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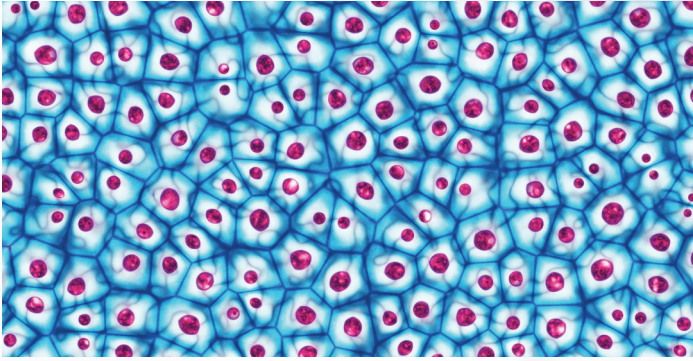


Laboratory Sciences

The Laboratory Sciences team at Biomere is focused on developing and executing assays to support downstream analysis of in-life and terminal samples from small and large animal preclinical models. The combination of *in vivo* study expertise and sample analysis positions Biomere to be a one-stop CRO for preclinical PK/PD and early toxicology studies.

Biomere has developed a portfolio of assays through a combination of in-house capabilities and partnerships with platform companies and service providers. Our in-house capabilities include cell isolation and tissue dissociation, clinical chemistry assays, quantitative RT-PCR or qPCR, flow cytometry panels, singleplex sandwich ELISA assays, and cytokine panels using the MSD platform. In addition to rodent and large animal samples, the team has experience working with human cell lines and blood samples.

The Lab Science team is led by PhD scientists who have extensive experience developing and running *in vitro* assays that generate valuable preclinical data. The team is continuously evaluating new platforms and assays – contact us at bd@biomere.com to discuss your study needs.



Tissue and Cell Culture Capabilities

Analysis in the Biomere lab typically starts with tissues collected at various time points from mice, rats or large animal models (including rabbits and non-human primates or NHPs) that have been treated with either control or a therapeutic. Biomere's *in vivo* scientists evaluate various modalities including oligos, LNPs, viral vectors, monoclonal antibodies and small molecules in a broad range of models. The team has experience in isolating pure cell populations from a tissue such as hepatocytes from liver or PBMCs from whole blood using enzymatic digestion, mechanical dissociation, density gradients or magnetic bead isolation (Miltenyi and StemCell Technologies).

The team has experience with cell culture methods for primary cell lines including human PBMCs as well as commercial cell lines that are used for *in vitro* assays such as cell viability, proliferation and apoptosis assays. The data deliverables include functional readouts such as proliferation, metabolic markers, apoptotic markers etc. and detailed documentation on the culture conditions and protocols especially for rare and sensitive cell lines. Additionally, we offer tissue homogenization services to generate whole lysates that can be used for gene expression profiling.

Gene Expression Profiling

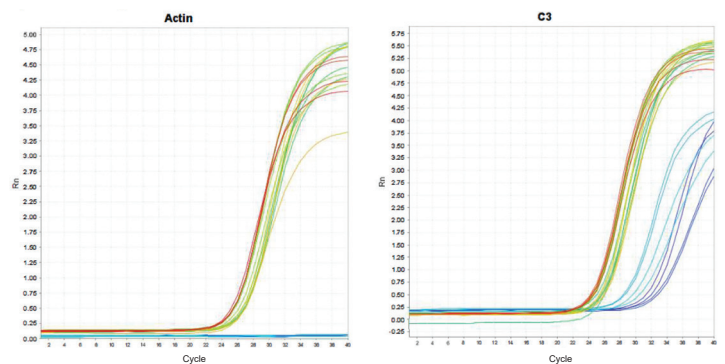
The Biomere team has developed several assays to evaluate gene expression changes in response to a therapeutic including quantitative RT-PCR (qPCR), single and multiplex ELISA-based assays and flow cytometry panels to evaluate cell surface and intracellular markers. Biomere also offers services using off the shelf and custom colorimetric ELISA and MSD assays to evaluate cytokines and other biomarkers in different sample types including blood,

sera, plasma, cerebrospinal fluid (CSF), and cell and tissue lysates. Most of the samples are tissues and biofluids from rodents, rabbits and NHPs that have been dosed with different therapeutic modalities. The data deliverables are customized for client needs and range from raw data to data reports that include standard curves, normalized data and fold-change analysis of specific markers.

qPCR Services

Biomere has recently developed expertise in both TaqMan and SYBR Green based quantitative RT-PCR using the QuantStudio 5 instrument. The primary sample types are cell and tissue lysates, isolated RNA from blood, PBMCs or other biofluids. The data deliverables can range from raw data (Ct values, melt curves etc.) to more in-depth analysis of fold-change in expression which is performed using QuantStudio software.

