Innovative Bioincubator and Pre-Clinical Contract Research Organization

Offering Extensive Research Discovery Products and Services

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Co-Founder, President, and CSO

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Accomplishments

- SBH Sciences is an innovative Bioincubator and Contract Research Organization (CRO).
- We have been operating for over 27 years, and have been providing over 350 biotechnology companies with high-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 in July of 2019.

Cell-Based Products

SBH Sciences has produced and commercialized 30 recombinant cytokines, 8 enzymes, and 40 Monoclonal Antibodies. Please contact for custom requests.

Recombinant Cytokines

- Activin-A
- Bone Morphogenic Proteins (BMP-2, BMP-7)
- CD22
- Growth Factors (HGF)
- GDF-15/MIC-1★
- IGF-BPs (IGF-BP-6)
- Interferon (IFN-b)
- Interleukins (IL-12, IL-23)★★
- Soluble receptors (s-IL-6R)
- TGF-Beta (TGF-b2)
- TNF Receptor (HVEM-Fc)

Enzymes

- 8 Glycosyltransferases

Monoclonal Antibodies

- Anti-TNF-alpha
- Anti-VEGF
- Anti-Gelectin-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

- 11 Biomarker Analysis platforms
- Cell-based Assays, over 500 cell lines
  - Cytokine, chemokine, oncology, inflammation, and TLRs
- T-Cell Activation
- Molecular Biology
- Gene and Cell Therapy
- Monoclonal Antibodies Development (in collaboration with Caerus)
- Development of Biologics
  - Cell Culture
  - Protein Purification
  - Analytical HPLC
  - ELISA / RBA (e.g., PD1/2 binding assay)
  - FACS
  - Formulation
  - Stability
  - Anti-Drug Antibody (ADA) assay

Comprehensive Biomarker Analysis Services

- SBH has 11 state-of-the-art biomarker analysis platforms including Luminex, MSD, Ella, Jess, SMCxPRO, FACS, and qRT-PCR.
- SBH is the first CRO to offer automated simple western blot services on “Peggy Sue”, “Wes”, and “Jess” (Protein Simple).
- SBH Diagnostics, our strategic partner company, is a Contract Research Organization providing biomarker analysis under CLIA certification and GLP guidelines.
- We assist companies and enable translation from non-regulated to regulated environment (clinical trials).

Eleven Platforms to assist with Biomarker analysis

BD Accuri C6
BD Biosciences

CLAIROstar
BMG Labtech

Ella
ProteinSimple

IsoLight
IsoPlexis

Jess
ProteinSimple

Luminex 200
Luminex

Peggy Sue
ProteinSimple

QuickPlex SQ 120
MSD

SMCxPRO
MilliporeSigma

StepOne PCR
Applied Biosystems

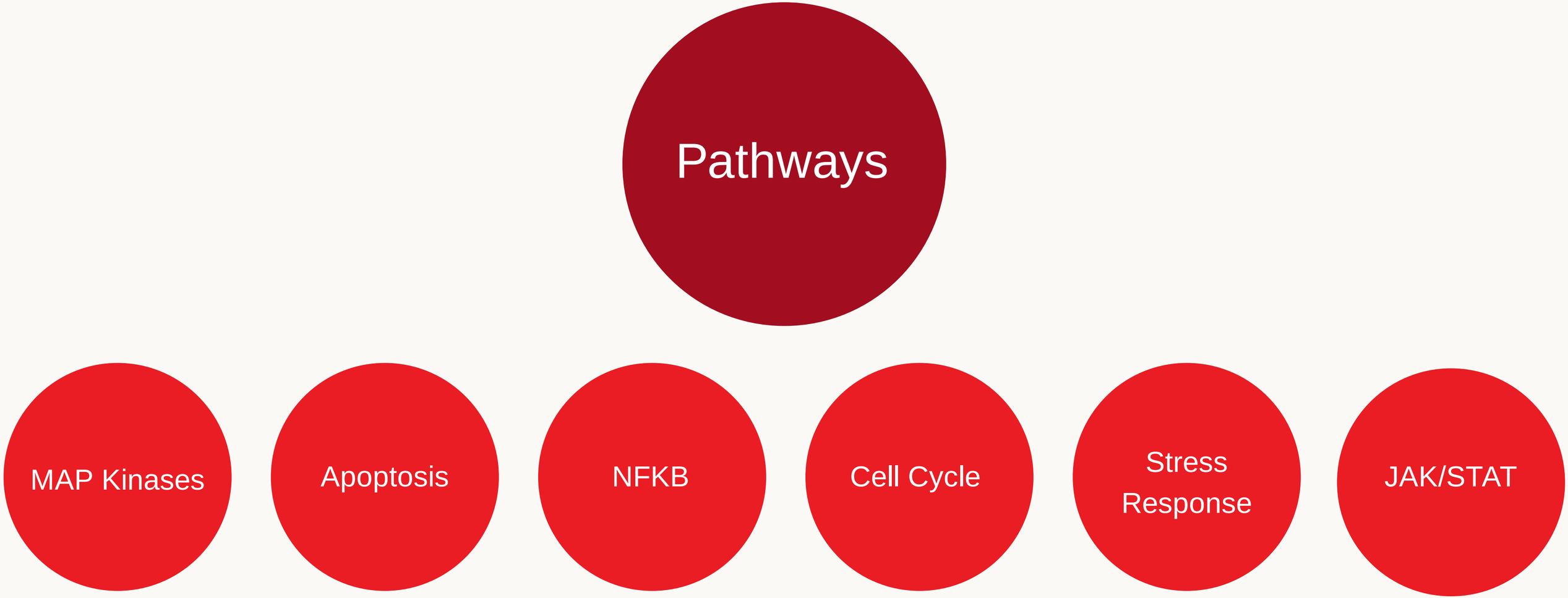
Wes
ProteinSimple

Bioanalytical Services

Analysis of biological matrix such as blood, serum, plasma, urine and tissue samples

- ELISA-Based Assays
- Receptor / Ligand - Binding Assay
- Anti-Drug Antibodies (ADA)
- Immunogenicity neutralizing antibody assays (Nab)
- Analytical HPLC
- Chromatography
- Pharmacokinetics (PK) and Pharmacodynamics (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

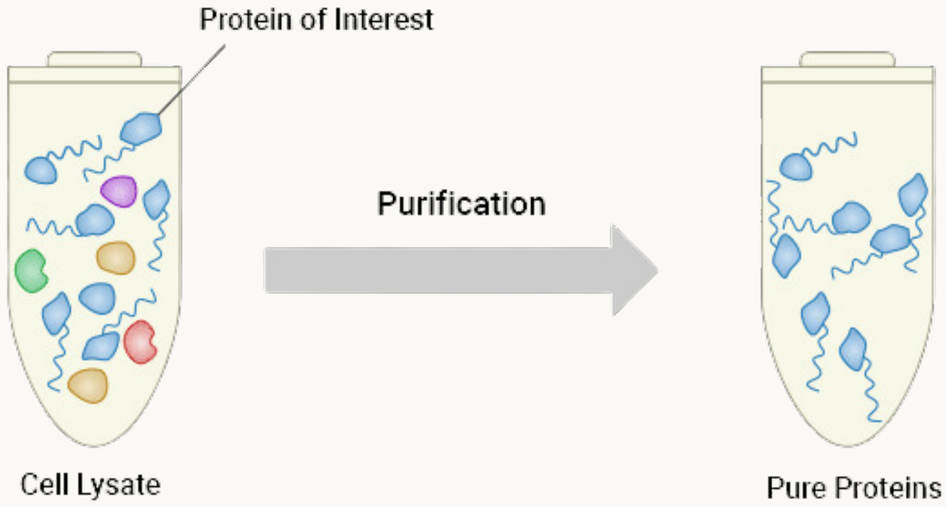
Mammalian and Insect Cells

- 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 cytokines stimulation
- Customized services (10 human primary cells and > 500 mammalian cell lines are currently available)
- Creation of new stable cell lines
- 2D and 3D assay capabilities including Organoids (in collaboration with Bonds Biosystems)
- Irradiation experiments (combination of anti-cancer therapy)
- Preparation and isolation of Exosomes
- Commercial production of cell culture spent media (8 years; 19 lots; > 150 L each lot)

