

THE MAQC PROJECT: ESTABLISHING QC METRICS AND THRESHOLDS FOR MICROARRAY QUALITY CONTROL

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Microarrays represent a core technology in pharmacogenomics and toxicogenomics; however, before this technology can successfully and reliably be applied in clinical practice and regulatory decision-making, standards and quality measures need to be developed. The Microarray Quality Control (MAQC) project involves multiple FDA Centers, major providers of microarray platforms and RNA samples, EPA, NIST, academic laboratories, and other stakeholders. The MAQC project aims to establish QC metrics and thresholds for objectively assessing the performance achievable by various microarray platforms and for assessing the merits of various data analysis methods for microarray datasets generated from different platforms. Two RNA samples will be selected for each of the three species (i.e., human, rat, and mouse), and differential gene expression levels between the two samples will be calibrated with microarrays and other technologies (e.g., QRT-PCR). The resulting microarray datasets will be used for assessing the precision and cross-platform/laboratory comparability of the microarray technology, and the QRT-PCR datasets will enable evaluation of the nature and magnitude of any systematic biases that may exist between microarray and QRT-PCR technologies.

Two pilot studies (i.e., RNA Sample Selection Pilot and Tissue Mixture Titration Pilot) have been completed with about 400 hybridizations. As a result, two commercial RNA samples (i.e., the brain RNA sample from Ambion and the Universal Human Reference RNA (UHRR) from Stratagene) and two mixtures (25:75 and 75:25, brain:UHRR) have been selected for the human MAQC main study, which is expected to be completed by September 2005. Each of the microarray platforms from seven vendors (Affymetrix, Agilent, Applied Biosystems, Combimatrix, Eppendorf, GE Healthcare, and Illumina) will be evaluated using the same set of four samples in five technical replicates by at least three test sites per platform, resulting in more than 420 hybridizations. QRT-PCR assays (Applied Biosystems) for more than 1,000 genes and QuantiGene assays (Genospectra) for more than 200 genes will be conducted using the same set of samples. The MAQC benchmark datasets, which are being accumulated in the FDA's ArrayTrack system, will be made available to the public in early 2006. Guidelines for microarray quality control and data analysis will be developed.

The availability of the calibrated RNA samples combined with the resulting reference datasets from the MAQC project will allow individual laboratories to more easily identify and correct procedural failures. The MAQC project will help improve the microarray technology and foster its proper applications in the discovery, development and review of FDA-regulated products. More information about the MAQC project can be found at <http://edkb.fda.gov/MAQC/>. We apologize for being unable to list the names of all MAQC participants due to the limitation of space. Views expressed in this abstract do not necessarily represent those of the authors' employers.