
Accelero Bioanalytics GmbH

Berlin • Germany

Your Partner in DMPK Research.
GLP Compliant Ligand Binding Assays.

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GLP Services

1. **Ligand binding assays** in 96/384 well plates
2. Capillary gel electrophoresis
3. RP/IEX/SEC HPLC
4. LC-MS/MS
5. Gas chromatography
5. Gel electrophoresis, Northern/Southern/Western blot
6. Pharmacokinetics
7. Pharmacodynamics
8. Statistics

For

1. siRNA, miRNA mimics and antagomirs, aptamers, antisense oligos
2. Therapeutic proteins, biosimilars, monoclonal antibodies, peptides
3. Antibiotics PD research

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GLP Services

1. More than 12 years experience in the field of nucleic acid drugs
2. **Preclinical experience:**
 - dose range finding (rat, mouse, cynomolgus)
 - acute & subchronic tox (rat, cynomolgus)
 - biodistribution (rat, mouse)
 - in matrices like plasma, urine, liver, heart, kidney, spleen, etc
3. **Clinical experience:**
 - pharmacokinetics (human)
 - pharmacodynamics (human)
 - antibody detection assay (ADA)
4. In vitro applications:
 - monitoring of nanocarrier siRNA load procedures

All assays are validated in accordance to the EMA guidance on bioanalytical method validation (2011).

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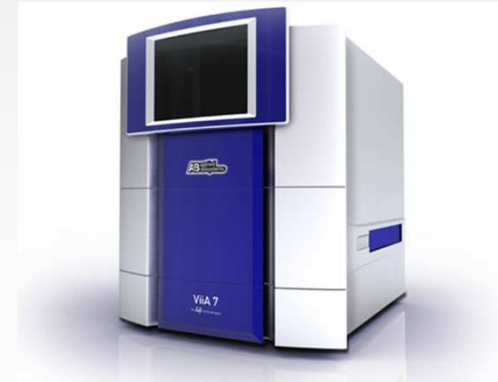
Ligand Binding Assay Equipment

1. Biotek Synergy 2 Multiwell Plate Reader

6well – 384well plates (fluorescence, absorption, luminescence)
21 CFR part 11 compliant

2. Applied Biosystems ViiA7 Dx Real-Time PCR System

IVD Label
384 well plates
21 CFR part 11 compliant



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Ligand Binding Assay Portfolio

1. Sandwich Hybridization Assay
2. ELISA (Cytokines, biosimilars PK, etc)
3. AlphaLISA®, AlphaScreen®
4. Immunogenicity Testing (ADA Assays)
5. Complement Activation
6. Real-Time qPCR
7. Real-Time RT-qPCR
8. Immuno qPCR
9. TaqMan® Arrays (384well expression patterns)
10. Immunoprecipitation
11. In vitro plasma binding studies
12. Label-free Biodistribution & ³H labelled (non-GLP)
13. Rapid amplification of cDNA ends (RACE)
14. Bead-based assays

AlphaLISA®, AlphaScreen® are trademarks of Perkin Elmer Inc.
TaqMan® is a registered trademark of Applied Biosystems Inc.

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Assay Portfolio For siRNA Pharmacokinetics

- Simply select from our assay portfolio!
- As an example, a double-stranded, chemically unmodified siRNA targeting human ICAM-1 (1) was spiked into human plasma, and the guide strand was quantified by applying three different assay principles:
 1. one-step capturing & detecting, followed by immobilization (2),
 2. two-step capturing & detecting, followed by immobilization (3),
 3. Real-Time RT-qPCR (4).

References:

- (1) Clark PR et al (2007), Nucleic Acids Res 36(4): 1081-97.
- (2) Brown-Augsburger P et al (2004), J Pharmacol Biomed Anal 34: 129-39.
- (3) Drolet DW et al (2000), Pharm Res 17(12): 1503-10.
- (4) Seitzer J et al (2011), J Pharmacol Toxicol Methods 63: 168-73.

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1. Simultaneous Capturing & Detecting