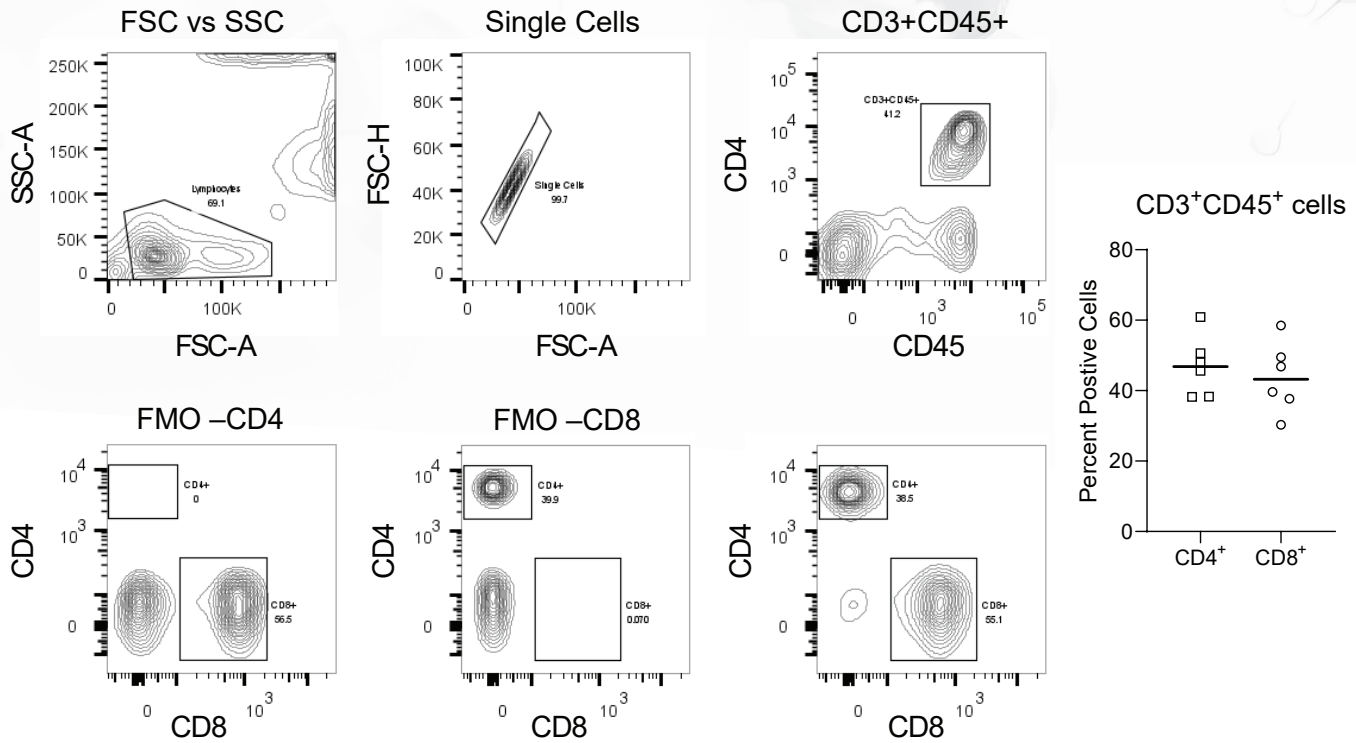
Figure 1: Representative qPCR data showing expression curves for beta-actin (left) and complement C3 gene (right).



Flow Cytometry

Biomere offers a growing portfolio of flow cytometry assays including high-parameter immune cell profiling, cell phenotyping, receptor occupancy analysis and functional assays. Our scientists use the CytoFLEX LX cytometer to develop custom flow panels that typically cover 13-15 colors to ensure high quality detection of cell surface and intracellular markers. The primary sample inputs are blood and cell samples from mice, rats or nonhuman primates that have been exposed to one or more therapeutic. In addition to flow cytometry analysis, Biomere offers cell sorting in partnership with Sauve Bio a startup based in Worcester MA. The main types of data deliverables are either raw data (FCS files) or complete reports that include the identification of specific cell populations and quantitative signal analysis.

Figure 2: Blood samples collected from 6 NHPs stained with anti-cyno-specific antibodies targeting CD3, CD45, CD4, and CD8 to measure the percentage of CD3+CD45+ CD4+ and CD3+ CD45+ CD8+ positive T-cell populations by flow cytometry. (FMO – fluorescence minus one).



