



Innovative Bioincubator and
Pre-Clinical Contract Research Organization

Offering
Discovery Research Products and Services

January 2024



- SBH Sciences is an innovative Bioincubator and a Contract Research Organization (CRO) which has been operating for over 26 years, providing over 300 companies with quality products and services.
- SBH Sciences has supported many start-up companies. We have collaborated with three companies through all stages of drug development, bringing seven NCE's to clinical trials. One of the seven drugs – Xpovio was granted FDA approval (07/2019).



**SBH Sciences has produced and commercialized
30 recombinant cytokines, 8 enzymes, and 40 MAb**

Activin-A

Bone Morphogenic Proteins

(BMP-2, BMP-7)

CD22

Growth Factors (HGF)

GDF-15/MIC-1 *

IGF-BPs (IGF-BP-6)

Interferon (IFN- β)

Interleukins (IL-12, IL-23) **

Soluble receptors (s-IL-6R)

TGF-Beta (TGF- β 2)

TNF Receptor (HVEM-Fc)

Enzymes (8 Glycosyltransferases)

Monoclonal Antibodies:

Anti-TNF α ; Anti-VEGF, Anti-Galectin-3

Anti-T, Anti-Tn, Anti-STn

* Only company that produces GDF-15/MIC-1 naturally from human cells

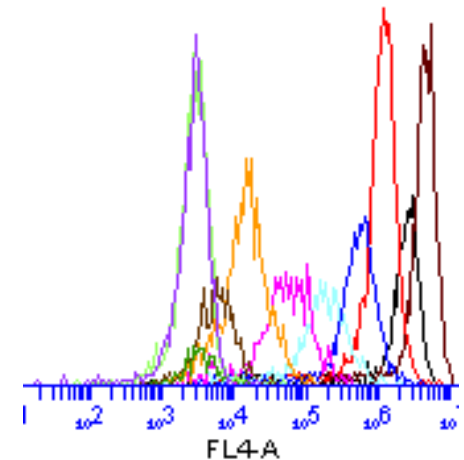
** Licensed human IL-12 process technology to Neumedicines, a California based company, and collaborated with them to develop IL-12 for Acute Radiation Syndrome. The project was supported by BARDA and DoD and is in Phase II / III clinical trials.

Extensive Services Offered to Support and Accelerate Your Research Programs

- Biomarker Analysis [11-platform]
- Cell-Based Assays
[cytokine, chemokine, oncology, inflammation, TLRs]
- T-Cell Activation
- Development of Biologics
 - Cell Culture
 - Protein Purification
 - Cell-based assays
 - Analytical HPLC
 - ELISA / RBA [e.g., PD1/2 binding assay]
 - FACS
 - Formulation
 - Stability
 - Anti-Drug Antibody (ADA) assay
- Molecular Biology
- Gene and Cell Therapy



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Gate: (P2 in all)



Comprehensive Biomarker Analysis Services

- We offer 11 innovative platforms for the analysis of biomarkers including SMCxPRO and Isolight.
- First CRO to offer automated simple western blot services on “Peggy Sue”, “WES” and “Jess” [ProteinSimple].
- First CRO to offer Simple Plex assays on “ELLA”.
- SBH Diagnostics, our strategic partner company, is a contract research organization providing biomarker analysis under CLIA certification and GLP.
- We assist companies and enable translation from non-regulated to regulated environment [clinical trials].



Eleven Platforms to Assist with Biomarker Analysis



- AlphaScreen® and AlphaLISA®
- MultiPlex: ProteinSimple ELLA
- ELISA [Tecan]
- Flow Cytometry – FACS Analysis
- HTRF®/ TR-FRET
- Luminex®200 [Multiplex Analysis]
- MSD QuickPlex SQ 120
- Automated Western Blot [Peggy Sue / Wes / Jess]
- Isolight [IsoPlexis]
- qRT-PCR
- SMCxPRO [MilliporeSigma]



Bioanalytical Services

- ELISA-Based Assays
- Receptor/ Ligand - Binding Assay
- Anti-Drug Antibodies [ADA]
- Analytical HPLC
- Chromatography
- Pharmacokinetics (PK) and Pharmacodynamic (PD)
- Multiplex Services (Luminex, ELLA, MSD, Isolight)
- Automatic Western Blot [Jess / WES]
- Endotoxin
- Cell-Based Potency Assays
- Flow-Cytometer Based Assays



Comprehensive Pathway Analysis

(Companion Biomarkers)



Cell Culture Services (Mammalian & Insect Cells)

- Production of recombinant proteins, monoclonal antibodies, and vaccines.
- Optimization of growth conditions (media optimization and serum-free adaptation).
- Multi-liter supply of any mammalian cell line, before or after cytokine stimulation.
- Customized services (10 human primary cells and > 500 mammalian cell lines are currently available).
- Creation of new stable cell lines.
- Commercial production of cell culture spent media [8 years ; 18 lots ; > 150 L each lot].
- 2D and 3D assay capabilities.
- Irradiation experiments (combination of anti-cancer therapy).
- Preparation and isolation of Exosomes.



Protein Purification Services for Biologics

- Development of scalable, well-validated, and reproducible purification processes.
- Liquid chromatography capabilities (Ion Exchange, HIC, Affinity, Metal, HA, SEC).
- HPLC (Preparative and Analytical methods development).
- Protein formulation and stability studies.

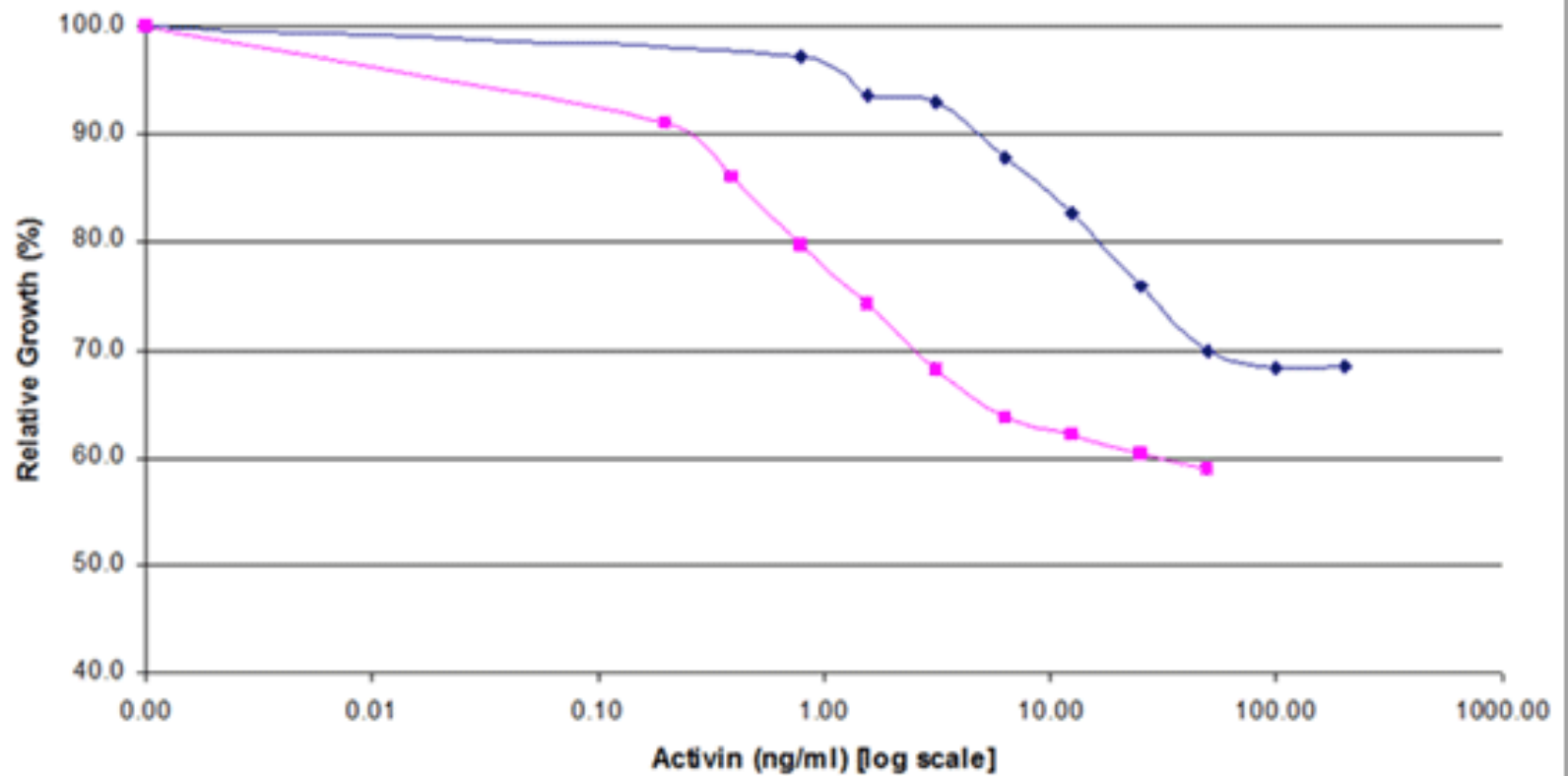
Cell-Based Assay Capabilities

- Inflammation, oncology, and fibrosis are the therapeutic areas where SBH Sciences is best positioned to assist you
- 330 cell-based assays to measure cytokine activity (cytokine-induced proliferation, cytokine-induced killing, cytokine release assays, and cytokine neutralization)
- GPCR activation and determine chemokine activity (e.g., IL-8, GRO, MCP1)
- Screening of therapeutic antibodies for specific activity (includes receptor binding assays, ADCC, ADCP, ADC, CDC assays, as well as immunocytokine)
- 370 different human cancer cell lines to facilitate in-vitro lead drug optimization (cytotoxicity, invasion, migration and adhesion assays)
- Cell-based disease models for compound selection (inflammation/fibrosis – THP-1, RAW 264.7, BEAS-2B, SW-982, human Lung Fibroblast, PBMC and immortalized liver cell line)
- T-Cell Activation (e.g., T-cell-engaging IgG-like antibody targeting FLT3 on AML cells and Activation of the 4-1BB/CD137 pathway on T cells)
- Co-Culture Experiments [e.g., RAW264.7 and ID8 cancer cells]
- Testing for the presence of anti-Adeno-Associated Virus (AAV) in pig serum
- Immunostimulation [e.g., transfection of h-PBMC with c-di-AMP (CDN) that activate h-STING and resulted in the secretion of IFN-alpha that enhance anti-cancer activity]
- TLRs activity [e.g., cytokine induction by TLR agonists]
- Microglial Activation
- Exosome uptake by human macrophages



