Novel therapy may prove effective in treatment of 30 percent of cancers

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A ground-breaking Canada-wide clinical trial led by Dr. Katherine Borden, at the Institute for Research in Immunology and Cancer (IRIC) of the Université de Montréal, has shown that a common anti-viral drug, ribavirin, can be beneficial in the treatment of cancer patients. Published in the journal *Blood* (First Edition), the study demonstrates that ribavirin suppresses the activities of the eIF4E gene in patients. This gene is dysregulated in 30 percent of cancers including breast, prostate, head and neck, colon and stomach cancer.

The study, inspired by the exciting discoveries made by Dr. Borden at IRIC, was a joint project between her research group, who monitored molecular events in trial patients, and Dr. Sarit Assouline of the Segal Cancer Centre, Jewish General Hospital, who led the clinical part of the trial.

The integration of these two teams made it possible to rapidly move from a research lab to patient tests. The study team targeted the gene by giving trial participants a mimic of its natural target, ribavirin. "Our results are the first to show that targeting eIF4E in humans is clinically beneficial," explains Dr. Borden. "We also found that ribavirin not only blocks eIF4E, it has no side effect on patients."

The trial studied patients with M4/M5 acute myeloid leukemia who had undergone several other treatments that had previously failed. "We had striking clinical improvements with even partial and complete remissions," indicated Assouline.

Dr. Wilson Miller, director of the Clinical Research Unit, Jewish General Hospital, and co-investigator in the trial added: "It's rare that discoveries in basic research move to clinical so quickly and successfully."

The next challenge for this team is to overcome the resistance that develops over time to ribavirin. "Combination therapy with chemotherapeutic agents may enhance the efficacy of this treatment," explains Borden, "Trials in the near future are planned to overcome this and we are looking forward to more complete remissions. We also hope to test whether ribavirin is as effective in the treatment of other cancers with dysregulated eIF4E. Our laboratory studies suggest this is likely."

The study team also included Drs. Brian Leber from McMaster University/Hamilton Health Sciences (Ontario) and Denis-Claude Roy from Hôpital Maisonneuve-Rosemont in Montreal. The study was made possible thanks to a $600,000 grant awarded to Dr. Borden by The Leukemia and Lymphoma Society (USA).

More information: Sarit Assouline, Biljana Culjkovic, Eftihia Cocolakis, Caroline Rousseau, Nathalie Beslu, Abdellatif Amri, Stephen Caplan, Brian Leber, Denis-Claude Roy, Wilson H. Miller Jr, and Katherine L.B. Borden. "Molecular targeting of the oncogene eIF4E in AML: a proof-of-principle clinical trial with ribavirin" Blood First Edition Paper, prepublished online May 11, 2009; DOI 10.1182/blood-2009-02-205153

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