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

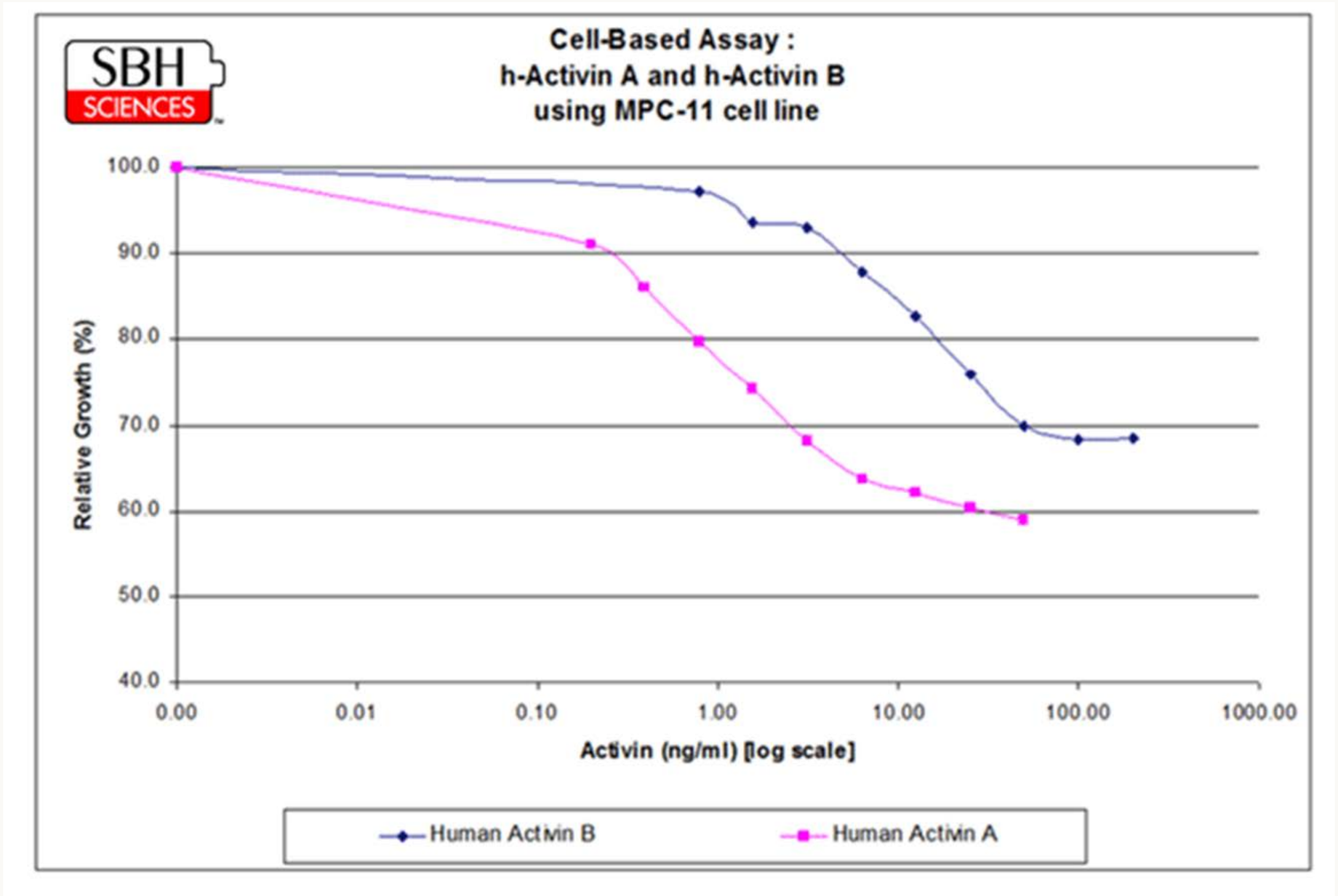


Cell-Based Assay Capabilities

- SBH Sciences is best positioned to assist you in therapeutic areas such as inflammation, oncology, and fibrosis
- 350 cell-based assays to measure cytokine activity (cytokine-induced proliferation, cytokine-induced killing, cytokine release assays, and cytokine neutralization)
- GPCR activation to determine chemokine activity (e.g., IL-8, GRO, MCP1)
- Screening of therapeutic antibodies for specific activity which includes receptor binding assays, ADCC, ADCP, ADC, CDC assay, and immunocytokines
- 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)

Cell-Based Assay Capabilities (Continued)

- 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 activates h-STING and results in the secretion of IFN-alpha that enhances anti-cancer activity]
- TLRs activity [e.g., cytokine induction by TLR agonists]
- Microglial Activation
- Exosome uptake by human macrophages


SBH
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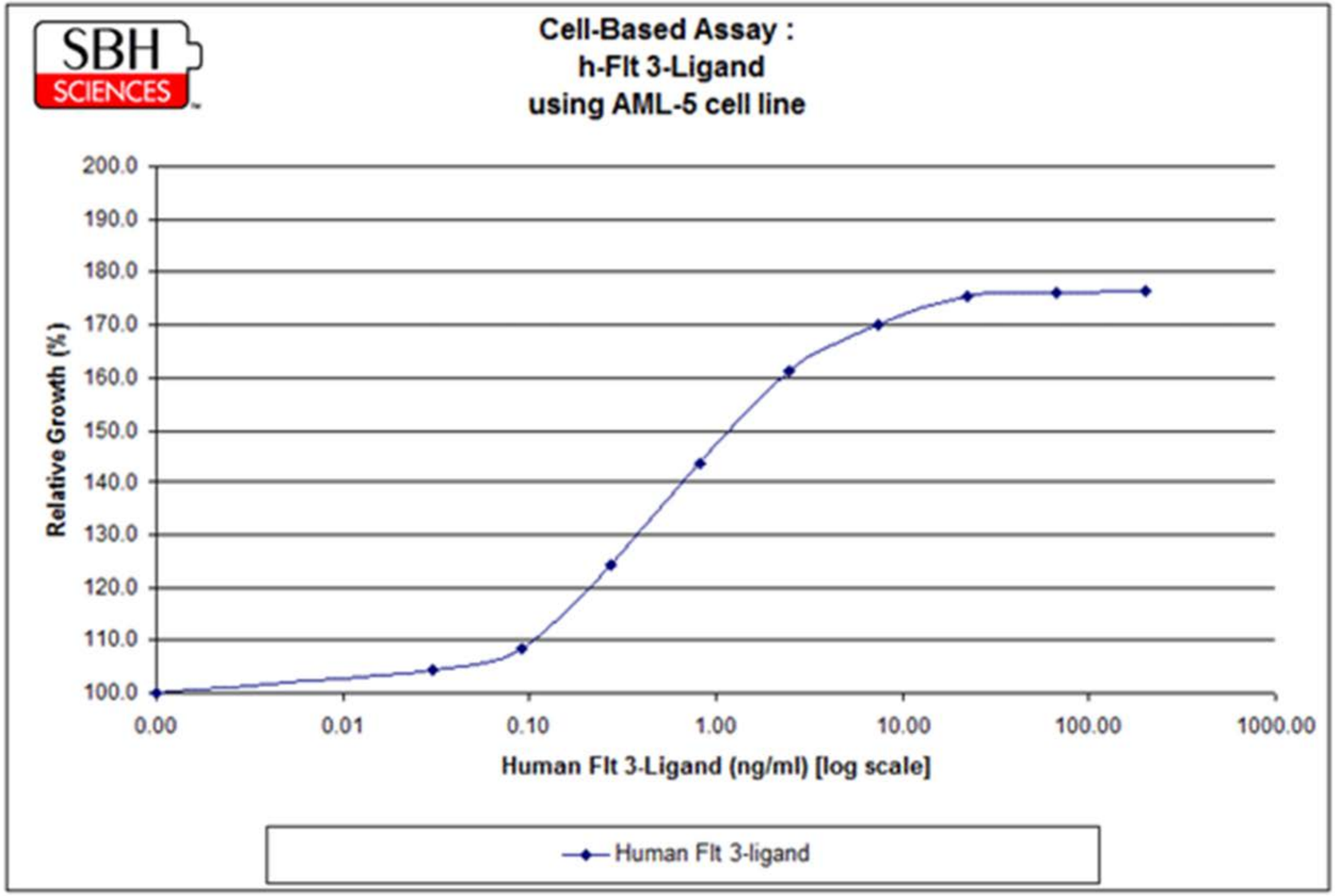
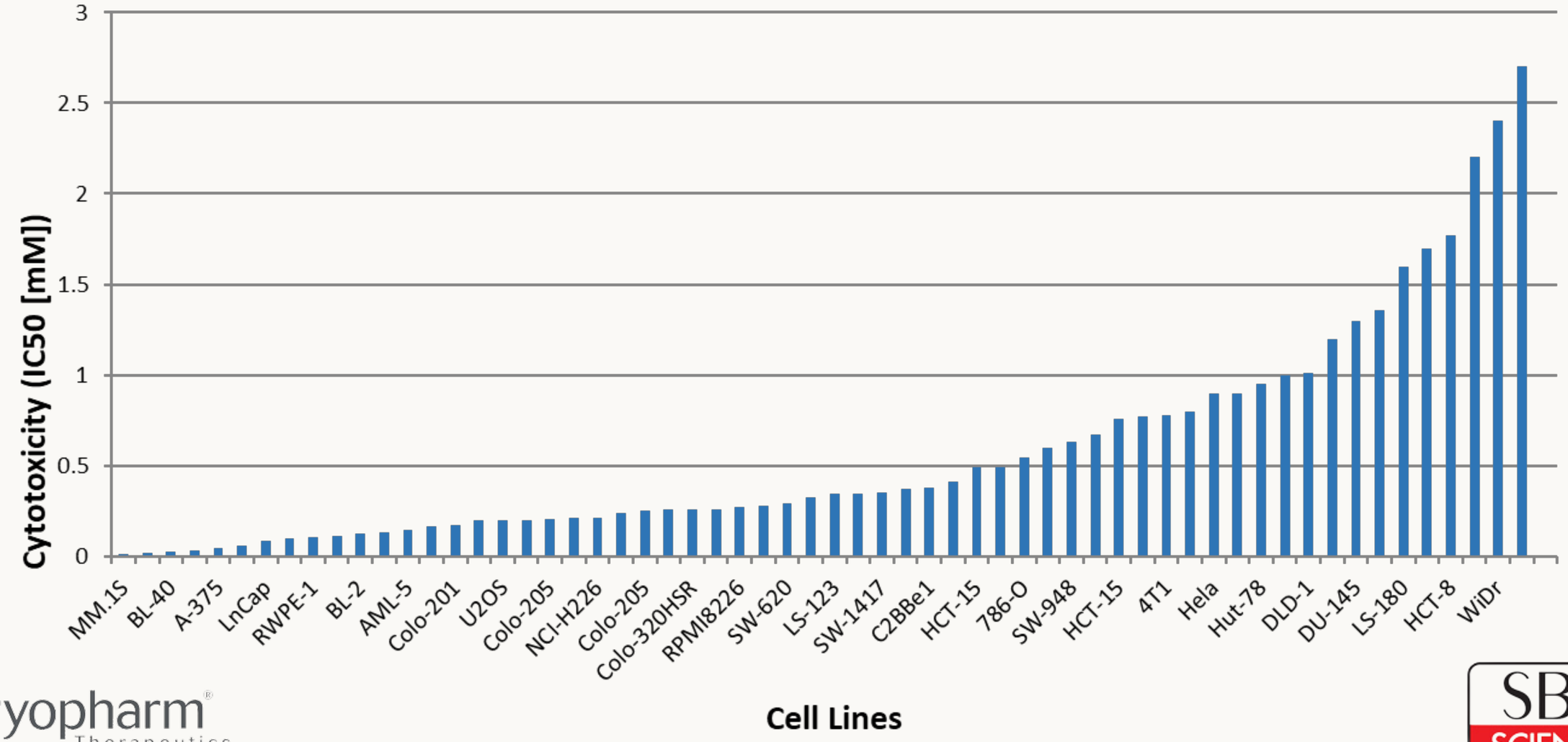
Cell-Based Assay :
h-Activin A and h-Activin B
using MPC-11 cell line
100.0
90.0
80.0
70.0
60.0
50.0
40.0
Relative Growth (%)
0.00
0.01
0.10
1.00
10.00
100.00
1000.00
Activin (ng/ml) [log scale]
Human Activin B
Human Activin A


SBH
SCIENCES
Cell-Based Assay :
h-Flt 3-Ligand
using AML-5 cell line
Relative Growth (%)
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
0.00
0.01
0.10
1.00
10.00
100.00
1000.00
Human Flt 3-Ligand (ng/ml) [log scale]
Human Flt 3-ligand

