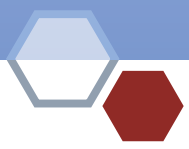
Australian Government
Department of Health

Medical Research Future Fund

# Stem Cell Therapies Mission

## Implementation plan

October 2021



# Background

Research advances over the past 10 years have shown the potential to develop new treatments using human stem cells. Stem cells may restore function to damaged tissues, be used to engineer replacement tissues and organs, or boost the body's ability to heal itself.

Human stem cells can also be used in the laboratory to create models of human tissues, allowing us to better understand what happens to the body during disease and potentially revolutionising drug development practices.

Both of these broad applications of stem cells could provide innovative treatments for many chronic and inherited diseases that have major unmet clinical needs.

The goal of the Medical Research Future Fund (MRFF) Stem Cell Therapies Mission is to support world-leading translational stem cell research that develops and delivers innovative, safe and effective stem cell medicines to improve health outcomes, in partnership with patients and carers.

This plan supports the implementation of the Stem Cell Therapies Mission roadmap and establishes a strategic plan to address the mission's goals within the context of the MRFF 10-year plan. This implementation plan should be read in the context of the mission roadmap, which describes the mission's scope, goals and principles.

## Scope of mission

The mission will invest in 'novel' stem cell research, such as new treatments involving stem cells or stem cell–derived tissues/derivatives, or new applications of human stem cells or stem cell–derived tissues to develop new drugs or therapies.

Within the Stem Cell Therapies Mission, the term 'stem cells' encompasses:

### Tissue stem cells

Tissue stem cells are stem or progenitor cells isolated from, or residing within, adult tissue for the purposes of tissue turnover, repair and homeostasis. Such stem cells may be developed as the therapeutic agent in situ, ex vivo or in vivo, or used to model the tissue in vitro for compound screening and drug development.

This stem cell type is pertinent to research funded through Aims 1, 2 and 3.

### Pluripotent stem cells

A pluripotent stem cell is a cell type capable of differentiation into any other cell type. Such stem cells may be differentiated into a required cellular endpoint or into multicellular tissues. The resulting cells and tissues, but not the initial pluripotent stem cells, can either represent the therapeutic agent or the tissue model for compound screening and drug development.

This stem cell type is pertinent to research funded through Aims 1, 2 and 3.

### Cancer stem cells

A cancer stem cell is the cell type present within a cancer that can give rise to all other cells within a neoplasm. As such, this is the primary target for a cancer therapy. Cancer stem cells can be used as generic or personalised models of cancer initiation and progression, and used for compound screening and drug development.

This stem cell type is pertinent to research funded through Aims 2 and 3.

## Mission research priorities

The research priorities described in the Stem Cell Therapies Mission implementation plan address key parts of the translation pipeline from discovery (of a new potential therapy or model to test therapies) through to early phase clinical trials to support commercialisation. The mission has identified three interrelated aims (areas of research) that require support for the stem cell treatment sector in Australia to realise its potential.

Funding will focus on:

- accelerating the development of safe, effective and affordable stem cell–based therapies (stem cell treatments)
- generating new treatments using human tissues made from stem cells (disease modelling for drug development)
- building the health system and commercial sector to deliver these transformative treatments for the community (a sector prepared to deliver stem cell treatments)

A coordinated funding approach across the translation pipeline is required to enable the mission to successfully achieve its goal. The implementation plan supports the funding of short-term discovery projects at entry to the pipeline throughout its timeline. Targeted programmatic funding at various intervals

will provide multidisciplinary teams with the ability to develop new stem cell therapies or new drug options to be screened and evaluated ready for clinical trial. The sequential funding of Phase I/IIa evaluation of novel therapies/drugs to facilitate commercialisation is envisaged across the timeline. To facilitate building the health system and commercial sector capabilities required to deliver stem cell treatments, funding is likely to be dispersed via discrete projects and via encapsulation into the programmatic development projects.

