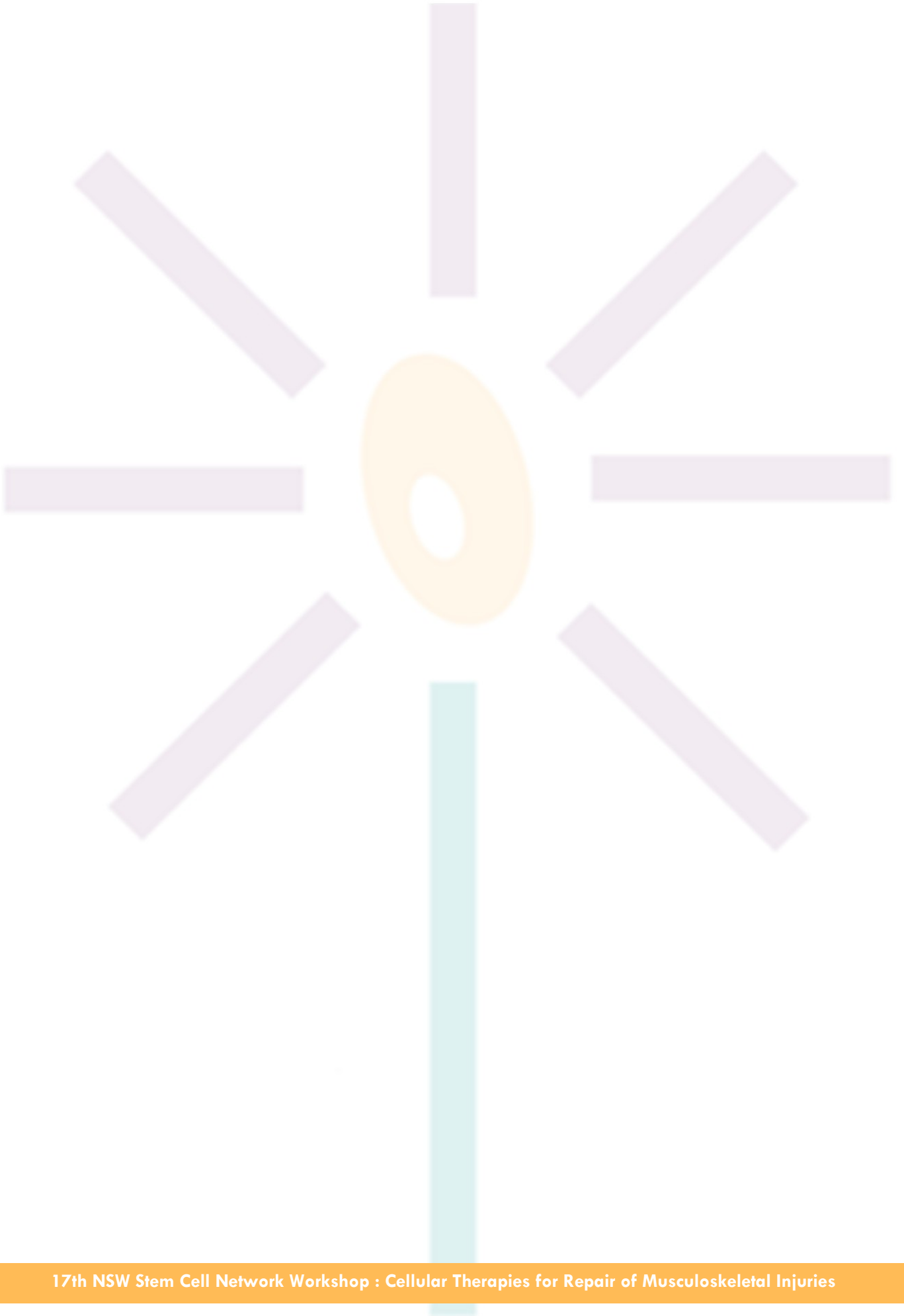


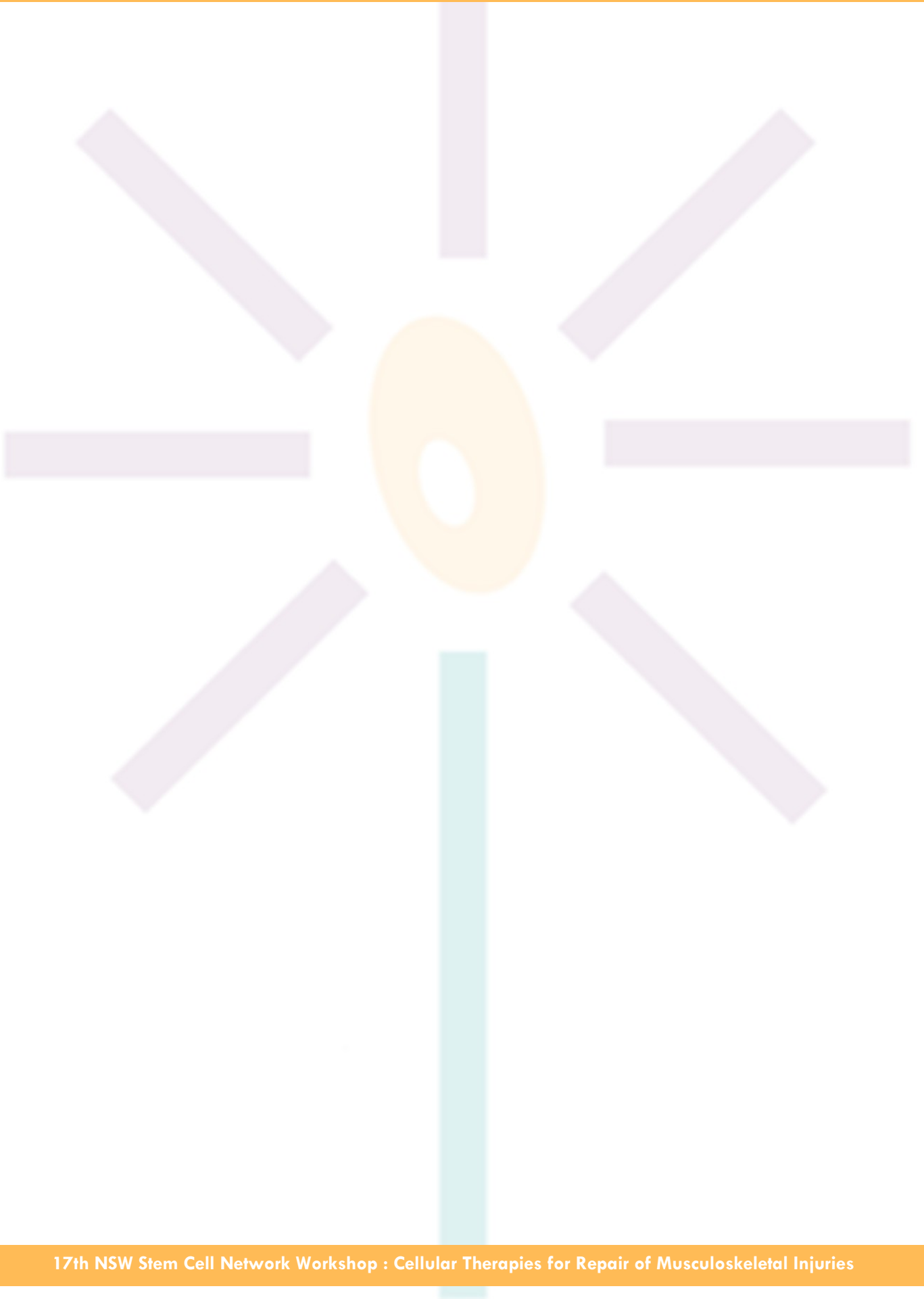
# 17th NSW Stem Cell Network Workshop

## Cellular Therapies for Repair of Musculoskeletal Injuries

Trades Hall Inn,  
Goulburn St, Sydney.  
Wednesday, October 31st, 2012







## NSW Stem Cell Network

### WELCOME

Welcome to the 17th Workshop of the NSW Stem Cell Network.

Just as with the 16<sup>th</sup> Workshop held in April, this one is devoted to a particular theme, *Cellular Therapies for Repair of Musculoskeletal Injuries*.

A reason the Network's Executive chose to hold a Workshop in this area of stem cells is because it is rapidly expanding clinically. Autologous cells being used for treatment of arthritis and other musculoskeletal disorders are mostly derived from the vascular stromal fraction of tissue removed by liposuction. Platelet rich plasma also is being used. And yet, there appears to be little hard evidence, as yet, from clinical trials to show that it works. Despite this, patients are queuing up privately to receive these therapies, and anecdotally, there are many success stories.

Several of the key Australian companies offering these therapies, in Sydney and Melbourne, are speaking today. These include Macquarie Stem Cells, Magellan Stem Cells, Lakeside Sports Medicine Centre and South Sydney Sports Medicine Centre. We look forward to hearing their experiences.