Cancer Cell Cytotoxicity

370 human cancer cell lines are ready for immediate studies



Karyopharm® Therapeutics

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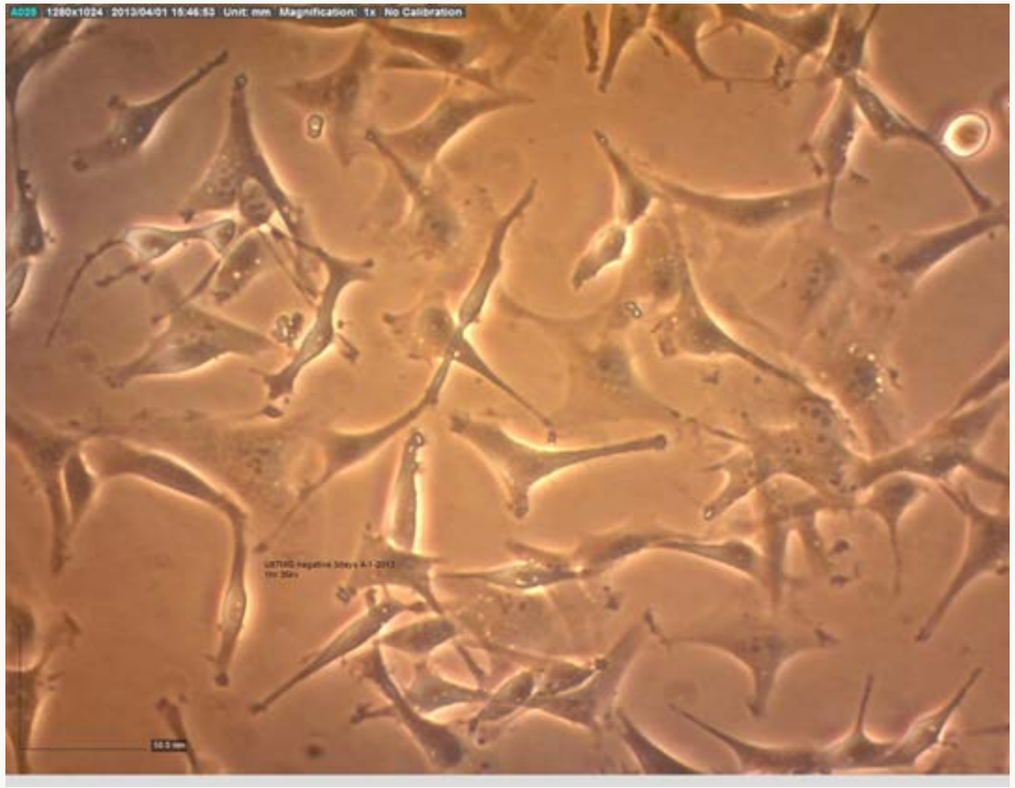
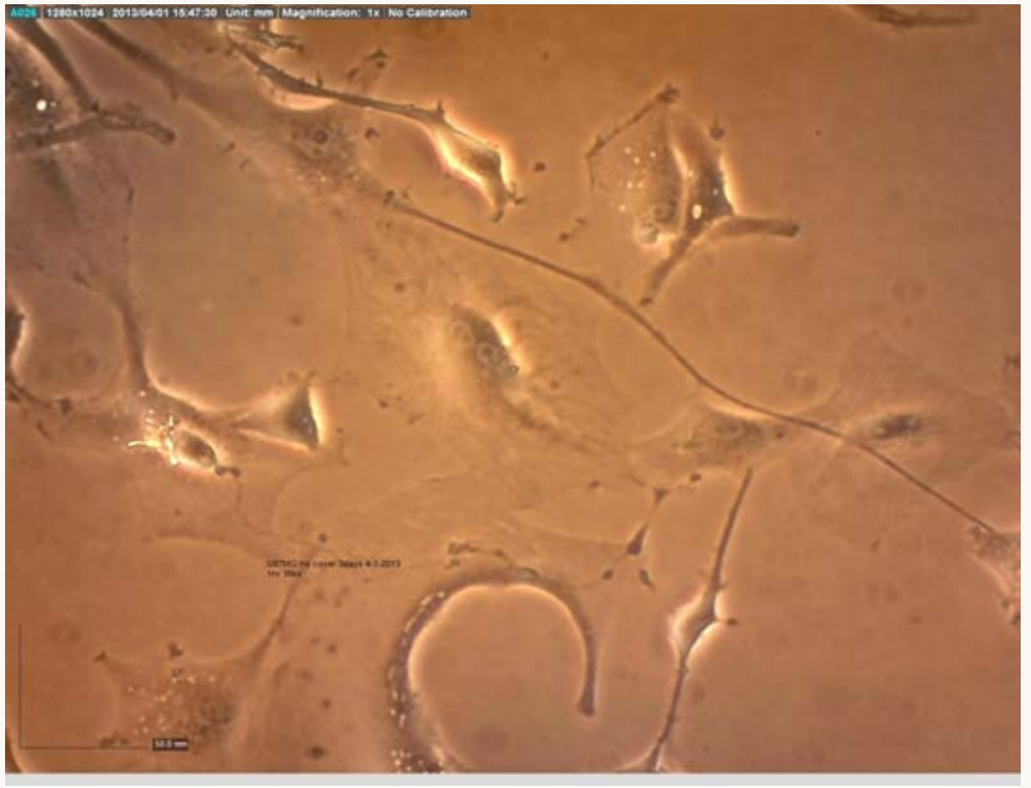
Irradiation Capability

U87MG cell line

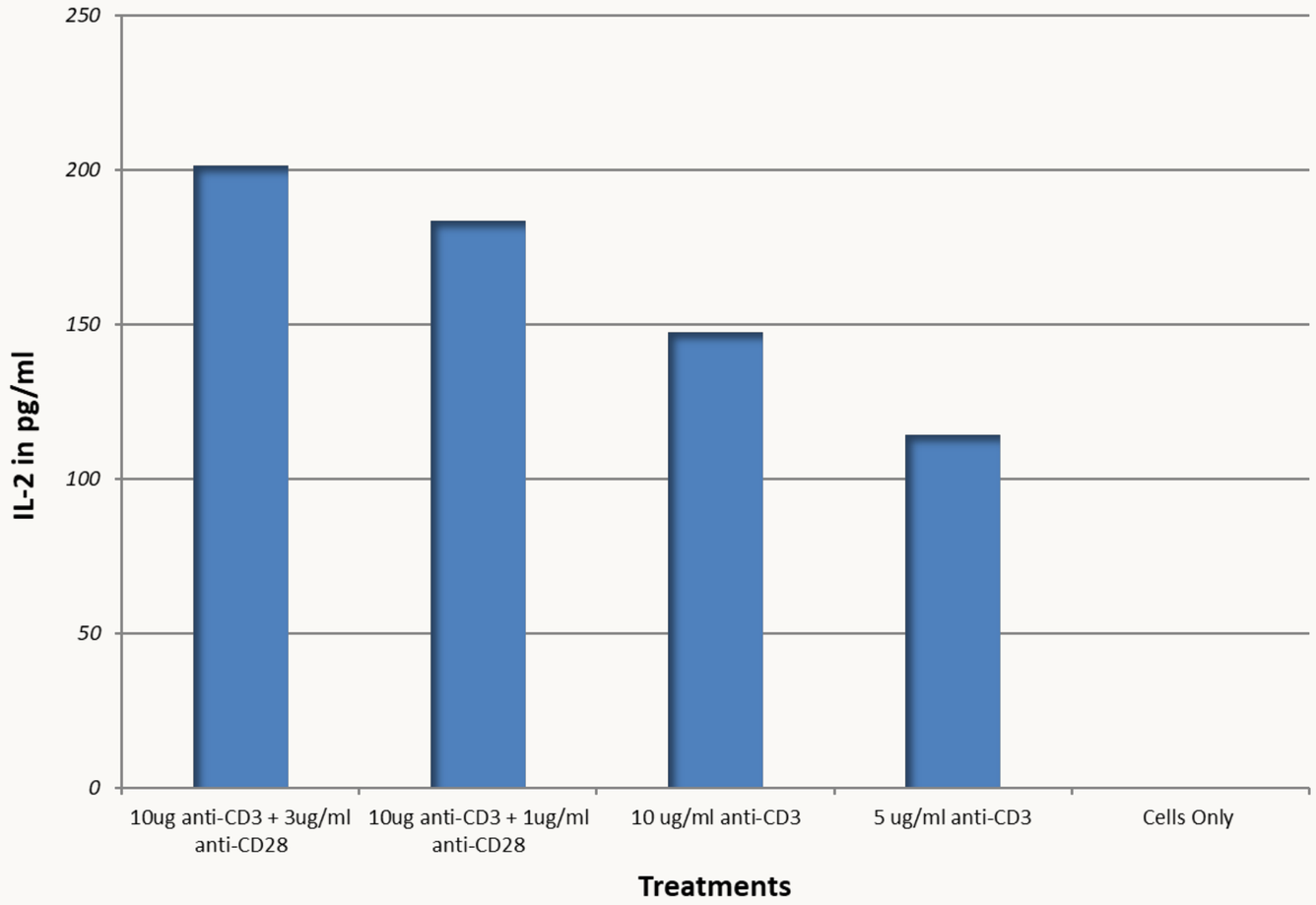




Low-dose radiation can cause cell morphology changes in U87MG as a post-radiation model system.

T-Cell Activation

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



Drug Development Solutions

Examples of discovery projects supported by SBH Sciences in the last 3 years

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.

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Drug Development Solutions

Examples of discovery projects supported by SBH Sciences (continued)

VI. Optimization of adeno-associated virus (AAV) vector design and function in cell lines, primary cells, and 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 particles containing CpG-A DNA to stimulate TLR9 activity.