## Aim 1. Accelerate the development of safe, effective and affordable stem cell–based therapies

**The challenge:** Development of novel therapies using stem cell and regenerative medicine has been slow, leading to new treatments being delayed. Internationally, the demand for stem cell therapies has opened up an opportunity for unproven treatments using poorly defined cell types, often through direct-to-consumer marketing and outside of an appropriate regulatory framework. Safe and effective stem cell treatments are required to meet community expectations. The development of such treatments based on sound evidence must be prioritised to accelerate delivery for Australian patients.

**The opportunity:** Regenerative stem cell–based treatments are a promising option for the treatment of many chronic and inherited conditions. Capacity building across the clinical and biotechnology sector will ensure that we can deliver emerging stem cell treatments to Australian patients.

This aim is envisioned to encompass the direct use of stem cells in the treatment of disease. Stem cell treatments may include the:

- activation or modification of tissue stem cells within the patient to improve repair
- generation of required cell types from stem cells for delivery into a patient
- delivery of stem cells themselves into a patient to generate new tissue in vivo

This aim will support projects that:

- establish evidence to support the development of a novel stem cell–based treatment (Priority area 1.1)
- develop novel stem cell–based treatments (Priority area 1.2)
- support early stage (Phase I/IIa) clinical studies of novel stem cell–based treatments (Priority area 1.3)

## Aim 2. Generate new treatments using human tissues made from stem cells for pre-clinical therapeutic development

**The challenge:** Current models of human diseases are poor, resulting in ineffective, expensive and potentially unsafe treatments. There is an urgent need for potential new treatments to fail early in the development pathway, rather than later at the clinical trial phases.

**The opportunity:** Human stem cells can more accurately model human disease (including inherited disease, complex disease, infectious disease and cancer) than cell lines or animal models. Using human stem cell–based models will speed up the pre-clinical evaluation of potential new treatments and reduce the chance of failure at clinical trial.

This aim is envisioned to encompass the use of stem cells to model human tissues in vitro to enhance screening for the development of drug and gene therapies.

This aim will support projects that:

- develop disease model platforms (Priority area 2.1)
- evaluate and screen new treatments using human tissues derived from stem cells (Priority area 2.2)

Capacity building will be a key component of projects funded through Aims 1 and 2. Capacity building across the clinical and biotechnology sectors may include training opportunities to address key technical, regulatory and ethical considerations and support for:

- critical skillsets for large multidisciplinary teams within the cell therapy ecosystem required for the Stem Cell Therapies Mission to succeed
- critical skillsets for the translation of stem cell–based products

In addition, research on the ethical, legal and social issues associated with the development and use of stem cell–based treatments and disease modelling is critical for understanding and supporting community adoption of these technologies.

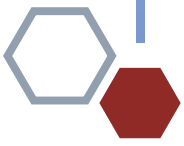
## Aim 3. Build the health system and commercial sector to deliver these transformative treatments for the community

**The challenge:** Health systems, clinicians, regulators, industry and the community are not prepared for stem cell and regenerative medicine therapies. This lack of preparedness includes a lack of appropriate frameworks for public engagement and involvement.

**The opportunity:** Social policy, health economics, legal and ethics research will ensure that patients are able to benefit from treatments that are safe, effective, affordable and equitable in availability.

This aim is envisioned to underpin the sector development required to ensure delivery of products developed within Aims 1 and 2.

This aim will support ethics, legal, health economics and social research into the development and use of stem cell–based treatments and disease modelling (Priority area 3.1).



# Overview

To target activities to achieve the objectives of the mission within the 10-year plan, the following aims and priority areas for research investment have been identified.

| Aim | Priority areas for investment |
|---|---|
| **1**. Accelerate the development of safe, effective and affordable stem cell–based therapies | **1.1** Establish evidence to support the development of novel stem cell–based treatments |
| | **1.2** Development of novel stem cell–based treatments |
| | **1.3** Early clinical studies (Phase I/IIa) to evaluate safety and efficacy of novel stem cell–based treatments |
| **2**. Generate new treatments using human tissues made from stem cells for pre-clinical development | **2.1** Develop disease model platforms |
| | **2.2** Evaluation and screening using stem cell–derived tissue models |
| **3.** Build the health system and commercial sector to deliver these transformative treatments for the community | **3.1** Ethics, legal, health economics and social research into the development and use of stem cell–based treatments and disease modelling |