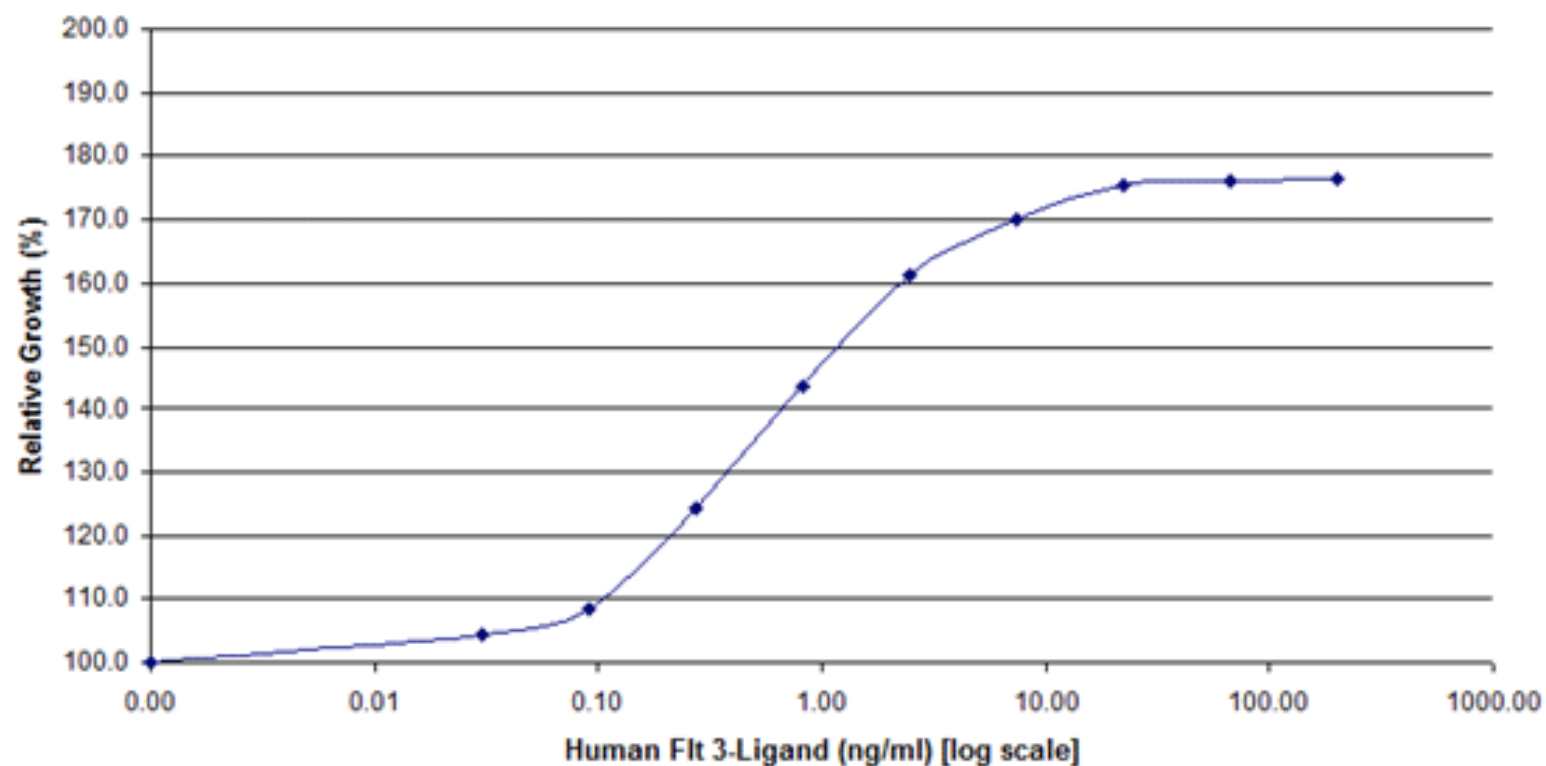


Cell-Based Assay :
h-Activin A and h-Activin B
using MPC-11 cell line





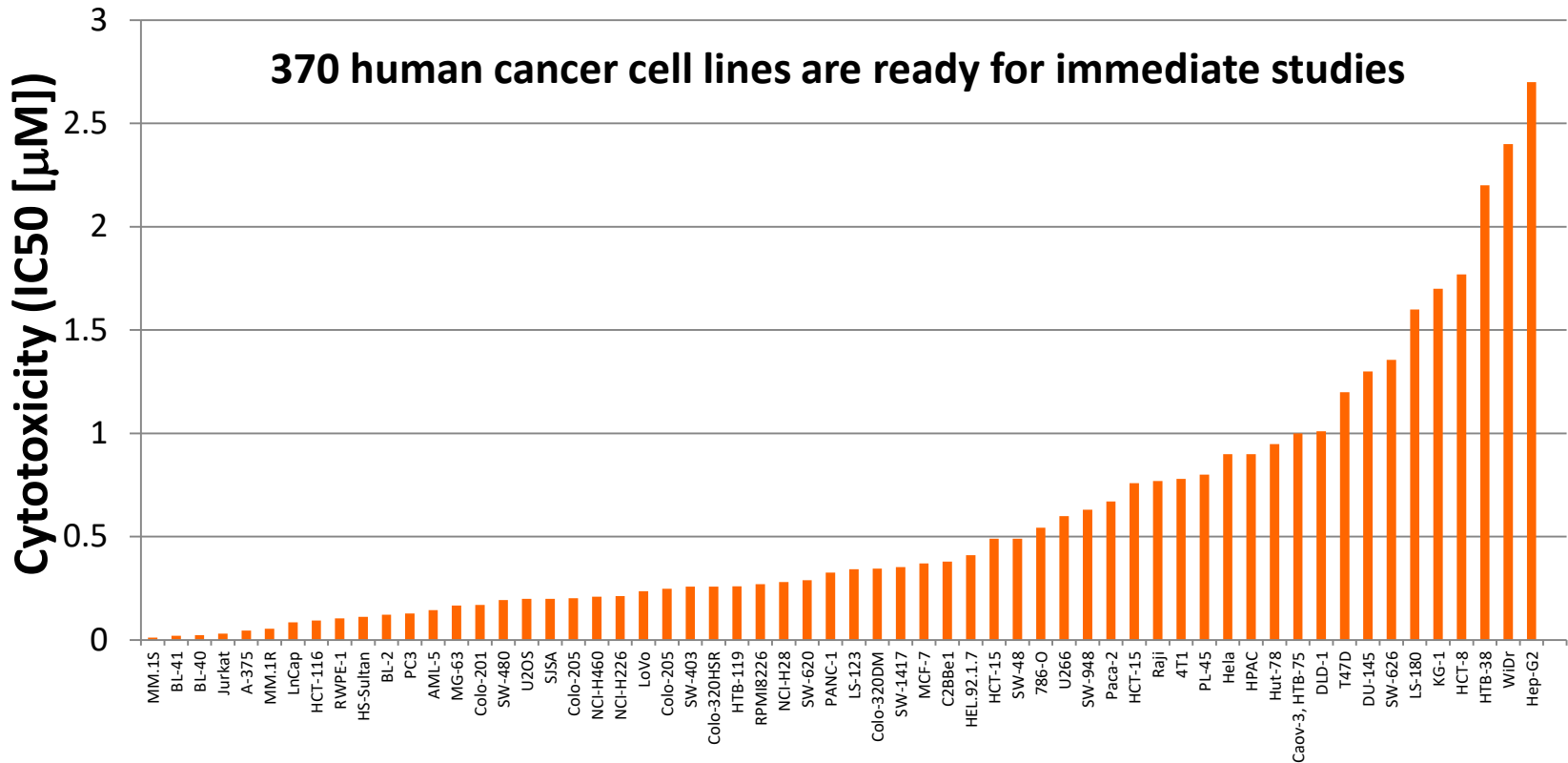
Cell-Based Assay :
h-Flt 3-Ligand
using AML-5 cell line



—•— Human Flt 3-ligand

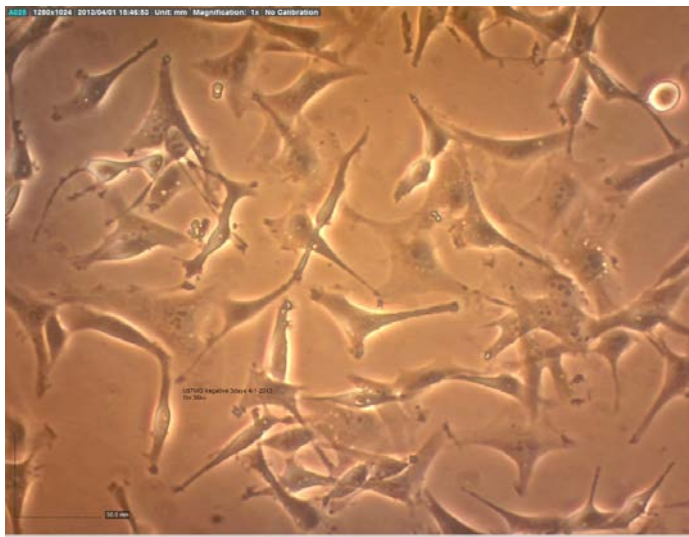
Cancer Cell Cytotoxicity

(72 hours)