XIII. Screening of hundreds of peptides against multi-targets (e.g., TL1A).

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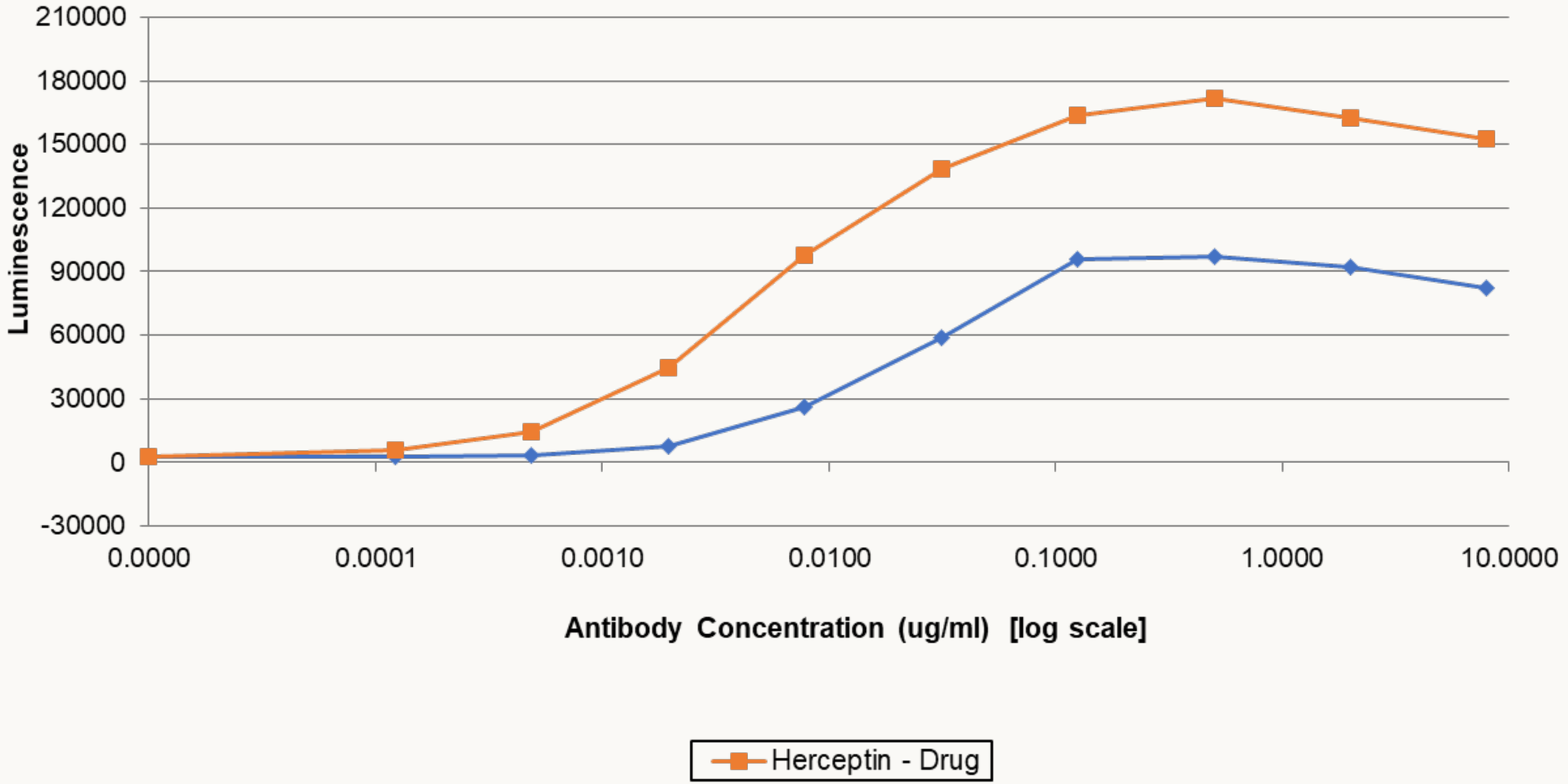
Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC)

Promega Kit (G7010; 12.8-Fold Effector-to-Target) Using SK-BR-3 Cells



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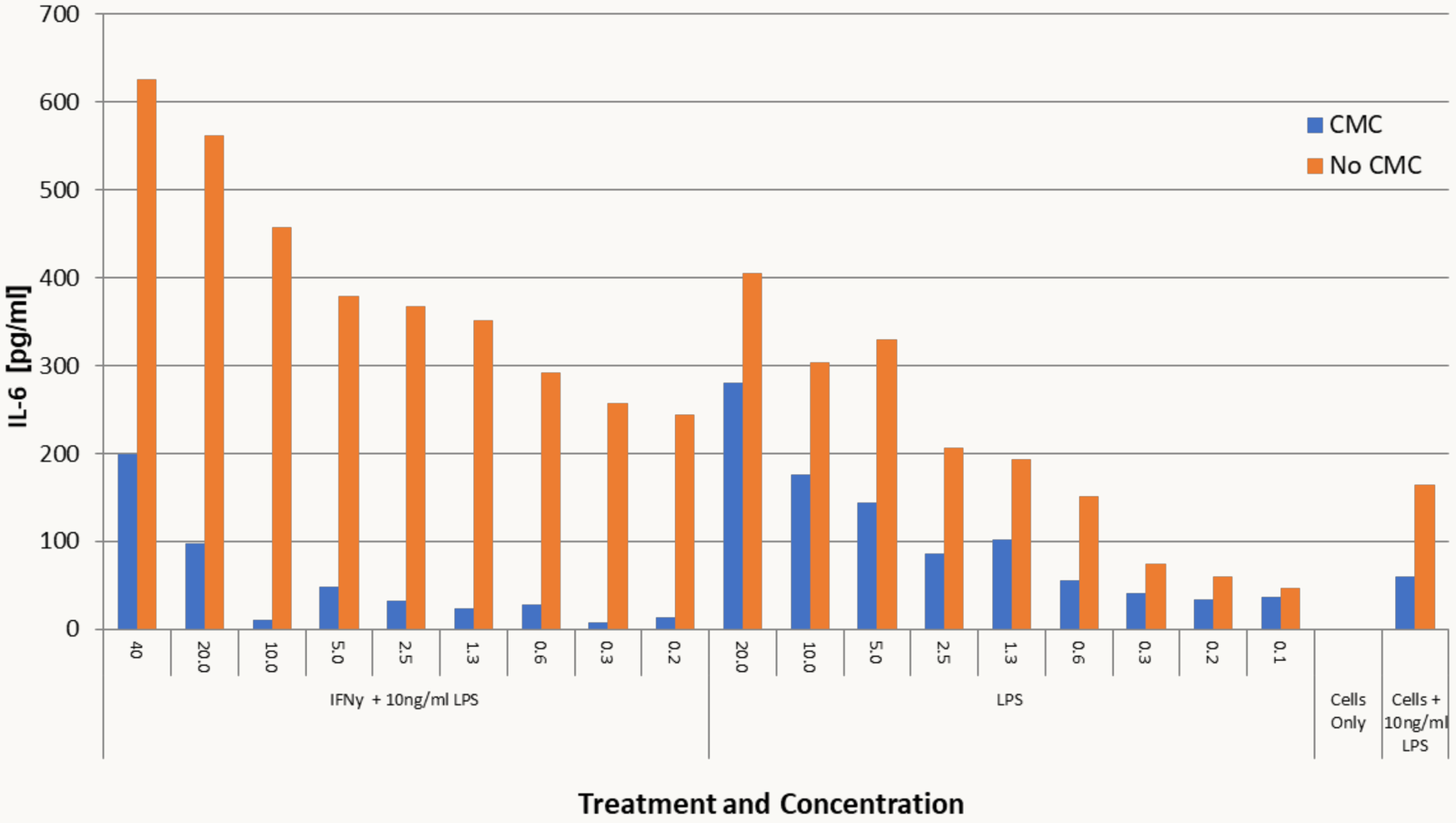
Human IL-6 secretion by THP-1 cells stimulated with LPS alone or in combination with IFN-gamma after Complete Media Change (CMC) to remove PMA or No Media Change



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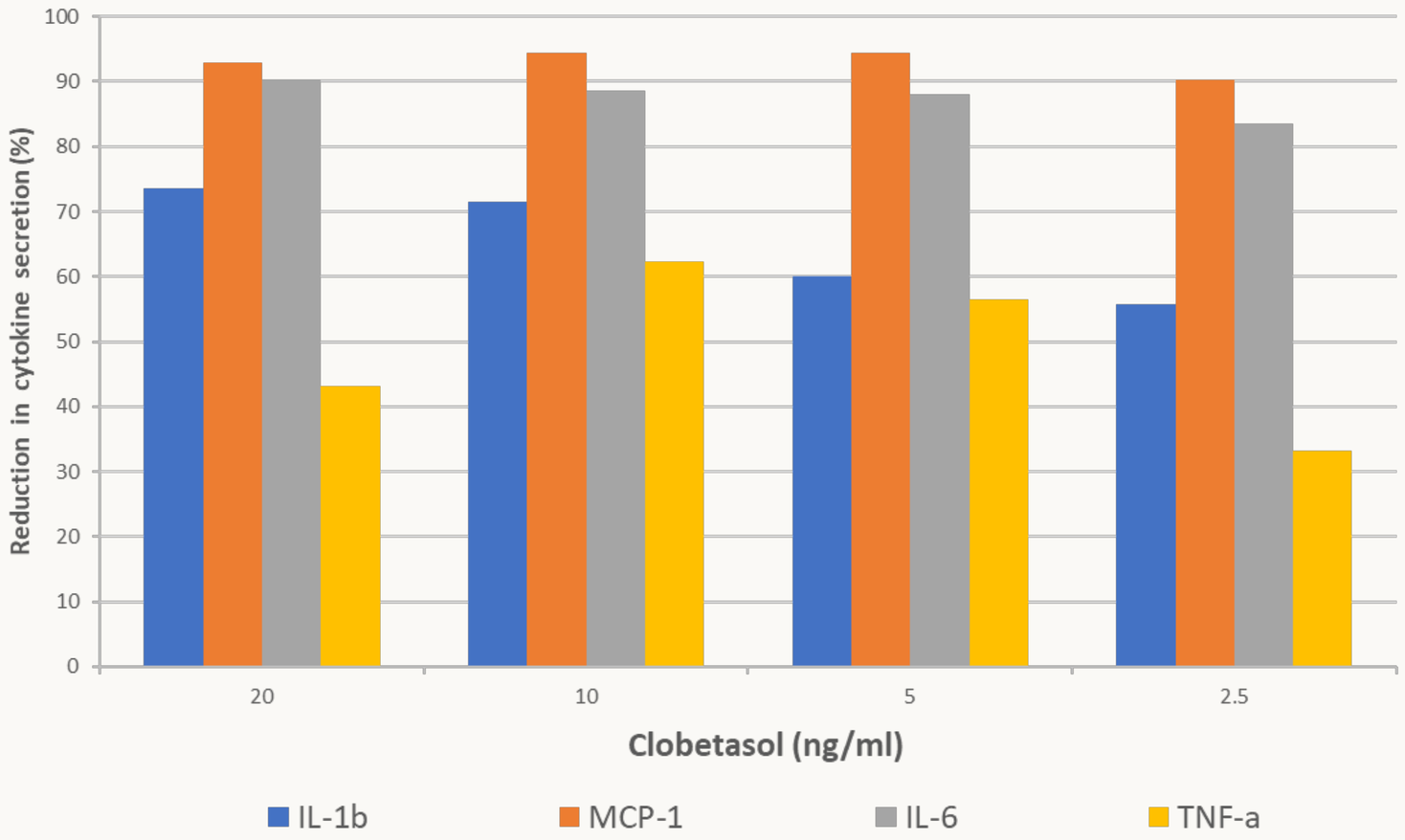
In-Vitro Inflammation Model 1

