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INTRODUCTION

About Us

MLM Medical Labs is a leading specialty and central laboratory with comprehensive research services and diagnostic capabilities in Europe and the United States. Offering a range of standard and fully customizable analytical services across a variety of therapeutic areas, we add value at every stage of the product development process from early stage R&D through phase IV clinical trials that serve to enhance and accelerate research programs to their next milestones. Each disease area is supplemented extensively by different models and batteries of *in vitro* and *ex vivo* analyses, offering answers to your therapeutics’ effect on different biological systems. With our strong reputation for scientific expertise, passionate approach to customer care, and adherence to providing quality data, we empower clients ranging from emerging biotech to Top Ten Global Pharma companies to reach confident clinical decisions that ultimately serve to improve patient lives.

We approach each project uniquely, hosting discussions to learn as much about our sponsors’ programs as possible including the overall objectives of the study and the potential mechanisms of the test items upfront. We approach each customer with transparent sharing of information, coordinated decision-making processes, and a high level of flexibility, offering you global service without the bureaucracy. We run off-the-shelf models, customize existing models and develop novel approaches, whether it be a new model, delivery method or assessment. Furthermore, our biomarker development and clinical services teams will collaborate with our customers to realize diagnostic assays or *in vitro* diagnostic devices. We are committed to creating a lasting partnership that ensures delivery of the most informative and comprehensive data package possible from each study we perform.

Our Core Values

Scientific Excellence

Personal Accountability

Customized Agile Solutions
IN VITRO CAPABILITIES
Screening and Mechanism of Action Studies

Cell Based Assays
Primary and immortalized cellular assays for compound screening, cytotoxicity testing, proliferation, cytokine production, disease modeling and more.

Flow Cytometry
Characterize complex cellular populations of interest with our standard and custom panels for immunophenotyping with BD LSR Fortessa.

Protein Analytics
Analyze biomarkers through singleplex, multiplex or ELISA-based technologies (up to 30 analytes per sample), Western Blot capabilities.

Histopathology
Our fully-equipped and GLP-compliant histopathology laboratory can provide in-depth tissue analysis through histological staining and immunohistochemistry on fresh frozen and FFPE samples.

Molecular Analytics
Analyze specific genes or pathways through PCR, DNA methylation determination, mRNA/miRNA expression levels and Next-Gen Sequencing.

Custom Assay Development
We specialize in assay development and validation to meet our customers’ complex analytical needs. Contact us today to discuss a customized assay solution!
IN VIVO CAPABILITIES
Models for Efficacy and Pharmacology Studies

Our scientists aim to provide the biotech and pharmaceutical community with relevant disease models that translate to the clinic because the development of life-saving therapeutics depends on it. We offer traditional, well-characterized rodent models of numerous diseases and disorders that can be found in publications across the literature, and we continually develop new models on the background of existing models.

Combining the right models with the necessary readouts, both in vivo and ex vivo, brings a higher degree of applicability to the clinic in later stages of development and ultimately accelerates our client programs forward.

Drug Administration
All standard routes (IV, IP, Intradermal, etc) as well as intranasal, oral aspiration and infusion pump delivery.

Tissue Sampling and Histopathology
Harvesting of all tissue types for ex vivo analysis of biomarkers. Traditional pathological assessments as well as digital imaging and quantitative image analysis.

Model and Method Development
Small animal model development as well as method development to address unmet study needs.

New Chemical Entities (NCE), Biologics and Medical Devices
Experience in handling small molecules, biologics, cell-based therapies, natural compounds, medical devices and combination products.
CELL CULTURE MODELING

In Vivo & In Vitro Assays

We offer a variety of in vivo models and in vitro assays for evaluating select pathways. Sponsors can select pathways of interest, choose between stimulation or inhibition assays, evaluate in cell based or whole animal systems.