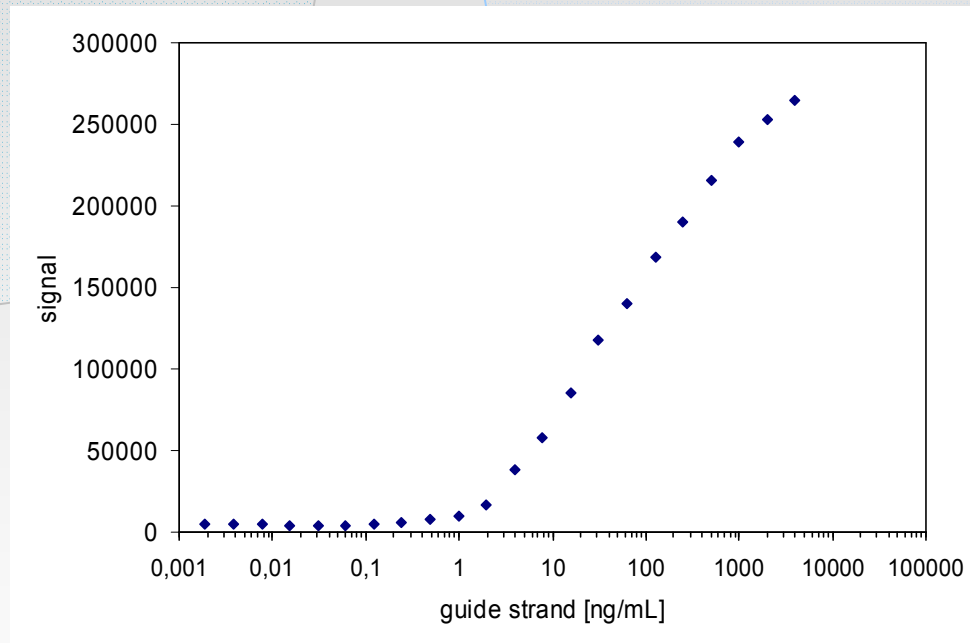


Figure 1. ICAM-1 siRNA Calibration Standards in Human Plasma.

Double-stranded siRNA targeting human ICAM-1 was spiked into human plasma, and the guide strand was assayed by applying a one-step, dual-probe liquid phase assay.

LLOQ = 3.91 ng/mL

References:

Clark PR et al (2007), Nucleic Acids Res 36(4): 1081-97.

Brown-Augsburger P et al (2004), J Pharmacol Biomed Anal 34: 129-39.

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2. Successive Capturing & Detecting

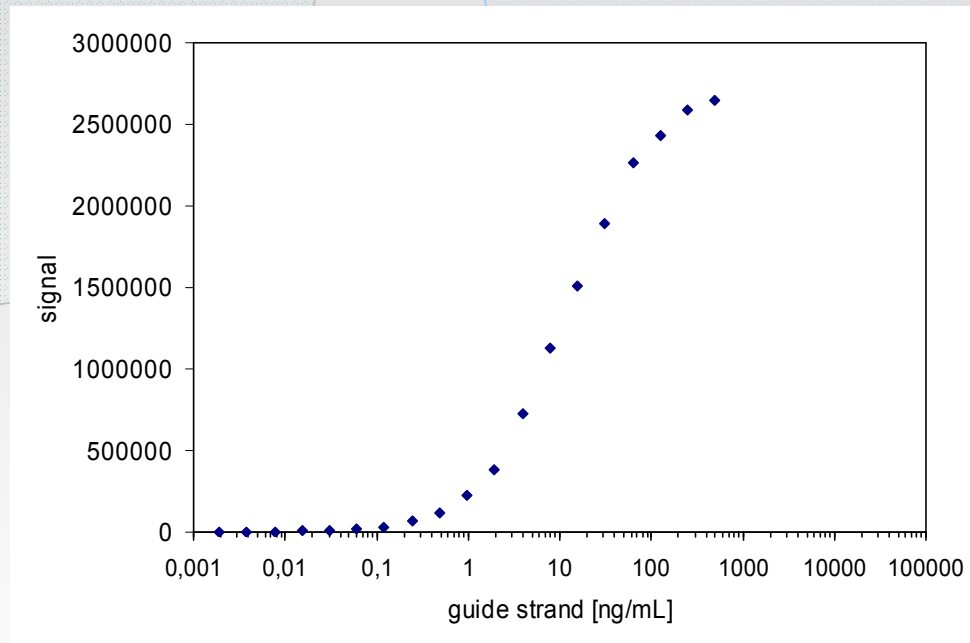


Figure 2. ICAM-1 siRNA Calibration Standards in Human Plasma.

Double-stranded siRNA targeting human ICAM-1 was spiked into human plasma, and the guide strand was assayed by applying a two-step, dual-probe liquid phase assay.

LLOQ = 0.03 ng/mL

References:

Clark PR et al (2007), Nucleic Acids Res 36(4): 1081-97.
Drolet DW et al (2000), Pharm Res 17(12): 1503-10.