Differentiated THP1, Positive Control: Clobetasol

Stimulation by: 1.25 ng/ml LPS + 0.5 ng/ml IFN-gamma

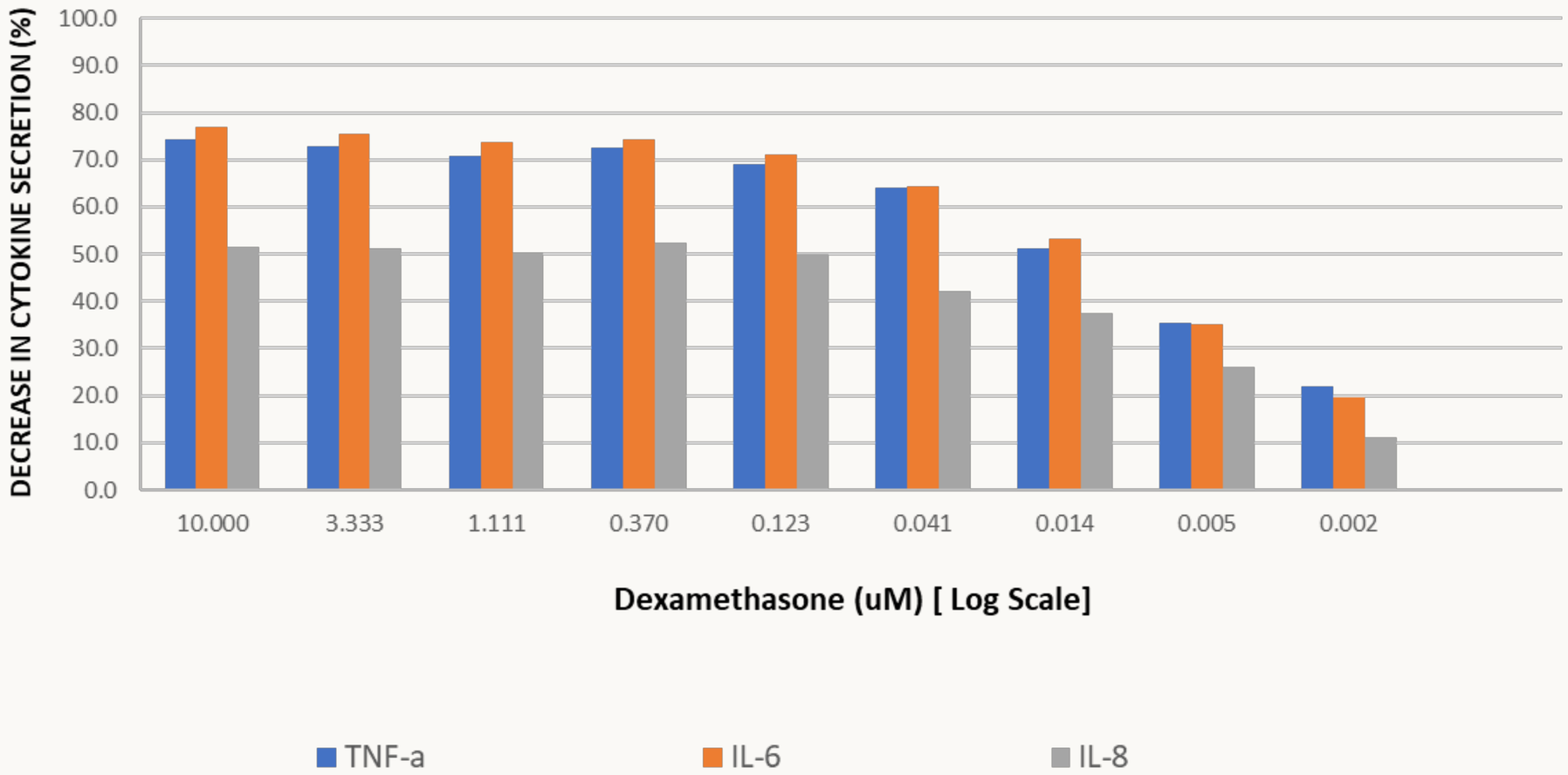


In-Vitro Inflammation Model 2

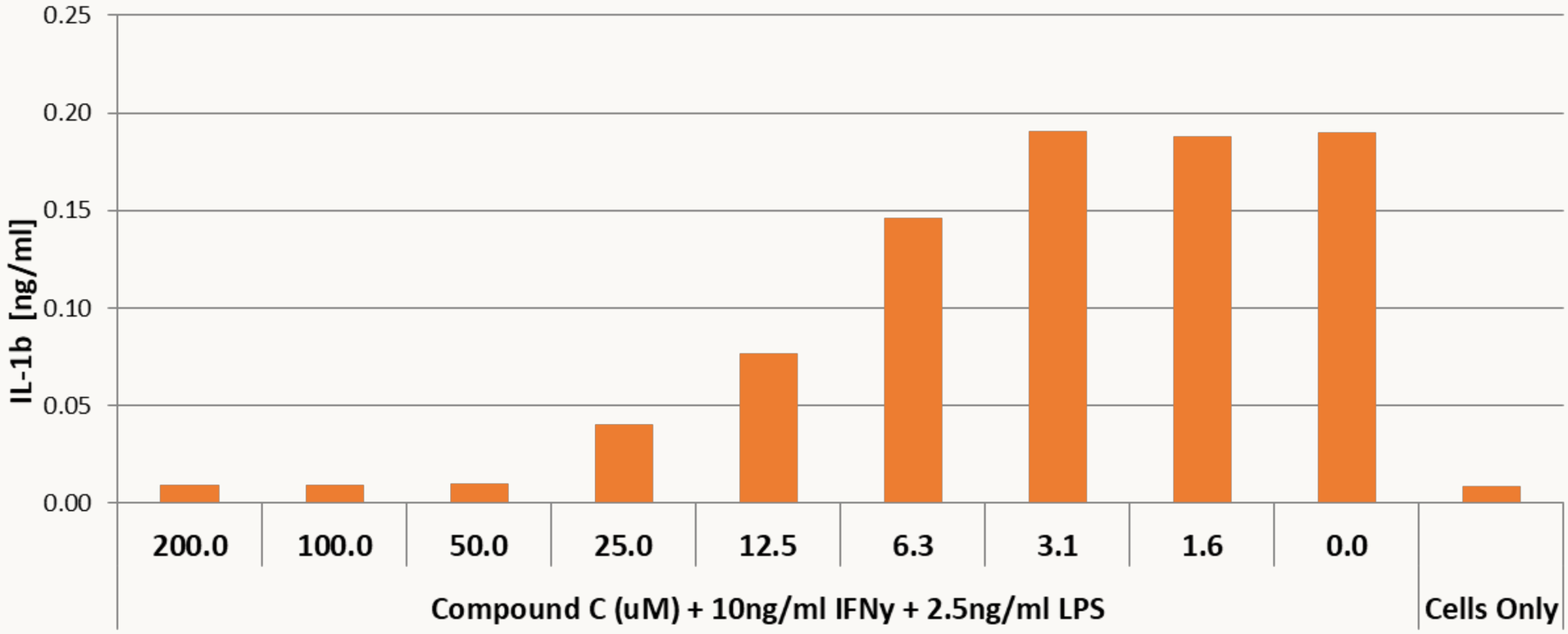
Treatment of human PBMC by 10 ug/ml R-848

Assay Positive Control: Dexamethasone

24 Hrs. of Exposure

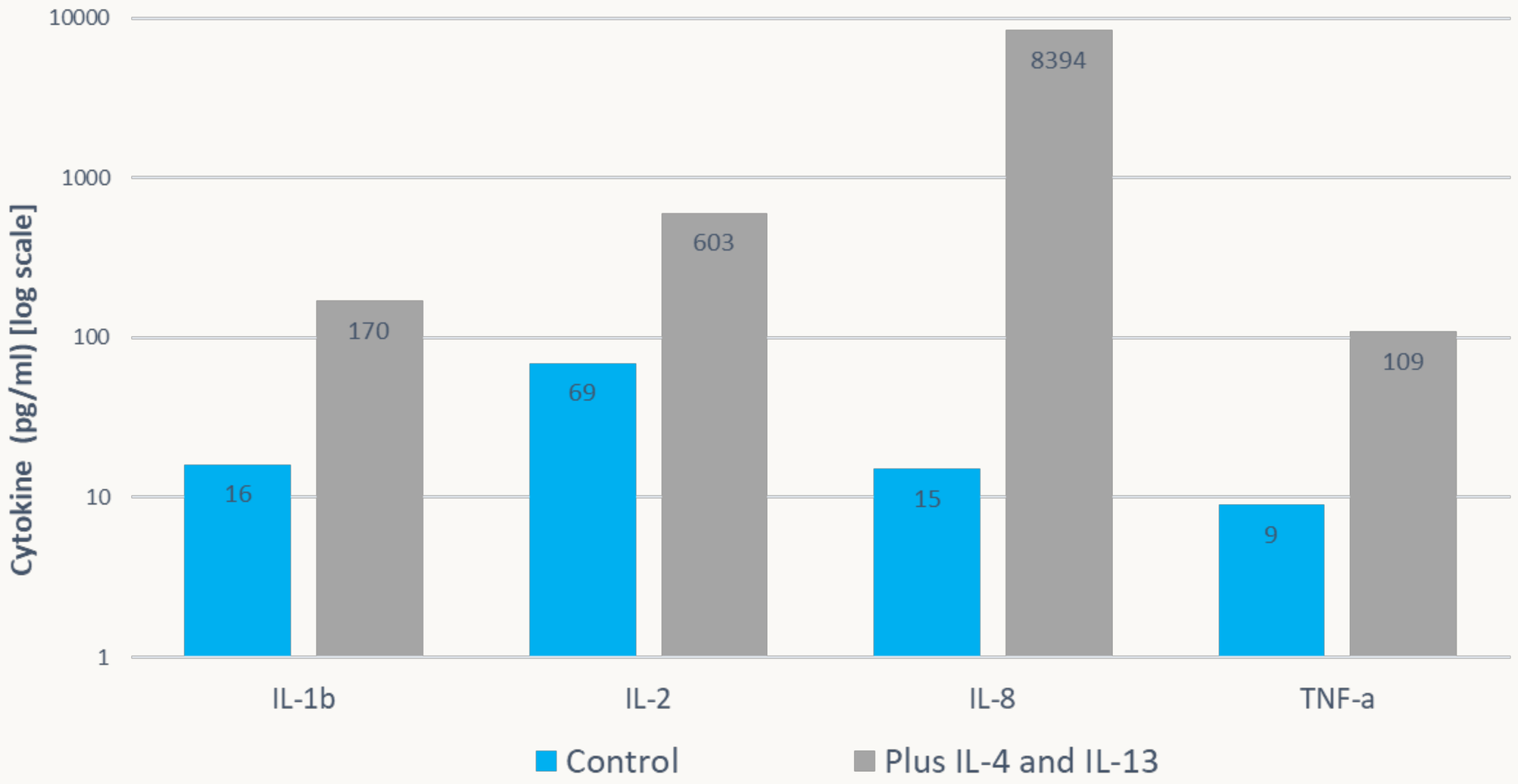


h-IL-1b Secretion by THP-1 Cells Treated with Compound C in Combination with 10ng/ml IFN-gamma and 2.5ng/ml LPS for 3 Days (M1) (Pre-Treatment with PMA for 3 days prior to the experiment)



