Milner Consortium Call 2024 long list of interest topics

Cross-cutting and priority themes

Emerging science Senescence | Fibrosis | RNA | Immune modulation
Technologies Disease model development | Novel modalities | Computational research and AI | RNA technologies
Priority themes (Pfizer) Anti-infectives (anti-viral/anti-bacterial) | RNA therapeutics – including in vivo cell reprogramming

Neuroscience

Relevant companies: Astex, Bristol Myers Squibb, Eisai, Eli Lilly and Company, GSK, J&J Innovation, Shionogi, Astellas, Pfizer, GSK, MSD

Diseases of interest

- **Neurodegenerative disorders (e.g. Alzheimer's and Parkinson's diseases**, **Huntington's, FTD, ALS (including ALS-C9orf72), dementia** and other diseases that involve degeneration of motor neurons)
- Behavioural and psychological symptoms of dementia (BPSD)
- **Genetic diseases with a neurodegenerative component** g. lysosomal storage diseases, mitochondrial diseases, leukodystrophies, CMT, poly Q diseases and MS)
- **Repeat expansion disorders**
- Retinal degeneration disorders
- Hearing loss owing to hair cell degeneration or ribbon synapse loss
- **Mood disorders (e.g. major depression, anxiety, ADHD, autism, PTSD, bipolar disease, schizophrenia)**
- **Neuropathic and chronic pain**
- Neurological disorders (such as epilepsy, sleep-wake disorders inc. sleep disorders linked to neurodegenerative pathology /diagnosis)
- Sleep apnoea, including methods to identify contributing factors, resistance mechanisms to current therapies such as continuous positive air pressure, muscle control in the upper airway, drug repurposing
- Addiction (e.g. drug abuse, opioid, alcohol, gambling)
- Multiple Sclerosis

Target identification and validation, approaches to therapeutic intervention and disease understanding

- **UPR/proteostasis**, **mitochondrial function, mitophagy, autophagy**, **lysosomes,** intracellular trafficking, inflammation, DNA damage repair, ferroptosis
- **Astrocyte biology** in maintenance of brain homeostasis and mechanisms to restore normal astrocyte function
- **Lipid homeostasis**
- **Cellular senescence**
- Contraction or removal of expanded nucleotide repeats
- Sporadic Alzheimer's disease target ID using gene profiles from patient samples; target validation (in animal models or iPSCs); methods for patient stratification and biomarker for proof of mechanism in response to HDAC2

- **Neuroinflammation** e.g. mechanisms in neurodegeneration and mood disorders
- **Synaptic plasticity e.g. in mood disorders**
- Glymphatic clearance
- Gut:brain axis and the role of the microbiome as a biomarker, e.g. in Parkinson's Disease
- Neuronal regeneration and repair, including neurogenesis
- Mitochondrial Biogenesis
- Oxidative stress
- ER stress and lipid biogenesis
- Microglia in cerebral infarction and multiple sclerosis

Technologies and approaches

- **Cellular and *in vivo* models that are better predictive of disease, including human and patient iPSC derived neurons/glia, organoids, microfluidic-based cellular model systems**
- Biophysical, cellular, imaging and functional assays to study ion channels, including those present in the lysomsomal pathway
- CRISPR screens in organoid models or using neurons derived from iPSCs for target ID and validation
- *In vivo* chimeric human iPSC rodent models
- *In vivo* transdifferentiation of cells e.g. astrocytes to neurons
- Novel *in vitro* model systems translatable to human biological processes
- Genetics and biomarkers (including digital) for the early detection/diagnosis of disease and patient stratification, e.g. for Parkinson's, dementia, depression, schizophrenia and rarer proteinopathies
- Novel 'omics approaches (including lipidomics, metabolomics and proteomics) for target ID and validation and pre-clinical and clinical biomarker discovery
- Imaging receptor occupancy using PET in animal models of CNS disease
- Assessing functional connectivity using fMRI and/or EEG in animal models of CNS disease
- Targeted modulation of gene transcription and translation (including endogenous non-coding RNA / RNA regulation/epigenetics
- Cell and Gene Therapy, including technologies for targeting the blood-brain barrier and specific cell types
- AAV mediated gene therapy in the CNS, retinal degenerative diseases or hearing loss (e.g. hair cell regeneration or ribbon synapse regeneration), and technology to deliver AAVs to the brain.
- T cell engagers
- BiTEs
- Diagnostics, stratification and therapeutic approaches for sensorineural hearing loss (including synapse or hair cell regeneration, prevention of ear inflammation and oxidative stress)

Novel modalities

A full list of modalities is at the Technologies list. In the context of neuroscience, there is interest in coupling novel chemical or biological entities, cellular or genetic approaches with improved mechanisms for delivery to the brain.

