Daiichi Sankyo Sponsored Research

Guidelines for Application

Application is on email basis. Please send us one page summary of the proposal at the program office (External_Innovation@dsi.com).

Eligibility: Researchers affiliated with universities and research institutions, who have ideas which may lead to drug discovery. The program is not open to undergraduate or graduate students.

Research Budget: up to $230,000 for one year including overhead/indirect costs

Term: 1-3 years. Successful program(s) will be considered for staging into collaborative research.

Selection Criteria:

- Matching needs (Research interests)
- Originality and uniqueness of research
- Drug discovery potential
- Feasibility of research plan
- Non-redundancy with Daiichi Sankyo's internal research projects and current collaboration

Deadline: Rolling application (untill March 2024)

Research Interests

Oncology

I. Novel targeted protein degradation technologies such as tumor/tissue selective E3 ligands and degradation mechanism other than ubiquitin proteasome system
II. Novel, biologically-tractable, tumor-associated antigens and their binders such as monoclonal antibody/antibody mimetics/Fab/scFv/sdAb
III. Novel IO targets for which mechanisms are confirmed in human-derived samples
IV. Adoptive cell-therapy technologies that can successfully treat solid tumors
V. Pancreatic cancer in vivo model that reflects human pancreatic ductal adenocarcinoma
VI. In vitro assay system that reflects in vivo epigenetic status and mechanism analysis of epigenetics targeting small molecule compounds

Non-Oncology

I. Novel disease relevant target identification research by using patient tissue samples or genetical analysis for the following target diseases (* both are neuroinflammation perspective)
    a) Immune diseases: refractory immune diseases and lung fibrosis
    b) Neurodegenerative diseases*: Alzheimer's disease, Perkinson's disease and ALS
    c) Psychiatric diseases*: Schizophrenia, Autism spectrum disorder, addiction & anxiety, major depression disorders

   d) Rare diseases: CNS, liver (mono or double genetic)
   e) Heart failure & Liver disease: (HFrEF & HFpEF) & NASH (not TG reducer)
   f) Ophthalmological disorders (AMD, RP and PDR)

II. Novel in vitro (iPSC derived) and in vivo models that recapture human pathological mechanisms/conditions of immune and CNS disorders described above
III. Biomarker research for patient stratification in neuroinflammation derived disease described above
IV. Drug delivery technologies for siRNAs to brain, heart, lung & kidney
V. Novel RNA targeting small molecules & editing technologies (not RNase2, Ago2 & ADAR) with CNS diseases and rare diseases target
VI. AAV platform: new capsid library (CNS target)

Further information is available on our website below.

https://www.daiichisankyo.com/rd/strategy_operations/open_innovation/our_interests/

Parallel Application to Other non-Daiichi Sankyo Grants

Public Grant

DS may accept an application for a research topic by an individual that has already applied for a public grant for such research topic so long as the applicable intellectual property is controlled by either the PI and/or university.

Pharma-Sponsored Grant

DS may accept an application for a research topic by an individual that has already applied for a private grant for such research topic, but DS reserves the right to decline such application for any reason, including if such individual accepts a private grant.

Please feel free to contact us for any inquires (External_Innovation@dsi.com).

Daiichi Sankyo Wish List 2023

A1: Oncology

Immuno-oncology

A1-01

Novel targets or research on tumor immunotherapy to overcome ICI insensitivity or resistance

- Focused cell types or mechanisms:
  - Suppressive immune cells
    - MDSCs
    - Innate lymphoid cells (ILCs)
  - Tumor cells
    - Enhancement of tumor antigenicity
  - T cell dysfunction including T cell exhaustion

Epigenetics

A1-02

Epigenetics regulation for break-through anti-cancer drug

- An approach to elucidate the mechanism of action of small molecule compounds targeting epigenetics related molecules for patient stratification and/or efficacy prediction
- Novel in vitro assay model/system that have been validated to reflect in vivo epigenetic status

Drug discovery for undruggable protein

A1-03

- **Novel hit / lead finding technology targeting “undruggable” proteins**
- **Method or technology of identifying hidden binding pockets (cryptic binding pockets) for small molecules on “undruggable” proteins**

- **Interested in research for epigenetics**

Disease model for pancreatic cancer

A1-04

Pancreatic ducutal adenocarcinoma (PDAC) models which reflects human PDAC features, and better than known genetically engineered mouse models (GEMM) like KPC (KRAS, TP53) in some points of following features

