Biguanides and Neoplasia

October 6–9

FUNDED BY **Oliver Grace Cancer Fund**

ARRANGED BY **M. Pollak,** McGill University, Montreal, Quebec, Canada
K. Struhl, Harvard Medical School, Boston, Massachusetts

Interest in potential roles of biguanides such as metformin in treatment and/or prevention of neoplastic disease continues to increase since the topic was last discussed at Banbury in 2011. Participants in the 2013 meeting discussed the nature of the primary site of action in mitochondria, the alterations in cellular energetics and metabolism caused by biguanides, and the genetic factors that influence these effects. Additionally, the effects of biguanides at the whole-organism level were reviewed, including modulation of both inflammatory responses and the endocrine environment. An important discussion centered on strategies for optimizing drug exposure to target tissues, which may differ from those important in diabetes treatment. Finally, the use of preclinical findings to optimize the design of future trials was reviewed.

Welcoming Remarks: J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory

Introduction: K. Struhl, Harvard Medical School, Boston, Massachusetts

Overview of Progress Since Last Meeting: M. Pollak, McGill University, Montreal, Quebec, Canada

SESSION 1

Chairperson: M. Pollak, McGill University, Montreal, Quebec, Canada

J. Hirst, The Medical Research Council, The Wellcome Trust/MRC Building, Cambridge, United Kingdom: Effects of biguanides on mitochondrial complex I.

M. Schwab, University Hospital of Tuebingen, Stuttgart, Germany: Metformin and drug disposition: Update and future perspectives.

B. Kahn, Beth Israel Deaconess Medical Center, Boston, Massachusetts: AMPK and the regulation of food intake, body weight, and metabolism.

SESSION 2

Chairperson: K. Struhl, Harvard Medical School, Boston, Massachusetts

L. Cantley, Weill Cornell Medical College, New York: AMPK and cancer.

R. Shaw, Salk Institute for Biological Studies, La Jolla, California: LKB1/STK11 genotype dictates therapeutic response to phenformin.

J. Pouyssegur, University of Nice, France: Targeting glycolysis (lactate transporters) sensitizes tumor cells to phenformin.

M. Pollak, McGill University, Montreal, Canada: Serine deficiency sensitizes neoplastic cells to phenformin.

K. Birsoy, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts: Metabolic liabilities of cancer cells to nutrient limitation.

SESSION 3

Chairperson: R. Shaw, Salk Institute for Biological Studies, La Jolla, California

M. Stampfer, Harvard University, Brigham and Women's Hospital, Boston, Massachusetts: Metformin and prostate cancer prevention.

N. Fleshner, Princess Margaret Hospital, Toronto, Canada: Rationale for metformin in prostate cancer.

C. Dang, University of Pennsylvania, Philadelphia: Activities of biguanides and metabolic inhibitors in human pancreatic cancer xenografts.

N. Hay, University of Illinois, Chicago: Targeting glucose metabolism for cancer therapy

P. Puigserver, Dana-Farber Cancer Institute, Boston, Massachusetts: Therapeutic implications of metabolic and energy flexibility in melanoma tumors.

M. Keiser, SeaChange Pharmaceuticals, Inc. San Francisco, California: Prediction and testing of a new target for metformin with a potential role in neoplasia.

H. Udono, Okayama University, Japan: Metformin-induced reversion of immune-exhaustion in tumor microenvironment.

SESSION 4

Chairperson: R. Jones, McGill University, Montreal, Quebec, Canada

J. Schlessinger, Yale University, New Haven, Connecticut: Targeting receptor tyrosine kinases.

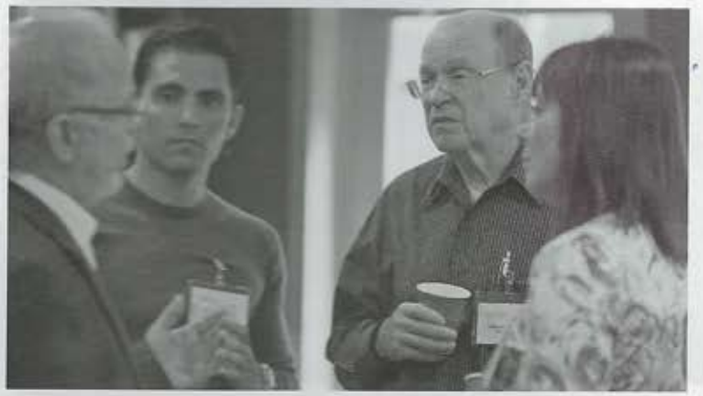
K. Struhl, David Geffen School of Medicine, Los Angeles, California: Metformin mediates anticancer effects by inhibiting the inflammatory pathway.

J.D. Watson, Cold Spring Harbor Laboratory: Exercise vs. metformin.

K. Vousden, Beatson Institute, Glasgow, United Kingdom: Regulation of metabolism through the p53 pathway.

G. Thomas, University of Cincinnati, Ohio: Metformin in the treatment of HCC?

N. Sonenberg, McGill University, Montreal, Quebec, Canada: Translational control of mitochondria function via mTOR.



M. Pollak, F. Cabreiro, N. Sonenberg, K. Vousden

J. Hirst