Drug Discovery 2017

ACC, LIVERPOOL

3rd - 4th October 2017

DRUG DISCOVERY IN THE 4TH DIMENSION
Tuesday 3rd October 2017: HALL 1C

Session Chairs: Jon Hutchinson (GlaxoSmithKline) **& David Swinney** (iRND3)

Drug discovery in the 4th dimension will give the audience a better understanding of the potential value of binding kinetics to drug discovery and the challenges to realise the value. Most target-based discovery programmes optimise compounds using measures of potency or affinity at equilibrium. However, a significant proportion of approved drugs operate by non-equilibrium mechanisms within their therapeutic context. One determinant of non-equilibrium conditions is slow dissociation kinetics (long residence time), which can extend the pharmacodynamic effect beyond the half-life of the drug, provide kinetic selectivity over other targets and/or give an efficacy advantage where the drug competes with an endogenous ligand or substrate under non-equilibrium conditions. These potential advantages, which directly affect the drug's therapeutic index and utility, are becoming more widely appreciated and experimental methods for measuring binding kinetics in higher throughput have advanced. The questions posed in this session are whether the timely and rational application of drug-target binding kinetics remains an unrealised opportunity in drug discovery, with the potential to reduce attrition? Can we define an optimum kinetic profile and build it in during lead optimisation?

The session will begin with an overview of the value of binding kinetics to drug discovery, followed by a review of experimental methods for their measurement and description of a novel experimental approach to monitoring binding kinetics in cells. We will then highlight computational modelling of binding kinetics using molecular dynamics before finishing with case studies addressing the optimisation of structure-kinetic relationships in kinase drug discovery, structural and kinetic aspects in GPCR discovery and the incorporation of binding kinetics into PK-PD models to support translation to in vivo efficacy.

CONFIRMED SPEAKERS

David Swinney (iRND3) - **Session Keynote**
Chun-wa Chung (GlaxoSmithKline)
Kelly Gatfield (GlaxoSmithKline)
Yibing Shan (D E Shaw Research)
Gerhard Mueller (Mercachem)
Rob Cooke (Heptares)
Peter Tonge (Stony Brook)

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