# Implementation strategy

The implementation strategy has been developed to guide research investment over the life of the mission. Investment aims to build capability and knowledge, as well as facilitate translation of advancements to clinical practice, to achieve the mission's objectives. The implementation strategy is intended to make the research purpose and direction transparent, and provide certainty to stakeholders. It also establishes how the outcomes of each priority area will be evaluated in terms of benefit to Australian patients, which will help to clarify the intended outcome and facilitate tracking of the mission's progress towards its objectives.

Research activities will be, or contribute to, large programs of work of national strategic importance that are informed by the key priority areas outlined in this implementation plan. The research activities are expected to foster collaboration and harness resources across the system to deliver improved health outcomes for Australians.

The MRFF Monitoring, evaluation and learning strategy provides an overarching framework for assessing the performance of the MRFF, focused on individual grants, grant opportunities, initiatives (eg the Stem Cell Therapies Mission) and the entire program. The strategy sets out the principles and approach used to monitor and evaluate the MRFF. It outlines the need for evaluations to be independent and impartial. The strategy aims to be transparent in process and outcomes, and agile to the needs of the MRFF, its consumers and stakeholders (such as the health and medical research industry). The Stem Cell Therapies Mission and grants funded under this initiative will be evaluated against the strategy.

For each aim and priority area for investment, the implementation plan identifies additional research and other activities required outside of the mission to facilitate and support the MRFF-funded research and long-term implementation.

The following enablers will provide overarching support for the Stem Cell Therapies Mission's implementation:

- key national infrastructure, including Therapeutics Innovation Australia and Phenomics Australia
- an ecosystem that encompasses the whole therapy development pathway for stem cells
- national and international advances in cellular manufacturing and cell-based clinical trial expertise
- international research, development and commercialisation partnerships and linkages to maximise investments through the mission
- effective collaborations with allied groups – including foundations, alliances and networks – to coordinate effort and avoid duplication to improve mission impact

AIM 1

# Accelerate the development of safe, effective and affordable stem cell–based therapies

## Priority area 1.1

Establish evidence to support the development of novel stem cell–based treatments

| **Research to begin in the ...** | **Priorities for investment (research questions and objectives)** |
|---|---|
| **short term**<br>1–2 years<br>**medium term**<br>2–5 years<br>and<br>**long term**<br>6–10 years | Throughout the Stem Cell Therapies Mission, short-term, small-scale development projects will support studies to establish the feasibility of novel cellular therapies. Such development projects should involve novel applications of human tissue or pluripotent stem cells. |

## Opportunities to use additional investment and other research to support the priority areas include, but are not limited to:

- Charities and patient advocacy groups
- State government health departments
- Cooperative Research Centre projects, National Health and Medical Research Council and government departments (eg industry, education, defence)
- Private and public hospitals
- Early-stage Australian venture capital funds, including the Biomedical Translation Fund
- MRFF initiatives, including for research infrastructure
- Philanthropists

## Activities required to support the research and facilitate long-term implementation include, but are not limited to:

- Access to clinical-grade (current Good Manufacturing Practice [GMP]) stem cell lines
- Clinician enablement and training
- Cell storage and banking and delivery processes
- Patient engagement and preparedness (for the research and the implementation of the treatments)

## Priority area 1.2
### Develop novel stem cell–based treatments

| Research to begin in the ... | Priorities for investment (research questions and objectives) |
|---|---|
| **medium term** 2–5 years to **long term** 6–10 years | Novel stem cell-based treatments developed by disease-focused, multidisciplinary teams that leverage partner funds and can articulate:<br>• a final product or therapy<br>• a feasible path to market<br>• an approach to regulatory processes<br>• a competitive advantage over comparable products<br>• appropriate consideration of the ethical, legal and social issues associated with treatments<br>• a strategy for enhancing sector capacity of key clinical, manufacturing and commercial skillsets<br>• potential funding leverage |