- High desmoplasia and stroma content
- low vasculature that reflects human PDAC
- established methodology to monitor PDAC tumor growth in pancreas
- possible strategy and plans to monitor antibody distribution to PDAC in pancreas

Target protein degradation

A1-05

- **Heterobifunctional molecule utilizing tissue/tumor specific E3 ligase**
  - Out of scope: conventional PROTACs with well-known E3 ligases (CRBN/VHL/IAP/MDM2)
- **Application of novel degradation mechanism (other than UPS) for protein degrader**
- **Novel technologies for identification of “monovalent (non-chimera) protein degrader” or “molecular glue” as an alternative approach for protein degradation**

Antibody-related research

A1-06

Unique antibodies or binders, applicable to mono- or multi-specific antibodies and/or cell therapy, against tumor-associated antigens, which include tumor, immune, and stromal cell targets.

- Binders include antibody mimetics, Fab, scFv, sdAb.

Cell therapy

A1-07

Novel technologies for adoptive T cell therapy

- Novel molecular targets/mechanisms to potentiate T-cell functions
- Novel molecular targets/mechanisms to enhance efficacy in solid tumor
- Novel conditional activation machinery at tumor sites (On/Off switch etc.)

A2: Central Nervous System

Psychiatric disease

Unique research on psychiatric diseases which can pave the way to novel drug development.

- Focused diseases: Major Depression Disorder, Anxiety disorder, Schizophrenia, Autism Spectrum Disorder

A2-01

Neuroinflammation

Novel target and psychiatric disease animal model induced by primary neuroinflammation, with human translatability by biomarker, suitable to judge the therapeutic potential of drug or target.

A2-02

New targets

Research for finding brand new therapeutic target to tackle UMN of psychiatric disease based on human disease information.

A2-03

Research for endogenous ligand, receptor, or pathway which is expected to be involved in abnormal activity of specific brain area causing psychiatric disease. Abnormal activity of specific brain area reported in patient and reproducibility in rodent model is recommended.

Neurodegenerative disease

Unique research on neurodegenerative diseases which can pave the way to novel drug development.

- Focused diseases: Alzheimer's Disease, Progressive Supranuclear Palsy, Frontotemporal Lobar Degeneration, Parkinson's Disease, Multiple System Atrophy, Dementia with Levybody, Amyotrophic Lateral Sclerosis

A2-04

Neuroinflammation

Novel research on glial cell function which can reveal relevance of the progression of neurodegenerative diseases. Ideas with high originality regarding neuroinflammation, cellular metabolism and senescence are of particular interest.

A2-05

New targets

Research for finding novel therapeutic target utilizing clinical information regarding prognosis and/or data from clinical trials.

As an example, research to identify new drug targets based on the clinical information that thin people progress faster in ALS and that calorie intake is the standard of care in the early stages of the disease.

A2-06

Novel research which focuses on neuroprotection to prevent disease progression. In addition to approach for direct neuroprotective effects, approach to elucidate novel, glial cell-mediated neuroprotective mechanism will be highly valued.

A2-07

Disease model

Translational disease model of neurodegenerative diseases.

A3: Ophthalmic Disease

Age-Related Macular Degeneration

A3-01

Research on establishment of animal models that mimic non-exudative age-related macular degeneration.

A3-02

Research on Drug Target Molecules/Mechanism for intermediate or non-exudative age-Related Macular Degeneration.

- Limitation: The target molecules will be limited to those with proven efficacy in animal models or those expected from analysis of patient samples.

Retinitis Pigmentosa

A3-03

Research on Drug Target Molecules/Mechanism for Gene-independent Therapy of Retinitis Pigmentosa.

- Limitation: The target molecules will be limited to those with proven efficacy in multiple animal models or those expected from analysis of patient samples.

Evaluation technology

A3-04

in vivo model for evaluation of visual function to detect photoreceptor-mediated signals.

- e.g., color vision evaluation in monkeys, method to evaluate higher order visual function in rodents, etc.

A4: Immune-related disease

Immune diseases/fibrosis

A4-01

Novel therapeutic targets or novel target identification involved in refractory immune diseases or fibrosis.

New targets are those that have not been tested in clinical trials and may also be known molecules.