In Vivo Immune Response Models:

<table>
<thead>
<tr>
<th>Category</th>
<th>Species</th>
<th>Response</th>
<th>Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellular Immunity</td>
<td>Mouse</td>
<td>Th1 response</td>
<td>Cytokine panel, FACS</td>
</tr>
<tr>
<td>Cellular Immunity</td>
<td>Mouse</td>
<td>Th2 response</td>
<td>Cytokine panel, FACS</td>
</tr>
<tr>
<td>Cellular Immunity</td>
<td>Mouse</td>
<td>Th17 response</td>
<td>Cytokine panel, FACS</td>
</tr>
<tr>
<td>Cellular Immunity</td>
<td>Mouse</td>
<td>CD8 T cell response</td>
<td>Cytokine panel, FACS</td>
</tr>
<tr>
<td>Non-specific Immunity</td>
<td>Mouse</td>
<td>Innate</td>
<td>Cytokine panel, FACS</td>
</tr>
<tr>
<td>Humoral Immunity</td>
<td>Mouse</td>
<td>B cell response</td>
<td>FACS, cytokines</td>
</tr>
<tr>
<td>Humoral Immunity</td>
<td>Mouse</td>
<td>B cell activation</td>
<td>FACS</td>
</tr>
<tr>
<td>Allergy/Hypersensitivity</td>
<td>Mouse/rat</td>
<td>Th1</td>
<td>Cytokines panel, FACS</td>
</tr>
<tr>
<td>Allergy/Hypersensitivity</td>
<td>Mouse</td>
<td>Th2</td>
<td>Cytokines panel, FACS</td>
</tr>
</tbody>
</table>
In Vivo Immune Response Models:

<table>
<thead>
<tr>
<th>Model</th>
<th>System</th>
<th>Stimulant(s)</th>
<th>Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>Custom Model</td>
<td>Custom</td>
<td>Custom</td>
<td>Cell proliferation, multiplex cytokine panel, ELISA, qPCR, FACS</td>
</tr>
<tr>
<td>PBMC Cellular Inflammation Model</td>
<td>Peripheripheral blood mononuclear cells (PBMC)</td>
<td>Lipopolysaccharides (LPS), Sponsor Compound</td>
<td>Cell proliferation, multiplex cytokine panel, ELISA, qPCR, FACS</td>
</tr>
<tr>
<td>T Cell Activation</td>
<td>PBMC</td>
<td>antiCD3/CD28, ConA, PHA, Sponsor Compound</td>
<td>Cell proliferation, multiplex cytokine panel, ELISA, qPCR, FACS</td>
</tr>
<tr>
<td>In vitro B-cell stimulation/activation</td>
<td>PBMC or B-cells</td>
<td>anti-CD40, anti-IgM/IgG, IL-4, Sponsor Compound</td>
<td>Cell proliferation, multiplex cytokine panel, ELISA, qPCR, FACS</td>
</tr>
<tr>
<td>M0/M1/M2 Macrophage Polarization Assay</td>
<td>Monocyte cell line THP-1</td>
<td>phorbol 12-myristate-13-acetate (PMA), LPS, IFN-gamma, IL-4, IL-13, Sponsor Compound</td>
<td>Cell proliferation, multiplex cytokine panel, ELISA, qPCR, FACS</td>
</tr>
<tr>
<td>TH17 Cell Differentation</td>
<td>CD4+ T cells</td>
<td>MACSiBeads (loaded with CD2, CD3, CD28 antibodies), Th-17 differentiation cocktail containing TH17 polarizing cytokines (IL-1β, IL-6, IL-23, TGF-B1, anti-IFNγ, anti-IL-4), Sponsor Compound</td>
<td>Cell proliferation, multiplex cytokine panel, ELISA, qPCR, FACS</td>
</tr>
<tr>
<td>Fibroblast-like Synoviocyte Inflammation Assay</td>
<td>Healthy Human Fibroblast-like Synoviocytes (HFLS) or Rheumatoid Arthritis Patient (HFLS-RA)</td>
<td>TNF-α, Sponsor Compound</td>
<td>Cell proliferation, multiplex cytokine panel, ELISA, qPCR</td>
</tr>
<tr>
<td>Colonic Epithelial Cell Inflammation Assay</td>
<td>Colonic Epithelial Cells</td>
<td>TNF-α, IL17a, Sponsor Compound</td>
<td>Cell proliferation, multiplex cytokine panel, ELISA, qPCR</td>
</tr>
</tbody>
</table>
# INFLAMMATION

