IBN SEMINAR SERIES

Drug Resistance and the Microenvironment: Strategies to Improve the Clinical Benefit from Chemotherapy

Dr Ian Tannock
Princess Margaret Cancer Centre and University of Toronto, Canada

Tuesday, November 18, 2014 • 9:00am to 10:00am
Aspiration Theatrette, Level 2M • The Matrix, 30 Biopolis Street, Biopolis

ABSTRACT

Most studies of resistance to anticancer drugs have evaluated molecular mechanisms in single cancer cells. Equally important, but rather neglected, is drug resistance due to the solid tumour microenvironment. Blood vessels and blood flow in tumours are irregular leading to large gradients in nutrient concentration, and we have shown that there are similar gradients in drug concentration within tumours following treatment with chemotherapy. Cells distant from functional blood vessels tend to be resistant, both because they are exposed to lower concentration of drugs, and because they are slowly proliferating.

We have investigated two strategies to overcome drug resistance that is due to the microenvironment of solid tumours. One approach is to use hypoxia-activated pro-drugs, such as TH-302, that are activated in hypoxic regions of tumours, and can then act selectively against hypoxic and neighbouring cells that are distant from tumour blood vessels. TH-302 has given promising results in clinical trials for pancreatic cancer and is now in phase 3 trials. The second strategy depends on the observation that poorly nourished or stressed tumour cells use the process of autophagy to recycle cellular components to facilitate their survival. Autophagy depends on fusion of autophagosomes with acidic lysosomes, and can be inhibited by higher doses of proton pump inhibitors, such as pantoprazole. We have shown that autophagy is upregulated following treatment with several anticancer drugs, and that inhibition of autophagy by pantoprazole increase the effects of docetaxel and doxorubicin against several human tumour xenografts. We have completed a phase I trial of high-dose i.v. pantoprazole with doxorubicin, and a phase II trial of pantoprazole and docetaxel for men with metastatic castration-resistant prostate cancer is in progress.

ABOUT THE SPEAKER

Dr Ian Tannock is Professor of Medicine and Medical Biophysics at Princess Margaret Cancer Centre and University of Toronto. He obtained his PhD in London, England and his MD at University of Pennsylvania, Philadelphia, USA. His clinical research investigates methods related to cancer clinical trials, and he chaired trials for men with metastatic prostate cancer that led to licensing of previous (mitoxantrone) and current (docetaxel) standard chemotherapy.

His laboratory research evaluates effects of the tumour microenvironment on outcome of cancer therapy. He is an editor of the Basic Science of Oncology textbook, now in its 5th edition, that is used by trainees in all branches of oncology. Dr Tannock was a member of the Board of Directors of the American Society of Clinical Oncology (ASCO) from 2001-2004. He received the alumnus award from M.D. Anderson Hospital, Houston, USA (1989), the Warwick Prize from the National Cancer Institute of Canada (2003), an honorary degree (DSc) from London University, UK (2009), and the European Society of Medical Oncology (ESMO) award (2012), the first non-European to receive this award. He chairs the scientific audit committee of the European Organisation for Research and Treatment of Cancer (EORTC) and is a member of the EORTC Board.

Dr Tannock was appointed a Member of the Order of Canada in December 2013.

This seminar is free and no pre-registration is required.
For any enquiries, please contact: announcements@ibn.a-star.edu.sg.
www.ibn.a-star.edu.sg

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