Digital therapeutics

- Novel evaluation methods or technologies for cognitive functional domains in CNS diseases
- Novel evaluation (diagnosis) methods in clinical setting using digital biomarkers for CNS disease

- **Digital solutions e.g. smartphone applications, computer software (In particular for Alzheimer's disease and dementia)**
- **Non-drug treatments for CNS diseases or chronic pain e.g. smartphone applications, computer software**
- Medical devices for non-drug treatments (e.g. Virtual Reality-based therapeutics for chronic back pain)

Immunology & inflammation

Relevant companies: Bristol Myers Squibb, Ferring, GSK, J&J, Pfizer, Astellas, Eli Lilly and Company, MSD

Disease areas:

- **Immuno-oncology** (see also oncology)
- **Neuroinflammation** (see also neuroscience)
- **Gastro-intestinal disease**
    - IBD, IBS, Crohn's Disease, ulcerative colitis, refractory coeliac disease, cilial disease; Approaches targeting the adaptive immune pathway; Approaches to enhance Treg function and abundance and activation of co-inhibition pathways; Looking beyond live microbial consortia to specific small molecule therapeutics that target pathogenic strains and metabolites derived from microbial strains, intestinal fibrosis

- **Rheumatology**
    - Systemic rheumatic diseases; Rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, SLE and LN, Sjogren's syndrome, Scleroderma, Polymyositis; Targeting mechanisms that address adaptive and innate immunity activation as well as adaptive counter-regulation; Complement mediated alternative pathway activation; Nucleic acid sensing; Novel combination approaches; Novel targets to address for SLE and LN

- **Dermatology**
    - Psoriasis, Atopic Dermatitis, Hidradenitis suppurativa; palmoplantar pustulosis, Alopecia, Vitiligo, Hiradenitis Suppurativa; Acne, pemphigus and systemic approaches to these diseases

- Lung immunity
- Heart disease and inflammation
- Fibrosis and inflammation
- Immunology & Inflammation in reproductive medicine and women's health
- Peanut allergy and celiac disease (including antigen specific and other immune modulating treatments)
- ANCA associated vasculitis
- Autoimmune diseases with defined autoantigens
- Pathways that are specific to patient-stratified populations in inflammatory disease

Biological understanding and therapeutic approaches:

- Innate and adaptive immunology
- Non-immune side of immunology: stromal interactions and tissue barrier function
- Tissue-immune system crosstalk in disease pathology: tissue-resident immune cells

- Immunomodulation, including novel targets in innate lymphoid cells
- Senescence
- T cell exhaustion
- Regulatory T cells, including engineered or optimized Tregs
- Regulatory B cells
- Myeloid cells that might promote immune resolution including engineered or optimized macrophages
- Biological pathways that selectively govern the induction of immunoregulatory cells, such as Tregs, macrophages, mesenchymal stem cells, dendritic cells and regulatory innate lymphoid cells
- Nucleic acid sensing
- Microbiome (for IBD and IBS)
- Complement
- Il-23 Pathway (including small molecule and other oral approaches for this pathway)
- Immune system modulation through the manipulation of mitochondria

Technologies and modalities

- Senolytic / senomorphic approaches to resolve fibrosis and inflammation
- Diagnostic tests to validate known prognostic disease biomarkers
- RNA as a therapeutic modality
- Immune cell reprogramming

Infectious disease

Relevant companies: GSK, Shionogi, Pfizer, Astellas

- SARS-COV-2
- HBV and HIV
    - HBV Immune therapeutics (TLR/RIG-I agonists, immune activation in the liver, checkpoint and MDSC inhibitors); and HBV antivirals (targeting cccDNA, replication inhibitors, HBX pathway, nucleic acid therapeutics). For HIV, this includes molecules / pathway expertise in "HIV Cure" approaches (latency reversing agents, bNAbs, immune clearance of reactivating cells; and Novel HIV vaccine approaches (therapeutic or prophylactic Vx; also interest in cure instead of chronic treatment)