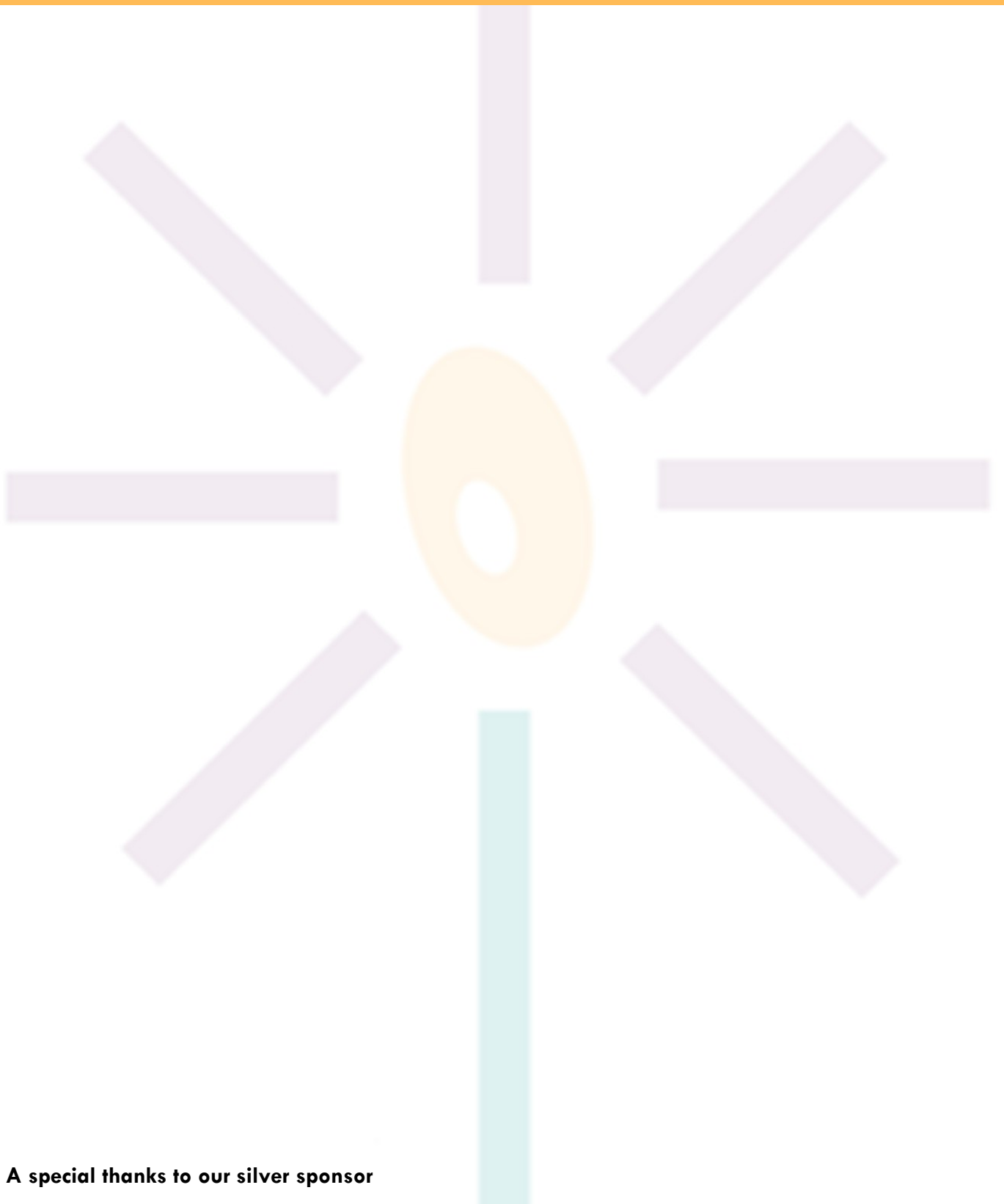
Subsequently, you will hear from Mesoblast that allogeneic progenitor cells also are being trialled for bone and cartilaginous repair. Regulatory approval for this therapy requires clinical trials to be conducted, as advised by the Therapeutics Goods Administration, but not for the autologous therapies. This seems an anomaly.

You will hear from the International Society for Cellular Therapy its views about what it believes is needed to manage the situation. The National Health and Medical Research Council via its expert committees is currently debating issues of this nature, as is the Australasian Society for Stem Cell Research. The Australian Health Practitioner Regulation Agency, which is responsible for ensuring the registration of all clinicians, appears currently to have little interest in the matter.

Because there are likely to be varying views on the best pathway forward to ensure efficacy and safety of the autologous therapies being offered, it was decided to hold a panel discussion on whether the Regulations for Autologous Cell Therapies in Australia should be changed. The Senior Manager in Research & Government of Stem Cells Australia, Associate Professor Megan Munsie, will be the moderator.

It is hoped that from the Workshop we will all be better informed about what is actually occurring in Australia at present with these novel therapies. It is also hoped that a pathway forward will be found to satisfy most that efficacy of these treatments will be examined in an objective manner. Moreover, if evidence is forthcoming supporting the continued use of these cells, this will be done in a safe manner with minimal risk to the recipients, and where patients give fully informed consent.

