

The Department of Orthopaedic Surgery is the oldest orthopaedic department in Australia and was one of the first sub-specialty surgical departments at St. Vincent's.

About us

As an academic division of the University of Melbourne's Department of Surgery, the Department of Orthopaedic Surgery is the first adult academic orthopaedic department in Melbourne. Consisting of 13 surgeons and five research staff, the department's clinical activity is underpinned by a vibrant basic science and clinical research program.

Our basic science program focuses on the mechanisms of osteosarcoma growth and spread and how these processes can be controlled by targeting specific genetic signals with small molecules. Our objectives are to improve current understanding of bone tumour biology and to translate this into new treatment strategies for reducing drug toxicities, improving survival and increasing the potential for limb-sparing surgery.

Our clinical research program has developed from our strengths as the state centre for joint replacement surgery and the state referral centre for musculoskeletal tumours. Performing almost 700 joint replacements per year for arthritis, our clinical activity provides a unique opportunity to study the impact of factors such as obesity and surgical technique on patient outcomes, as well as the pathways that are important for delivering effective, timely and efficient patient care. Our experience with managing several hundred tumours per year also allows us to develop innovative ways of limb-sparing surgery while providing the necessary clinical data to drive improvements in patient management.

Projects in progress or completed

Basic science research

- Development of an *invivo* model of chondrosarcoma
- The role of RECK in osteosarcoma and chondrosarcoma biology
- The regulation of osteoclast function via PEDF
- The importance of early phase genes in osteosarcoma behaviour
- Development of nanoparticles for delivery of bioactive agents.

Clinical science research

- Prognostic factors for outcomes and complications following joint arthroplasty in obese patients
- The prognostic significance of obesity in joint arthroplasty: a prospective observational study in 1,100 patients

- A prospective longitudinal study of bone remodelling after cemented total hip arthroplasty using triple taper stem design
- The influence of prosthetic alignment on length of stay after total knee arthroplasty
- Language as a barrier to good outcomes after joint replacement.

Research applications in the clinical setting

Our research has identified that obesity is associated with increased postoperative complications and the specific risk is that of infection. Moreover, we identified that the absence of suction drains following joint arthroplasty in obese patients was associated with a greater risk of infection. These results have highlighted the need for careful wound closure and mandated the use of suction drains in patients with BMI greater than 30.

Our randomised control trial, which compared the outcome of total knee arthroplasty between computer navigated and conventional techniques, demonstrated that achieving mechanical alignment within three degrees of neutral was associated with better function, improved patient satisfaction and shorter length of stay. This has highlighted the importance of the need for greater accuracy when undertaking joint arthroplasty and this has motivated the uptake of computer-guided surgery by our surgeons when undertaking this type of surgery.

Research outcomes in relation to patient care

There have been fewer joint infections amongst obese patients.

The team

Prof Peter Choong, Prof and Director Orthopaedics; Dr Toru Akiyama, International Research Fellow; Dr Jonathan Clark, Research Fellow; Dr Crispin Dass, Senior Research Officer; Michelle Dowsey, Clinical Trials and Research Coordinator/PhD Candidate; Mei Lin Tan, Honours student

Highlights

Dr Jonathan Clark

- Peter Ryan Prize for Surgical Research

Michelle Dowsey

- Best Student Poster (Clinical) St. Vincent's Research Week, August 2008
- NHMRC Public Health Postgraduate Scholarship (#502021) 2008

Higher degrees conferred in 2008

- Eugene Ek, PhD, University of Melbourne
- Mei Lin Tan, Honours, Melbourne University

Grants

Choong P

John Mitchell Crouch Fellowship. Royal Australian College of Surgeons, (2008), \$82,000

Choong P, Dass C

PEDF as a potential anti-osteosarcoma agent. Liddy Shriver Sarcoma Initiative, (2008), \$64,000

Clark J, Choong P, Dass C

The influence of the human RECK protein on osteosarcoma and chondrosarcoma. Royal Australian College of Surgeons, (2008-2009), \$55,000