- Respiratory Pathogens
    - Targets for pan-respiratory infections
    - Novel influenza antivirals (especially Influenza B)
    - Novel rhinovirus or human metapneumovirus antivirals / host pathways implicated in viral pathogenesis; novel inhibitors of pNTM (human non-tuberculosis mycobacteria)
    - Novel host targets or therapeutics that selectively suppress excessive inflammation caused by respiratory infections, including suppression of ARDS

- Ideas for host immune system modulation to develop novel anti-viral, anti-bacterial, antifungals or antimalarial
- Clinical/translational research for an identification of etiological factors affecting severities and outcomes of infectious diseases
- Antibacterial resistance and hard to treat microbial infection

- Novel compound or technology (Vaccines also in scope), in particular to control Pseudomonas aeruginosa infection; Infection following acute exacerbation of COPD, infection in CF or non-CF Bronchiestasis patients and polymicrobial infection; Concepts of biofilm formation or persistence (excluding general drug resistance mechanism)

- Global Public Health
- MRSA (Methicillin resistant Staphylococcus aureus)
- Chlamydia
- ETEC (enteropathogenic E. Coli)
- Targets for antimalarial vaccine
- Drug targets for preventing severe Malarial infection
- Targets for a universal vaccine
- Mycobacterial infection

Therapeutic approaches

- Pathogen and host targets
- Novel dengue virus or pan-flavivirus antivirals or vaccines
- Understanding of the immune pathways that need to be increased or decreased to reach a sweet spot between fighting infection or conversely limiting tissue damage
- Targets and strategies that can be used for other diseases e.g. pan-respiratory
- RNA-based vaccines
- EBV
- **Pandemic preparedness** (e.g. Lassa, Nipah)
- Novel approaches to adjuvants

Technologies

- Development of smart pills e.g. to improve/ensure compliance of HIV patients
- New technology that would induce immune response in mucus in mouth and at local infection site
- New (humanised) models to study chronic viral infection of hepatitis B, papilloma virus
- New pre-clinical models for human rhinovirus infection
- New technologies for the administration, evaluation and design of new vaccines
- Next generation antibody technology

Oncology

Relevant companies: Astex, AstraZeneca, Bristol Myers Squibb, Eisai, Eli Lilly and Company, Ferring, GSK, J&J Innovation, Pfizer, Astellas, Shionogi, MSD

Cancer types

- **Hematologic malignancies** (e.g. B-cell malignancies, multiple myeloma, myeloid malignancies, AML)
- **Lung**
- **Colorectal**
- **Breast**
- **Ovarian**
- **Prostate**

- Uro-oncology, including Bladder, Upper tract urothelial cancer (UTUC) and prostate
- Gastrointestinal
- Sarcoma
- Pancreatic cancer
- **Any tumour type where there is a recognisable targetable sub-population of interest**
- **Novel targets in indications with limited existing, targeted therapies,** g. small cell lung cancer or glioblastoma

Target identification and validation, approaches to disease understanding and therapeutic intervention

- **DNA damage response**
- **Chromatin regulation**
- **Epigenetics**
- Cell cycle
- **Cellular senescence**
- Fibrosis
- Understanding the role of the microbiome
- Protein homeostasis and degradation
- Validated and novel E3 ligands and/or tissue or disease specific E3 ligands
- Novel approaches to target undruggable proteins
- Retrotransposons and LINE1 elements
- R-loop pathobiology
- Cell surface proteins expressed specifically on solid tumour cells
- **Tumour heterogeneity and evolution**
- **Tissue-immune system crosstalk and tissue-resident immune cells**
- **Tumour microenvironment**
- Tumour intrinsic biology
- Long-term survivors
- Mechanisms of drug tolerance and drug-tolerant persister cells (DTPs)
- Screening platform for multi-specific antibodies. i.e. antibodies that bind more than one antigen
- Technologies that impact mitochondrial protein homeostasis, DNA variation and mutation

Immuno-oncology

- **Immune senescence**
- Immune Therapy
- **Developing next-generation I-O therapies, including targeting the microbiome**
- Directed T cell therapies
- Regimens that trigger potent, specific T cell immunity
- **Immune biomarkers**, including minimally invasive biomarkers of immune cell activity in the tumour microenvironment and tumour destruction
- Mechanisms to circumvent IO resistance
- Tumour microenvironment related to immunology including spatial distribution and relation to outcome
- Macrophage biology
- Natural killer cell biology
- Immune cell reprogramming
- Overcoming T cell exhaustion; enhancing antigen presentation
- CD3 engagers