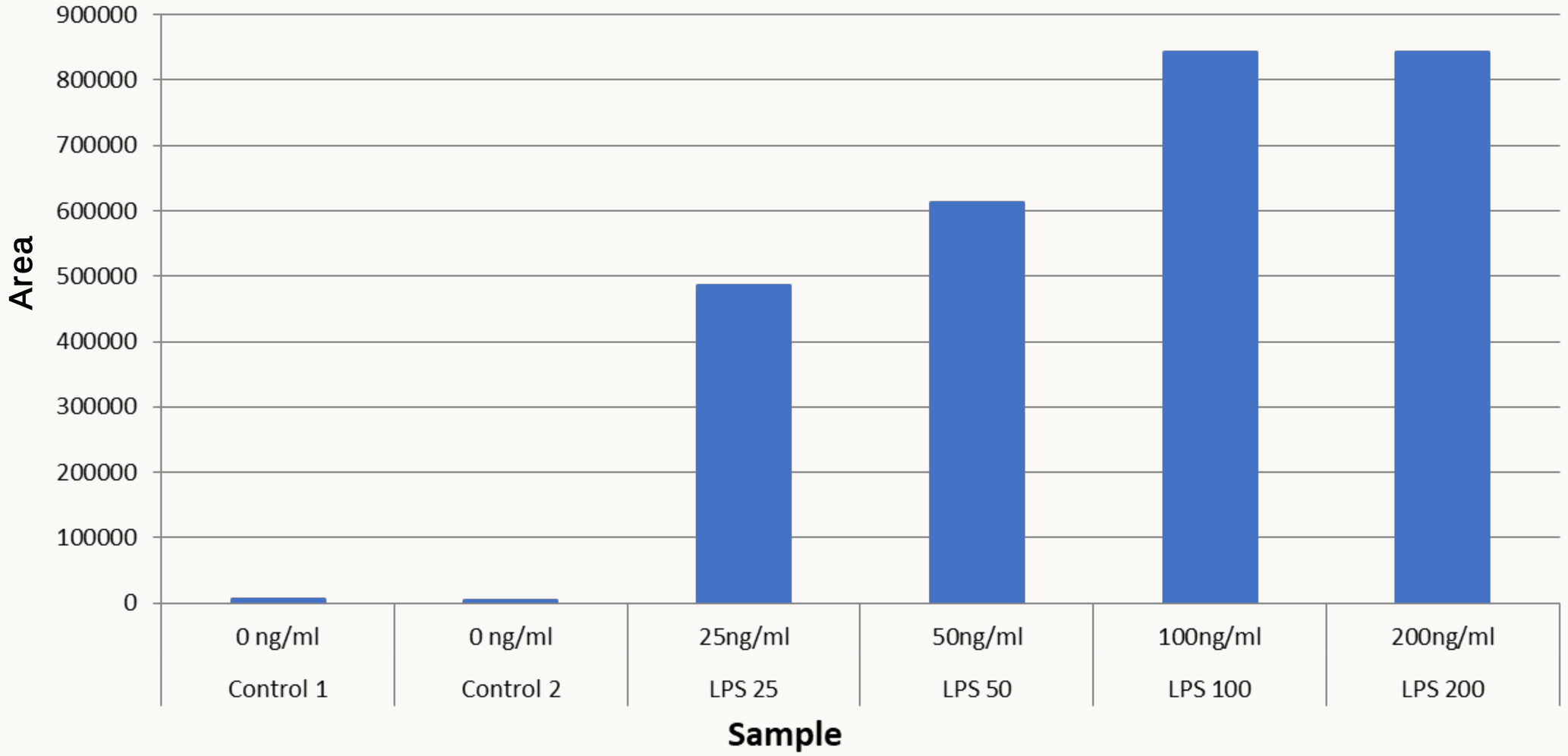
Please note: Up to 100 uM Compound C did not cause any cytotoxicity effect on the cells.

Polarization / Differentiation of THP1 Cells (M2)

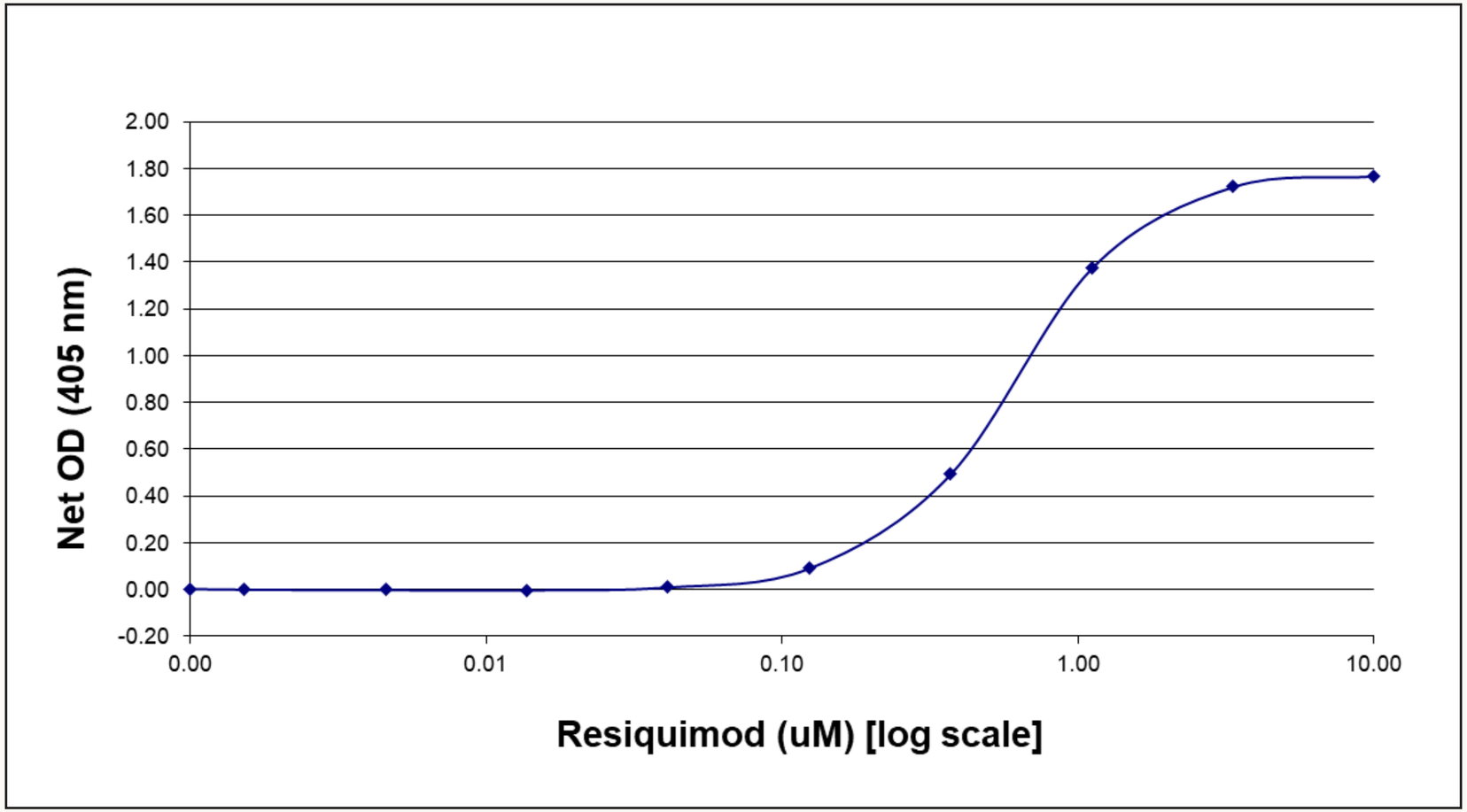


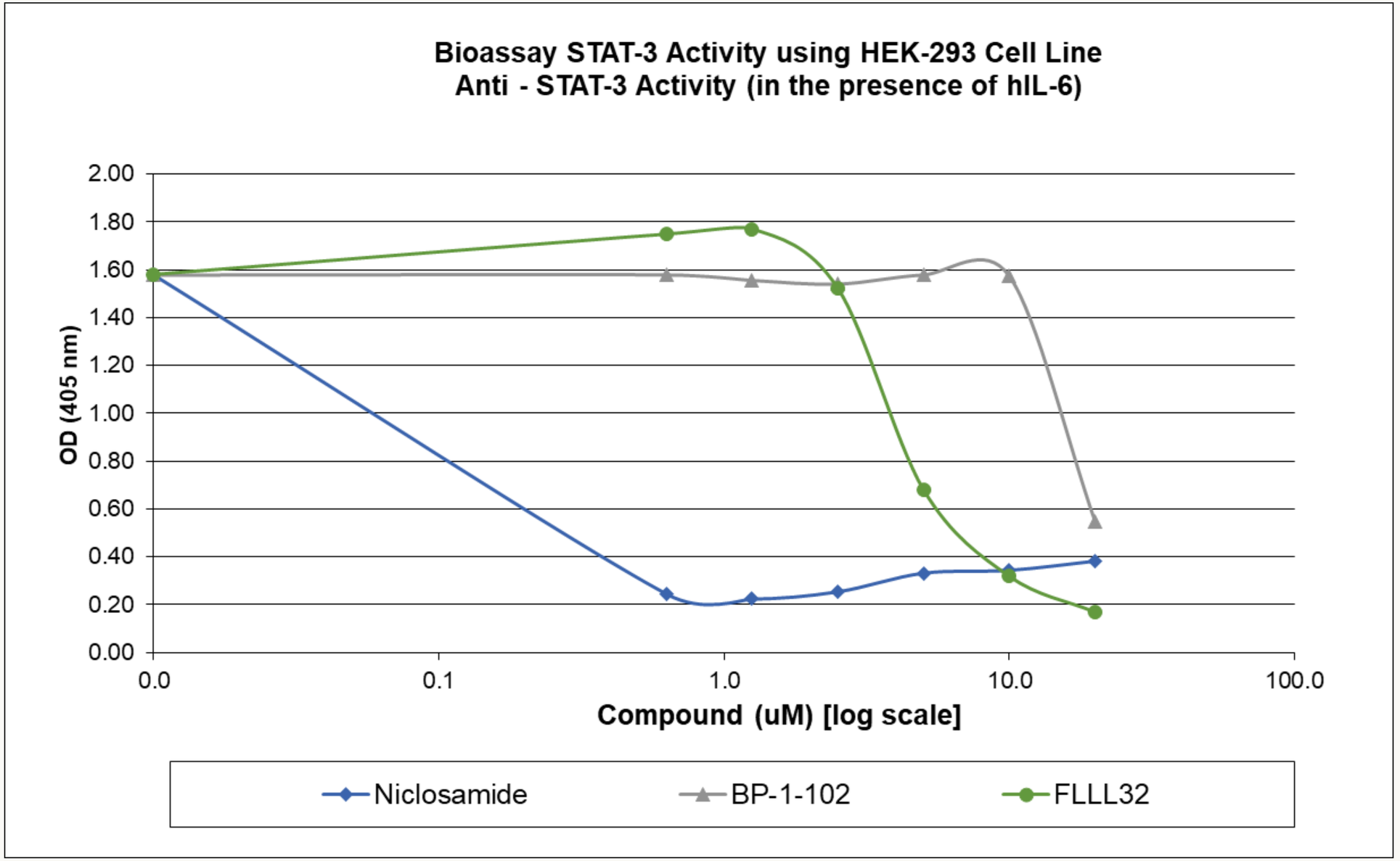
RAW 264.7 Cells

iNOS Peak Area with WES Analysis (ProteinSimple)



