Ultrasound is perhaps the most recognized form imaging technology as a result of its common use monitoring fetal development through the course of pregnancy. First described for medical purposes in the 1940s by Dr. George Ludwig[45] and Dr. Jon Wild,[46] this technique depends on the generation, reflection, and subsequent detection of reflected sound waves. The typical sonography system generates a series of pulses in the ultrasound frequency range (typically 2–18 MHz) at the surface of the skin. The sound waves are reflected back as echoes, the intensity and angle of which is dictated by the nature of the tissue encountered and its acoustical impedance. This technique can be used to visualize most regions of the body and does not require radioactive material, but image resolution is not as good as that available with other imaging techniques.[47] The relatively low cost of ultrasound as compared to the previously described techniques, however, has led to the wide application of ultrasound devices across the medical and clinical community.

THE PRACTICAL APPLICATION OF BIOMARKERS

Although there are a wide variety of biomarkers available to choose from, the application of any particular biomarker in a given program is at least in part dependent on the nature of the disease or condition under investigation. Biomarkers can be used to determine whether or not a candidate compound is capable of reaching the target of interest, provide an early indication of efficacy (or lack thereof), predict toxicity, and even identify patient populations that are more likely to respond to therapeutic agents. At the end of the day, the purpose of biomarkers and translational medicine is to increase the speed and efficiency of the identification of novel therapeutics. In order to accomplish this goal, the selection of biomarkers must be aligned with the goals of the program and the program scientist must be willing to objectively respond to the results even if the data support project termination. While this is not the most satisfying of outcomes, projects closed at an earlier stage expend less resources than those that are closed at a later point, allowing limited funds and time to be redirected to other priorities and projects. The importance of biomarkers in the drug discovery and development process is best demonstrated through a review of some real world examples of the impact of biomarkers. The following examples provide an illustration of programs whose key decision points would have been far more difficult to evaluate in the absence of biomarkers.

DPP-IV Inhibitors (Januvia®)

The development of inhibitors of the enzyme dipeptidyl peptidase IV (DPP-IV), a serine protease, for the treatment of type 2 diabetes is an interesting case. A number of biochemical biomarkers that provided