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### An unfamiliar consequence of *BRCA1* inactivation

Familial *BRCA1*-associated breast cancers display a distinctive histopathology and profile of gene expression. Loss of the cell cycle regulator, p27, is a common finding, yet the functional relationship between

*BRCA1* and p27 has not been well defined.

Researchers in Melbourne, Australia, have recently created a transgenic mouse expressing a dominant negative allele of *BRCA1* in the mammary gland [9]. This mouse was found to have delayed mammary development. Contrary to expectation, it also displayed elevated levels of p27 and reduced proliferative capacity. *In vitro* studies confirmed that acute loss of *BRCA1* did indeed augment p27 expression. This was not due to altered proteosomal degradation, but probably reflects an increased level of the mRNA.

In contrast, expression of the *BRCA1* transgene on a p27 heterozygote background resulted in normal mammary gland development. However, there was an associated increase in the number of cells in S phase. Surprisingly, p27 was the only cell cycle regulator affected by *BRCA1* inactivation, suggesting that this molecule

is central to the observed phenotype.

Extrapolating these results to humans, it appears that p27 could initially accumulate in response to germline *BRCA1* mutations. This would presumably counteract the effects of *BRCA1* inactivation by inducing growth arrest. However, subsequent events favour reduced p27 and an increased proliferation rate. Loss of p27 is therefore likely to be a prerequisite for *BRCA1*-associated tumourigenesis. It is possible that in future, drugs designed to maintain elevated levels of p27 might block this effect, allowing prevention, rather than cure, in patients harbouring familial *BRCA1* mutations.

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## Business

### Collaborations

#### Peakdale and Cyprotex collaborate on drug-like screening compounds

Peakdale Molecular (<http://www.peakdale.co.uk>) and Cyprotex (<http://www.cyprotex.com>) have announced their collaboration in the application of ADME technology to maximize the drug-like properties of Peakdale's unique screening compounds. Cyprotex will use its CloeScreen™ HTS technology to evaluate the ADME properties of approximately 8500 novel lead-like compounds developed and synthesized by Peakdale.

The ADME data generated from the collaboration will be used to develop predictive models that will form the basis for the enhancement of the design of novel compounds. The provision of compounds with enhanced ADME profiles enables Peakdale to offer its clients superior starting points from which to discover new drugs, in addition to making substantial improvements in the efficiency of subsequent optimizations.

'Consistent, high quality compound data are essential for efficient drug discovery because it enables you to predict the potential of new compounds before

they've even been synthesized,' commented David Leahy, Cyprotex's Chief Scientific Officer. 'Combining our predictive models with Peakdale's unique chemistry will offer drug-like leads that will be ready for trials earlier and offer a greater chance of success.'

Gareth Jenkins, Peakdale's Business Development Manager, added: 'Our customers already benefit from our novel chemistry expertise. Now they can benefit further from better quality compounds, faster development times and reduced risk from failure in clinical trials.'

#### Strand and Bio-Rad

Strand Genomics (<http://www.strandgenomics.com>) has entered into an agreement with Bio-Rad (<http://www.bio-rad.com>) with a view to integrating Strand Genomics' predictive human pharmacokinetic models into Bio-Rad's KnowItAll® platform for *in silico* ADME-Tox assessment. Strand's ADME-Predict™ uses the chemical structure of potential drug candidates to generate predictions for human pharmacokinetic parameters that are applicable to drug discovery, including bioavailability, volume of distribution and protein binding.

Kas Subramanian, Strand's Chief Scientific Officer, remarked: 'We are pleased to combine this expertise and technology along with Bio-Rad's award winning KnowItAll™ platform. This combined expertise will allow medicinal chemists and pharmacologists to design and optimize leads and candidates that have the greatest chance of succeeding in the clinic.'

'We look forward to working with Strand Genomics in moving forward to accelerate drug discovery,' added Gregory Banik, General Manager, Bioinformatics Division at Bio-Rad. 'The addition of these predictors emphasizes Bio-Rad's continued commitment to offer the most comprehensive ADME-Tox prediction portfolio to the drug discovery community.'

Strand Genomics is a Bangalore-based life sciences informatics company focusing on software for drug discovery and development. Strand's core strengths lie in data mining and analysis, knowledge management and workflow processes to develop its products and provide high-end technology consulting services.

#### GenData and Battelle to collaborate on the identification of predictive diagnostics for COPD

GenData (<http://www.gendata.org>) and Battelle (<http://www.battelle.org>) have entered into a collaborative study for the

discovery, development and commercialization of biomarkers for diagnostic and therapeutic applications in chronic obstructive pulmonary disease (COPD), the fourth leading cause of death in the USA.

