TRANSIL^{XL} AGP Binding Kit

A Fast High-Throughput Assay for α_1-Acid Glycoprotein Binding

FEATURES AND BENEFITS

- Fast, requires only 20 minutes total assay time
- Accurate, measures the affinity of drug candidates to α_1-acid glycoprotein (AGP) to predict plasma protein binding under diverse disease conditions
- Reliable with highly reproducible results, and robust correlation to equilibrium dialysis method. Fully quality-controlled binding estimates
- Rapid compound quantification due to immoblized plasma proteins
- Kit includes a spreadsheet for calculation of final results and traffic light system for data quality rating

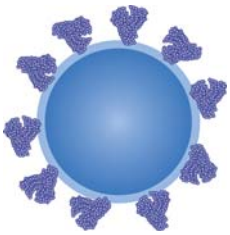

Fig. 1: Illustration of a TRANSIL AGP Binding bead with α_1-acid glycoprotein immobilized in random orientation to expose all binding sites.

TECHNICAL DESCRIPTION

The TRANSIL^{XL} AGP Binding Kit estimates the binding of drugs to α_1-acid glycoprotein (AGP) and is essential for predicting plasma protein binding under disease states. The assay kit measures the affinity constant (K_D) of drugs to AGP and hence allows the calculation of AGP under disease dependent protein concentration ranging from 0.4 to 2.8 g/L. In combination with TRANSIL^{XL} HSA Binding Kit it is possible to obtain accurate prediction of plasma protein binding in a highly controlled and reproducible assay environment.

The kit consists of ready-to-use 96-well microtiter plates. One plate can be used for measuring AGP binding of up to 12 compounds. The assay requires only 5 steps: (i) addition of drug candidate, (ii) mixing and incubation for 12 minutes, (iii) removal of beads by centrifugation, (iv) sampling of supernatant, and (v) quantification of drug candidate.

CAPABILITIES

- Detection system
  - LC/MS/MS
  - Scintillation counting
  - Others
- Parameters estimated and predicted
  - Affinity constant (K_D) of drugs to AGP
  - Unbound fraction of drug in AGP solution
  - Unbound fraction of drug in plasma
  - Concentration dependet plasma protein binding

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Validation of the TRANSIL^{XL} AGP Binding Kit

Human serum albumin (HSA) and human α_1-acid glycoprotein are the most important plasma binding proteins. TRANSIL binding assays are available for both proteins. The TRANSIL^{XL} AGP Binding Kit employs immobilized AGP with a random orientation. This makes sure that all binding sites are available and that the assay reproduces exactly the binding of drugs to AGP in solution (fig. 2). The TRANSIL^{XL} AGP Binding assay is designd to predict plasma protein binding in conjunction with the TRANSIL^{XL} HSA Binding assay (fig. 3) and to model plasma protein binding under a broad range of disease conditions. Differences in relation to plasma binding arise through variations in plasma composition, due to lipids blocking binding sites in native plasma, and occasionally due to binding to other plasma proteins with low abundance. Figure 4 illlustrates that AGP can contribute primarily to plasma binding of acidic or neutral drugs.

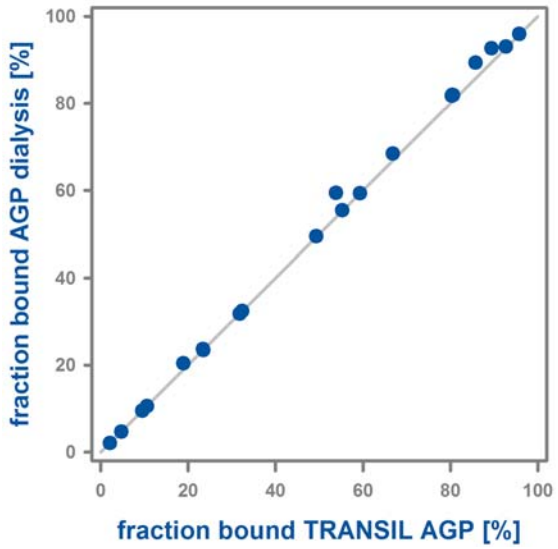


Fig. 2: Comparison of AGP binding measured using the TRANSIL^{XL} AGP Kit and by dialysis with AGP.