**Bernie Tuch**  
Director, NSW Stem Cell Network



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## Program

8.00am	Registration opens
8.20am	Opening Address – <b>Professor Jim Patrick, Cochlear Limited</b> The Commercialisation of the Cochlear Implant
Session 1 Chair	<b>Autologous Therapies For Musculoskeletal Injuries</b> <b>Professor Jill Cook, Monash University</b>
8.30am	<b>Dr. Ralph Bright, Macquarie Stem Cells</b> Setting the Scene with Autologous Therapies
8.55am	<b>Dr. Dan Bates, Lakeside Sports Medicine Centre</b> Adipose derived stromal vascular fraction for the treatment of degenerative joint disease
9.20am	<b>Professor Richard Boyd, Magellan Stem Cells</b> The Victorian Experience
9.45am	<b>Dr. Luke Inman, South Sydney Sports Medicine Centre</b> Autologous Platelet Rich Plasma injections to aid in the regeneration of knee particular cartilage lesions. Case studies
10.15am	Morning Tea/Refreshments
Session 2 Chair	<b>Regulation of Cellular Therapies and Managing Community Expectation</b> <b>A/Professor Megan Munsie, Stem Cells Australia</b>
10.40am	<b>Professor Peter Ghosh, Mesoblast</b> Allogeneic Progenitor Cells in Preclinical and Clinical Studies
11.05am	<b>A/Professor Dominic Wall, International Society for Cellular Therapy</b> Ethical, Commercial and Professional Perspectives on Unproven Therapies
11.30am	<b>Dr Mary Boyd Turner, Therapeutic Goods Administration</b> Regulating human cell- and tissue-based therapies in Australia
11.45am	<b>Discussion with Panel: A/Professor Dominic Wall, Dr Ralph Bright, Dr Dan Bates &amp; Professor Peter Ghosh</b> Should the Regulations for Autologous Cell Therapies in Australia be Changed?
12:40pm	Finish

**Professor Jim Patrick - Cochlear Limited**

The Commercialisation of the Cochlear Implant

This presentation will describe how the cochlear implant was taken from a scientific proof of concept in a research laboratory to the commercial success that it is today. It will give an overview of the methods used to prove device safety and efficacy, as well as the approaches that led to acceptance by sceptical medical and scientific communities. It will describe how ongoing scientific and technological advances have assisted adoption by both professionals and candidates and the importance of cost-effectiveness data for reimbursement for different market segments. It will conclude with an overview of the Regulatory requirements and timetables for new product introduction in different regions.

**Professor Jim Patrick** is Chief Scientist at Cochlear Limited and recognized as a world authority on cochlear implants. He joined Professor Graeme Clark's research team at Melbourne University in 1975. With training in physics and communications engineering, and an interest in how electrical stimulation might be used to help people hear, he led the successful development of "UMDOLEE", the ten channel cochlear implant developed by the Departments of Otolaryngology and Electrical Engineering.



When initial proof of concept generated Federal Government support for commercial development in 1981, Jim moved to Sydney as a member of the Cochlear "Tiger Team", established by Paul Trainor inside the Nucleus group to develop a 'clinically applicable' cochlear implant. Jim was responsible for systems engineering, and the digital aspects of the implantable stimulator, playing the key leadership role in the development of the commercial medical implant.

Since 1981 he has been a member of Cochlear's senior management team, holding a number of technology management roles, including responsibility for R&D, Quality and Manufacturing. Currently, Jim is responsible for Cochlear's global research programme, exploring how novel forms of signal processing can improve the performance of the cochlear implant, and how advances in biology and electro-neural interfaces can be applied to future implant designs. He has an honorary appointment as Associate Professor, The University of Melbourne.

## Speaker: Dr Ralph Bright - Macquarie Stem Cells

### Dr Ralph Bright - Macquarie Stem Cells

Setting the scene with autologous therapies

Stem cells from fat have been coming since Patricia Zuk published her work in 2001. Thousands of animals have been successfully treated and thousands of humans are following. Now doctors who are early adopters are performing this procedure in greater numbers. The technology has simplified and in the near future this procedure will be offered by General Practitioners.

Adipose derived stem cells have created a difficulty for the laboratory based scientists. They do not have unlimited access to fresh fat and willing patients as clinicians do so they culture. Cultured cells are 10 times larger than fresh cells (fresh cells average 7microns, same as red blood cells) and cause problems with arterial blockage and not passing easily through the lungs. Fresh cells go anywhere red cells will go. Cultured cells are not as effective as the cocktail of cells that come from fat.

Adipose derived cells now have a three year history of safety. Knowing that we should 'first cause no harm' we now need to discover how best to use these cells. Inject them into a knee and some will leave that knee and travel all over the body "homing" to areas of need and treating problems you had not intended to treat. Things such as memory, vision and energy all improve. Having said that, they are not the elixir of life. Many things do not improve.