Dowsey M, Choong P

Prognostic significance of obesity in joint arthroplasty. National Health and Medical Council, (2008-2009), \$42,100

Select international presentations

Choong P

- Invited speaker, 'John Mitchell Crouch Oration – The evolution of sarcoma management: from machines to molecules', Royal Australian College of Surgeons Annual Scientific Meeting, Hong Kong, May 2008
- Invited speaker, 'Modern management of sarcoma', 13th Hong Kong Medical Forum, Hong Kong, May 2008
- Plenary speaker, 'Generation Y – slick or slack' and 'International medical graduates – friend or foe' Australian Orthopaedic Association 68th Annual Scientific Meeting, Hobart, Australia, October 2008

Dass C

- Speaker, 'Involvement of the uPAR in PEDF-mediated antisarcoma activity', and 'Nanoencapsulated DNzyme-assisted silencing of c-jun leads to inhibition of osteosarcoma, liposarcoma, breast and prostate cancers', ASEAN Scientific Conference in Pharmaceutical Technology, Penang, Malaysia, June 2008
- Plenary speaker, 'A DNzyme nanoparticle for cancer gene therapy', Melbourne Gene Therapy Symposium, Melbourne, Australia, May 2008

Miki Y

- 'Clinical significance of size change during radiotherapy of soft tissue sarcoma', Asia Pacific Musculoskeletal Tumour Society Meeting, Beijing, China, September 2008

Collaborations

International

- National Institute of Health (NIH) USA
- Tokyo University

National

- Monash University
- Peter MacCallum Cancer Centre
- Prince of Wales Hospital
- University of Melbourne
- University of New South Wales

Publications

Akiyama T, Dass CR, Choong PF 2008, 'Novel therapeutic strategy for osteosarcoma targeting osteoclast differentiation, bone-resorbing activity and apoptosis pathway', *Mol Cancer Ther*, 7, 11, 3461-9

Barrington MJ, Olive DJ, McCutcheon CA, Scarff C, Said S, Kluger R, Gillett N, Choong P 2008, 'Stimulating catheters for continuous femoral nerve blockade after total knee arthroplasty: a randomised, controlled, double-blinded trial', *Anesth Analg*, 106, 4, 1316-21,

Choong PF, Rudiger HA 2008, 'Prognostic factors in soft-tissue sarcomas: what have we learnt?' *Expert Rev Anticancer Ther*, 8, 2, 139-46

Choong PF, Dowsey MM, Stoney JD 2008, 'Does accurate anatomical alignment result in better function and quality of life? A prospective randomised controlled trial comparing conventional and computer-assisted total knee arthroplasty', *J Arthroplasty*

Clark JC, Dass CR, Choong PF 2008, 'A review of clinical and molecular prognostic factors in osteosarcoma', *J Cancer Res Clin Oncol*, 134, 3, 281-97

Clark JC, Dass CR, Choong PF 2008, 'Current and future treatments of bone metastases', *Expert Opin Emerg Drugs*, 13, 4, 609-27

Dass CR 2008, 'Drug delivery in cancer using liposomes', *Methods Mol Biol*, 437, 177-82

Dass CR, Choong PF 2008, 'Cancer angiogenesis: targeting the heel of Achilles', *J Drug Target*, 16, 6, 449-54

Dass CR, Choong PF 2008, 'Chitosan-mediated orally delivered nucleic acids: a gutful of gene therapy', *J Drug Target*, 16, 4, 257-61

Dass CR, Choong PF 2008, 'C-jun: pharmaceutical target for DNAzyme therapy of multiple pathologies', *Pharmazie*, 63, 6, 411-4

Dass CR, Choong PF 2008, 'Gene therapy for osteosarcoma: steps towards clinical studies', *J Pharm Pharmacol*, 60, 4, 405-13

Dass CR, Choong PF 2008, 'Pigment epithelium-derived factor (PEDF): drug developmental challenges ahead for a budding anti-angiogenic', *Pharmazie*, 63, 1, 4-6

