TT 20: Challenges of Free and Total Macromolecule Quantification

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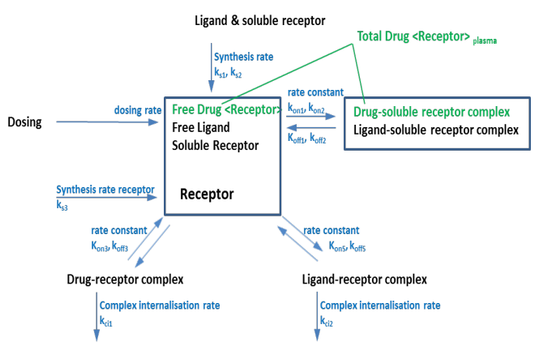
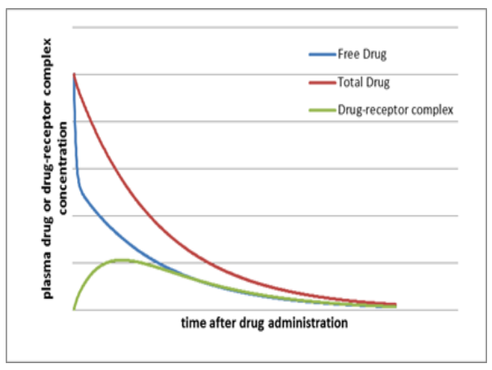
Background and Aim

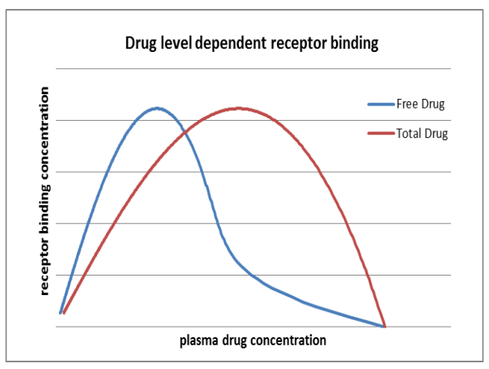
- ❑ What is Free and Total?
- ❑ Relevance of differentiation between Free and Total Drug
- ❑ Roadmap
- ❑ Discussion of AAPS White paper (Lee et al.,The AAPS journal; 2011 Mar;13(1):99-110)
- ❑ Interference test – case studies
- ❑ Modeling approach (Staack et al., Bioanalysis. 2012 Feb;4(4):381-95)
- ❑ Data interpretation done by different Pharma companies using a case study

Team Members

- Daniela Stoellner, Novartis, Team lead on-leave
- Sherri Dudal, Novartis, GBC team lead L3
- Marianne Scheel Fjording, Novo Nordisk, Team lead
- Margarete Brudny-Kloeppel, Bayer HealthCare
- Marie-Helene Pascual, Sanofi-Aventis
- Eva Vieser, Amgen Research
- Roland Staack, Roche
- Gregor Jordan, Roche
- Michaela Golob, Merck-Serono

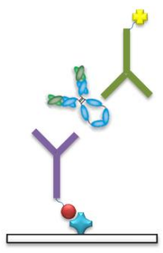


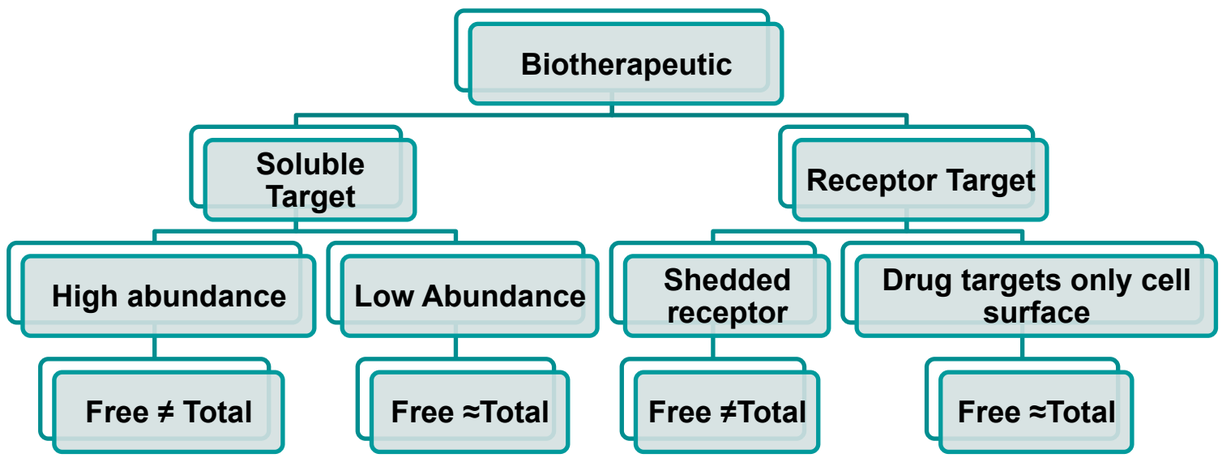




Ongoing Activities and Current Results

- ❑ Starting point: Discussion on applying the methods used in the free versus total paper (Lee et al.,The AAPS journal; 2011 Mar;13(1):99-110)
  - ❑ method for target interference to define free vs total assay works for some methods but not all
  - ❑ Dependent on KD and the drug QC value used when titrating in target.
  - ❑ What methods exist for defining free and total assays? Comparisons.
  - ❑ What are the consequences of under or over estimating the absolute drug values?
  - ❑ Recommendations on the characterization of assays.





- ❑ Interference –
  - ❑ Define types of target
  - ❑ Share examples of ELISA setup
  - ❑ Determine how to present interference data to define assay
  - ❑ Collection of data
  - ❑ Compare cases to determine whether current methods fit the data

Future Plans

- ❑ Collection of data
- ❑ Evaluation of interference testing
- ❑ Elaborate a EBF consolidated approach for assay characterization:
  - ❑ True total assay?
  - ❑ True free assay?
  - ❑ Interference?
- ❑ EBF position paper: to increase awareness among stakeholders of what forms of drug/ligand are measured and what are the advantages and limitations of ligand-binding assays.