a unique opportunity… it is rare to find a small, fast-moving company that also has a broad, multi-product portfolio of promising small-molecule compounds addressing some of the targets pharmaceutical markets in the world.'

Michael Schubert appointed VP, R&D at Bruker Daltonics

Bruker Daltonics (http://www.bruker-biosciences.com) has appointed Michael Schubert as Vice President for Research and Development. Schubert will be responsible for the management of the company's R&D activities worldwide.

Commenting on his appointment, Schubert said: 'I am looking forward to leading our global R&D efforts at such an exciting time in the growth of life-science applications of mass spectrometry. We will use our resources and strategic partnerships to offer systems and solutions for expression proteomics, clinical proteomics and metabonomics applied to drug discovery and development.'

Bruker Daltonics is an operating company of Bruker BioSciences, a parent company of Bruker AXS – a leading developer and provider of life science and advanced materials research tools based on X-ray technology.

People was written by
Joanne Clough

Contributions to *Monitor*

We welcome recommendations of papers for review within *Monitor*, in the fields of combinatorial chemistry, pharmacogenomics, pharmacoproteomics, bioinformatics, new therapeutic targets, high throughput screening, new drug delivery technologies and other promising lines of research.

Details of recent papers or those *in press* should be directed to
Dr Steve Carney, Editor, *Drug Discovery Today*, Elsevier,
84 Theobald's Road, London, UK WC1X 8RR.
tel: +44 207 611 4132, fax: +44 207 611 4485,
e-mail: DDT@drugdiscoverytoday.com

1359-6446/04/$ – see front matter PII: S1359-6446(04)03079-X