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



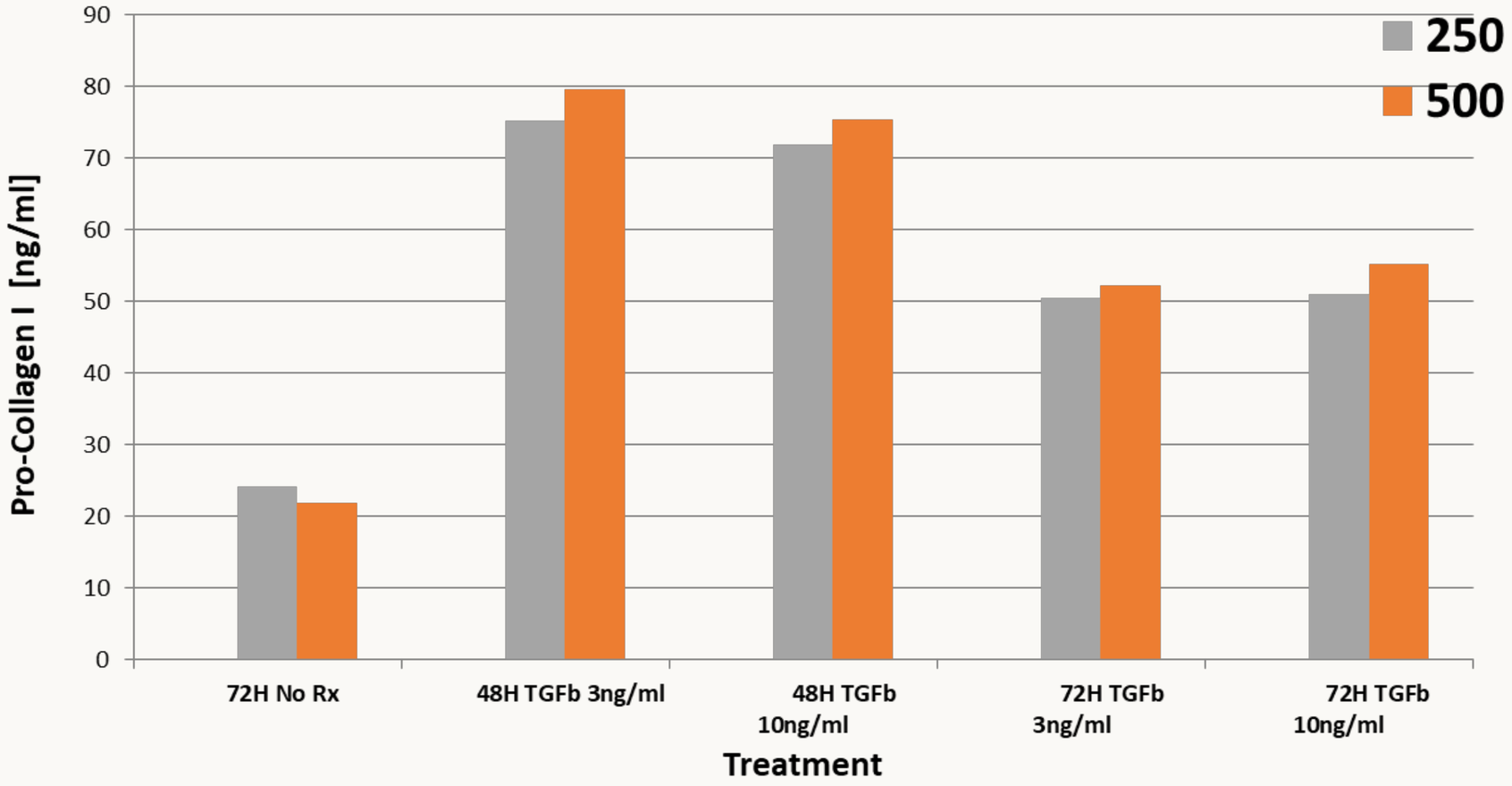

Bioassay STAT-3 Activity using HEK-293 Cell Line
Anti - STAT-3 Activity (in the presence of hIL-6)
OD (405 nm)
2.00
1.80
1.60
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
0.0
0.1
1.0
10.0
100.0
Compound (uM) [log scale]
Niclosamide
BP-1-102
FLLL32

In-Vitro Fibrosis Model

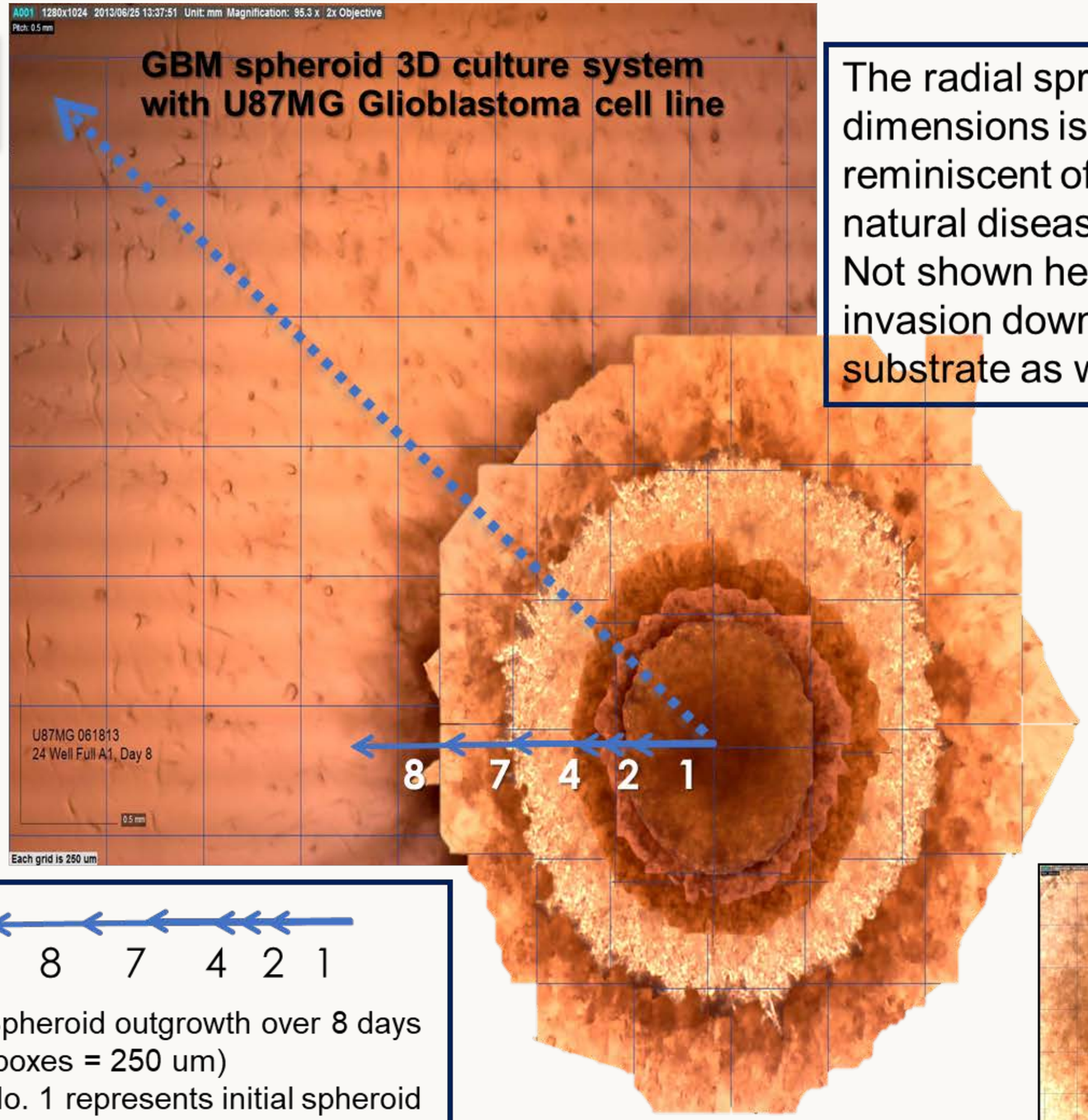
h-Pro-Collagen I Production by human Lung Fibroblast Cells

Treated with 3 and 10 ng/ml TGF-b1 for 48 or 72 Hours

(Diluted 1:250 or 1:500 Fold prior to ELISA)

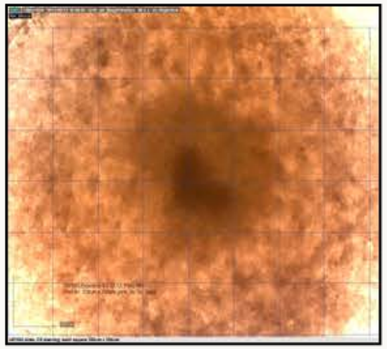


Untreated GBM



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 was 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