The combination of GenData's extensive longitudinal clinical treatment data and Battelle's signature technology in inhalation toxicology will afford the best-characterized population of COPD. In the future, it is hoped that this population can be used to elucidate the mechanisms of this disease and to identify the underlying genetic factors associated with COPD. Furthermore, the treatments that are currently available for COPD only afford temporary relief of the symptoms to the sufferer and GenData and Battelle are aiming to develop more-effective therapies for this disorder.

John Hoidal, Managing Director at GenData, commented: 'This is a great opportunity for us to leverage 20 years of clinical experience and genetic research to better understand the pathways

involved in the onset and progression of this deadly disease.'

Mark Gritz, Vice President of Battelle's Division of Health and Life Sciences, added: 'We are excited to bring Battelle's signature technologies in inhalation toxicology and bioanalytical methodology, as well as our development of experimental models of COPD, to expedite the development of new predictive diagnostic procedures and therapeutic regimes for prevention and more effective treatment of COPD.'

### Announcement

#### Benitec settles infringement litigation against GenScript

Benitec (<http://www.benitec.com.au>) has announced the settlement of its pending patent infringement case against GenScript (<http://www.genscript.com>). The infringement dispute began when Benitec initiated suits against Nucleonics (<http://www.nucleonicsinc.com>), Ambion

(<http://www.ambion.com>) and GenScript to protect its RNAi gene silencing technologies.

As part of the settlement, GenScript has taken from Benitec a worldwide non-exclusive license to make and sell DNA-directed RNAi-based products (ddRNAi). This settlement completely resolves all claims asserted in the original dispute between Benitec and GenScript that was filed in the US District Court for the District of Delaware.

John McKinley, Chairman and CEO of Benitec, commented: 'I am pleased that we have again been able to settle an infringement dispute by the granting of non-exclusive license to GenScript. Based upon our expanding issued ddRNAi patent estate, we are committed through our licensing strategy to enable the widest use of ddRNAi in both products and research licenses to protect both Benitec and our ddRNAi licensees.'

Business was written by  
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## People

### Appointments

#### Antares Pharma appoints Jack E. Stover as CEO and Director

Antares Pharma (<http://www.antarespharma.com>), an emerging specialty pharmaceutical company, has announced the appointment of former President and Chief Operating Officer Jack E. Stover to the additional roles of CEO and Director.

Stover joined Antares from Sicor (<http://www.sicor.com>), where he was Executive Vice President and Chief Financial Officer. Prior to joining Sicor, Stover held various senior management and operating roles with proprietary and pharmaceutical and global medical device companies, and brings more than 15 years of relevant industry experience to his new appointment.

Commenting on his new responsibilities, Stover said: 'I am excited about the opportunity to utilize my skills in the generics, branded and medical device industries in leading Antares Pharma as it transitions to a market-oriented specialty pharmaceutical company.'

Jacques Gonella, Antares Pharma's Chairman, added: 'We are very confident that Mr Stover's prior experience will provide the guidance and leadership the company needs as it continues its rapid evolution as a specialty pharma business.'

#### John Sperzel joins Axis-Shield as President of US operations

Axis-Shield (<http://www.axis-shield.com>), the *in vitro* diagnostics company, has announced the appointment of John Sperzel as President of Axis-Shield USA. The US division of Axis-Shield is currently being established, with its key responsibility being the development of the presence of the company in the US point-of-care market. In his new appointment, Sperzel will concentrate on strengthening the company to manage and support a network of distributors to serve the physician's office laboratory market for Axis-Shield's point-of-care products.

Sperzel joins Axis-Shield from Bayer Diagnostics, where he was Vice President of World Wide Marketing and Business Development for Near Patient Testing.

Sperzel has previously worked for several major diagnostic companies in the USA and brings extensive experience in the marketing of point-of-care in the USA and internationally to his new position.

'We are very pleased to have been able to attract someone of John's caliber to this important position,' remarked Svein Lien, Axis-Shield's CEO, on Sperzel's appointment. 'We look forward to seeing our new company generate substantial growth for our pioneering AFINION point-of-care system in this key marketplace.'

### Awards

#### Reid Coleman awarded 2004 AMDIS Award for Achievement in Applied Medical Informatics

Reid Coleman, Chief Medical Informatics Officer at Lifespan (<http://www.lifespan.org>), has been recognized by the Association of Medical Directors of Information Systems (AMDIS) for his pioneering work in implementing computerized physician order entry (CPOE) at the company. As the physician