- Small molecule immune-modulators and combinations with immunotherapies
- Novel approaches to modulate the tumour microenvironment
- Mitochondrial biology involved in immunometabolism, particularly in T cell activation and macrophage differentiation

Technologies and approaches in oncology

- Identifying and targeting early-stage disease
- Preventing overtreatment
- Methods to better understand tumour microenvironment, including spatial analyses
- New approaches to local therapy
- **Single cell sequencing** e.g. to understand resistance
- **Direct tumour targeting**
- **Liquid biopsies and cfDNA**
- Cell and gene therapy
- **Novel and rational combination/synthetic lethality-driven treatments**
- **Improved models of disease (e.g. patient-derived)**
- Innovative target identification and validation using novel technologies or model systems
- Microbiome
- New imaging approaches
- RNA as a drug, small molecule RNA binders
- **Novel modalities** (e.g. PROTACs, ADCs, Small molecule chaperones, Protein stabilisers, Protein degraders, Nitrases)

Microbiome

Relevant companies: Ferring, Shionogi, Astellas

- Gut dysbiosis, host-microbiome signals
- Role of microbiome in uro-oncology
- Respiratory microbiome
- Studies supporting microbiome treatment as strategy for other disease areas
- Microbiome-based solutions for prevention/interception of childhood allergic disease or celiac disease
- Novel microbiome targets and/or Dx for adenoma occurrence or recurrence
- Technology that lets probiotic bacteria settle at specific sites in the human gut
- *In vitro* models of human gut microbiota
- *In vivo* models that simulates human gut microbiota
- Contribution of microbiome to maternal health and reproductive medicine
- Identification of bacteria that drive response to cancer immunotherapy
- Microbiome interaction with existing Tx in IBD (e.g. drug metabolism, efficacy of small molecules or biologics.)
- Identification of microbiome associated with disease course in IBD
- Microbiota in small intestine and their roles in in triggering and maintaining inflammatory diseases

Metabolic and cardiovascular disease

Relevant companies: J&J Innovation, Pfizer, AstraZeneca, Eli Lilly and Company, Astellas

- Metabolism and cardiovascular risk factors
- Heart failure

- Pulmonary hypertension and adjacencies, including Idiopathic Pulmonary Fibrosis
- NASH and NAFLD (including targeting senescence to improve metabolic dysfunction)
- Cachexia
- Obesity
- Diabetic/chronic kidney disease, AKI
- Common retinal degeneration conditions: Age-Related Macular Degeneration (Wet, Dry / Intermediate, Geographic Atrophy), Diabetic Macular Edema / Diabetic Retinopathy, Retinal neuroprotection
- Rarer inherited retinal diseases: e.g. Stargardt Disease, Retinitis pigmentosa

- Type 1 Diabetes
    - BMs/tests that anticipate β-cell destruction
    - Treatments suppressing impact of environmental triggers
    - Treatments suppressing immune activation
    - Treatments that maintain normal insulin production in those susceptible to T1D
    - Adjunctive therapies to insulin in T1D that result in substantial HB1Ac lowering
    - Clinical data sets

- Type 2 Diabetes

Technologies

- Better in *vitro/in vivo* models for predicting liver damage
- Gene therapies
- Extended release technologies

Musculoskeletal disease

Relevant companies: Shionogi, Pfizer, Eli Lilly and Company, Astellas

- Novel drug targets or lead compounds for sarcopenia
- Neuromuscular disease
- Duchenne muscular dystrophy
- Mitochondrial biology, including Ca^{2+} signalling and biology, and apoptosis

Rare disease

Relevant company: Pfizer, Astellas

- Rare haematology
- Rare cardiac disorders
    - Rare inherited, dilated & arrhythmogenic hypertrophic cardiomyopathy; Amyloid light-chain amyloidosis (AL-Amyloidosis); Rare heart rhythm disorders

        - Novel concepts underlying the cause of disease such as mutant or modifier genes or signalling pathways
        - Novel treatments that reverse existing pathology