## Opportunities to use additional investment and other research to support the priority areas include, but are not limited to:

- Charities and patient advocacy groups
- State government health departments
- Cooperative Research Centre projects, National Health and Medical Research Council and government departments (eg industry, education, defence)
- US National Institutes of Health, the Department of Defense, the Defence Advanced Research Projects Agency or other non-Australian grants
- Public and private hospitals
- Early-stage Australian venture capital funds, including the Biomedical Translation Fund
- Biotechnology and pharmaceutical companies
- Philanthropists
- Australian Government Department of Industry, Science, Energy and Resources (including through MTPConnect)
- MRFF's Researcher Exchange and Development within Industry initiative, and Medical Research Commercialisation initiative (which supports the Biomedical Translation Bridge and BioMedTech Horizons initiatives)
- National Collaborative Research Infrastructure Strategy

AIM 1

## Activities required to support the research and facilitate long-term implementation include, but are not limited to:

- Specific capacity building, including cellular manufacturing, biotechnology and specific cell therapy–based clinical trial expertise
- Australian-based cellular manufacturing
- Funding of cellular manufacture platforms and infrastructure
- Access to clinical-grade (current GMP) stem cell lines
- Generation of, and access to, appropriate current GMP lines for clinical trials
- Cell storage and banking and delivery processes
- National guidelines for the use of stem cell therapies
- Harmonised patient consent practices for stem cell clinical trials
- Clinician enablement and training
- Clinical trial design and infrastructure specifically for the delivery of stem cell products
- A vibrant national network of clinical trial centres delivering stem cell treatments
- Dedicated ethics approval committees to oversee stem cell trials
- Patient engagement and preparedness (for the research and the implementation of the treatments)
- Clinical trial centres enabled to deliver cellular therapies
- More ready access to regulatory and GMP advice
- Vibrant and skilled business development sector with experience in cellular products
- Review of legislation, regulation and policy around delivery of cellular products in Australia
- Review of regulation around the generation of chimeric animals in pre-clinical studies
- Improved international visibility for the sector in stem cell products and/or clinical trials

## Priority area 1.3

### Early clinical studies (eg Phase I/IIa) to evaluate the safety and efficacy of novel stem cell–based treatments

For novel stem cell treatments to reach patients, clinical data are needed to examine safety (that is, to determine how the treatment will be given and any side effects) and determine whether the treatment is efficacious. Exploratory (pilot) studies examining feasibility and acceptability may also be conducted with safety and efficacy studies such as Phase I/IIa trials. Data from these clinical studies are needed for the regulatory approval of a stem cell treatment.

| **Research to begin in the ...** | **Priorities for investment (research questions and objectives)** |
|---|---|
| **short term**<br>1–2 years<br>**medium term**<br>2–5 years<br>and<br>**long term**<br>6–10 years | Throughout the Stem Cell Therapies Mission, early stage clinical trials (Phase I/IIa) of new stem cell therapies will be funded. These activities will include:<br>• exploratory (pilot) studies to assist the design of clinical studies that will evaluate the safety and preliminary efficacy of novel stem cell–based treatments<br>• clinical studies such as Phase I/IIa trials for novel stem cell–based treatments to demonstrate safety and/or initial efficacy<br><br>Ideally, data from these clinical studies will be incorporated into regulatory approval strategies for the novel stem cell–based therapies. |

## Opportunities to use additional investment and other research to support the priority areas include, but are not limited to:

- Charities and patient advocacy groups
- State government health departments
- Cooperative Research Centre projects, National Health and Medical Research Council and government departments (eg industry, education)
- US National Institutes of Health, the Department of Defense, the Defence Advanced Research Projects Agency or other non-Australian grants
- Public and private hospitals
- Early-stage Australian venture capital funds, including the Biomedical Translation Fund
- Biotechnology and pharmaceutical companies
- Philanthropists

