

a single verified report whereby breeding or radiation and/or chemical mutagenesis resulted in a toxin, allergen or other hazard that was not known to exist before. These facts support the conclusion that DNA insertions and other types of mutations do not pose unreasonable risks to the environment or to human and animal health, regardless of how they came about.

#### COMPETING FINANCIAL INTERESTS

The authors declare competing financial interests: details are available at <http://www.nature.com/doi/10.1038/nbt.2347>.

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Although relatively new compared with its genomic and proteomic predecessors, research in the field of metabolomics has already led to the discovery of biomarkers for disease, fundamental insights into cellular biochemistry and clues related to disease pathogenesis<sup>1,2</sup>.

The success of metabolomics over the past decade has relied largely on advances in mass spectrometry instrumentation, which make it possible to detect thousands of metabolites simultaneously from a biological sample. Coupled with developments in bioinformatic tools such as XCMS Online (<https://xcmsonline.scripps.edu/>)<sup>3</sup>, it has now become relatively routine to comprehensively compare the intensities of thousands of metabolite peaks in one sample group to those in another in an untargeted manner. This approach, called untargeted metabolomics, has the potential to implicate unexpected pathways with a unique phenotype or disease process.

Despite the attractiveness of having a comprehensive and unbiased approach for profiling metabolites that is analogous to those used in the other ‘omic’ sciences, an overwhelming proportion of the metabolomic community exclusively uses a targeted platform in which only a specified list of metabolites is measured. The benefit of such a targeted platform is speed. Unlike the untargeted platform, after the targeted mass spectrometry methods are established, minimal effort and resources are required to profile these specific metabolites over a large number of samples. In contrast, the major bottleneck of untargeted metabolomics has been the challenge of determining the identities of the peaks found to be dysregulated in the untargeted profiling data.

Traditionally, the untargeted metabolomic platform involves multiple steps (Fig. 1). The first step is acquiring global mass spectrometry data for each of the samples. Next, these data are analyzed using bioinformatic software that performs quantitative analyses to find peaks that are significantly different between sample groups. The investigator then typically searches the mass-to-charge ( $m/z$ ) ratios of the peaks of interest manually in metabolite databases. Searches that return hits within the mass accuracy of the instrument are considered to be putative identifications. To confirm the identifications, tandem mass spectrometry (MS/MS) data from the research sample are then compared to the MS/MS data of a commercial standard. To obtain the MS/MS data, a targeted MS/MS analysis is typically performed on one of

## Broad consent in biobanking

### To the Editor:

The Feature in the February issue by Scott *et al.*<sup>1</sup> on the policy challenges of biobanking characterizes broad specimen donor informed consent as “ethically contentious.” A survey of public attitudes is cited. This same survey found that a significant percentage of individuals are prepared “to consent broadly to future research use and to forego additional choices as a result”<sup>2</sup>.

With our perspectives in patient advocacy or at research centers aimed at bringing new regenerative therapies to patients, we have consistently emphasized the value of research donors’ perspectives. In the context of protocols for creating immortalized cell lines for banking and distribution, we have also witnessed support for broad consent. Indeed, enthusiasm is even more pronounced among those touched by disease, and patient donors actually express concern that study-specific

consent can be burdensome and impede research.

This experience suggests to us that broad consent is ethically responsible, provided there is comprehensive oversight and a robust informed consent process. With the continued support of donors, we look forward to applying this model in biobanking efforts.

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## An accelerated workflow for untargeted metabolomics using the METLIN database

### To the Editor:

Metabolites, which are typically recognized as small molecules that are involved in cellular reactions, provide a functional signature of phenotype that is complementary to the upstream biochemical information obtained

from genes, transcripts and proteins. The high correlation between metabolites and phenotype has created a surge of interest in the field that is reflected in the number of metabolomic publications growing from just a few articles in 1999 to over 5,000 in 2011.