- Rare renal disorders

- Focal Segmental Glomerulosclerosis, IgA Nephropathy, Alport Syndrome, or Autosomal Dominant Polycystic Kidney Disease:
    - Novel targets/pathways to improve glomerular filtration
    - Mechanisms to reduce IgA deposition or slow renal decline post deposition
    - Mechanisms to reduce cyst size, growth, formation and downstream effects on renal function

- Rare metabolic/ endocrine diseases
- Neuromuscular disease
    - Emerging science on repeat expansion diseases, DNA damage response, replicative stress and cellular senescence
    - AAV based approaches for gene therapies

- Mitochondrial diseases

Reproductive medicine and maternal health

Relevant company: Ferring

- Male infertility: novel targets/mechanism or treatment approaches
- Female infertility: novel targets/mechanism or treatment approaches
- Organoid models, including endometrium, ovarian and testicular, to better understand the biology of fertility
- Disease understanding, novel targets or treatments for endometriosis, preterm birth, preeclampsia and polycystic ovary syndrome
- Novel *in vitro*/*ex vivo*/*in vivo* models to study reproductive medicine or maternal health
- Computational Biology/AI-driven approaches to identify novel potential drugs/targets in reproductive medicine/maternal health

Technologies

This list includes novel methods and technologies that are potentially relevant across different disease areas and are of interest for many of the Consortium companies. Please also see the technologies that are particularly relevant to specific disease areas.

There is strong interest in teams who are developing technologies, methods or modalities in other disciplines and working with researchers to apply these in disease biology.

Computational biology

- **Novel approaches for interpreting cfDNA**
- Immuno-informatics methods
- Translational expression methods in single cells
- Differential expression and crosstalk in organoid or complex cell models
- **Novel approaches to guide unique gene editing capabilities**
- AI and Machine Learning for drug discovery, biomarkers and novel applications
    - The application of novel 'omics approaches, including metabolomics and proteomics
    - Spatial methodologies (including their integration with H&E samples and omics data)

    - Multi-modal integration including phenomics
    - Digital biomarkers
- AI or another technology to analyse chemical or protein structure for potential toxicological profile
- **Mechanisms to aggregate or stimulate datasets in a coherent way**
- Applications of AI in chemistry and other disciplines
- In silico approaches for the design of functional proteins
- In silico chemical synthesis to identify chemical structures with reduced off target toxicity of a known compound or small molecule
- Methods for studying the biology of DNA nucleotide repeats and their contribution to disease
- Technology related to mutagenicity risk of nucleic acid analogues
- Methods to predict clinical efficacy based on polypharmacology
- Bioinformatics

Sequencing, multi-omic approaches and protein biochemistry

- Proteomics, Epigenomics or Metabolomics
- Integrative multi-omics approaches
- Immunophenotyping (single-cell and spatial 'omics)
- Single cell genomics and proteomic platforms
- scRNAseq multiplexing
- Novel high throughput proteomics platform with high sensitivity

Functional Genomics

- CRISPR screening methods in organoids / complex cell systems
- Functional genomics screening with high-dimensional protein-level readouts
- Methods to integrate single-cell perturbation data with single-cell disease atlases for target discovery

RNA drug discovery

- Technology to predict secondary and tertiary structures of RNA molecules (mRNA, non-coding RNA etc.)
- Technology to identify secondary and tertiary structures of RNA molecules (SHAPE technology, DMS technology etc.)
- Small molecule RNA binders and inhibitors
- RNA as small molecule target (approaches, modelling and targets)
- Approaches to improve understanding causal links between non-coding elements and gene expression
- Efficient mRNA modification technologies
- Novel approaches that enable *in vivo* mediated cellular reprogramming
- Novel non-viral vectors or lipid nanoparticles

RNA-based Therapeutics

- In vivo or in situ cell reprogramming for cancer therapy (modification of immune cells (T-cell, myeloid cells) tumor cells, Immuno-oncology or inflammation & immunology (eg fibrosis) using mRNA and (lipid) nanoparticles
- Approaches that enhance tissue, organ or cell-type specific targeting of (lipid) nanoparticles

Disease models

There is strong interest in models that are patient-derived and have been demonstrated to be disease relevant. Key considerations will include how well the model reflects and predicts disease pathology, how well it can be used for screening assays and whether it could be scalable.