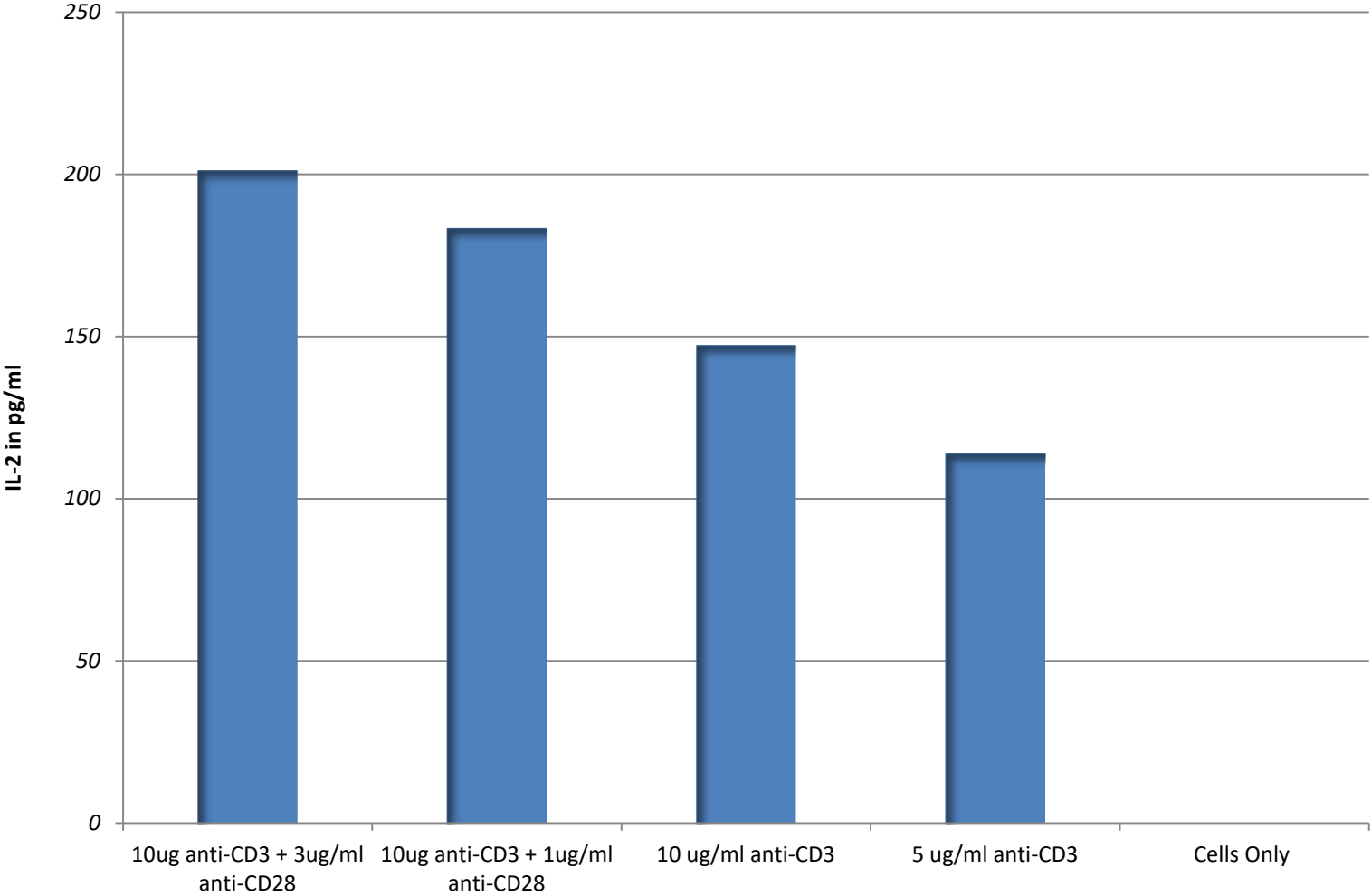
Irradiation Capability

U87MG cell line



T-Cell Activation

Human IL-2 secreted by Jurkat clone E6-1 cells after stimulation with immobilized anti-CD3 and soluble anti-CD28





2019 - 2023 - Drug Development Solutions

Examples of discovery projects supported by SBH Sciences

I. Inflammation:

Differentiation of THP-1 cells to:

- M1 [IFN-gamma & LPS]
- M2 [IL-13 & IL-4]

WES Analysis of iNOS expression by RAW 264.7 cells

Measurement of TLR-4, TLR-5, TLR-7, TLR-8 & TLR-9 agonist activity using the SEAP reporter HEK293 or THP1 cell lines

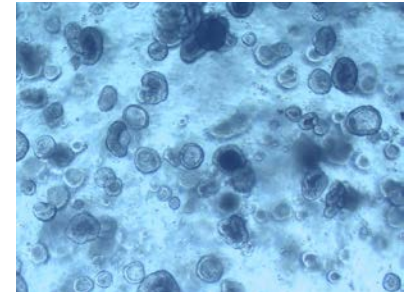
Screening Agonist / Antagonist compounds targeting CB1 & CB2 receptors

II. Experiments using isolated: Neutrophil, Eosinophils, Basophils

III. Modulation of T-cell activation

IV. Isolation of Stem Cells from Human Milk

V. Pig, Rat and Mouse – Scale up of intestinal organoids [ileum & duodenum] and transfect and create stable cells prior to in-vivo transplantation





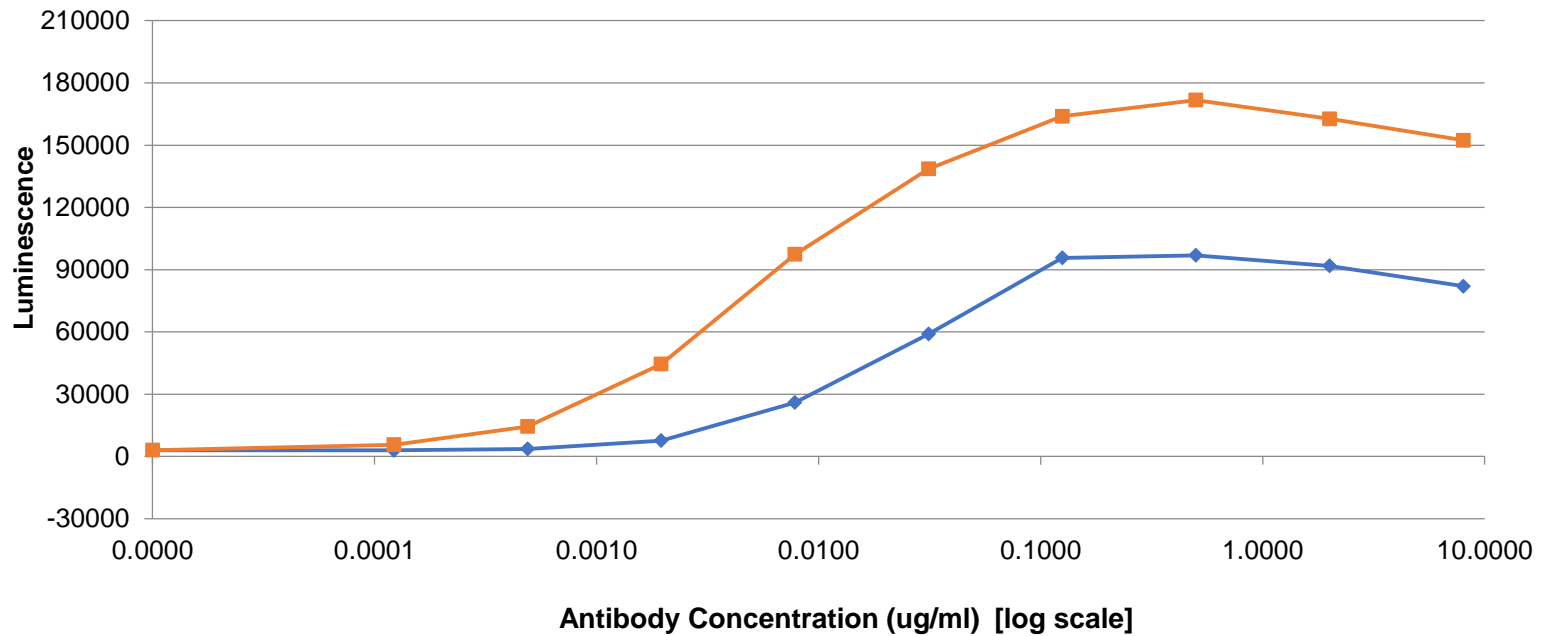
2019 - 2023 - Drug Development Solutions

Examples of discovery projects supported by SBH Sciences

Continue:

- VI. Optimization of adeno-associated virus (AAV) vector design and function in cell lines, primary cells, ex-vivo tissues and organoids.**
- VII. Transfection of mouse and human pancreatic beta-cell lines.
Transduction of pancreatic beta cell lines and mouse and human islets.**
- VIII. qPCR assays for vector copy number and AAV titer.**
- IX. Investigate the potential of IL2/IL12 fusion protein to induce potent anti-tumor immunity.**
- X. Isolation of NK cells from human PBMC and investigate the role of NKG2D receptor - MICA interaction by FACS analysis.**
- XI. Screening RNA-targeting therapeutics compounds as an innovative anti-cancer drug.**
- XII. Development of cell-based assay to assess the activity of virus-like particle containing CpG-A DNA to stimulate TLR9 activity.**
- XIII. Screening of hundreds peptides against multi-targets (e.g., TL1A).**