The TGA have ruled that this procedure will not be regulated by them. Our ultimate responsibility is to ourselves, our patients and the medical board. How do we fulfil our professional obligations?



**Dr Ralph Bright** worked in general practice for many years before starting cosmetic medicine and surgery in 1998. A strong interest in liposuction and fat transfer led to an interest in stem cells in fat. He injected his first patient with adipose derived stem cells in April 2009 and now treats six patients per week on average. He has continued to refine the procedures and protocols. As a founding director of Cell Innovations he now sells the ultrasonic cavitation technique to companies in Australia and around the world.

Dr Bright is invited to speak at conferences in Australia and overseas. He has a strong interest in research and a passionate belief in the industry.

**Dr Dan Bates - Lakeside Sports Medicine Centre**

Adipose derived stromal vascular fraction for the treatment of degenerative joint disease.

The use of mesenchymal stem cells (MSCs) has opened new and exciting possibilities for the treatment of degenerative joint disease. Cellular studies indicate that MSCs can differentiate into cartilage and be used to promote the proliferation of already differentiated chondrocytes. Animal studies have shown the ability of MSCs to cover cartilage defects in vivo and, in models of osteoarthritis, slow the degenerative process. Early human case series have shown intra-articular injection of MSCs repair cartilage defects with hyaline-like, or fibrocartilage. Human studies of osteoarthritis are yet to show convincing evidence of reversal or slowing of the disease process but do indicate that MSCs are able to modify patient pain and symptoms. We will review the evidence to date and outline our research moving forward.

**Dr Dan Bates** completed a science degree with an honours thesis at the University of Melbourne in 1995. He then studied medicine at the University of Newcastle completing his degree in 2001. He served as a registrar for a number of years before pursuing his passion for sport, specialising in Sports Medicine. Dan is currently working at Lakeside Sports Medicine Centre in Melbourne, and is the head doctor for Melbourne Football Club. Dan became interested in the use of biological therapies while working at the Sydney Swans in 2009 and is currently working with Monash Immunology and Stem Cell Laboratories (MISCL) and Australian Catholic University in the area of stem cells and degenerative joint disease.



## Speaker: Professor Richard Boyd - Magellan Stem Cells

### Professor Richard Boyd - Magellan Stem Cells

#### The Victorian Experience

There has been no precedent for the excitement and hope that stem cells offer to millions of patients. Embryonic stem cells (ESC) initially raised great expectation but they have major safety concerns. Accordingly much research now targets “adult” stem cells, particularly mesenchymal stem cells (MSC) which primarily form bone, muscle, fat and also nerves, but most importantly have very strong anti-inflammatory properties and can induce tissue repair. Many studies now focus on tissue and organ-specific stem cells present throughout the body. Of great interest are the stem cells also available at birth - umbilical cord blood HSC and MSC and pluripotential amniotic epithelial stem cells. Very recently breast milk has also evolved as an important source of stem cells. However as exciting as stem cell research is, there is a practical problem – unless they are derived from the patient themselves, the stem cells will be rejected. We have developed new technologies to overcome this problem, based on self tolerance mechanisms. Haemopoietic stem cells (as bone marrow transplants) have been used successfully to save lives for nearly forty years, by rebuilding the blood system in cancer patients following high dose chemotherapy or radiation and a wide range of other haematological and immunological disorders. MSC, however, are now the most frequently used non-HSC stem cells clinically, being used in ~ nearly 200 registered clinical trials: cancer (improvement of HSC engraftment, prevention of GvH); bone repair, cardiovascular disease/stroke, musculo-skeletal/osteoarthritis and exploratory treatments such as diabetes (type I and II), macular degeneration of the eye, autoimmunity and diseases of the kidney, liver, lungs and nervous system. Stem cell therapies, however, are fundamentally dependent on carefully controlled clinical trials. These are now underway, particularly for immune and inflammatory conditions.

**Professor Richard Boyd** is a Professor of Monash University, and Director of Monash Immunology and Stem Cell Laboratories where he also Heads the Immune Regeneration laboratory of approximately 25 people. He is also Chief Scientific Officer of biotechnology company Norwood Immunology and the newly formed Magellan who have supported the translation of his research to clinical trials in Australia and the US . Much his research has focussed on the formation and growth of the immune system and its repair following damage through infection, radiation, chemotherapy, autoimmunity and natural aging process. He has also given over 500 public lectures on immunology and stem cells. He has recently been awarded two prestigious grants from the Californian Institute for Regenerative Medicine.