- Novel cell surface targets
- Novel intracellular targets

If the target has been acquired,

- **The targets can be either specific subset of pathogenic cells or molecules involved in these disease mechanisms.**
- **The targets are desired to be scientifically validated in a preclinical study.**
- **For cell surface targets, antibodies have been obtained**

In the case of target identification studies,

- **An exploratory study of novel therapeutic targets utilizing patient sample collection and omics data analysis before and after administration of existing therapeutic agents.**
- **Transcriptome analysis (scRNA-seq, CITE-seq, LIBRA-seq, and Spatial transcriptomics), GWAS and/or PheWAS analysis or whole exome analysis from human samples.**

Evaluation technology

A4-02

Novel drug target validation tools which mimics pathological mechanism of refractory immune-inflammatory disorders (such as pulmonary fibrosis diseases, interstitial lung disease, and autoimmune disease with neuropsychiatric symptoms)

- Novel validation tools using patient cells-derived iPS cells and organoids
- Novel validation tools using Organ on a chip technology
- Novel animal models
- Validation of drug targets using above tools
  - Novel cell surface targets
  - Novel intracellular targets

A5: Cardiovascular and metabolic diseases

NASH

A5-01

- **Novel therapeutic target for NASH and/or target identification for NASH based on unique screening platform**
  - Out of scope: MOA reducing TG in liver
- **Exploratory research to identify novel therapeutic target for NASH based on unique screening platform using iPS cells or organoid derived from NASH patients**

Chronic Heart Failure

A5-02

Innovative research to provide novel therapeutic targets for HFrEF, HFpEF using human myocardial samples or organoid derived from HF patients

Disease model

A5-03

Research for disease model to evaluate compounds which improves microcirculation.

- e.g., type II myocardial infarction, coronary artery disease, Raynaud's phenomenon, Scleroderma, Buerger's disease, cerebral small vessel disease, atrial fibrillation, HFrEF

A6: Mechanism based strategy

Gene therapy

A6-01

- **Novel target genes whose expression needs to be repressed for therapeutic purposes**
  - Our focus is CNS, but the scope is not limited to CNS. Our scope also includes liver, muscle, heart, pancreas and so on.
- **Novel secreted factors, such as proteins, peptides, or biologics which can be delivered by gene therapy vector for therapeutic purposes.**
  - The target organ for gene expression is liver, but organs where the secreted factor exhibits efficacy are not limited.

mRNA-related research

A6-02

Non-coding RNA or NMD-sensitive mRNA which work as therapeutic target.

- Especially, we are interested in those targeted with oligonucleotides by following mechanisms:
  - Convert endogenous non-coding RNA or NMD-sensitive mRNA into functional RNA by either changing a splice site or RNA editing
  - Block function of non-coding RNA by either changing a splice site or RNA editing
- Out of scope:
  - Micro RNA
  - Therapeutic targets for cancer

Protease related disease

A6-03

Diseases which can be treated by protease inhibition.

- Especially, we are interested in the disease with following characteristics
  - Can expect dramatical improvement by single protease inhibition
  - No toxicity or little toxicity is expected by systemic inhibition of the protease
  - Target validation has been completed using animal model or at cellular level
  - Preferably an animal model of the disease is available
- Out of our scope:
  - Diseases which need to inhibit multiple protease to treat
  - Proteases without extracellular secretion
  - Diseases treated well by existing drugs
  - Research for Cancer

B1: DDS technology

Nucleic acid

B1-01

Novel nucleic acid therapeutics

- Novel delivery platforms or organ (ex. CNS, lung, kidney, cancer, immune cells, heart, etc.) selective targeting ligands for antisense oligonucleotides, siRNA or mRNA

Nanoparticle

B1-02

Novel nanoparticle-based DDS technology for CNS or cancer-targeting

- Nanoparticles bearing CNS-targeting ligands that can be used for delivery of various therapeutic modalities to the brain.
- Nanoparticles bearing cancer-targeting ligands that can be used for delivery

of various therapeutic modalities to cancer tissue cells.

- In vivo data proving the concept of the technology is required.
- Out of scope: technology to physically open the BBB, ADC, conjugated drug.

Formulation (local administration)

B1-03

Formulation technologies for local administration and action

- Novel formulation technologies for local administration for low, middle and high molecular weight compounds
- transdermal and pulmonary delivery technologies for peptides and nucleic acids (non-invasive) including transition enhancement into cells
- sustained release necessary in case of infrequent administration (inner ear, intra-articular, etc.)
- technologies regarding to CNS delivery such as nose to brain, intrathecal administration etc. also included
- Out of scope: modification or conjugation technologies (lipid or sugar conjugation, etc.)

