SIA Preclinical Services in Drug Development

At Science in Action Ltd. (SIA), we offer tailor-made preclinical in-vivo and in-vitro studies to assess drug safety and efficacy. Our services cover wide range of therapeutic areas, disease models and research techniques. We are committed to highest standards of research along with optimal flexibility in meeting your scientific needs.

This brochure describes in vitro assays offered as a part of SIA's R&D services. Please note that our experience includes, but is not limited to, the models and systems that appear below. All of our services are tailored to the specific requirements of our customers' applications. For free consultation, please contact us 972-52-4263400, raanan.margalit@gmail.com.

IN VITRO SERVICES

1. Tissue Culture Services.

   We provide tissue culture services for cell cultivation and storage as well as establishment and testing of primary rodent cell cultures. SIA's cell bank contains over 70 cell lines including normal and transformed cells of human and other origins. Cancer cell lines are cultivated for no more than 20 passages and routinely tested for parasites (e.g. mycoplasma) to insure the integrity of the original cells.

   A team of qualified cell scientists is dedicated to perform a wide repertoire of tissue and cell culture techniques to address your drug development programs.

2. Transient/stable Transfection

By insertion of DNA plasmid containing the gene of interest into the cells transient transfection induces or enhances the synthesis of target gene product. Target gene silencing can be achieved by a transfected small nucleic acid such as siRNA or miRNA to inhibit gene expression. In transient transfection the foreign DNA does not integrate into the genome of the host cells, rather certain number of DNA copies persist in the cells temporary, typically 6-10 days.

The advantage of transient transfection is that there is no need for long and expensive stable cell line establishment. Hence, application of transient transfections is preferable for initial drug candidate screen and for fast production of small quantities of protein for activity evaluation.

Stable transfection allows long-term integration of foreign DNA into host cell genome through a process of careful selection. Once, the introduced DNA is integrated, it passes to the descendent cells during replication. Stable transfection is useful for studies on long-term regulation of genetic mechanisms and gene therapy.

3. Cell Viability Assay

Cell viability assay is based on highly sensitive and accurate fluorometric detection method for quantifying the number of metabolically active viable cells. The assay is used for an in vitro assessment of the effect of biologically active materials on cell viability. Examples of research systems that may utilize cell viability assay is when the test item is designed to provide neuroprotection or hinder the growth of cancer cells.

4. Enzyme-Linked Immunosorbent Assay (ELISA)

ELISA is used to detect and quantify a variety of secreted factors such as cytokines, chemokines, proteins or peptides in cell supernatant, body fluids or cell extracts. The advantage of ELISA method is its high sensitivity, specificity

and the ability to obtain fast and accurate results by simultaneously testing multiple samples.

5. DNA, RNA and Protein Analysis.

DNA and RNA purification and analysis services include isolation of genomic DNA, mRNA, small DNA and RNA sequences from cells or tissues and analysis by quantitative real time PCR (QRT-PCR). SIA has vast experience in isolation and analysis of RNA and DNA sequences by PCR and QRT-PCR.

Gene expression analysis services include all steps form mRNA isolation through cDNA preparation and quantitative real time PCR analysis (QRT-PCR).

Protein Analysis by Western Blotting and Immunofluorescence is used to assess the specific proteins of interest, their amounts, stability, posttranslational modifications and localization within cells. Co-staining of two cellular proteins or cellular protein and a molecule of interest, may reveal co-localization and possible interaction.

Immunohistochemistry (IHC) services include immunolocaliztion of either one or several antigens of interest in frozen, paraffin-embedded tissue sections and cell samples. We utilize various detection methods such as immunofluorescence, alkaline phosphatase, and immunoperoxidase.

6. In vitro Migration/Invasion Assays

In vitro migration and invasion assays provide a simple and fast quantitative platform to measure cellular migratory or invasive phenotypes, in vitro. In this assay, cells are allowed to migrate through an artificial membrane towards a chemo-attractant gradient. The efficiency of this process is assessed by fluorometric analysis.

Migration through a membrane coated with basement membrane components provides a model system to study invasive potential of the cell culture.

7. In Vitro Differentiation Assays

In vitro differentiation assays are used to determine the effect of novel compounds or exogenous factors on cell fate, morphology and signal transduction processes.

Neurite outgrowth assay permits to study regulatory pathways involved in neuronal differentiation and axonal growth. In this assay, the effect of compound of interest on neurites formation and length is monitored. Understanding neurite outgrowth can provide the opportunity to improve therapeutics for neurodegenerative diseases and injuries of central nervous system.

Skeletal muscle differentiation assay. Myoblast differentiation is essential for the development of functional myotubes and regeneration of skeletal muscles. Skeletal muscle differentiation assay may be used to identify novel therapeutic targets and to screen drug candidates for diseases and conditions associated with severe muscle weakness and frailty.

Adipocyte differentiation assay. Adipocyte differentiation of mesenchymal stem cells and multipotent cell lines is a multistep process mediated by sequential activation of several groups of transcription factors that orchestrate the adipogenic network. Mature adipocytes are characterized by intracellular accumulation of lipid droplets as well as transcription of adipocyte-specific genes. Adipocyte differentiation models are used in the research of obesity, adipose biology and tissue engineering.

Osteogenic differentiation assay. Osteogenic differentiation of mesenchymal stem cells towards osteoblasts is a process involving induction of complex endogenous molecular pathways that is controlled by various extracellular

signals through. Dysfunctions in osteogenic commitment as well as disturbances in later stages of osteogenic differentiation may result in various bone diseases and systemic disorders, such as osteoporosis and cancer. Osteogenic differentiation assay permits to investigate the mechanisms engaged in stimulation of osteogenic differentiation and may provide important insights for tissue engineering applications.

8. Ex-vivo Studies

   SIA has a fully equipped facility for in-vivo research in rodents. Upon sample collection from mice or rats, cells can be isolated for further research in tissue culture. Ex vivo models can be used for evaluation of toxicity tests, assessment of peripheral nerve grafting repair, effect of specific agents on cardiovascular systems as well as manipulations with blood samples and cultivation of lymphocytes.

9. Lymphocyte Activation Assay is an example for ex-vivo study where lymphocytes isolated from lymph nodes/spleen can be activated in culture in the presence of test item. Lymphocyte activation is examined by detection of cell proliferation and cytokine secretion monitoring by ELISA.

10. Fluorescent-Activated Cell Sorting (FACS) analysis.

    Flow cytometry is rapid and reliable method for quantification, characterization and functional analysis of fluorescently labeled cells. FACS analysis is often used to assess cell cycle distribution and to determine whether apoptosis or necrosis took place following application of cytotoxic agents or other effectors. FACS may also be used for isolation of specific cell populations.

The above assays represent examples of research options offered by SIA. Please remember that our services are all tailored to our customers' specific needs and do not hesitate to contact us for more detailed information.

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