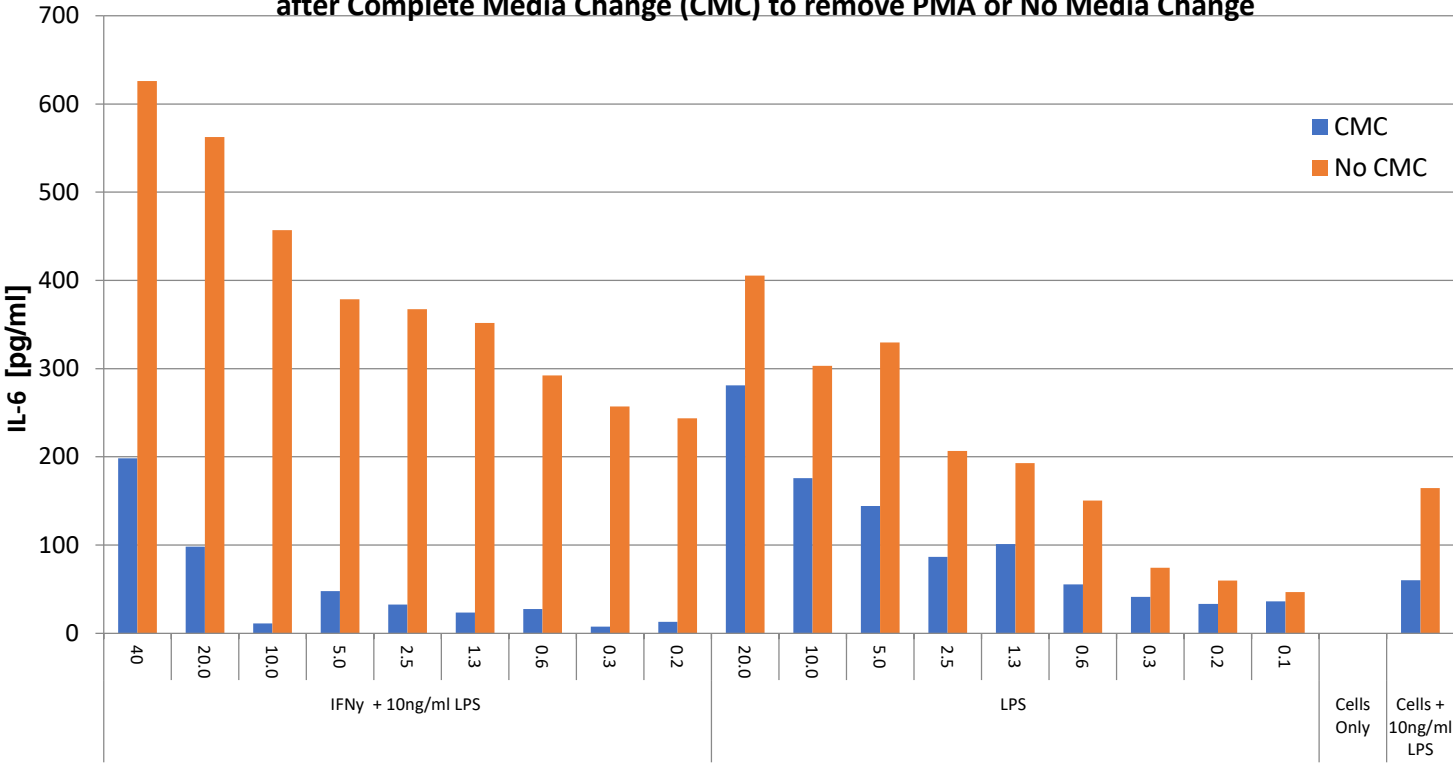
**Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC)
Promega Kit (G7010 ; 12.8-Fold Effector-to-Target)
Using SK-BR-3 Cells**



Herceptin - Drug

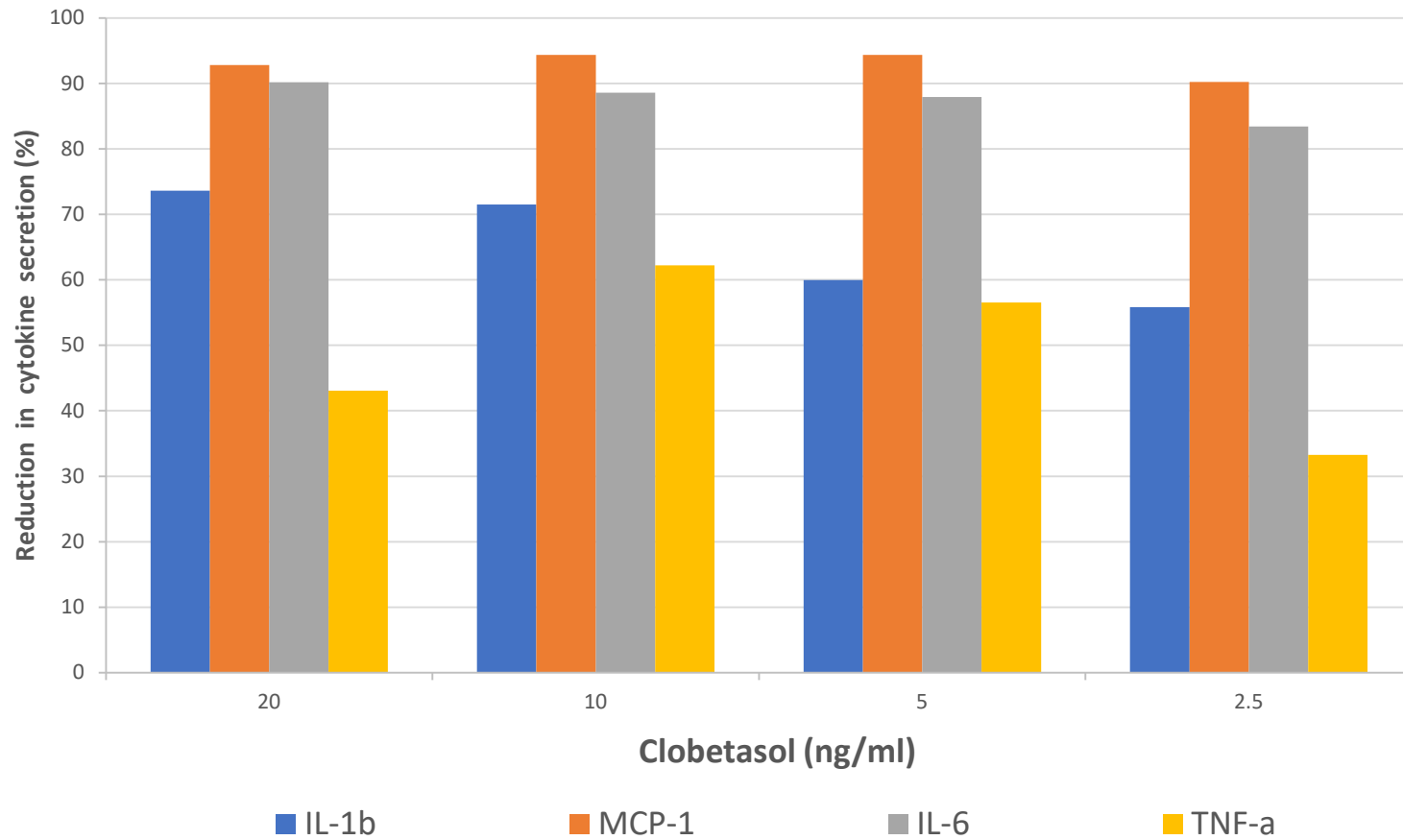
Human IL-6 production by THP-1 cells stimulated with LPS alone or in combination with IFN γ

after Complete Media Change (CMC) to remove PMA or No Media Change

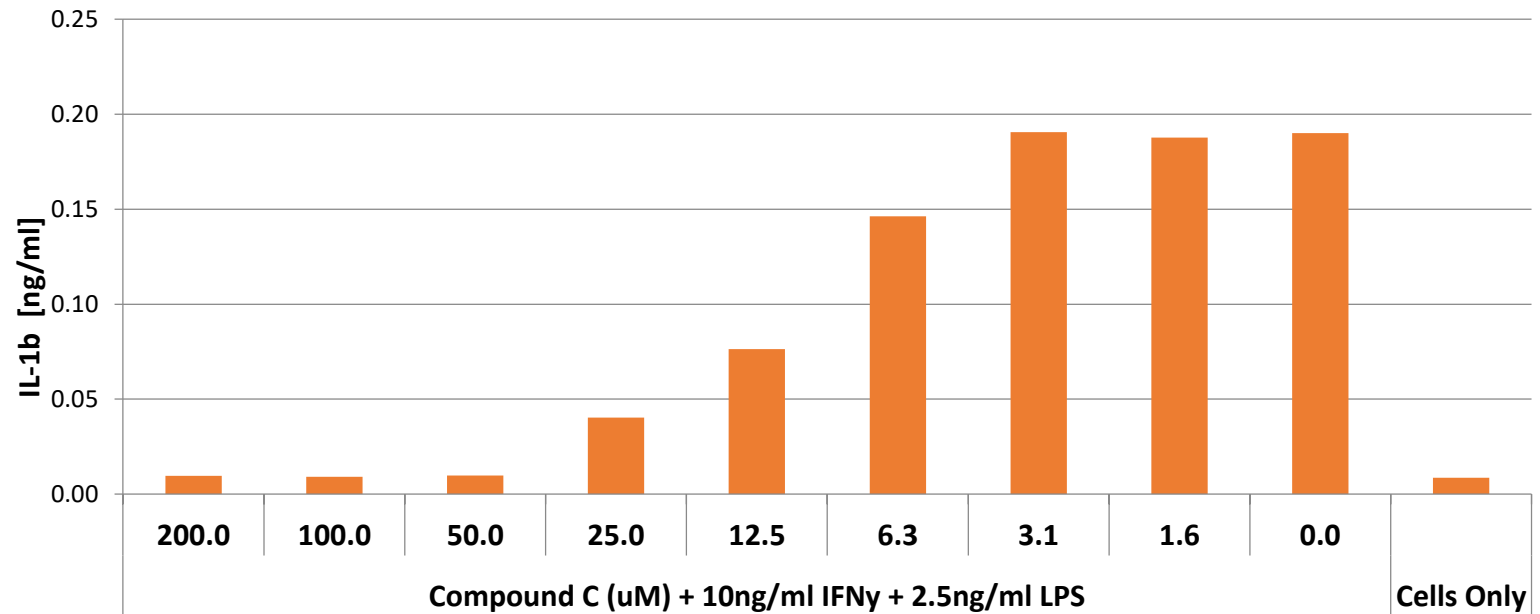


Treatment and Concentration

In-Vitro Model: Differentiated THP1
Positive Control: Clobetasol
Stimulation by: 1.25 ng/ml LPS + 0.5 ng/ml IFN-gamma