AIM 1

## Activities required to support the research and facilitate long-term implementation include, but are not limited to:

- Australian-based cellular manufacturing, including GMP prototyping and production facilities
- Funding of cellular manufacture platforms/infrastructure
- Generation of, and access to, appropriate current GMP stem cell lines
- Clinician enablement and training
- Clinical trial infrastructure specifically for the delivery of stem cell products
- Dedicated ethics approval committees to oversee stem cell trials
- National guidelines for the use of stem cell therapies
- Harmonised patient consent practices for stem cell clinical trials
- Patient engagement and preparedness (for the research and the implementation of the treatments)
- More ready access to regulatory and GMP advice
- Clinical trial centres enabled to deliver cellular therapies
- A vibrant national network of clinical trial centres delivering stem cell treatments
- Review of legislation, regulation and policy around delivery of cellular products in Australia
- Improved international visibility for the sector in stem cell products and/or clinical trials
- System for reporting adverse events from stem cell therapies
- Improved consultation with the TGA to enhance pathways involved in bringing treatments to the clinic

## Evaluation approach and measures

- Publications generated from mission funding to stem cell therapies
- Patent submissions and granted patents generated from mission funding to stem cell therapies
- Identified ‘unmet needs’ in which a stem cell solution is being developed
- Number of proof-of-concept studies supported
- Successful pre-clinical and proof-of-concept studies for the use of stem cell treatments
- Number of clinical cellular candidates ready for evaluation in Phase II/III clinical trials
- Value of business plans developed by mission-funded programs
- Amount of funding leveraged within mission-funded programs
- Commercial investment in cellular product development

AIM 2

# Generate new treatments using human tissues made from stem cells for pre-clinical development

## Priority area 2.1

### Develop disease model platforms

Human stem cell–based models of disease provide an important ex-vivo method of assessing the potential of novel cellular or drug therapies before clinical trial.

| **Research to begin in the ...** | **Priorities for investment (research questions and objectives)** |
|---|---|
| **medium term**<br>2–5 years<br>to<br>**long term**<br>6–10 years | Research projects may include:<br>• development and validation of human stem cell–based models of disease, including genetic disease, infectious diseases and cancer<br>• development of high-content or high-throughput screening approaches<br>• generation of patient-derived stem cell lines for screening treatments |

## Opportunities to use additional investment and other research to support the priority areas include, but are not limited to:

- MRFF initiatives such as the Genomics Health Futures Mission, the Cardiovascular Health Mission and the Australian Brain Cancer Mission
- National Collaborative Research Infrastructure Strategy, including Phenomics Australia
- Australian Government departments (including Industry, Science, Energy and Resources)
- State government health departments
- National Collaborative Research Infrastructure Strategy
- Philanthropy, disease-focused charities and patient advocacy groups

## Activities required to support the research and facilitate long-term implementation include, but are not limited to:

- Development of patient consent for stem cell derivation
- Good integration with genomics technologies
- Improved national capacity to generate and gene-edit stem cell lines
- Stem cell line registers and repositories

## Priority area 2.2

### Evaluation and screening using stem cell–derived tissue models

Evaluation and screening using stem cell–derived tissue models will be undertaken by multidisciplinary teams that articulate:

- a final target product or therapy
- a feasible path to market
- an approach to regulatory processes
- a competitive advantage over other comparable products
- appropriate consideration of the ethical, legal and social issues
- a strategy for enhancing sector capacity of key clinical, manufacturing and commercial skillsets
- potential funding leverage

Research projects may include:

- screening of novel or repurposed drug candidates, silencing RNAs or therapeutic oligonucleotides or other modifiers of cellular function, including gene editing and base editing
- personalised identification of appropriate drugs based on patient-specific stem cell–derived tissues

| **Research to begin in the ...** | **Priorities for investment (research questions and objectives)** |
|---|---|
| **short term**<br>1–2 years | Application of stem cell–based screens for the development of treatments for inherited disease, complex disease, infectious disease and cancer. |
| **medium term**<br>2–5 years<br>to<br>**long term**<br>6–10 years | Large-scale projects involving multidisciplinary teams will focus on pre-clinical screening of new treatments using human tissues made from stem cells. |

## Opportunities to use additional investment and other research to support the priority areas include, but are not limited to:

- MRFF funding, including Genomics Health Futures Mission (eg funding for functional genomics), the Cardiovascular Health Mission and the Australian Brain Cancer Mission
- National Collaborative Research Infrastructure Strategy, including Therapeutic Innovation Australia
- Leveraged co-funding from commercial partners
- Angel investors and philanthropists
- Early-stage Australian venture capital funds, including the Biomedical Translation Fund
- Pharmaceutical partners
- Charities and patient advocacy groups
- State government departments

Late:

- Venture capital funds
- Pharmaceutical and biotechnology companies
- MRFF Clinical Trial Activity initiative funding

## Activities required to support the research and facilitate long-term implementation include, but are not limited to:

- Funding for clinical trials to test emerging treatments
- TGA acceptance of human stem cell tissue models as an acceptable surrogate for pre-clinical data, which may require communication with the FDA and an FDA lead
- Development of patient consent for stem cell derivation (work with the Genomics Health Futures Mission)
- Good integration with genomics technologies (work with the Genomics Health Futures Mission)
- Improved high-throughput screening capacity

## Evaluation approach and measures

- Publications generated from mission funding to stem cell models
- Patent submissions generated from mission funding to stem cell models
- Identified ‘unmet needs’ in which a stem cell model is being applied
- Number of clinical candidates ready for development
- Amount of funding leveraged within mission-funded programs
- Number of new companies or commercial investment by existing companies in teams using stem cell models for product development

AIM 3

# Build the health system and commercial sector to deliver these transformative treatments for the community

## Priority area 3.1

### Ethics, legal, health economics and social research into the development and use of stem cell–based treatments and disease modelling

Ethical, legal and social implications (ELSI) policy and health economics research will address broad issues in the stem cell sector, such as consent and participation in pre-clinical and clinical research, or discrete issues associated with a particular product, screening platform or treatment.

This research is envisioned to underpin the sector development required to ensure products developed within Aims 1 and 2 are accessible in the clinic for all Australians.

| **Research to begin in the ...** | **Priorities for investment (research questions and objectives)** |
|---|---|
| **short term**<br>1–2 years<br>**medium term**<br>2–5 years<br>and<br>**long term**<br>6–10 years | MRFF investment will focus on the following priority areas:<br>• appropriate ethical and regulatory frameworks<br>• ownership and use of cells and cellular products<br>• community understanding and expectation in stem cell therapies, including approval processes<br>• health economics assessments and evaluations |

## Opportunities to use additional investment and other research to support the priority area include, but are not limited to:

- Australian Research Council (ethical, legal and social implications [ELSI] research)
- Australian Government Department of Industry, Science, Energy and Resources (including through MTPConnect)
- State government departments of health, and industry or development
- Hospitals
- Superannuation funds
- Philanthropy

## Activities required to support the research and facilitate long-term implementation include, but are not limited to:

- Better engagement with the community around what stem cell treatments can do and what they cannot do
- Increased community understanding of the regulatory approval processes for autologous and allogeneic cellular therapies
- Better alignment with relevant international guidelines and regulatory frameworks for appropriate governance of such treatments
- Patient engagement and preparedness (for the research and the implementation of the treatments), including increased visibility around opportunities to participate in clinical trials
- More ready access to regulatory and GMP advice
- Harmonised patient consent practices for stem cell clinical trials
- Dedicated ethics approval committees for stem cell treatments
- Clearer reporting of research outcomes and their significance in terms of progress towards stem cell therapies

## Evaluation approach and measures

Advances in the following ELSI areas:

- Publications generated from mission funding around ELSI of stem cell research and therapies
- Improvement to national guidelines related to stem cell research and clinical translation based on findings from funded research, including those from government agencies and medical specialty colleges
- Deeper understanding of views and concerns of Australians relating to stem cell research and its translation, as reflected in targeted education initiatives and other policy activities
- More standardised approach to ethics committee approval processes for clinical trials of stem cell–based interventions, including development of uniform national consent process for patients to enter stem cell trials
- Development of uniform national consent processes for patients to provide cells for research
- More comprehensive understanding of the health economics impact of stem cell therapies