Effects of serum matrix on molecular interactions between drugs and target proteins revealed by GMR biosensor technology

Investigations of molecular interactions between drugs and biomolecules are indispensable for understanding the mechanism of drug actions and their pharmacokinetics/pharmacodynamics. However, analyses of protein interactions are typically performed in buffered salt solutions which lack many components that are present in the original biological matrix, and thus has significant effects on the binding behaviors observed. This limitation of not being able to conduct binding kinetic studies in relevant biological matrices is a result of using an inadequate technology. The standard technology for such studies is based on surface plasmon resonance (SPR) measurements where nonspecific binding due to blood proteins distorts the kinetic data for samples with more than 1% serum. Therefore, detailed kinetic studies in relevant biological matrices are unavailable.

In a recent study published in *J. Pharm. Biomed. Anal.* **198**, 114015 (2021), Saito, *et al.,* used the Giant Magneto Resistance (GMR) platform from MagArray to investigate the binding characteristics of three molecular pairs in a serum-based matrix compared with a buffer-only matrix. The pairs were: quercetin and cAMP-dependent protein kinase A (PKA), Infliximab and tumor necrosis factor alpha (TNFα), and Bevacizumab and vascular endothelial growth factor (VEGF). They found that the presence of serum had different effects on the binding kinetics of the pairs compared to buffer-only measurements. Protein pairs were not as affected as were the small molecules. Saito et al., attributed the differences to the hydrophobic and electrostatic characteristics of the drug molecule, target protein, and serum proteins, which could only be evaluated with the GMR technology. They concluded that the real-time monitoring of molecular interactions in a more relevant biological matrix, enabled by the GMR platform, was a powerful tool to investigate such complicated, yet real-life, molecular interactions. Additionally, the method would allow the analysis of any kind of effects by a third molecule on the interaction between two other molecules, for example, an inhibitor drug's interactions between two kinds of proteins. Such capabilities expand the depth of drug discovery and characterization.

To learn more about how the MagArray GMR platform can also help your drug discovery and characterization efforts, click here: www.magarray.com/lifesciences, or contact Kalidip Choudhury, Ph.D., at MagArray Lifesciences kalidip.choudhury@magarray.com