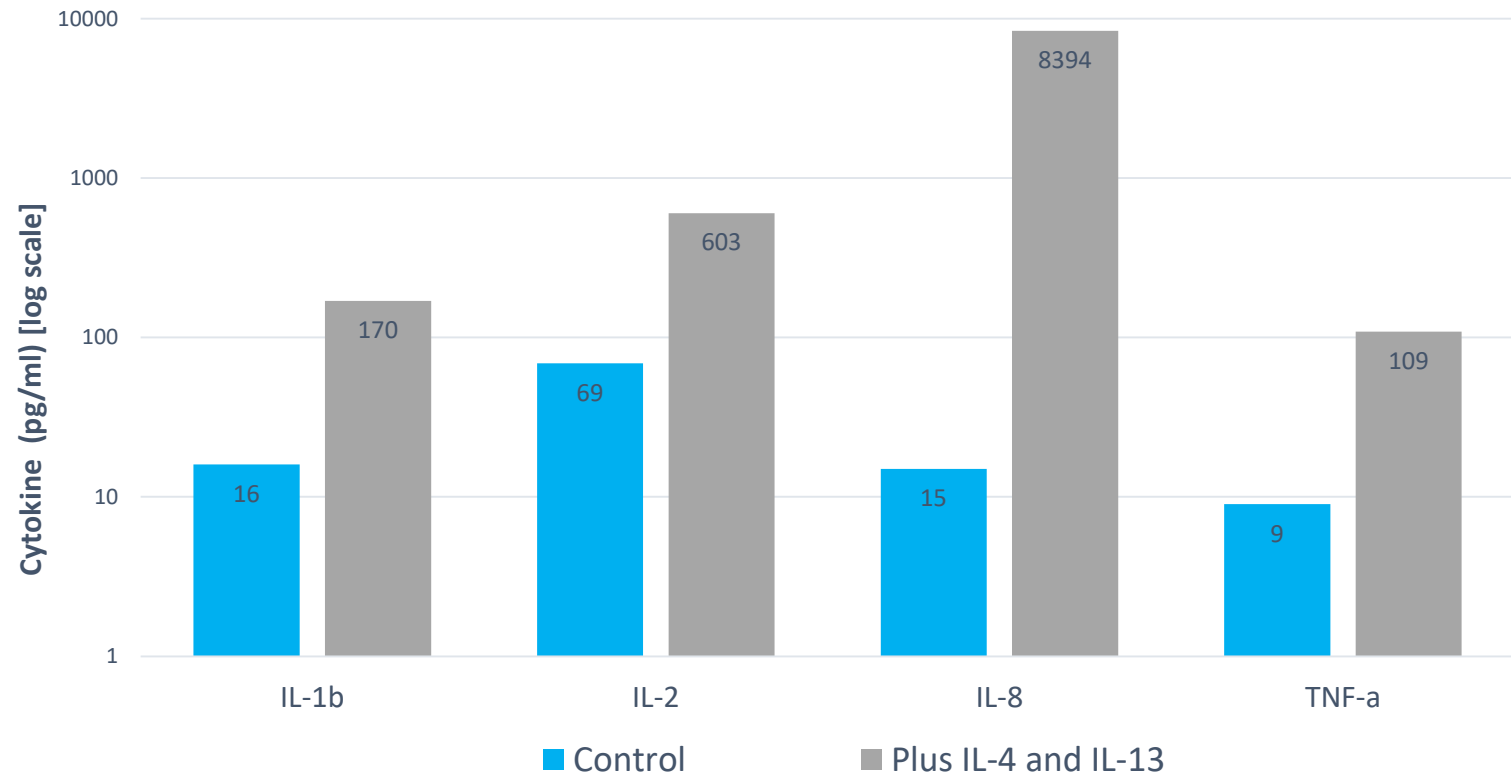


**h-IL-1b Production by THP-1 Cells Treated with Compound C
in Combination with 10ng/ml IFN γ and 2.5ng/ml LPS for 3 Days [M1]
[Pre-Treatment with PMA for 3 days prior to the experiment]**

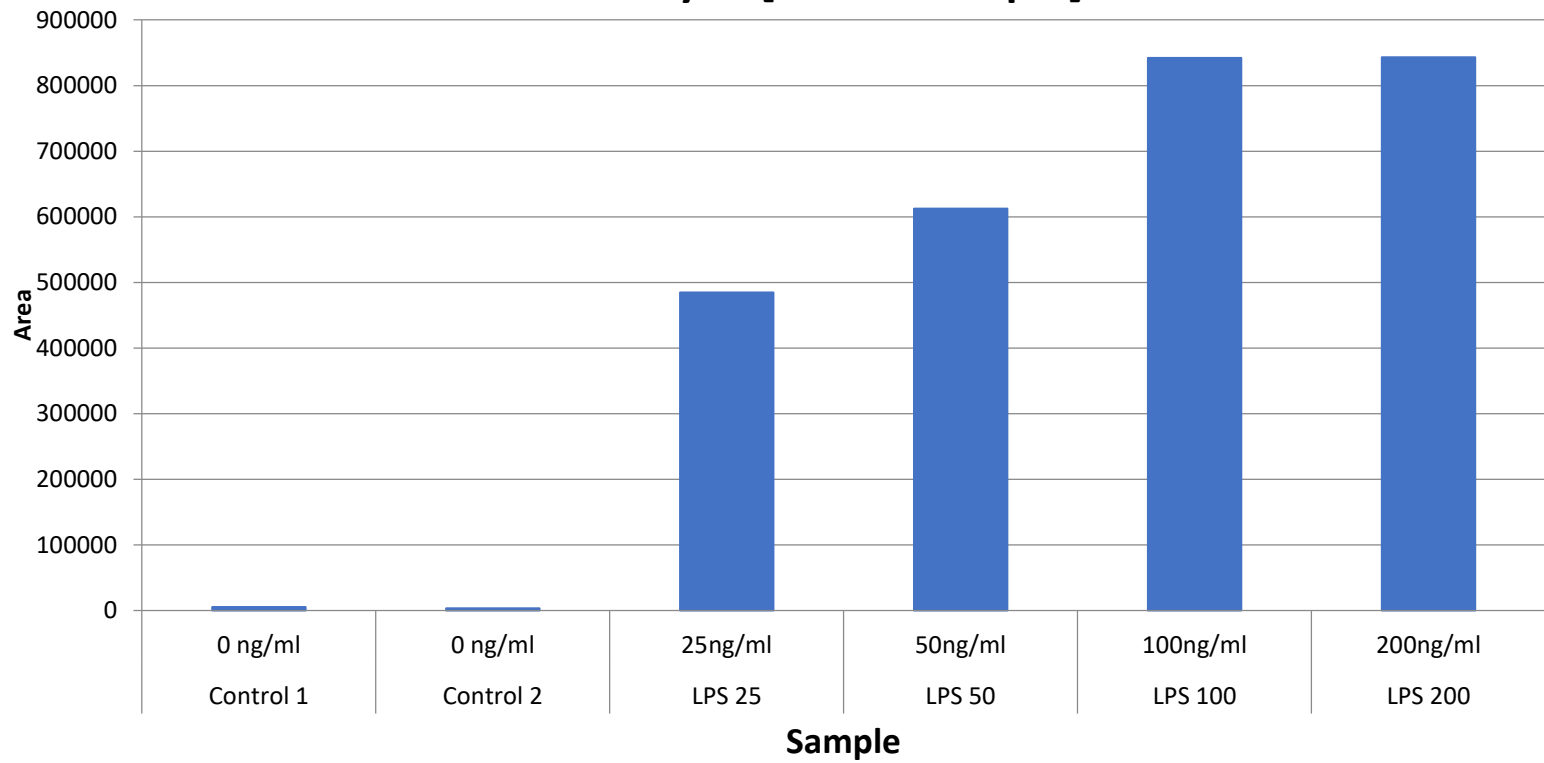


Please note: Up to 100 uM Compound C did not cause any cytotoxicity effect on the cells.