**Dr Nathan Gibbs - South Sydney Sports Medicine Centre**

*Presentation by Dr Luke Inman, MB,BS. FACSP registrar*

Autologous Platelet Rich Plasma injections to aid in the regeneration of knee articular cartilage lesions. Case studies

Knee joint arthritis is a major disability for those who suffer from it. It is a progressive condition that ultimately leads to major surgery in the form of joint replacement. In its early stages it often starts with focal articular cartilage lesions. This talk will present numerous case studies showing the ability of Autologous Platelet Rich Plasma injection therapy to aid in reversing or regenerating these lesions in a hope to prevent their natural progression. The author has found best results are achieved using a protocol of monthly injections for 6-9 months until serial MRI's show regeneration of the lesion. These serial MRI's will be presented.

**Dr Nathan Gibbs** has been involved in sports and musculoskeletal medicine for nearly 30 years. He was a professional rugby league player prior to then becoming a team doctor for professional rugby league teams including South Sydney, Manly, NSW State of Origin, and Australia. He has been the Sydney Swans AFL team doctor for the last 15 years. He is co-director and founder (since 1986) of the South Sydney Sports Medicine Centre in Kensington Sydney. He has been performing autologous platelet rich plasma injections for nearly five years on chronic joint and tendon injuries. His clinic has also recently commenced treatment using adipose tissue derived mesenchymal stem cells.

## Speaker: Professor Peter Ghosh - Mesoblast

### Professor Peter Ghosh - Mesoblast

#### Allogeneic Progenitor Cells in Preclinical and Clinical Studies

Using monoclonal antibodies that recognize specific antigens on the surface of mesenchymal progenitor cells (MPC) that are only expressed during the early stages of their development we have been able to obtain essentially pure cell lines with high plurogenic potential and low immunogenicity from bone marrow aspirates and other sources from healthy volunteers. These allogeneic cell lines have been evaluated as therapeutics in a wide variety of clinical indications including cardiovascular disorders, rheumatoid and osteoarthritis, degenerative disc disease, long bone fracture and bone non-unions, osteoporosis, macular degeneration and type 2 diabetes.

Here I present some of our preclinical and clinical studies with MPC on the repair of degenerate discs (DD) and describe some early stage experiments on methods for reconstituting new disc cartilaginous tissue within the cervical spinal column. A model of disc degeneration was induced in three adjacent discs (L3 – L5) of the lumbar spines of 24 adult sheep by the injection of an enzyme that depolymerises the proteoglycans of the nucleus pulposus [Chondroitinase-ABC (cABC)]. Three months later, 0.5 million MPC (Low dose) or 4 million MPC (High dose) suspended in a Hyaluronan (HA) carrier, were injected into the degenerate L3L4 discs, L4L5 remained untreated and L5L6 received HA alone. Animals were necropsied 3 and 6 months later. However, radiographs and MRI images were taken prior to cABC injections, 3 months post injection and just before necropsy.

At six months post treatment Low dose MPC injections had restored disc height to within normal control levels whereas HA alone did not. For the Low and High dose MPC-injected discs the recovery of disc height was accompanied by a significant reduction of MRI and histopathology degeneration scores. This preclinical study facilitated a phase II, FDA approved clinical trial to assess the safety and efficacy of MPC for treatment of patients with chronic discogenic low back pain to be undertaken. The results of this study will be available next year.

Fusion of the cervical spine is generally undertaken for symptomatic disc degeneration. However, spinal fusion is not a benign procedure. Is it possible to generate a new disc instead? We filled intradiscal spinal fusion cages with collagen sponges impregnated with MPC alone or MPC cryopreserved with a novel chondrogenic agent, Pentosan Polysulfate (PPS). Cages were surgically implanted into the excised disc space of the cervical spines of sheep. Three months later the cages and adjacent vertebral bodies were examined histologically and biochemically. MPC plus collagen favored bone formation, as expected from the success of MPC alone in spinal fusion, but local cartilage deposition was observed when MPC were implanted in the presence of PPS. These latter findings offer a potential means of generating new cartilaginous disc tissue in the cervical or lumbar spine as an alternative to traditional vertebral fusion.

## Speaker: Professor Peter Ghosh - Mesoblast



**Professor Peter Ghosh** has more than 45 years experience in Medical Research and is acknowledged internationally as an authority on osteoarthritis and intervertebral disc diseases including therapeutic modalities for their treatments. From 1974 – 2002 he was Associate Professor and Director of the Raymond Purves Research Laboratories in the Department of Surgery, University of Sydney and President and Director of the Institute of Bone and Joint Research (IBJR) at Sydney's Royal North Shore Hospital (RNSH) from 1999 until his retirement in 2002. He is Past President of the Australian and New Zealand Orthopaedic Research Society, the Matrix Biology Society of Australia and New Zealand and Board member of the Osteoarthritis Research Society International (OARSI).

Osteoarthritis Research Society International (OARSI).

