# New generation monitoring introduces six complementary approaches for improved donor specific antibody assessment

**Rico Buchli, Ying-Yu Wu, Leslie Wilmot, Jacob Collard**

*HLA Protein Technologies Inc., Oklahoma City, OK, USA*

hla protein Technologies Inc

DSA Discover Architecture

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## One platform • six modular capabilities • clinical interpretation • technical interrogation

### A | CONFIRM & QUANTIFY

**Is the donor-specific response confirmed, and how strong is the donor-specific response?**

**PURPOSE** **Confirm donor relevance and establish a quantitative DSA reference state.**

**CLINICAL VALUE**
Quantifies donor-specific response strength; compares donor targets; creates a baseline for future follow-up.

**OUTPUT**
Baseline phenotype, quantify donor-specific response.

TECHNICAL

| | |
|---|---|
| CORE TECHNOLOGY | Native HLA$^{bio}$ targets • Serum titration • Dose-response modeling • QC/reference system |
| PRIMARY OUTPUTS | logEC$_{50}$ [DilF] • Top/Asymptote • Hill slope • S/B • $R^2$ • Breadth |
| EXTENDED CAPABILITY | Base Landscape • within-patient target comparison • standardized quantitative baseline |

### B | RESOLVE

**What antibody populations are driving a complex or cross-reactive HLA pattern?**

**PURPOSE** **Dissect complex, cross-reactive, or discordant HLA reactivity patterns.**

**CLINICAL VALUE**
Clarifies dominant vs residual responses and cross-reactive vs independent antibody populations.

**OUTPUT**
Experimentally resolved antibody components.

TECHNICAL

| | |
|---|---|
| CORE TECHNOLOGY | Soluble-HLA blockers • paired reference/inhibition experiments • combinatorial blocking |
| PRIMARY OUTPUTS | Reference Profile • Inhibition Profile • Neutralization Profile |
| EXTENDED CAPABILITY | Reductive Profiling • Blocker-response matrix • Antibody-population deconvolution |

### C | ISOLATE

**Can the relevant HLA-specific antibody population be physically separated and recovered?**

**PURPOSE** **Physically capture defined HLA-specific antibody populations for direct study.**

**CLINICAL VALUE**
Provides direct specificity confirmation and physical access to the antibody population of interest.

**OUTPUT**
HLA-enriched antibody fractions.

TECHNICAL

| | |
|---|---|
| CORE TECHNOLOGY | HLA$_{mag}$ [HLA$^{bio}$ and streptavidin magnetic beads • HLA$_{smx}$ [HLA-coupled Sepharose matrix] |
| PRIMARY OUTPUTS | Sera input • Depleted flow-through • Enriched/eluted HLA-specific antibody |
| EXTENDED CAPABILITY | Epitope mapping • LC-MS/MS • Antibody proteomics • BCR/proteogenomic analysis • Fc glycosylation • Functional assays |

### D | CHARACTERIZE

**What biologic and functional features modify the donor-specific antibody response?**

**PURPOSE** **Add functional and molecular context to a defined donor- specific response.**

**CLINICAL VALUE**
Differentiates response quality beyond signal strength and defines subclass, complement, and Fc-related features.

**OUTPUT**
Functional and molecular DSA phenotype.

TECHNICAL

| | |
|---|---|
| CORE TECHNOLOGY | Isotype/subclass assays • Complement assays • FcγR interaction • Glycoanalysis • Functional systems |
| PRIMARY OUTPUTS | IgG/IgM • IgG1–4 • C1q/C3/C3d • FcγR engagement • Glycoform profile |
| EXTENDED CAPABILITY | NK-cell activation • FcγR reporter assays • Endothelial interaction • ADCC-associated / complement-dependent function |

### E | TRACK & MONITOR

**Is donor-directed humoral activity increasing, stable, resolving, rebounding, or responding to intervention?**

**PURPOSE** **Measure longitudinal change, persistence, rebound, and treatment response.**

**CLINICAL VALUE**
Defines trajectory, persistence, treatment response, rebound, and meaningful longitudinal change.

**OUTPUT**
Patient-specific DSA trajectory / Trajectory Landscape.

TECHNICAL

| | |
|---|---|
| CORE TECHNOLOGY | Matched serial titration • same HLA targets • same QC/reference framework • Longitudinal analytics |
| PRIMARY OUTPUTS | ΔlogEC$_{50}$ • ΔTop • Δbreadth • Landscape displacement • Emergence/disappearance |
| EXTENDED CAPABILITY | Trajectory classification • Persistence • Treatment response • Rebound • Rate/durability of change |

### F | MEMORY

**Does donor-reactive humoral memory persist even when circulating DSA is weak or absent?**

**PURPOSE** **Interrogate latent capacity to regenerate donor-reactive humoral responses.**

**CLINICAL VALUE**
Extends assessment beyond circulating antibody to persistence and functional recall potential.

**OUTPUT**
HLA-specific humoral memory / recall phenotype.

TECHNICAL

| | |
|---|---|
| CORE TECHNOLOGY | Native HLA fluorescent multimers • Flow cytometry • B-cell activation • FluoroSpot/ELISpot |
| PRIMARY OUTPUTS | HLA-specific memory B cells • B-cell phenotype • Antibody-secreting cells • Regenerated HLA-specific antibody |
| EXTENDED CAPABILITY | Culture-supernatant profiling • Recall-response breadth/ strength • BCR sequencing • Longitudinal memory assessment |

**CLINICAL VALUE** | **ACCESS** • **TRACK** • **UNDERSTAND** • **PROTECT**



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