- Organoids in which genetic changes have been causally linked to disease phenotypes (n.b. consideration of model limitations will be important)
- Senescence models e.g. to study senomorphic or senolytic agents
- Tissue slice methods and tissue explants
- Functional Genomics and phenotypic models
- Microphysiological systems for safety/metabolism for screening
- *in vitro/ex vivo* reconstitution of 3D tumours or other disease models
- Cell and Gene Therapy
- *In vivo* trans-differentiation of cells e.g. astrocytes to neurons
- Organ-on-a-chip technology that can be used to test pharmacokinetics (e.g. culture of intestinal, renal and hepatocyte cells)
- Kidney disease-relevant preclinical models

Structural biology

- Materials science/surface chemistry for EM-grids
- Accessing reagents for stabilising individual proteins and protein complexes and/or increasing the size of proteins for EM (Antibodies, Aptamers, Nanobodies Darpins etc)
- Incorporation of non-standard amino acids into proteins
- Novel methods for purifying/isolating/stabilising membrane proteins for structural studies (EM/X-ray)
- New expression systems, including cell free technologies, for membrane proteins
- Emerging protein structure determination platforms
- Next generation platforms for protein structure prediction
- Investigating docking of peptides to target proteins
- Labelling methods for medium-sized molecules (peptides, nucleic acids, etc.)

Imaging technologies

Super resolution imaging platforms (such as 3D bioprinter, intelligent image analysis tools, tissue imaging and real time single cell sorting/ purification based on machine learning)

Targeted delivery approaches

- Technologies for targeting the blood-brain barrier and specific cell types
- Technologies to deliver peptides or nucleotides to specific tissues or organs
- Novel approaches to enable peptide delivery to cells
- Novel technologies to improve peptide pharmacokinetics after oral or parental delivery
- Solid state stabilization of proteins to enable high-concentration parenteral delivery
- Biomolecular condensates
- Lipid nano particles (LNPs) or other non-viral based technology for gene modulation in cells
- Technologies directed toward enhancing GI absorption of poorly absorbed compounds or enabling novel delivery methods (colonic, intraoral, subcutaneous, intra-tumoral)
- Drug delivery systems using nasal aerosol

- Novel modalities that enable disease or tissue specific gene expression
- Approaches to enable multiple exposures to (redosing with) AAV based vectors
- Technologies and approaches for LAP (Long-acting parenteral formulation) drug discovery

Systems biology tools to evaluate pharmacologic/toxicologic responses

Chemistry and novel drug modalities

- Chemical biology tools to expand FBDD capabilities: Biological validation of novel binding sites; Cellular target engagement tools
- Chemoproteomics: Novel target ID (oncology and CNS), particularly for targets where we can deploy CryoEM (ion channels / GPCRs)
- Medicinal Chemistry: High throughput experimentation – automation for fragment elaboration, Reaction prediction, Encoded library technology
- Non-invasive approaches that quantitatively monitor the toxicology phenotype of a new therapeutic
- Novel approaches to predict ligand affinity
- Biomaterials the increase engraftment, survival and function of transplanted cells
- PROTACs and compounds that induce protein degradation or stabilization
- Molecular glues
- DUBTACs
- Small molecule chaperones
- Nitrases, a recently identified enzyme class with reported role in Parkinson's disease
- Antibody-drug conjugates (ADCs)
- ASO – ligand conjugates: antisense oligos with receptor binding moiety appended to facilitate internalisation
- Bi- and tri-specific antibodies
- Conjugated oligos (RNA / DNA)
- RNA as a drug
- T-cell engagers, BiTEs
- RNA-stabilizing or editing technologies, coupled with improved delivery e.g. to brain
- Gene therapy technologies to drive differentiation, maturation, or cell function
- Synthetic process automation of low-molecular-weight compounds using robots
- Automated synthesis + biocatalysis

Devices and non-drug technologies

- Digital solutions e.g. smartphone applications, computer software (In particular for Alzheimer's disease and dementia)
- Companion digital therapeutics that enhance delivery of care
- Controlled release technologies for drug delivery
- Drug delivery device technologies

Bioscience

- Cell cycle
- Novel approaches to target undruggable proteins
- Single cell sequencing e.g. to understand resistance
- Novel and rational combination/synthetic lethality-driven treatments (Dual CRISP)
- Methods to integrate single-cell perturbation data with single-cell disease atlases for target discovery

- Innovative target identification and validation using novel technologies or model systems
- New imaging approaches
- Cellular and in vivo models that are better predictors of disease