Since joining Mesoblast Ltd in 2005 as Senior Vice President, he has been responsible for the development and execution of their laboratory and preclinical research programs in Orthopaedics and Rheumatology using their propriety Progenitor Cells.

## Speaker: Dr Mary Boyd Turner - Therapeutic Goods Administration

### **Dr Mary Boyd Turner - Therapeutic Goods Administration**

Regulating human cell- and tissue-based therapies in Australia

In May 2011, the TGA introduced a regulatory framework for human cell- and tissue-based therapeutic goods, or 'biologicals'.

The framework was established subsequent to recommendations endorsed by all Australian State and Territory Health Ministers, and based on extensive industry and stakeholder consultation taking into account international practice. It provides improved clarity and regulation of these types of products in Australia. It enables access to treatment options while ensuring that the therapies are of an acceptable standard for their defined clinical uses. It also requires ongoing safety monitoring once the therapies have been approved for use in Australia.

The framework has been designed to have a low regulatory impact on established sectors such as human tissue establishments, and does not apply to fresh blood, viable organs, haematopoietic progenitor cells used for haematopoietic reconstitution or assisted reproduction tissues.

**Dr Mary Boyd Turner** is a medical graduate from the University of Adelaide. After graduation she undertook training in Paediatrics and attained a Fellowship of the Royal Australasian College of Physicians. She subsequently became a Fellow of the Royal Australasian College of Medical Administrators and worked in hospital management. This was followed by positions in government as a senior medical advisor. During this time, Mary developed interest and skills in evidence evaluation and evidence based practice. She joined the Therapeutic Goods Administration in 2007 and before commencing the Biological Sciences Section worked as an evaluator in the Offices of Product Review and Medicines Authorisation. Her extracurricular interests include the arts and music.