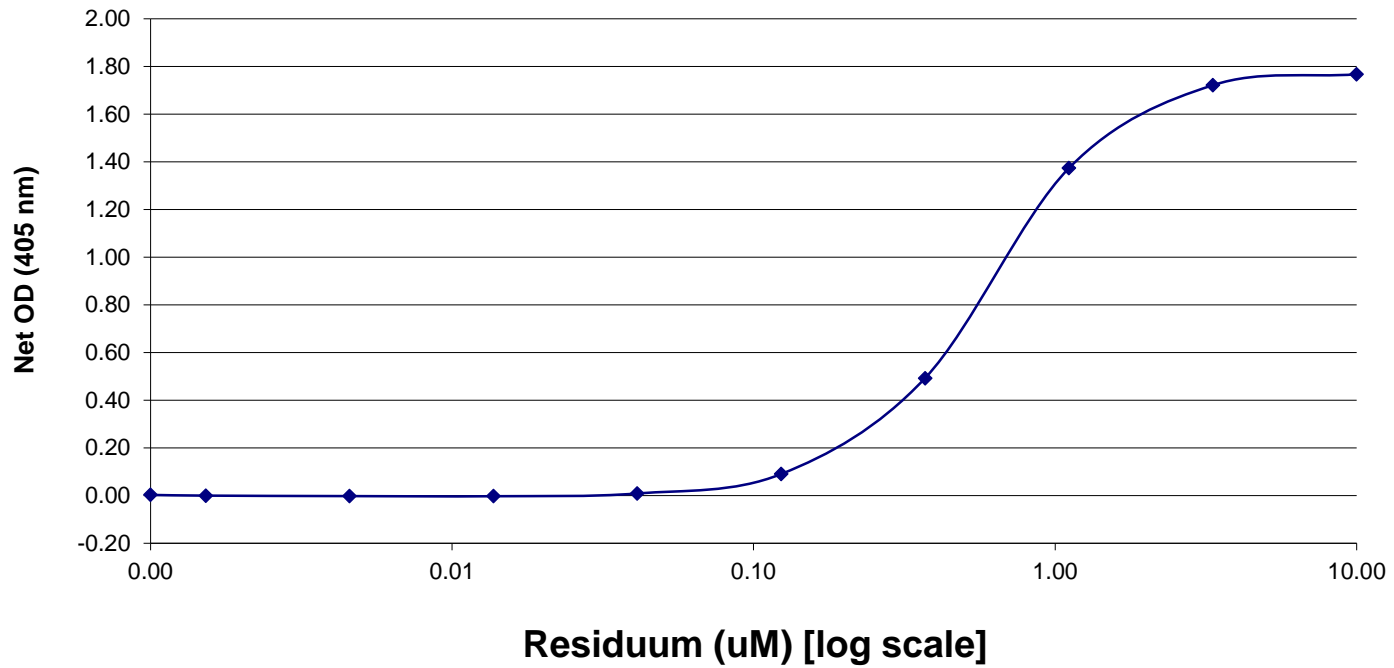
Polarization / Differentiation of THP1 Cells [M2]



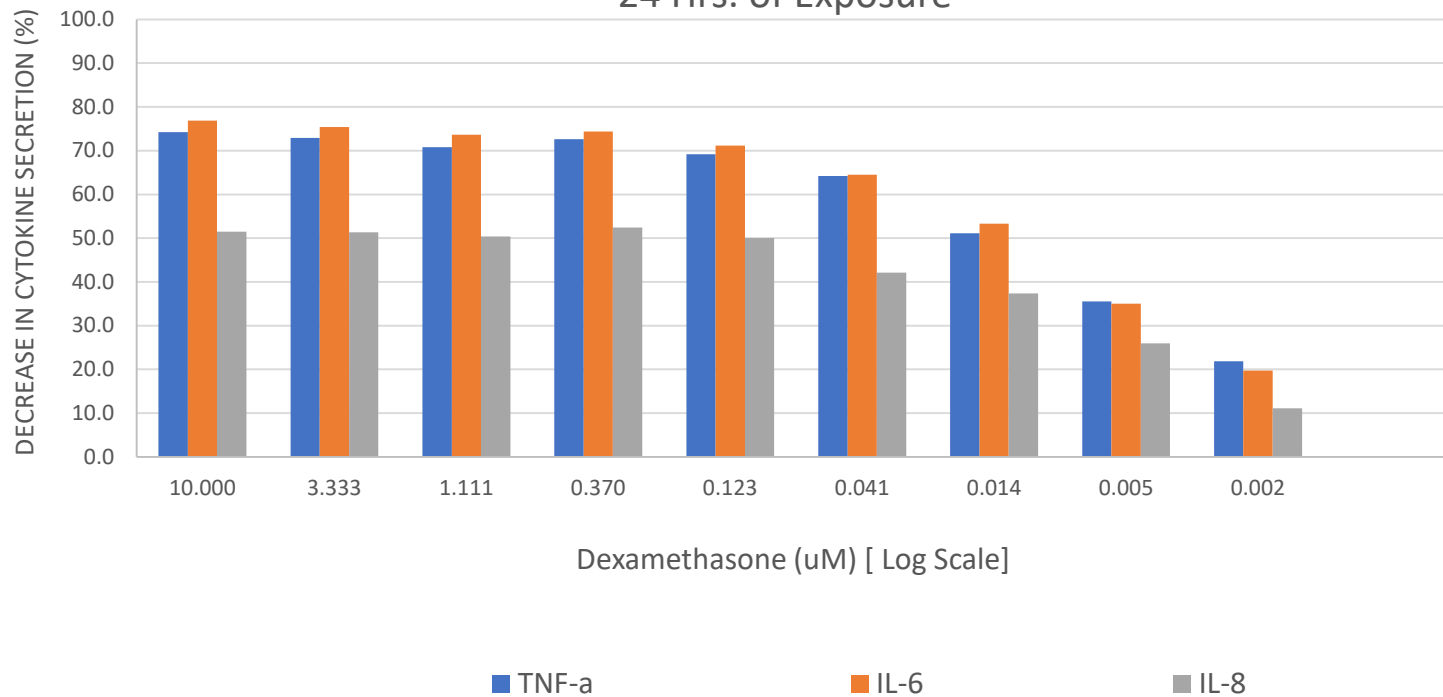
**RAW 264.7 Cells
iNOS Peak Area
WES Analysis [Protein Simple]**



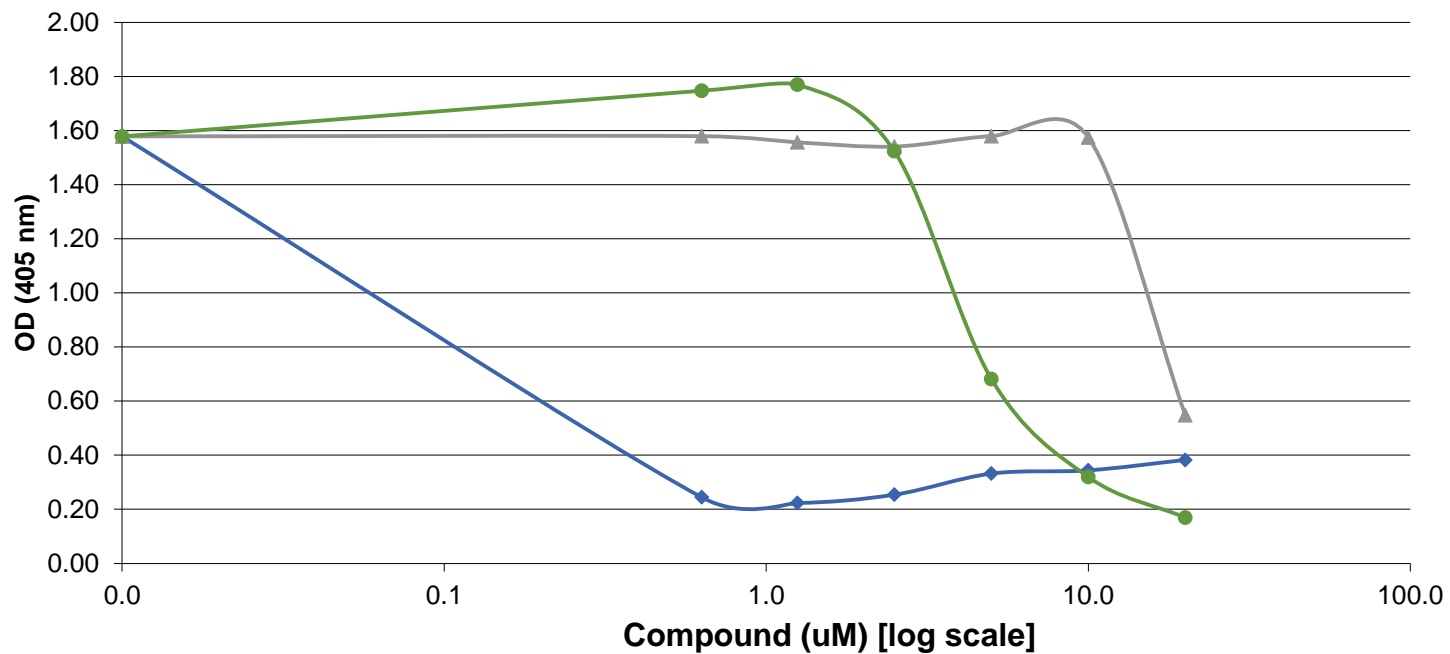
**HEK-TLR7 Cells
Bioassay of Residuum (R-848)
Treatment for 46 Hours
Alkaline Phosphatase Activity**



In-Vitro Inflammation Model
Treatment of human PBMC by 10 ug/ml R-848
Assay Positive Control: Dexamethasone
24 Hrs. of Exposure