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3. Real-Time RT-qPCR Assay

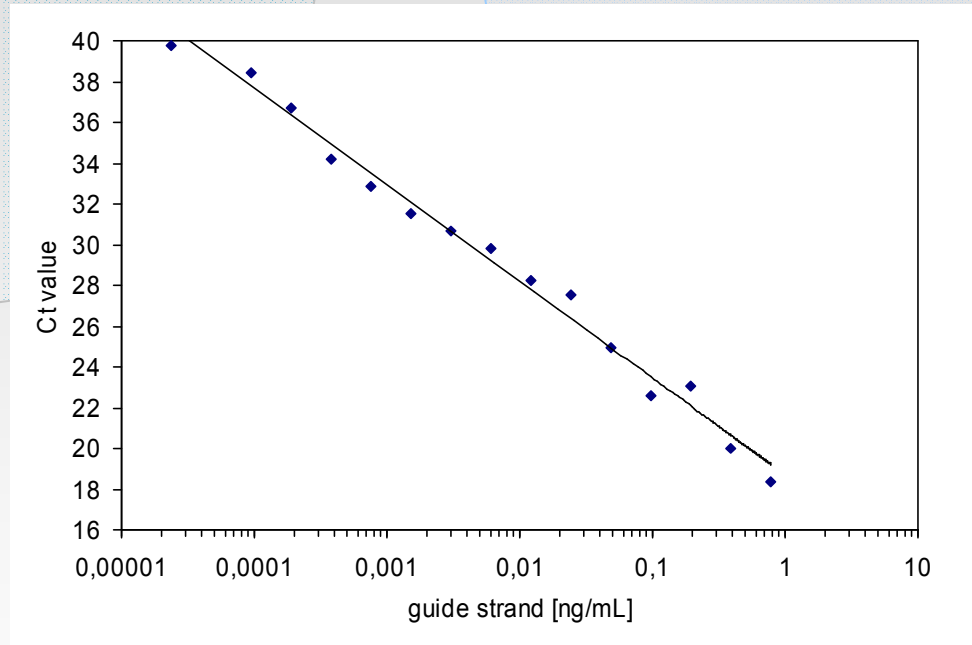


Figure 3. ICAM-1 siRNA Calibration Standards in Human Plasma.

Double-stranded siRNA targeting human ICAM-1 was spiked into human plasma, and the guide strand was assayed by applying a two-step, Real-Time RT-qPCR assay.

LLOQ = 0.0001 ng/mL

References:

Clark PR et al (2007), Nucleic Acids Res 36(4): 1081-97.

Seitzer J et al (2011), J Pharmacol Toxicol Methods 63: 168-73.

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We Provide Your Assay of Choice

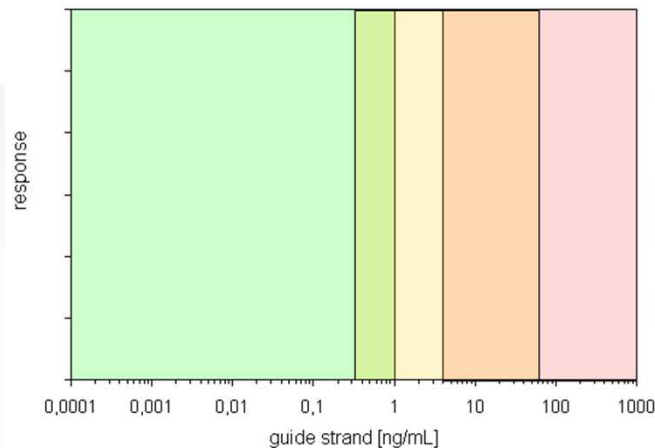
Table 1. Quantification of Double-Stranded siRNA Targeting Human ICAM-1 in Human Plasma.

	LLOQ [ng/mL]	ROQ [ng/mL]	LOD [ng/mL]
One-Step Dual Probe Assay	3.91	3.91-1000	39.1
Two-Step Dual Probe Assay	0.03	0.03 - 62.5	0.3
Real-Time RT-qPCR Assay	0.0001	0.0001 - 1	0.01

LLOQ = lower limit of quantification
 ROQ = range of quantification
 LOD = limit of detection

All three assays provide overlapping quantification windows:

-  one-step, dual probe hybridization assay
-  two-step, dual probe hybridization assay
-  Real-Time RT-qPCR assay



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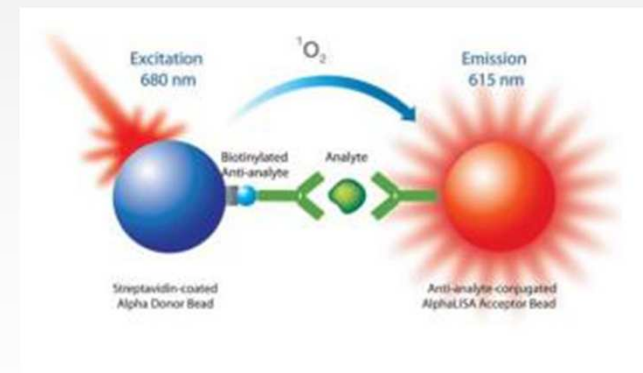


Customized Assay Development

1. AlphaLISA 384well Sandwich Hybridization Assay

6well – 384well plates (fluorescence, absorption, luminescence)
21 CFR part 11 compliant

2. Immuno qPCR Assay for the quantification of miRNA, siRNA in immuno-captured Ago2



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Summary

1. Accelerō Bioanalytics offers a broad range of PK and PD assays to **cover the complete drug development process** of any: siRNA, miRNA antagomir or mimic, antisense oligo, aptamer, etc from the preclinical stage up to Phase I clinical trials.
2. All **assays can be easily customized** to any nucleic acid drug sequence.
3. Benefit from our experience in this field.

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