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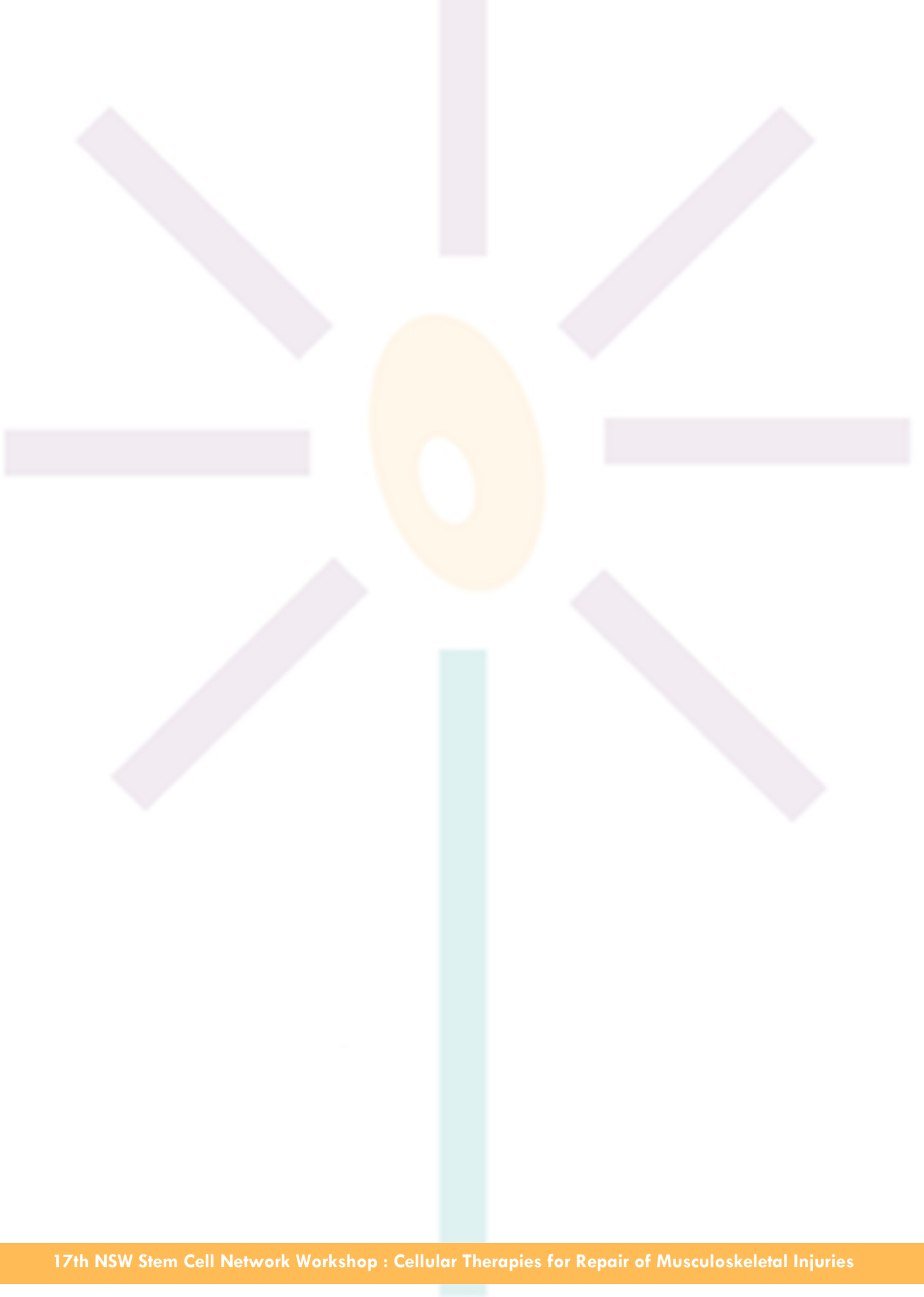
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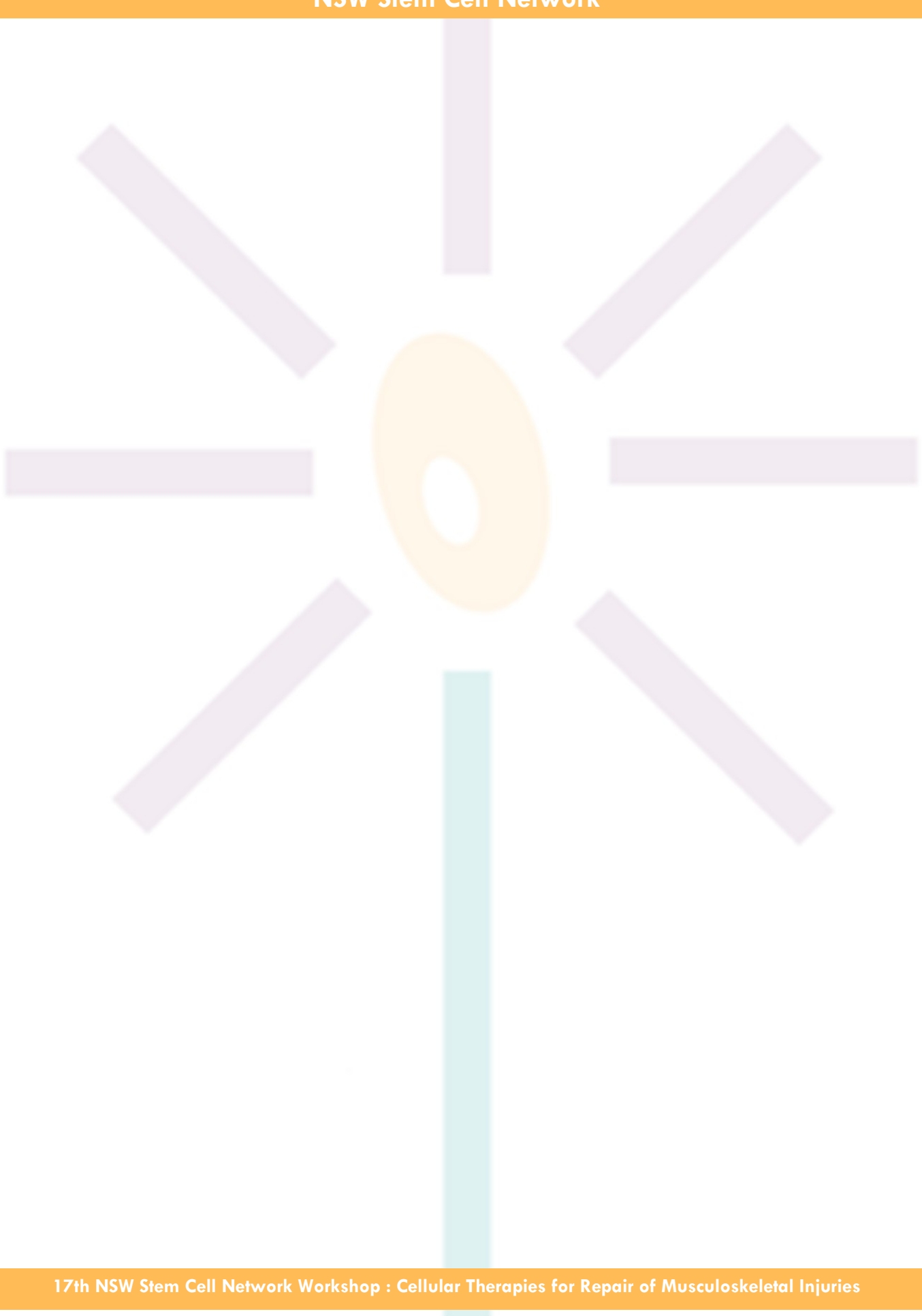
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