Sandwich ELISA and MSD assays

Biomere is proficient in running commercially available singleplex ELISAs that have colorimetric or fluorescent readouts and the team works closely with third party developers to transfer protocols for custom ELISA assays to support analysis of specific biomarkers. Additionally, our scientists have over 10 years' experience running assays on the MSD platform that uses multiplex electrochemiluminescence readouts for various markers including cytokines, serum proteins and cellular proteins. Most of the samples are from rodents or primates dosed with a specific therapeutic and since the MSD assays are optimized for small sample volumes the platform is ideal to analyze in-life and terminal for longitudinal analysis. Due to the long-standing collaboration, our scientists work closely with the MSD team to design and validate custom plates for specific client studies.

The team has experience with the different types of MSD panels including U-PLEX customized panels, V-PLEX validated kits and customizable antibody sets (R-PLEX) so MSD analysis for each client study can be customized.

The more popular MSD multiplex panels include:

- Cytokine Combo Panel
- Proinflammatory Combo Panel
- Viral Combo Panel
- Chemokine Combo Panel
- Custom Panels

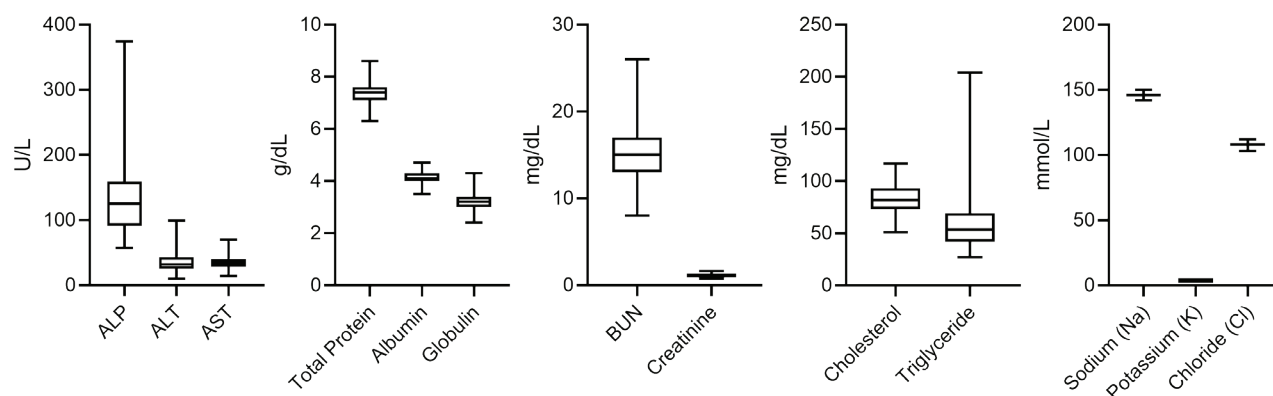
Clinical Chemistry Analysis

The Biomere clinical chemistry lab has developed assays to measure multiple endpoints in whole blood, serum, plasma and biofluids including urine, cerebrospinal fluid (CSF) and synovial fluid. The team uses the Sysmex XN-1000 for hematology analysis and the Beckman Coulter DXC 700 AU for chemistry analysis – both instruments are widely used in the clinical setting thus ensuring the translational value of the preclinical data. Additionally, both analyzers require small sample volumes ensuring that samples collected from mice and rat models can be analyzed.

Biomere offers a comprehensive portfolio of hematology endpoints including but not limited to counts of different white blood cells (lymphocytes, monocytes, eosinophils, basophils), platelet volumes and ratios, red blood cell counts and hematocrit. Clinical chemistry analysis includes the measurement of enzyme levels such as alkaline phosphatase, proteins, metabolite markers and electrolytes as well as specialty tests for custom markers including apolipoprotein forms, bile acids, lipids etc.

Clients have the option to use preset panels that combine different readouts such as CBC, differential markers and reticulocyte analysis. More recently, the team has launched coagulation assays to evaluate therapies that may cause uncontrolled bleeding or other clotting issues.

Figure 3: Representative data of clinical markers measured in NHP blood samples including liver markers, serum proteins, kidney function, lipids and ions.



Organ-Chip System – COMING SOON!

The Biomere team has partnered with Emulate Inc. to offer Organ-Chip Services for preclinical testing. The first system that is being validated is the Liver-Chip to measure drug induced liver injury (DILI).

Please contact us at bd@biomere.com if you are interested in collaborating on the development of specific Organ-Chip systems.



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