## Inflammatory Assessments Across Multiple Disease Areas

<table>
<thead>
<tr>
<th>Organ/Disease</th>
<th>Model</th>
<th>General Assessments</th>
</tr>
</thead>
</table>
| Rheumatoid Arthritis    | • Collagen Induced Arthritis (CIA)  
• Collagen Antibody Induced Arthritis (CAIA)  
• Carrageenan Air Pouch  
• Carrageenan Induced Paw Edema | Histology/IHC, Flow Cytometry, Biomarker Analysis, DNA/RNA Analysis, PK |
| Dermal Inflammation     | • Imiquimod (IMQ) Induced Psoriasis  
• IL-23 induced Psoriasis  
• DNBC/FITC Induced Atopic Dermatitis  
• Oxazolone Delayed Type Hypersensitivity  
• Passive Cutaneous Anaphylaxis | Histology/IHC, Flow Cytometry, Biomarker Analysis, DNA/RNA Analysis, PK |
| Respiratory/Lung        | • Ovalbumin (OVA) Asthma  
• Lipopolysaccharide (LPS) Lung Inflammation/Injury  
• House Dust Mite (HDM) Asthma  
• HDM + LPS Asthma  
• Bleomycin induced IPF | Histology/IHC, Flow Cytometry, Biomarker Analysis, DNA/RNA Analysis, PK |
| Fibrosis                | • Diet Induced NASH  
• Bleomycin Induced Systemic Sclerosis | Histology/IHC, Flow Cytometry, Biomarker Analysis, DNA/RNA Analysis, PK |
| Sepsis                  | • LPS-Induced Septic Shock  
• BSL-2 Grade Facility and can work under SPF conditions for microbiome related studies  
• Cecal-Ligation Puncture (CLP) | Histology/IHC, Flow Cytometry, Biomarker Analysis, DNA/RNA Analysis, PK |
| Inflammatory Bowel Disease | • Dextran sulfate Sodium (DSS)-induced ulcerative colitis  
• Trinitrobenzene sulfonic acid (TNBS)-induced Crohn’s Disease | Histology/IHC, Flow Cytometry, Biomarker Analysis, DNA/RNA Analysis, PK, Von Frey, Motor Function, Inflammation Score |
| Metabolic Disorder      | • Feed Intake  
• Diet-induced obesity | Histology/IHC, Flow Cytometry, Biomarker Analysis, DNA/RNA Analysis, PK, Von Frey, Motor Function, Inflammation Score |
HISTOPATHOLOGY
Histological Assessment of all Tissue Types

Histopathological evaluations form a highly valuable component of preclinical, translational, and clinical studies alike, providing additive spatial, contextual, and temporal information directly from tissues of interest. We offer a full-service GCLP and CLIA-certified histopathology laboratory that can provide in-house analysis of tissues, with capabilities for processing, embedding, microtomy, histochemical staining, immunohistochemical staining, immunofluorescent staining, and assessments. Our skilled team of histologists provide 20+ years of expertise to apply to each study that MLM performs, utilizing tissue specific staining optimization protocols for antibody validation and calibration, ensuring the highest quality of pathological assessment.

1a) IHC, MPO, skin punch, 20x
1b) IHC, MPO, AI Overlay, skin punch, 20x
2a) Chromogenic triplex, tonsil, (CD8-Teal_CD4-Yellow_CD3-Purple)
2b) IF Triplex, tonsil, (CD3-CY5_CD8-RG6_PanCK-FAM)
3a) H&E, Skin punch, 20x
3b) Masson Trichrome, Liver, 20x
To meet the ever-changing demands of our client research programs, MLM Medical Labs® offers unique *in vitro* and *in vivo* model development capabilities for analysis of pharmaceutical, biologic and medical device products. Our laboratory can import and utilize nearly any readily available rodent strain, and has extensive experience creating novel models for custom investigational purposes. Combining the right models with the necessary readouts, both *in vivo* and *ex vivo*, brings a higher degree of applicability to the clinic in later stages of development and ultimately accelerates our client programs forward. Collaborative cost-sharing and partnership opportunities are available for those interested in exploring areas outside our present focus. Contact our scientists to discuss model development for your study needs.

**Recently Validated Models**

- **CD4+ T-Cell Anergy Model** (Staphylococcal enterotoxin B-induced, performed in Balb/c mice)
- **Th17 Cell Differentiation Model** (Anti-CD3 antibody-induced, performed in C57/BL6 mice)
- **Hair Growth Model** (Performed in B6C3F1/J mice)
- **Scleroderma / Systemic Sclerosis Model** (mice CD-1 or C57BL/6)
- **NASH Model** (mice C57BL/6)

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CONTACT US!
Speak with a scientist today to discuss your next study!

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