NUS National University of Singapore | Department of Biological Sciences Faculty of Science

BIOLOGY COLLOQUIUM

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Hosted by A/P Ge Ruowen

RECENT SUCCESSES IN TARGETED ANTI-CANCER THERAPY

By **Alex Matter**

Experimental Therapeutics Centre (ETC) & D3, A*STAR

*Alex Matter is CEO of the Experimental Therapeutics Centre since April 2009 and since January 2012 CEO of the newly created D3 platform, A*STAR, Singapore. Previously, he had spent five and a half years as Director of the Novartis Institute for Tropical Diseases (NITD), from October 2003 to February 2009. Prior to this role, Dr. Matter was Global Head of Oncology Research for Novartis Pharmaceuticals Corporation. Dr. Matter played an important role in the success of several anticancer drugs, including Gleevec/Glivec® and more recently, Tasigna®, building and leading the teams that discovered these and several other anticancer drugs as well as one HIV protease inhibitor (Reyataz®) that is marketed by another company.*

Dr. Matter received his medical degree from the University of Basel. He also had fellowships at the Swiss National Science Foundation and the Swiss Academy for Medical Sciences. He has published more than 100 scientific articles and several book chapters in the area of oncology and hematology. He is emeritus Professor of the Medical Faculty of the University Basel and an Honorary Adjunct Professor of the Department of Pharmacology, YLL School of Medicine, NUS in Singapore.

He is a member of the American Association for Cancer Research, the Board of the Health Sciences Authority (HAS) and the Board of Curiox, a Singapore-based start up company. He is also a chair/member of several Scientific Advisory Boards. He is an elected member of the Swiss Academy of Medical Sciences.

Dr. Matter is the recipient of the Life-time Achievement Award from IBC Life Sciences, the 13th Warren-Alpert prize and the AACR-Bruce F. Cain Memorial Award. Recently he was awarded the 2013 Szent-Györgyi Prize from the US National Foundation for Cancer Research.

A targeted anti-cancer drug works through one or more closely related drug targets that are understood in terms of their epidemiology, pathophysiology and role in the maintenance of the cancer phenotype. Such drugs can be biologics (most frequently monoclonal antibodies), or small molecular weight compounds. The following discussion shall be limited to small molecular weight compounds.

There are now about twenty different and approved targeted anti-cancer drugs on the market, for a wide variety of indications. In molecularly well-defined cancers these drugs show clear benefit and an acceptable tolerability. Limitations of current cancer therapy reside in limited improvement of overall survival, relatively rapid emergence of resistance, limited tolerability and high cost. All of these problems need to be tackled through novel approaches. Novel agents can deal with drug targets that were deemed undruggable until quite recently or that have become resistant to the parent compounds. Judicious combination of two or more agents may help overcoming the emergence of resistance and thereby increase efficacy. Better use of available agents through application of pharmacokinetics-based drug dosing may help to improve tolerability, and the systematic use of pharmacodynamic biomarkers supports patient selection and patient stratification in clinical trials.

ETC has built up all the capabilities to perform state-of-the-art drug discovery while D3, its sister institute is taking care of the downstream activities including preclinical development and early clinical trials, up to and including Proof-of-Concept in man. All of the ETC projects are done in close collaboration with academic institutions in Singapore or overseas, or with industry, on a world-wide basis. Importantly, the academic partner brings deep disease knowledge, the validated drug targets and primary assays to the collaboration.

Two examples shall be discussed that illustrate the approaches taken by ETC and D3 in tackling above-listed issues. The first collaboration with the group of Prof. Tiong S. Ong (Duke-NUS, Singapore)concerns imatinib-resistant chronic myelogenous leukemia while the second one is with Prof. David Virshup (also Duke-NUS) in the field of Wnt inhibitors.

Artwork by Ann Nee, DBS, NUS