Dass CR, Choong PF 2008, 'The use of chitosan formulations in cancer therapy', *J Microencapsul*, 25, 4, 275-9

Dass CR, Choong PF 2008, 'uPAR mediates anticancer activity of PEDF', *Cancer Biol Ther*, 7, 8, 1262-70

Dass CR, Ek ET, Choong PF 2008, 'PEDF as an emerging therapeutic candidate for osteosarcoma', *Curr Cancer Drug Targets*, 8, 8, 683-90

Dass CR, Khachigian LM, Choong PF 2008, 'c-Jun is critical for the progression of osteosarcoma: proof in an orthotopic spontaneously metastasizing model', *Mol Cancer Res*, 6, 8, 1289-92

Dass CR, Khachigian LM, Choong PF 2008, 'c-Jun knockdown sensitises osteosarcoma to doxorubicin', *Mol Cancer Ther*, 7, 7, 1909-12

Dass CR, Choong PF, Khachigian LM 2008, 'DNAzyme technology and cancer therapy: cleave and let die', *Mol Cancer Ther*, 7, 2, 243-51

Dass CR, Galloway SJ, Clark JC, Khachigian LM, Choong PF 2008, 'Involvement of c-jun in human liposarcoma growth: supporting data from clinical immunohistochemistry and DNAzyme efficacy', *Cancer Biol Ther*, 7, 8, 1297-301

Dass CR, Friedhuber AM, Khachigian LM, Dunstan DE, Choong PF 2008, 'Biocompatible chitosan-DNAzyme nanoparticle exhibits enhanced biological activity', *J Microencapsul*, 25, 6, 421-5

Dass CR, Friedhuber AM, Khachigian LM, Dunstan DE, Choong PF 2008, 'Downregulation of c-jun results in apoptosis-mediated anti-osteosarcoma activity in an orthotopic model', *Cancer Biol Ther*, 7, 7, 1033-6

Dowsey MM, Choong PF 2008, 'Early outcomes and complications following joint arthroplasty in obese patients: a review of the published reports', *ANZ J Surg*, 78, 6, 439-44

Dowsey MM, Choong PF 2008, 'Obese diabetic patients are at substantial risk for deep infection after primary TKA', *Clin Orthop Relat Res*

Dowsey MM, Choong PF 2008, 'Obesity is a major risk factor for prosthetic infection after primary hip arthroplasty', *Clin Orthop Relat Res*, 466, 1, 153-8

Ek ET, Dowsey MM, Tse LF, Riazi A, Love BR, Stoney JD, Choong PF 2008, 'Comparison of functional and radiological outcomes after computer-assisted versus conventional total knee arthroplasty: a matched-control retrospective study', *J Orthop Surg (Hong Kong)*, 16, 2, 192-6

Kong GY, Rudiger HA, Ek ET, Morrison WA, Choong PF 2008, 'Reconstruction after external hemipelvectomy using tibia-hindfoot rotationplasty with calcaneo-sacral fixation', *Int Semin Surg Oncol*, 5, 1

Ta HT, Dass CR, Dunstan DE 2008, 'Injectable chitosan hydrogels for localised cancer therapy', *J Control Release*, 126, 3, 205-16

Tse LF, Ek ET, Slavin JL, Schlicht SM, Choong PF 2008, 'Intraosseous angiosarcoma with secondary aneurysmal bone cysts presenting as an elusive diagnostic challenge', *Int Semin Surg Oncol*, 5, 10

Wei Y, Wang L, Clark JC, Dass CR, Choong PF 2008, 'Elevated leptin expression in a rat model of fracture and traumatic brain injury', *J Pharm Pharmacol*, 60, 12, 1667-72

Xie Z, Choong PF, Poon LF, Zhou J, Khng J, Jasinghe VJ, Palaniyandi S, Chen CS 2008, 'Inhibition of CD44 expression in hepatocellular carcinoma cells enhances apoptosis, chemosensitivity, and reduces tumorigenesis and invasion', *Cancer Chemother Pharmacol*, 62, 6, 949-57