NATIONAL CENTER FOR PROFESSIONAL & RESEARCH ETHICS

ETHICS AWARENESS W·E·E·K

OCTOBER 8-12

UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN CAMPUS

When is Reproducibility an Ethical Issue?

Genomics, Personalized Medicine, and Human Error

Keith Baggerly
MD Anderson Cancer Center

Modern high-throughput biological assays let us ask detailed questions about how diseases operate, and promise to let us personalize therapy. Careful data processing is essential, because our intuition about what the answers "should" look like is very poor when we have to juggle thousands of things at once. Unfortunately, documentation of precisely what was done is often lacking. When such documentation is absent, we must apply "forensic bioinformatics" to infer from the raw data and reported results what the methods must have been. The issues are basic, but the implications are far from trivial.

We examine several related papers purporting to use microarray-based signatures of drug sensitivity derived from cell lines to predict patient response. Patients in clinical trials were allocated to treatment arms on the basis of these results. However, we show in several case studies that the results incorporate several simple errors that may have put patients at risk. One theme that emerges is that the most common errors are simple (e.g., row or column offsets); conversely, it is our experience that the most simple errors are common. We briefly discuss steps we are taking to avoid such errors in our own investigations, and discuss reproducible research efforts more broadly.

These issues have been the subject of an Institute of Medicine Review of the use of Omics-Based Signatures to Predict Patient Outcomes. Some of the issues raised and topics of debate will also be addressed.

FOR MORE INFORMATION
http://ethics.grainger.illinois.edu/

Tuesday, October 9
4:00 pm
Institute of Genomic Biology
Auditorium

Dr. Keith Baggerly is Professor of Bioinformatics and Computational Biology at the MD Anderson Cancer Center, where he has worked since 2000. His research involves modeling structure in high-throughput biological data, including various types of proteomic and array data. Dr. Baggerly is best known for his work on "forensic bioinformatics", in which careful reexamination of existing data shows the need for careful experimental design, preprocessing, and documentation. This work has been the subject of features in *Science*, *Nature*, the *New York Times*, and *60 Minutes*. In the past few years, his work led to the suspension and eventual termination of several ongoing clinical trials, to debate about the importance of reproducibility in high-throughput biology, and to a US Institute of Medicine (IOM) review of the level of evidence that should be required before omics-based tests are used to guide therapy in clinical trials.

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