NORDIC BIOMARKER

Antibody-Specific Interferences – and How to Reduce Them

Many substances in the human plasma sample to be analyzed, can interfere with the actual analysis and cause false results. Some interfering substances act by binding specifically to some part of the measurement system (e.g. antigen or antibody), whereas other interfering substances change the optical signal non-specifically without any binding.

An example of a common specific interference in immunological assays is that from Rheumatoid Factor (Rf). Rf is an immunoglobulin itself that can bind to several other immunoglobulins. If Rf is present in the patient sample to be analyzed, it may bring the antibodies used in the assays together without antigen being present, thereby causing false positives.

Another example of a specific interference is that from Human Anti-mouse Antibodies (HAMA). As mouse antibodies are sometimes used in pharmaceuticals, patients that have been given such drugs may have developed HAMA that will be present in the blood. If HAMA is present in the human plasma sample to be analyzed, it may cause false positives in much the same way as Rf.

One common way to reduce these effects from Rf and HAMA is to use various blocking substances present on the market. Although several of them have a good reducing effect, there are also some arguments for not using them. One drawback with a blocking substance is that it will increase the cost of the assay. Another problem could be that it will lure the user into a false belief that Rf and HAMA is no longer a problem, when, in fact, higher concentrations of these interfering substances still may cause false positives. Neither will blocking substance remove all other potential problems from interfering substances, known or unknown, which may be present in the sample.

Another common way to reduce the problems from Rf and HAMA is to refrain from using normal mouse antibodies to design immunological assays. Instead, F(ab) or Fab2 fragments can be used, which lack the Fc-region where Rf and HAMA may interact. However, this will increase the production costs of the assays even more than including blocking substances. But it works, and the effects are present even at high concentrations of Rf and HAMA.

If the increased costs for reducing interferences from Rf and HAMA are motivated, depends on the context. If the assay results at hand are heavily relied on to make the diagnosis, and if the outcome of a false positive is serious for the patient, then, yes, the increased costs are probably motivated.