S8. Promises and limitations of biomarkers

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In many 'omics' fields, extraordinary claims have been made about the accuracy of biomarkers for early detection of cancer, for predicting prognosis, and for predicting response to therapy. Yet such claims often turn out to be non-reproducible, and very few new markers have been brought out of the 'omics' pipeline into clinical application.

The disconnect between claims and reality can be explained in part by lack of attention to fundamental 'threats to validity' from 'chance' and 'bias'. Those problems have been discussed before; the purpose of this presentation is to explain possible approaches to address them. While there is no 'quick fix' or simple solution – like 'guidelines' or 'phases' – progress could be made by attention to several critical topics:

First, every study, even 'early' ones, should be 'reliable' in the sense that a study should not contain fatal flaws due to chance or bias. Journals have a major role in assuring a study's strength or reliability and its transparency.

Second, the quality of 'specimens' has an underappreciated role in helping to assure the reliability of a study's results. The central concept is that, after specimens are collected, a 'study' *has been done*, regardless of whether the process was ever conceptualized as a study. In other words, by the time specimens are collected, bias has – or has not – been hardwired into the study. Access to adequate specimens is the rate-limiting step in the field of biomarker research. High-quality specimens should be used even in 'early' studies, suggesting a compression of what we currently think of as 'phases'.

Third, important 'shortcuts' may available in marker research that are totally unavailable in drug development research.

Last, to solve the 'culture clash' that can occur when basic scientists and clinical researchers must collaborate in marker research, it may be useful to separate roles rather than to try to make each specialist into something he or she is not. While molecular markers hold great promise for use in diagnosis, prognosis, and predicting response to therapy, that promise cannot be realized until we appreciate – and apply – appropriate "rules of evidence" to conduct and interpret research.