Hope Funds for Cancer Research **Press Release**

Announces Newly Published Research in the journal *Molecular Cell* from Postdoctoral Fellow

For Immediate Release
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Newport, RI - February 2, 2015 - A paper was published in the journal *Molecular Cell*, from one of the Hope Funds for Cancer Research postdoctoral fellows, Dr. Simon Knott in Dr. Gregory Hannon's laboratory at Cold Spring Harbor Laboratory. The findings demonstrate an algorithm that predicts the likelihood of target knockdown by shRNAs.

"Dr. Knott's findings have developed a validated tool that could play a meaningful role in the discovery of new treatments for cancer," says David Garrett, a Hope Funds for Cancer Research Trustee. "We are very excited to be supporting this cutting-edge work."

The research published in the December 18, 2014 issue of the journal *Molecular Cell*, describes this novel work and its potential applications.

To View *Molecular Cell* Article, Click Here.

About Simon Knott, Ph.D.
Dr. Knott is working in the laboratory of Gregory Hannon, Ph.D. He is working to overcome the shortfalls of single-target therapeutics, by using combinatorial agents targeting critical notes of multiple pathways. Dr. Knott's research is building methods to identify high efficacy multi-targeted therapeutics. Simon received his B.Sc degree from Queen's University, Canada and his Ph.D. in Computational Biology from University of Southern California. After completing his Ph.D. in 2011, he joined Gregory Hannon's lab as a postdoctoral Fellow. In 2012, Simon became a Hope Funds for Cancer Research Fellow.

Loss-of-function RNAi screens that target tumorgenic genomic factors are a powerful and commonly drawn weapon in the war on cancer. However, using current tools, these screens often produce less than industrial strength results. Dr. Knott's research is aimed at improving the quality and robustness of these tools, thus he does not focus on a specific cancer per se.

RNAi screens, as they pertain to cancer research, are driven by the premise that oncogenic changes alter the dependencies of cells, making them vulnerable to the loss of driving oncogenes and to addictions that the transformed state creates. There are cases where this paradigm has proven successful, like Gleevec, Tarceva and B-RAF inhibitors. However, there are inevitably patients who fail to respond or, more commonly and perhaps predominately, initially respond but later acquire resistance to single-target therapies. The reasons for initial and outright resistance are several-fold. Chief among them is heterogeny in cancer cell populations due to additional mutations acquired between the time of the initial driver mutation and the time of treatment. For example, the chronic myeloid leukemia drug Gleevec, which targets the tyrosine kinase

enzyme ABL, is rendered ineffective in patients with additional mutations in the BCR-ABL enzyme. The mechanisms behind delayed and/or acquired resistance appear to be more complex. Cellular pathways are dense, highly connected and adaptable. Following the exposure of cancer cells to a targeted therapy, the pathways involved is typically up- or down-regulated as anticipated. However, having rapid rate of proliferation and anti-apoptotic tendencies, these cells can overcome this initial therapeutic onslaught by taking advantage of pathway plasticity. Up- or down-regulating parallel or related pathways, tumor cells are able to compensate for the loss of targeted gene/pathway. To overcome the shortfalls of single-target therapeutics, it is necessary to turn towards combinatorial agents targeting critical notes of multiple pathways. Dr. Knott's research is building methods to identify high efficacy multi-targeted therapeutics.

About Hope Funds for Cancer Research

The Hope Funds for Cancer Research was formed in 2006 by a group of concerned individuals who have experience in oncology, intellectual property law, investment banking, philanthropy, sociology, and the arts to establish a funding vehicle that would take a rational scientific, medical, and investment approach to granting money to the most interesting and promising research efforts to address the most difficult-to-treat cancers, including pancreatic, lung, liver, sarcomas, esophageal, brain, gastric, and ovarian cancers. These cancers are insidiously aggressive illnesses that kill most of their victims within months, even with aggressive chemotherapy. The Trustees of the Hope Funds for Cancer Research believe that funding research that could lead to breakthroughs in these areas and increase life expectancy in these types of cancers is at the core of our mission. The Hope Funds for Cancer Research is a 509 (a)(1) charity under 501(c)(3) of the Internal Revenue Service's code. For additional information about the organization, please visit http://www.hope-funds.org or call 401-847-3286.

Hope Funds for Cancer Research: Advancing Innovative Research in Understudied Cancers

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