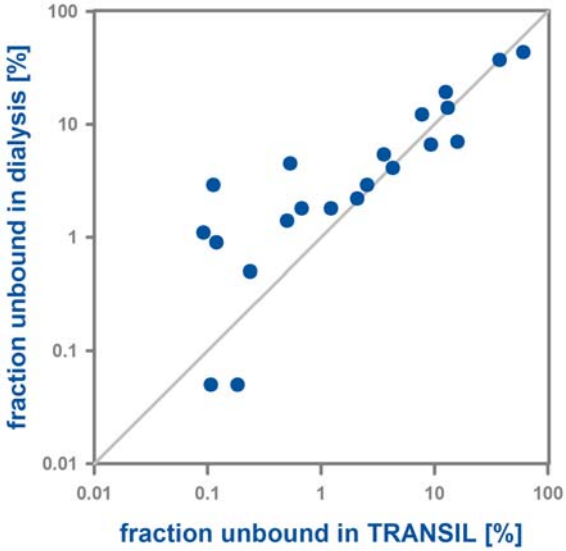


Fig. 3: Comparison of plasma protein binding predictions based on the TRANSIL^{XL} HSA and AGP assay and serum dialysis.

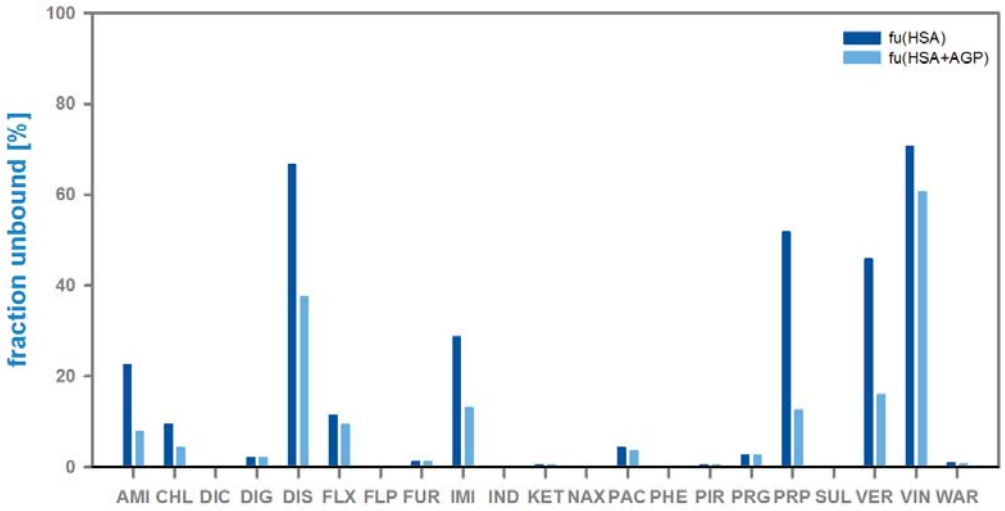
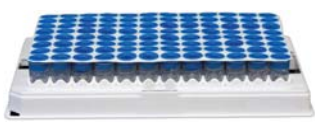


Fig. 4: HSA and AGP contribution to plasma protein binding represented as decrease in drug unbound as a consequence of binding to AGP. AMI: amitriptyline, CHL: chlorpromazin, DIC: diclofenac, DIG: digitoxin, DIS: disiopyramid, FLX: fluoxetine, FLP: flurbiprofen, FUR: furosemid, IMI: imipramin, IND: indomethacin, KET: ketoprofen Wdh, NAX: naxopren, PAC: paclitaxel, PHE: phenylbutazon, PRG: progesteron, PRP: propranolol, SUL: sulfasalazine, VER: verapamil, VIN: vincristine, WAR: warfarin

PRODUCT INFORMATION

Order Number	Name
TPB-0211-2096	TRANSIL^{XL} AGP Binding Kit



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