**Bioassay STAT-3 Activity using HEK-293 Cell Line
Anti - STAT-3 Activity (in the presence of hIL-6)**

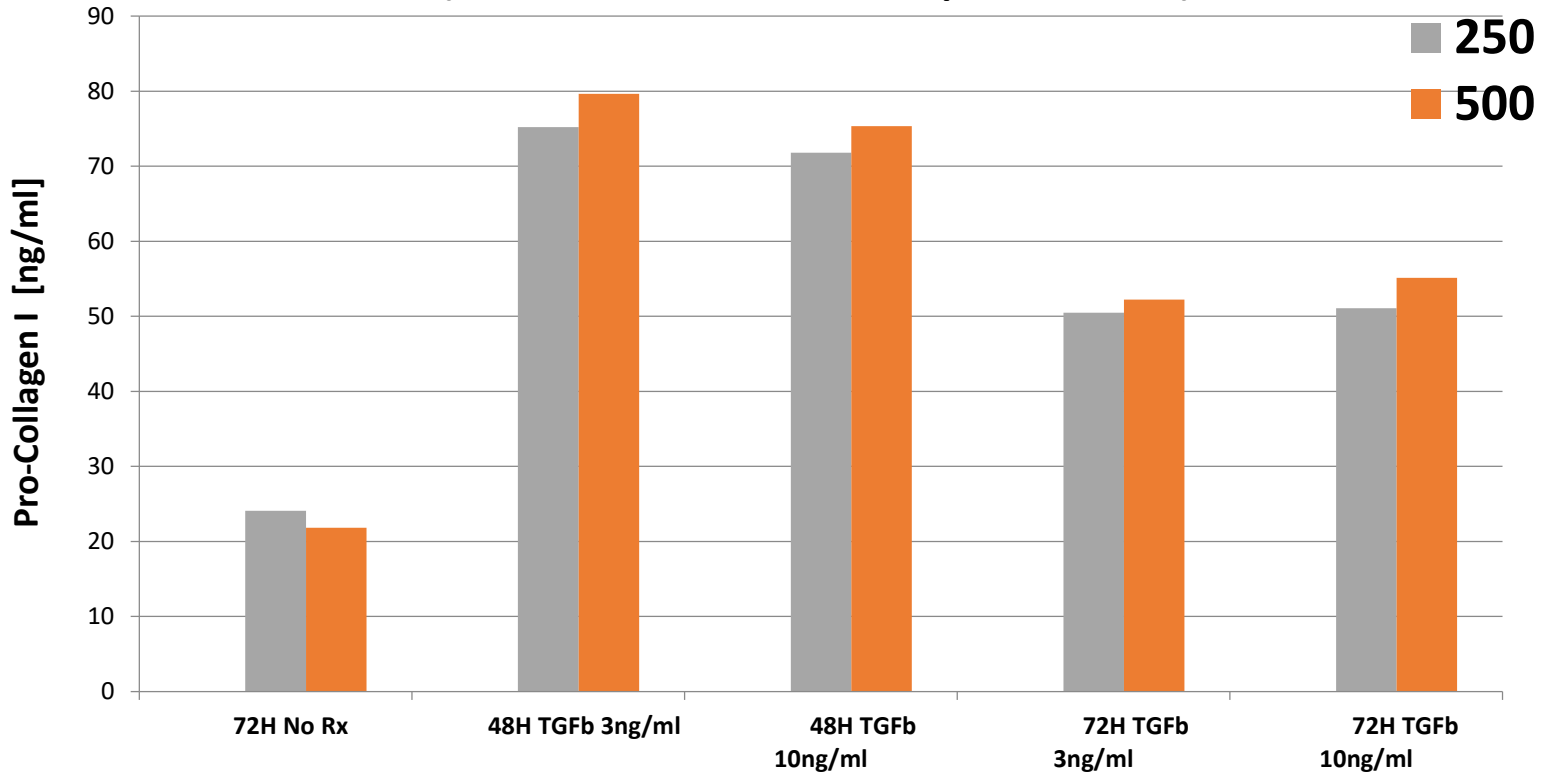


◆ Niclosamide

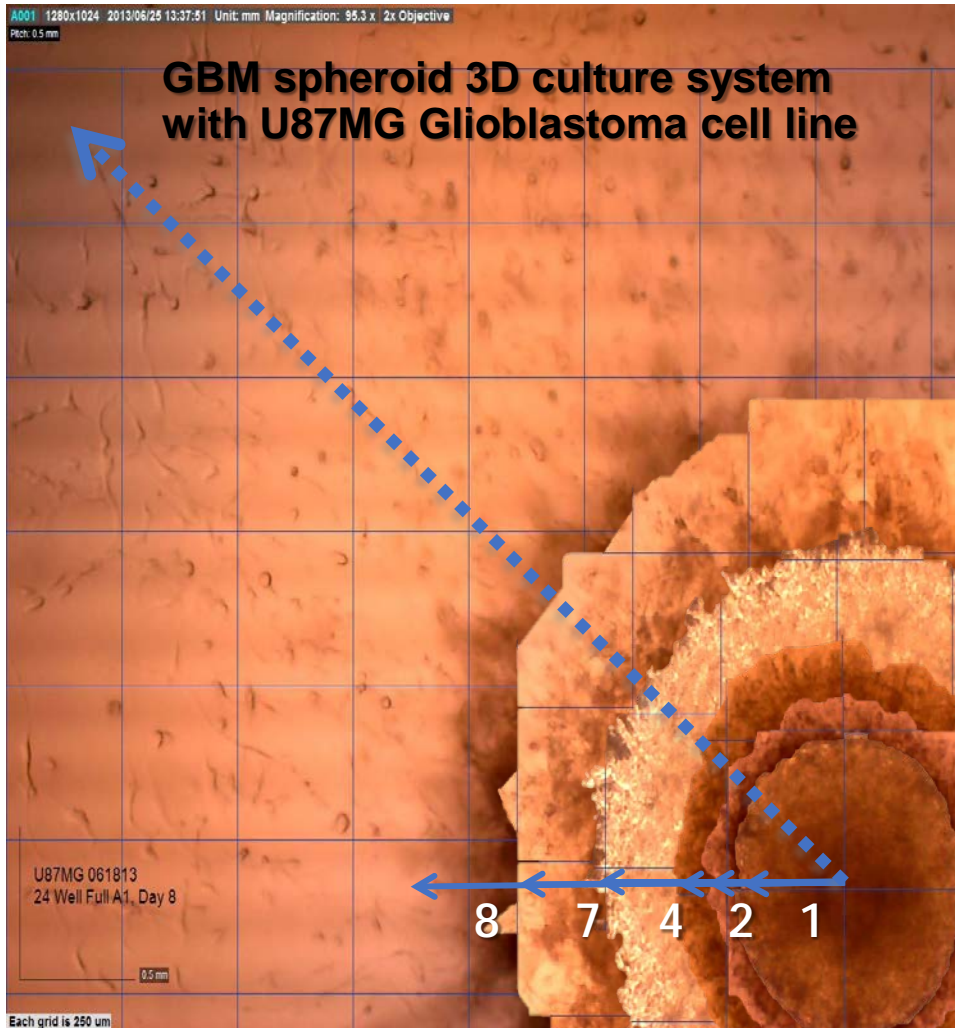
▲ BP-1-102

● FLLL32

**h-Pro-Collagen I Production by human Lung Fibroblast Cells
Treated with 3 and 10 ng/ml TGF-b1 for 48 or 72 Hours
(Diluted 1:250 or 1:500 Fold prior to ELISA)**



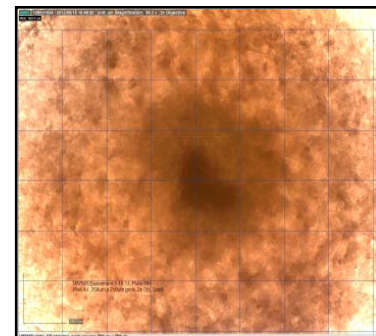
Untreated
GBM



The radial spread in two dimensions is reminiscent of the natural disease. Not shown here is the invasion down into the substrate as well.



Spheroid outgrowth over 8 days
(boxes = 250 um)
No. 1 represents initial spheroid
plated



Clinical Product Development - Case Study: human IL-12 a Novel Radiation Medical Countermeasure

- Proprietary human IL-12 production process was developed by SBH Sciences
- COA established for commercial release to the R&D market
- Neumedicines, Inc. (CA) licensed the technology from SBH Sciences
- In 2008, both companies collaborated to secure a Biomedical Advanced Research and Development Authority (BARDA) contract to develop IL-12 for Acute Radiation Syndrome
- In 2009, SBH Sciences optimized the process, scale-up, and transferred the technology to a GMP manufacturing
- 2011 – Submission of IND and First-In-Human for Toxicity studies

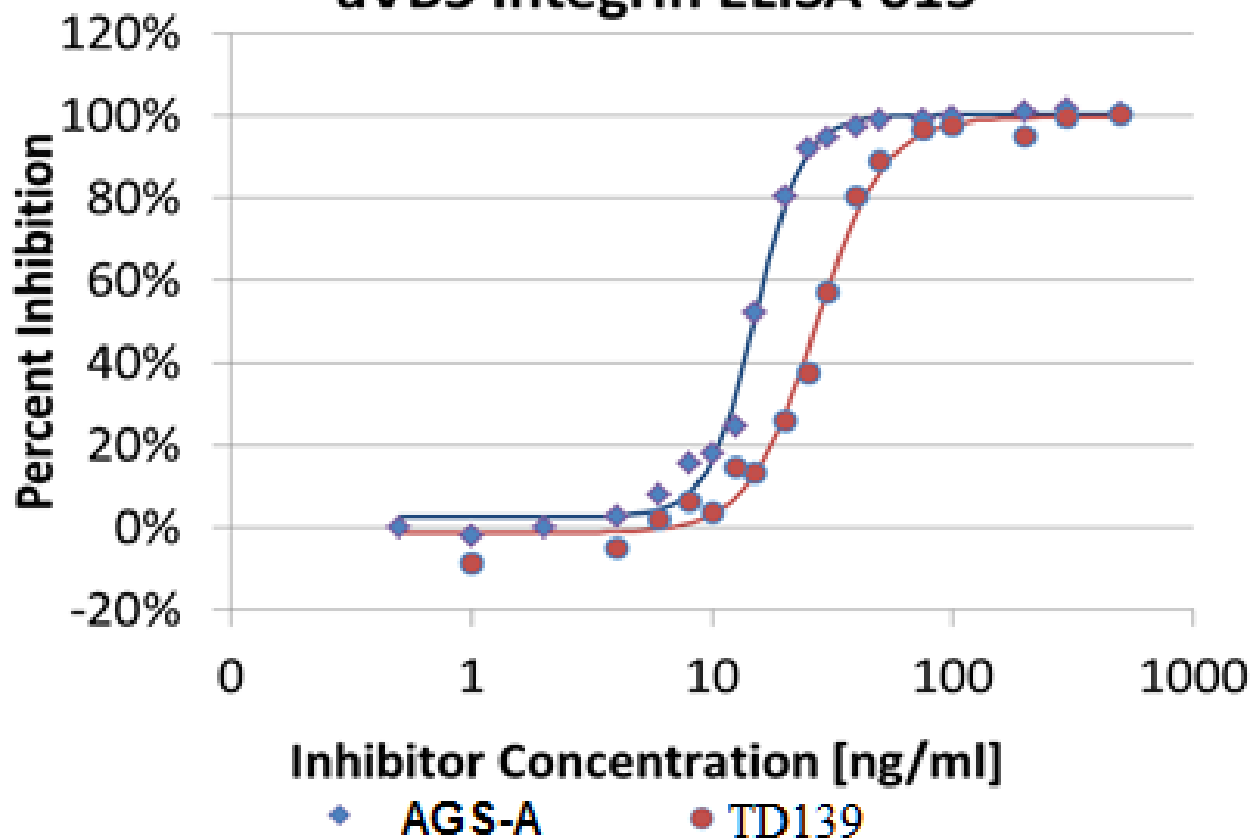


January 2014
Galectin Therapeutics and SBH Sciences,
announce the formation of
Galectin Sciences, LLC,
a Collaborative Venture for Research and Development
Galectin Inhibitors
for Oral Administration

