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The war on cancer: an end in sight?

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The *Annual Meeting of the American Association for Cancer Research* (AACR) is the world's premier cancer research conference, featuring the latest discoveries in the aetiology, diagnosis, prevention and treatment of cancer. This year's event, which was held on 16–20 April 2005 in Anaheim, CA, USA, covered the latest developments in the full range of scientific disciplines involved in cancer research.

The programme was organized in parallel sessions, ensuring that all participants always had something to interest them throughout the conference. Key topics at meeting included the discovery of new small molecule cancer drugs post-Gleevec and advances in genomics and/or proteomics for novel therapeutic modalities. As regards to the diagnosis and prevention of cancer, the identification of clinical biomarkers and the role of diet as cancer-causing risk were also extensively discussed.

Current status of the field

The fight against cancer stands at a turning point in its history. The explosion of information and progress in our understanding of the cellular and molecular biology of cancer in recent years present tremendous opportunities for the future discovery and development of new diagnostic and therapeutic agents for the control of this terrible disease. The key challenge facing the cancer research community at this time remains the translation of this basic knowledge into more efficacious, preventative, diagnostic and therapeutic products.

Andrew von Eschenbach (Director of the US National Cancer Institute) challenged the cancer community to eliminate the suffering and death due to cancer in the USA by 2015, and the mood among the participants felt overwhelmingly positive. However, it should not be forgotten that difficult barriers need to be overcome and researchers must work together effectively if this challenging target is to be met. Some of these barriers to progress inherent in the system for management and administration of cancer research were outlined by Clifton Leaf [1], who claimed that the war on cancer was being lost, provoking considerable discussion within the cancer research community. Although acknowledging the dedication of the scientific community to the fight against cancer, the article highlighted several issues, such as availability of patient tumour samples, Intellectual Property and ownership barriers to the sharing of data and collaboration, and the tendency of the grant awarding bodies to encourage incremental progress and the acquisition of new data rather than more risky and adventurous research.

Emerging themes

Targeted therapeutics post-Gleevec

In recent years, considerable excitement has been associated with Gleevec (Novartis Pharmaceuticals) with regards to the promise of translating our basic knowledge in cancer biology into efficacious 'molecularly targeted' small molecule drugs. Although Gleevec has shown outstanding clinical activity as a single agent against chronic myelogenous leukaemia (CML) and other (relatively rare) cancers, this 'wonder drug' is not without shortcomings, most notably development of drug resistance and failure to produce durable remissions in cases of advanced disease. A new compound under development – AMN107 (Dana-Farber Cancer Institute and Novartis Pharmaceuticals) – demonstrated a response rate of >70% in advanced CML patients, and a response rate of >90% in patients with an early form of the disease [2]. In the AACR-Richard and Hinda Rosenthal Foundation Award Lecture, Charles L. Sawyers (Howard Hughes Medical Institute, University of California, Los Angeles, CA, USA) presented his research on Bcr-Abl, which was crucial to the development of Gleevec and post-Gleevec analogues.

Napoleone Ferrara (Genentech, San Francisco, CA, USA), winner of the AACR-Bruce F. Cain Memorial award, described the development of the anti-VEGF (vascular endothelial cell growth factor) antibody Avastin, the first anti-angiogenic drug to be approved by the FDA in February 2004.

Other highly promising contemporary molecular targets that still need to reach clinical fruition were also featured, the most important being phosphoinositide 3-kinase

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(PI3K), described by Lewis C. Cantley (Harvard Medical School, Boston, MA, USA), and telomerase, presented by Elizabeth Blackburn (University of California San Francisco, CA, USA).

Novel therapeutic modalities

The use of short interfering RNA (siRNA) to block the activity of specific genes involved in tumour growth has burgeoned in the cancer biology arena in recent years; however, to date, therapeutic exploitation of this technology has not been realized. The first study showing that the systemic administration of siRNA inhibits disseminated tumour growth was reported. Siwen Hu (Children's Hospital of Los Angeles and University of Southern California, CA, USA) described the design of a novel delivery system to transport gene silencing nanoparticles into tumour cells, inhibiting Ewing's sarcoma in an animal model [3]. siRNA designed to target a specific growth-promoting gene called *EWS-FLI1* (active only in Ewing's sarcoma) was encased in a sugar-containing polymer, forming a nanoparticle, that was, in turn, attached to transferrin, a protein that delivers iron into cells. Long-term treatment of a mouse Ewing's sarcoma model with this delivery system markedly inhibited tumour growth. Translation of this delivery system into human clinical trials is eagerly anticipated.

Clinical biomarkers

Diagnosis of cancer at its earliest stages through the identification of molecular biomarkers in the clinic was a continuous theme. One particularly promising avenue in this regard is the detection of informative molecular markers in bodily fluids. The recent reliable detection and isolation of mRNA from saliva and serum present exciting early disease diagnostic opportunities. Yang Li (University of California, Los Angeles, CA, USA) reported that genetic biomarkers isolated from saliva of 32 patients predicted oral squamous cell carcinoma in ~nine out of ten cases [4]. Future research will involve larger patient populations and also include studies in other difficult-to-detect cancers, such as ovarian and pancreatic.

Cancer chemoprevention

Advances in the early detection of tumours and cancer chemopreventative strategies, particularly against colorectal cancer, were discussed extensively throughout the meeting. For example, Bandaru S. Reddy (Rutgers University, Piscataway, NJ, USA) observed that a low-dose combination of the non-steroidal anti-inflammatory drug celecoxib, the cholesterol-lowering statin Lipitor® and aspirin dramatically lowered the incidence of invasive and non-invasive adenocarcinomas, with the optimal combination inhibiting 95% of the tumours that developed in untreated laboratory rats [5]. These data support the concept that combinations of low-dose chemopreventative agents could be a highly promising chemopreventative strategy. Oleg K. Glebov (National Cancer Institute, Bethesda, MD, USA) described how taking the cyclooxygenase inhibitor celecoxib led to the alteration of a specific 'signature' set of genes in the colons of patients at high risk of a hereditary form of colon cancer (hereditary nonpolyposis colon cancer or HNPCC) [6].

The elimination of the cancer-causing risks produced by a high-fat Western style diet in mouse models of intestinal cancer by the anti-inflammatory drug sulindac was described by WanCai Yang (Albert Einstein Cancer Center, Bronx, NY, USA) [7]. Sulindac appeared to offer protection against a lack of tumour suppressor genes and poor diet. Although it is too early to translate these findings in mouse models into recommendations on preventing human colon cancer, these data do illustrate the interplay between genes and common nutritional and medicinal agents in the development of intestinal cancer.

Conclusions

The NCI Director has laid down a bold challenge to the cancer community, and optimism is high within the field that rapid advances in early cancer diagnosis and the development of new preventative and therapeutic agents will finally make substantial inroads into reducing suffering and death from cancer within the next few years. To date, the lack of any substantial impact on survival rates from the biggest killers, such as lung cancer, reminds us that the fight against this devastating enemy is far from won, and that the cancer research community need to work effectively together to achieve its ultimate goal.

References

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Erratum

In the July 15 2005 issue of *Drug Discovery Today* (Vol. 10, No. 14), in the conference report entitled *Progress towards better understanding and treatment of major psychiatric illnesses*, Atheir Abbas should have been included as first author.

The editorial team apologize for any confusion this might have caused.

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