Partnerships

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

5 Provisional Patents have been submitted
2 Issued Patent

Galectin Therapeutics

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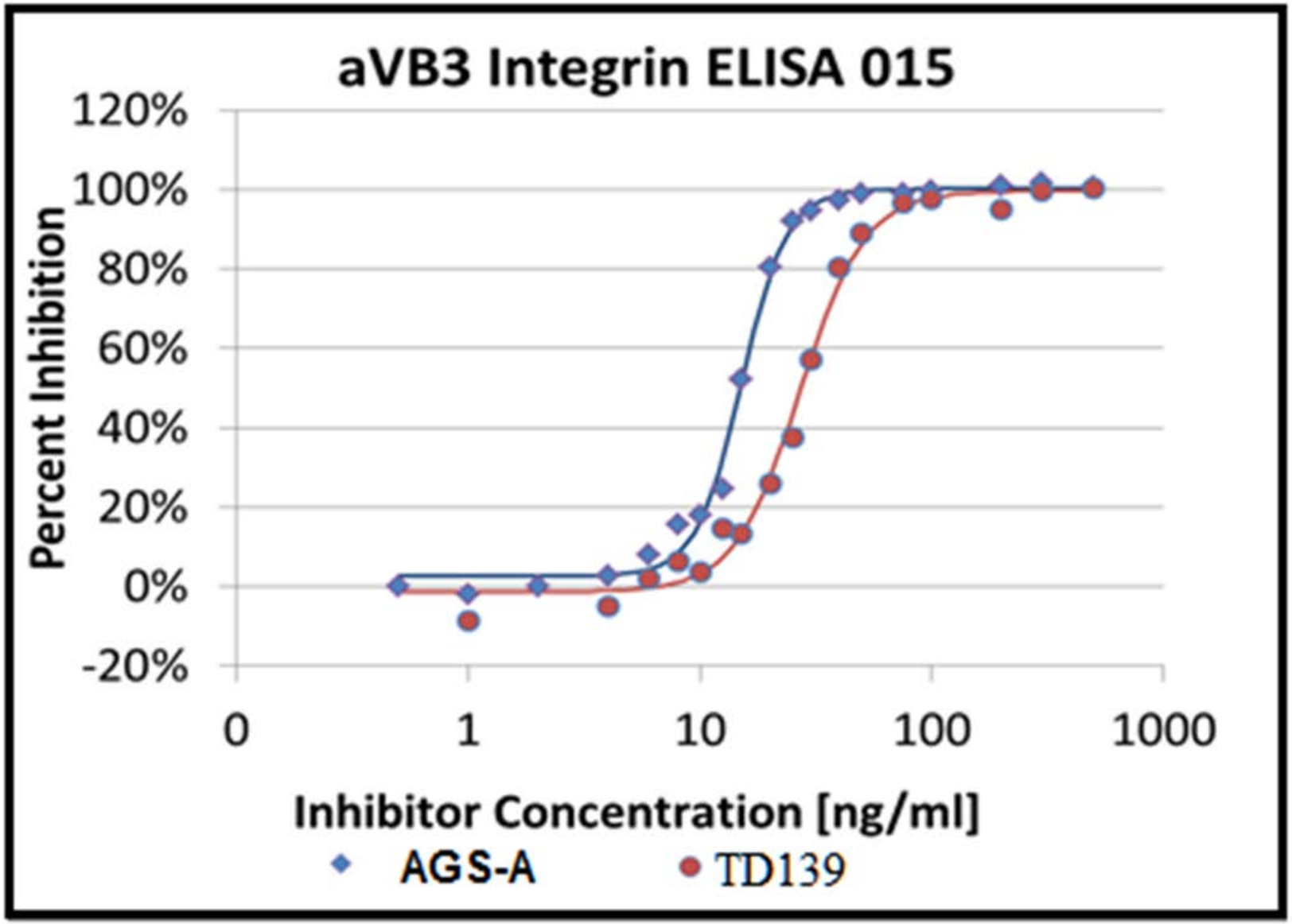
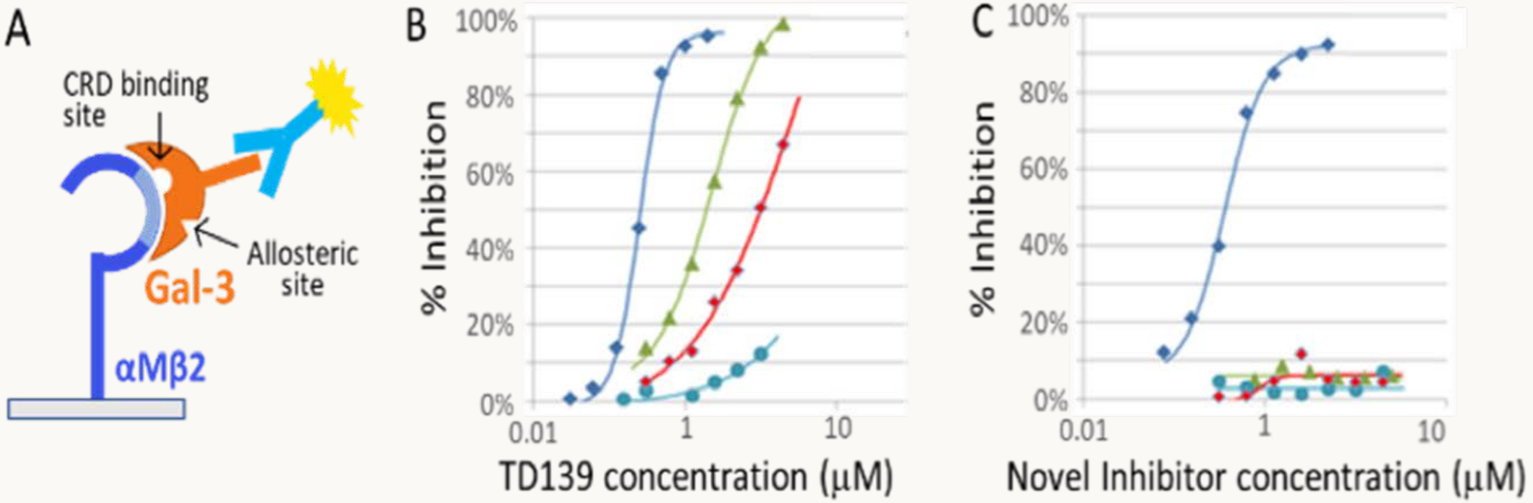

aVB3 Integrin ELISA 015
120%
100%
80%
60%
40%
20%
0%
-20%
Percent Inhibition
0
1
10
100
1000
Inhibitor Concentration [ng/ml]
AGS-A
TD139

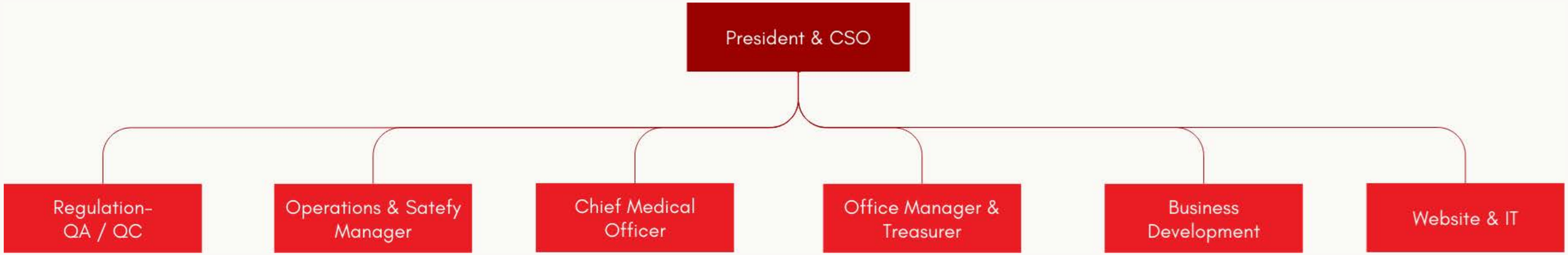
Improved specificity of Galectin-3 modulators

In a receptor-based ELISA (A), TD139 inhibits binding of multiple galectins to integrin αMβ2 (B).

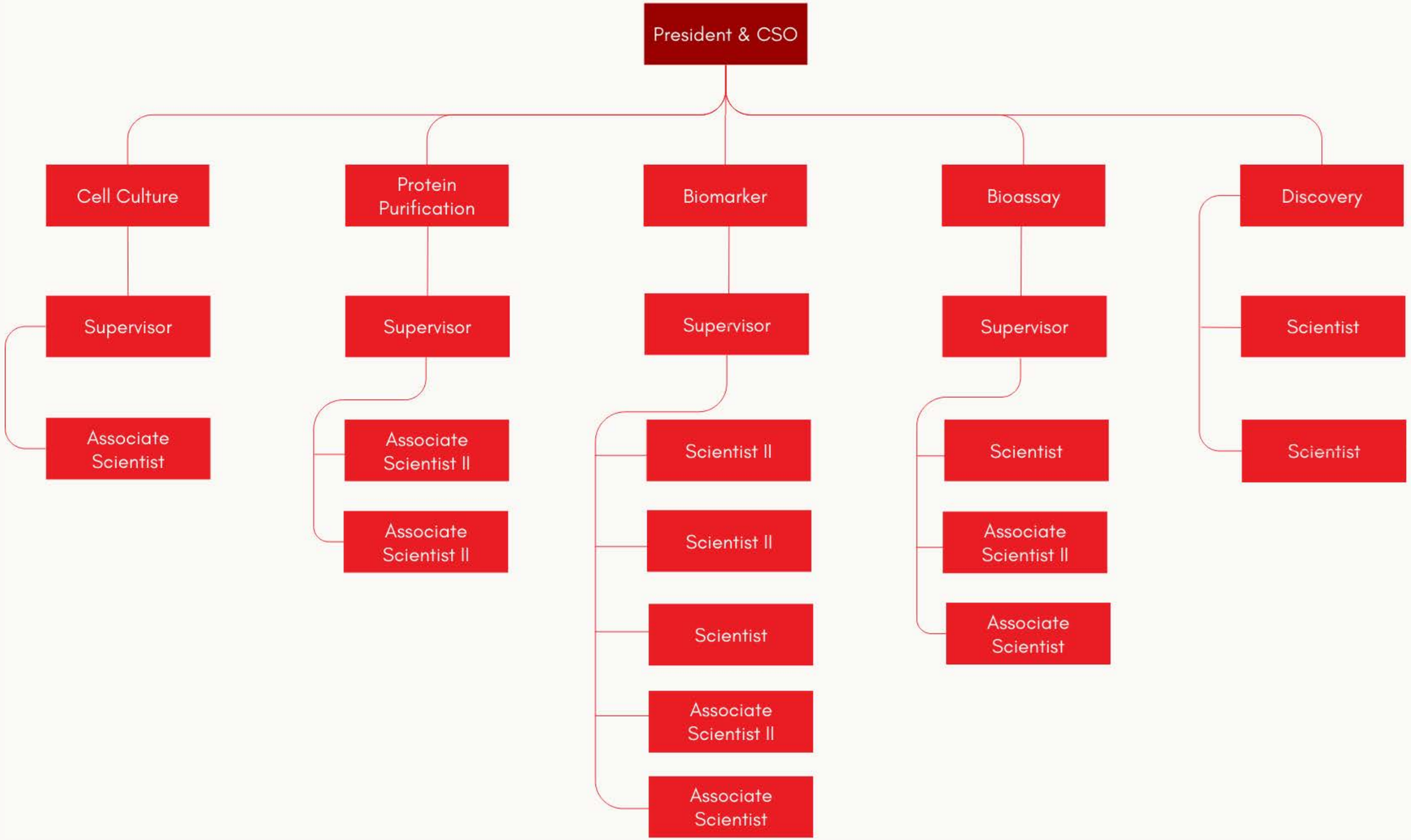
An allosteric Gal-3 inhibitor (G229) shows significantly greater specificity for Gal-3 over other galectins (C).



Key Roles at SBH



Company Structure



Create Your Competitive Advantage

Seamlessly Transition Your Product from Early Development to Preclinical and Clinical Stages

Partner with SBH Sciences
Your Pre-Clinical Contract Research Organizatior

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