5 Provisional Patents have been submitted
2 Issued Patent

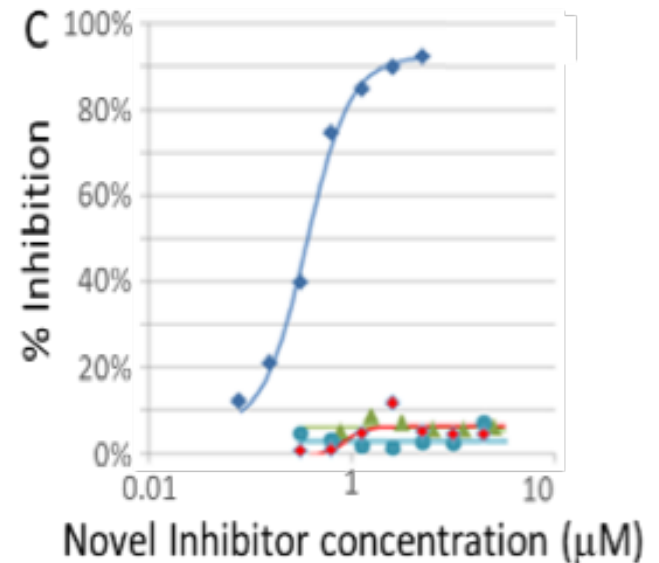
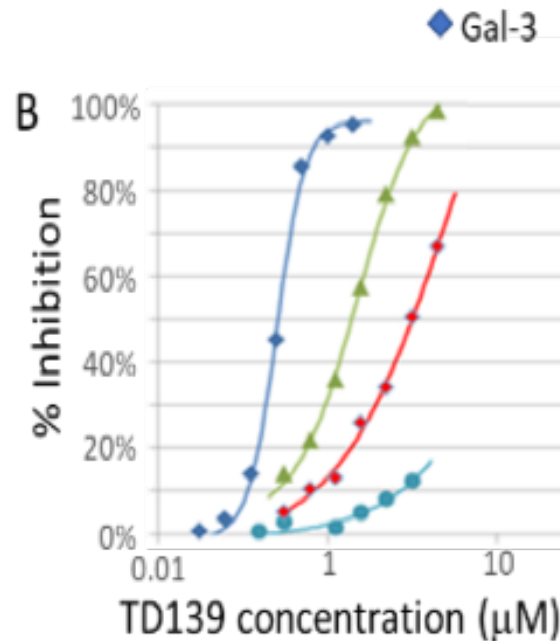
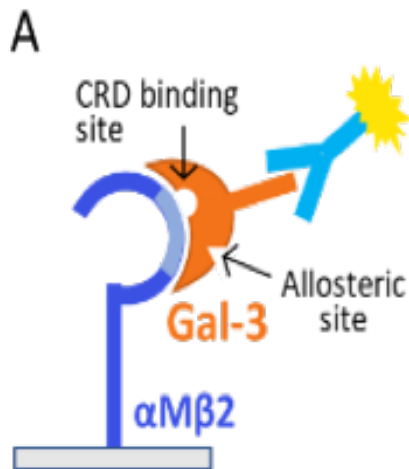


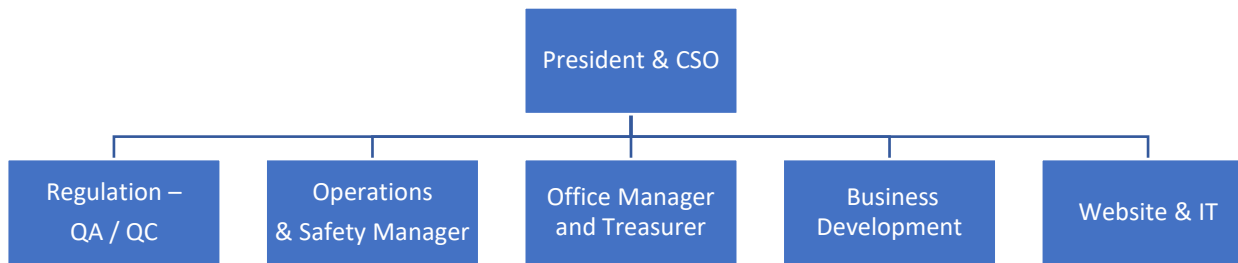
aVB3 Integrin ELISA 015

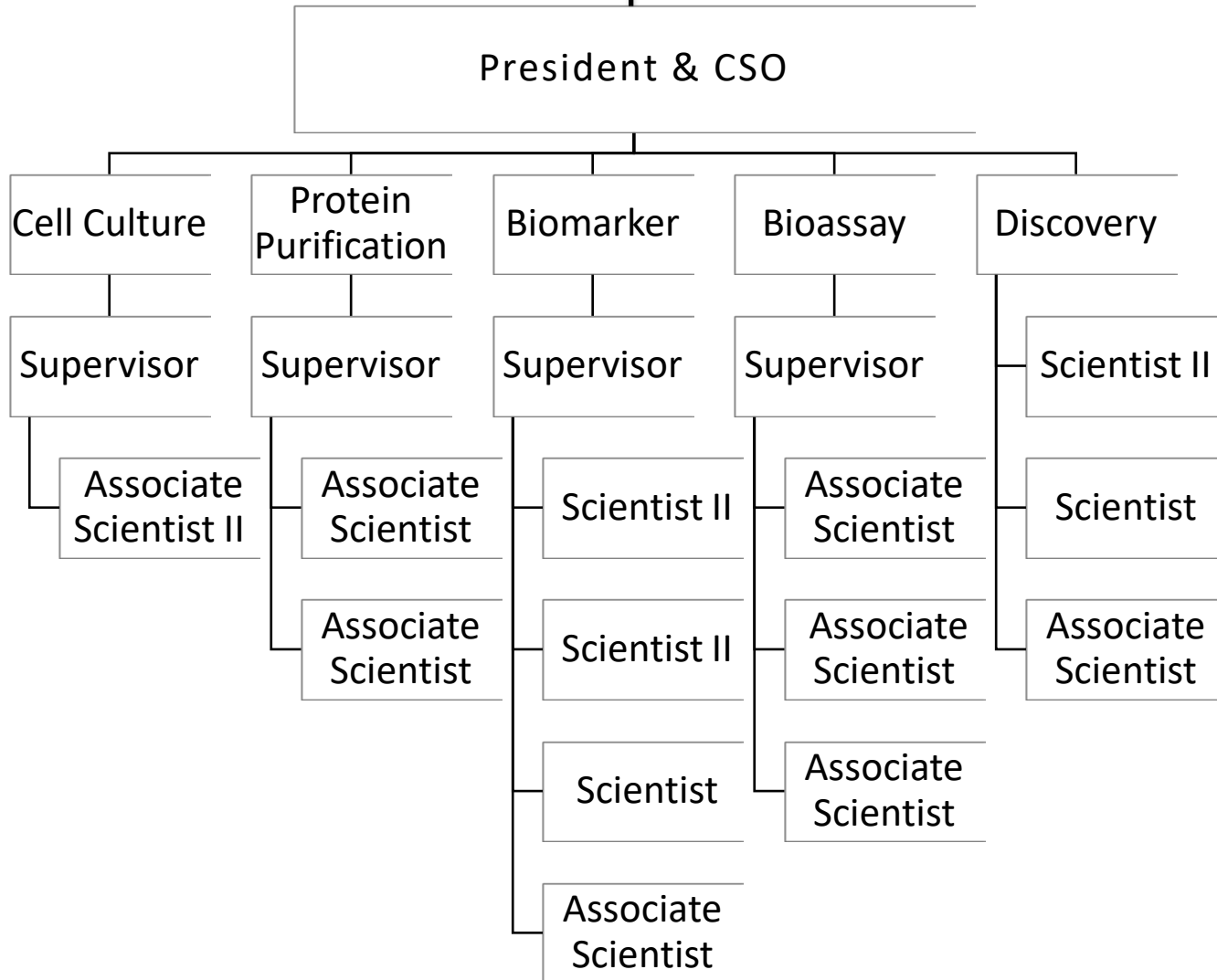


Improved specificity of Galectin-3 modulators

- In a receptor-based ELISA (A), TD139 inhibits binding of multiple galectins to integrin $\alpha M\beta 2$ (B). An allosteric Gal-3 inhibitor (G229) shows significantly greater specificity for Gal-3 over other galectins (C).







Create Your Competitive Advantage
Advance your product from early development
to pre-clinical and clinical Smoothly
SBH Sciences → SBH Diagnostics



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