Life Science Lecture

John M. Lambert, PhD.
EVP and Chief Scientific Officer
ImmunoGen, Inc., Waltham, MA, USA

»Antibody-drug Conjugates (ADCs):
Magic Bullets for Cancer?«

Date Thursday, 13th December 2012
5:00 p.m.

Venue Bayer HealthCare Pharmaceuticals
S 100 | Auditorium*
Müllerstr. 178 | 13353 Berlin-Mitte

The lecture is open to the public, registration beforehand is not necessary

*via videoconference at Wuppertal site at Bldg.459, room 129

Bayer HealthCare Pharmaceuticals

Dr. Joachim Krüger, Chemical Development, Process R&D,
Joachim.krueger1@bayer.com

Dr. Monika Lessl, Alliance Management, Global Innovation Sourcing
monika.lessl@bayer.com
John M. Lambert, Ph.D.

“Antibody-drug Conjugates (ADCs): Magic Bullets for Cancer?”

ABSTRACT:
Oncologists viewed monoclonal antibody technology with great optimism when the technology was first developed in the late 1970s and applied to the generation of antibodies that bound to a variety of tumor-associated antigens. Antibodies offered the promise of targeted elimination of tumor cells without the systemic toxicity associated with chemotherapy. Rituximab, which binds to CD20 expressed by B cells and B cell lymphomas, fulfills this promise; it has excellent single-agent activity and has become the backbone of treatment of non-Hodgkin’s lymphoma. However, over three decades of clinical research with many antibodies to many cancer cell surface targets has resulted in just two targets on solid tumors to which there are antibodies approved for therapy, namely HER2 and EGFR. In general, the immunological mechanisms for cell elimination induced upon antibody binding to cell surfaces have not proven effective against solid tumors without some other mechanism for enhanced potency.

One approach to enhancing the cell-killing activity of antibodies that bind to cell surface targets on tumor cells is to arm them with a cytotoxic effector agent (a “payload”) to create compounds known as antibody-drug conjugates (ADCs). The idea of such selective targeting of cytotoxic agents to diseased cells was first proposed a century ago by the German immunologist, Paul Ehrlich, who coined the term “magic bullets”. However, the early developments in the field of antibody delivery of cytotoxic agents to cancer cells were not successful due, in part, to the limited potency of the cytotoxic payloads used for the early ADCs, and to the failure of the early ADCs to provide markedly better side-effect profiles than “classical” chemotherapeutic agents.

Recently, with exciting clinical results emerging with ADCs employing cytotoxic agents designed specifically for antibody-targeted delivery, interest in the ADC field has been reinvigorated. With the approval in 2011 of brentuximab vedotin, and the impressive data reported with trastuzumab emtansine, it has become apparent that ADC technologies utilizing highly potent tubulin-acting agents are able to generate highly active, well-tolerated, anticancer agents that fulfill this long-awaited promise. Active compounds can be created against targets expressed on hematologic tumors as well as against targets expressed on solid tumors, and they can be generated from antibodies such as trastuzumab that have some intrinsic antitumor activity, as well as from antibodies such as brentuximab that have no activity as “naked” antibodies. In creating effective, well-tolerated, ADCs, each element in its design, from target selection to choice of antibody, cytotoxic “payload”, and linker, is important, and will be exemplified in the presentation.

It is exciting to report that, after nearly 30 years of research, the emerging clinical data with several compounds suggest that ADCs promise to make a real difference in the lives of patients with cancer. As more compounds advance, one can envisage a future where patients are treated with active anti-tumor agents, among them ADCs, that lack the severe toxicities associated with chemotherapy.
John M. Lambert, PhD

Bibliography (excluding abstracts and oral presentations):

Top 20 (from 105 articles)


2. Lambert JM, Jue R, Traut RR. Disulfide cross-linking of *Escherichia coli* ribosomal proteins with 2-iminothiolane (methyl 4-mercaptobutyrimidate): Evidence that the cross-linked protein pairs are formed in the intact ribosomal subunit. Biochemistry 1978; 17:5406-16.


John M. Lambert, PhD.
EVP and Chief Scientific Officer
ImmunoGen, Inc.
830 Winter Street
Waltham, MA 02451

TEL: 781 895 0600
john.lambert@immunogen.com

SHORT BIOGRAPHY:

Dr. John M. Lambert is Executive Vice President and Chief Scientific Officer at ImmunoGen, Inc., Waltham, Massachusetts.

Dr Lambert received a BA in Natural Sciences in 1972 from the University of Cambridge, England, and received a Ph.D. degree in Biochemistry in 1976, also from Cambridge University, for his research on the structure of multimeric glycolytic enzymes under the supervision of Professor Richard N. Perham.

He did his postdoctoral training in the laboratory of Dr Robert R. Traut in the Department of Biological Chemistry, School of Medicine, at the University of California at Davis, where he worked on the structure of ribosomes (1976 – 1980), and with Dr John R. Coggins in the Department of Biochemistry at the University of Glasgow in Scotland (1980 – 1982), where he worked on the arom multienzyme complex.

In 1982, Dr. Lambert was appointed Assistant Professor of Pathology at the Sidney Farber Cancer Institute (later called the Dana-Farber Cancer Institute), Harvard Medical School in Boston, where he joined the research program supported by ImmunoGen, Inc., to develop monoclonal antibody-based anticancer therapeutic agents (1982 – 1987).

In 1987, ImmunoGen established independent laboratories in Cambridge, Massachusetts to expand its research programs to develop immunoconjugates for treating cancer. Dr Lambert was appointed Director of Biochemistry in 1990, and Senior Director of Research in 1992. He joined the Senior Management team of the Company as a Vice President in 1994, and served in a variety of roles until becoming Executive Vice President and Chief Scientific Officer in 2009.