

*The Relationship Between Variability in Protein Expression and Function*

Drug companies are currently exploring the use of LC-MS-MS for the identification of possible targets for the drug development.<sup>1</sup> Stable isotope labeling is used to detect proteins that are being over- or under-expressed in a diseased state.<sup>2</sup> The precision of the mass spectrometer provides ion ratios within  $\pm 10\%$ .<sup>3</sup> As a result, the “normal” variations in protein expression can be easily detected. Therefore, it is important to establish guidelines that can be used in assessing the significance of differential expression measured when comparing a diseased state to a normal state. The following questions are raised.

How does the variation in protein expression within a defined system relate to protein function and can we use this relationship as a guide in determining the significance of differential protein expression measured in diseased cellular states?

This study seeks to measure the average biological variation in protein expression for a large set of carefully selected proteins under well-defined conditions to test whether there is a correlation between normal biological variation in expression and protein function. Proteins will be identified through the acquired MS-MS spectra and data-base matching. If a correlation is established, guidelines for assessing the significance of differential expression can be explored and developed.