B2: Modality based technology

Small molecule drug discovery

B2-01

Method of creating unique chemical library using untraditional chemical reactions, such as electrochemical reactions, photochemical reactions, enzymatic reactions, etc.

B2-02

Novel small molecules which selectively bind to proteins specifically expressed in disease causing cell.

- The proteins should be expressed with sufficient selectivity (>x100) in

disease cells compared to normal cells.

- The proteins should be expressed in sufficient quantity (>50nM).
- The small molecules should bind to the protein with sufficient selectivity to the other proteins (>x100).

B2-03

Novel technologies that can be used for identifying functional RNA-targeting small molecules

- Methods for identifying RNA motifs that are functionally relevant.
- Methods for degrading target RNAs induced by binding of small molecules.
- Unique approaches for modulating translation or splicing with RNA-targeting small molecules.

Nucleic acid therapy

B2-04

Novel nucleic acid therapeutics

- Novel oligonucleotide-based technology that can control mRNA level or change mRNA sequence by recruiting an endogenous molecule(s).
- Out of scope: technology related to RNase H、Ago2、ADAR

Gene therapy

B2-05

Novel AAV capsid library platform/technology to isolate promising novel capsids in vivo

- Out of scope: Platform using barcoded capsid library which have been already reported

B2-06

Novel technologies which can enhance gene expression or durability for in vivo gene therapy

- Novel oligonucleotide-based technology that can control mRNA level or change mRNA sequence by recruiting an endogenous molecule(s).

B2-07

Novel gene silencing/suppression technology/novel protein that show high suppression efficiency and can be delivered by viral vector

- Out of scope: Existing nuclease-related research, such as CRISPR/Cas9

B2-08

Unique high-order assay using human brain organ/tissue for evaluating distribution and infection of locally delivered AAV vector

- Out of scope:
  - Assay system related to BBB (Blood-brain barrier)
  - Assay system using animal tissues or samples

B3: Drug discovery technology

Computational chemistry

B3-01

Novel methods for sampling biologically relevant conformational space of middle size molecules such as target protein degraders (TPD) to consider their conformations on binding and/or on passing though membrane.

Omics analysis

B3-02

High-throughput and whole genome-wide omics profiling platform for drug-perturbated samples

- For omics, biologically related and interpretable omics such as proteomics, metabolomics, and isoform ratio in alternative splicing are preferable, but not for established omics like transcriptomics.
- For platform, high resolution, cost-effective and high throughput data

collection systems with small amount (i.e. <100 μL) of samples are preferable.

B3-03

Novel drug target exploration technology using multi-omics data

- Novel drug target discovery technology using multi-omics data linked to disease phenotypes
- Multi-omics data linked to disease phenotypes (Kind of database)
- Transcriptome analysis technology is acceptable if they also have the unique patient data.

Bioimaging/Bioanalysis

B3-04

Novel visualization techniques and novel imaging probes for biological tissue imaging

- We are interested in novel technologies for the following aspects of biological tissue imaging.
  - Probes for detecting changes in the intracellular environment
    - e.g., singlet oxygen, phosphorylation
  - Fluorescence, luminescence, MRI and PET imaging with higher resolution and sensitivity than conventional method.
  - Imaging of unlabeled materials, such as Raman spectroscopy and imaging mass spectrometry.
  - Probes that can combine imaging and omics analysis

B3-05

Novel high-throughput screening methodology to evaluate free fraction of highly bound drugs in plasma and tissues with a high precision

Extracellular vesicle

B3-06

Novel technology to isolate tissue-derived extracellular vesicles (including exosomes)

- Technology that can efficiently isolate extracellular vesicles (including exosomes) from human serum and plasma with high purity
- The word of "tissue" includes not only organs (such as the heart, liver, and brain etc.) but also cells that are present in organs (such as cardiomyocyte, hepatocyte, nerve cells and glial cells, etc.)
- Out of scope:
  - Technology isolating extracellular vesicles (including exosomes) from in vitro cultured cells
  - Technology directly isolating extracellular vesicles (including exosomes) from tissue homogenates

B3-07

Research for toxicity/AE expression mechanisms, especially of interstitial lung disease, caused by extracellular vesicles (exosome)