BRIGHAM HEALTH
BRIGHAM AND WOMEN'S HOSPITAL

FOR IMMEDIATE RELEASE

Contact: Haley Bridger
Brigham and Women's Hospital
617-525-6383, hbridger@bwh.harvard.edu

New Era for Blood Transfusions through Genome Sequencing

Whole genome sequencing makes it possible to type hundreds of important blood type differences, enabling more precise matching for future blood transfusions

Boston, MA — Most people are familiar with A, B, AB and O blood types, but there are hundreds of additional blood group "antigens" on red blood cells – substances that can trigger the body's immune response – that differ from person to person. Each year, up to 16 deaths reported to the Federal Drug Administration are attributed to mismatches in red blood cell antigens that are not related to differences in A, B and O blood groups. Currently, no method is available that can determine all blood antigens. But as whole genome sequencing becomes routine for patients, it may be possible to modernize therapy by identifying both rare donors and at-risk recipients before blood transfusions. In a new study, investigators from Brigham and Women's Hospital and Harvard Medical School, as well as from the New York Blood Center have leveraged the MedSeq Project – the first randomized trial of whole genome sequencing in healthy adults – to develop and validate a computer program that can comprehensively and cost-effectively determine differences in individuals' blood types with more than 99 percent accuracy. The team's results are reported in *The Lancet Haematology*.

"Blood transfusion complications are common in patients needing chronic transfusion, but with current technology it is not cost effective to do blood typing for all antigens." said first author William Lane, MD, PhD, director of Clinical Laboratory Informatics and assistant director of the Tissue Typing Laboratory in the BWH Department of Pathology. "But the algorithm we have

developed can be applied to type everyone for all relevant blood groups at a low cost once sequencing is obtained."

Blood transfusions are one of the most common procedures in medicine with more than 11 million units of blood transfused in the U.S. each year. Complications from blood transfusions can be life-threatening. When the body encounters foreign antigens on the donor cells, it can stimulate production of antibodies that can destroy the transfused donor cells. From birth, people have antibodies unique to their ABO blood type, but other antibodies against specific blood antigens can be stimulated during pregnancy from exposure to fetal cells or exposure to donor cells when receiving multiple blood transfusions.

"This approach has the potential to be one of the first routine clinical uses of genomics for medical care for patients needing blood transfusion," said co-first author Connie M. Westhoff, PhD at the New York Blood Center. "It could prevent serious or even fatal complications because once patients are sensitized they have a life-long risk of hemolytic transfusion reactions if blood transfusion is needed in an emergency."

Today, most testing for blood donors and patients include only ABO and Rh matching, but more than 300 red blood cell antigens and 33 platelet antigens are known. To create a way to cost-effectively type many people for these antigens, Lane teamed up with scientists directing the MedSeq Project and experts in blood group genetics at the New York Blood Center to build a database and develop a computer software algorithm, known as bloodTyper, that could rapidly and accurately predict an individual's blood group antigen profile from genomic sequences. Lane, Westhoff and colleagues validated the software by comparison using traditional more labor intensive methods. bloodTyper was more than 99 percent accurate when typing from the MedSeq Project participants' genomes. Lane notes that this work would not have been possible without access to samples from the MedSeq Project, and collaborated closely with MedSeq's principal investigator, Robert Green, MD, MPH, and co-investigator, Heidi Rehm, PhD.

"This report demonstrates a previously unanticipated use case and benefit that will accrue as whole genome sequencing become a routine part of medical care," said Green, one of the senior authors on the study, director of the Genomes2People Research Program at BWH and professor

of medicine at Harvard Medical School. “Genome sequencing can now identify potential transfusion recipients who need rare blood types and the individuals who can safely provide them.”

Funding for this work was provided through the Clinical Sequencing Exploratory Research Consortium of the National Human Genome Research Institute and National Institutes of Health, Doris Duke Charitable Foundation, NHS Blood and Transplant, National Institute for Health Research, and Wellcome Trust.

The Genomes2People Research Program at Brigham and Women’s Hospital, the Broad Institute and Harvard Medical School is directed by Robert C. Green, MD, MPH and conducts empirical research in translational genomics and health outcomes. NIH-funded research within G2P seeks to understand the medical, behavioral and economic impact of using genetic risk information to inform future standards for implementing genomic medicine. The BabySeq Project is recruiting families of both healthy and sick newborns into a randomized clinical trial where half will have their baby’s genome sequenced. The MilSeq Project is examining sequencing within the military. The MedSeq Project has conducted the first randomized clinical trial to measure the impact of whole genome sequencing on the practice of medicine. REVEAL Study has conducted several randomized clinical trials examining the impact of disclosing genetic risk for a frightening disease. And the Impact of Personal Genomics (PGen) Study examined the impact of direct-to-consumer genetic testing on over 1000 consumers of two different companies. Visit genomes2people.org for more and follow us on Twitter @Genomes2People.

Brigham and Women's Hospital (BWH) is a 793-bed nonprofit teaching affiliate of Harvard Medical School and a founding member of Partners HealthCare. BWH has more than 4.2 million annual patient visits and nearly 46,000 inpatient stays, is the largest birthing center in Massachusetts and employs nearly 16,000 people. The Brigham’s medical preeminence dates back to 1832, and today that rich history in clinical care is coupled with its national leadership in patient care, quality improvement and patient safety initiatives, and its dedication to research, innovation, community engagement and educating and training the next generation of health care professionals. Through investigation and discovery conducted at its Brigham Research Institute (BRI), BWH is an international leader in basic, clinical and translational research on human diseases, more than 3,000 researchers, including physician-investigators and renowned biomedical scientists and faculty supported by nearly $666 million in funding. For the last 25 years, BWH ranked second in research funding from the National Institutes of Health (NIH) among independent hospitals. BWH is also home to major landmark epidemiologic population studies, including the Nurses' and Physicians' Health Studies and the Women's Health Initiative as well as the TIMI Study Group, one of the premier cardiovascular clinical trials groups. For more information, resources and to follow us on social media, please visit BWH’s online newsroom.

About New York Blood Center: Founded in 1964, New York Blood Center (NYBC) is a nonprofit organization that is one of the largest independent, community-based blood centers in the world. NYBC, along with its partner organizations Community Blood Center of Kansas City, Missouri (CBC), Innovative Blood Resources (IBR), Blood Bank of Delmarva (BBD), and Rhode Island Blood Center (RIBC), collect approximately 4,000 units of blood products each day and serve local communities of more than 45 million people in the Tri-State area (NY, NJ, CT), Mid Atlantic area (PA, DE, MD), the Kansas City metropolitan area, Minnesota, Nebraska, Rhode Island, and Southern New England. NYBC and its partners also provide a wide array of transfusion-related medical services, including Comprehensive Cell Solutions, the National Center for Blood Group Genomics, the National Cord Blood Program, and the Lindsley F. Kimball Research Institute, which — among other milestones — developed the Hepatitis B vaccine and a patented solvent detergent plasma process innovating blood-purification technology worldwide.

###