

Head

Professor Dorothy Keefe, MBBS, FRACP, MD

Current Appointments:

The Cancer Council South Australia Professor of Cancer Medicine, Faculty of Health Sciences, University of Adelaide

Clinical Director, Royal Adelaide Hospital Cancer Centre

Chair MBBS Curriculum Committee (Operations)

Staff:

Dr Rachel Gibson, Cancer Council South Australia Research Fellow

Dr Joanne Bowen, Royal Adelaide Hospital Research Fellow

Dr Richard Logan, Head, Department of Oral Pathology, University of Adelaide

Higher Degree Students:

Dr Richard Logan, PhD

Ms Andrea Stringer, PhD

Ms Ann Yeoh, PhD

Mr Wilson Chan, PhD

Ms Avanita Prabowo, Honours

Ms Noor Al-Dasooqi, Honours

Ms Zhi-Yi Ong, Honours

Laboratory Research Focus:

Mucositis is a common, costly and unpleasant side effect of anti-cancer treatment that has previously been under-researched. The Mucositis Research Group investigates patho-biology and possible treatments for alimentary (oral and gastrointestinal) mucositis. We have developed animal models of both chemotherapy- and radiotherapy-induced mucositis, and use these to investigate the changes over time post-treatment both along the alimentary canal and through its depth. We can then investigate new agents as potential anti-mucotoxic treatments. The group has an international reputation in this area, with Professor Keefe acting as a consultant to many of the Pharmaceutical companies that have drugs in development for mucositis, as well as collaborating to investigate new agents in our animal model.

The Triad Burden of Illness studies are prospectively investigating the clinical and quality of life implications, as well as health-care costs associated with mucositis from multi-cycle chemotherapy and chemo-radiotherapy.

Current Funded Research 2006-2007:

Equipment grants

2007: Automated image analysis system for the high throughput immunohistochemical analysis of clinical and experimental samples. Tilley WD, Owens JA, Norman RJ, Findlay D, Rodgers RJ, Roberts CT, Wittert G, Ricciardelli C, Musgrave I, Robertson SA, Callen DF, Keefe D. NHMRC equipment grant. \$100, 695.

2007: Automated image analysis system for the high throughput immunohistochemical analysis of clinical and experimental samples. Tilley WD, Owens JA, Norman RJ, Findlay D, Rodgers RJ, Roberts CT, Wittert G, Ricciardelli C, Musgrave I, Robertson SA, Callen DF, Keefe D. University of Adelaide, Faculty of Health Sciences Equipment Grant. \$25,000.

Project grants

2007: Triad Mucositis Burden of Illness Study: Chronic mucosal injury study, Elting, Keefe & Sonis. Amgen Inc. US \$900,000

2006: Triad Mucositis Burden of Illness Study: Acute mucosal injury cohort expansion, - Elting, Keefe & Sonis. Amgen Inc. US \$609,000

2006: Chemotherapy-induced diarrhoea: Characterisation of mechanism, D Keefe. The Cancer Council South Australia. \$70,500

2006: Oral mucositis: clinical presentation, histological features and pro-inflammatory cytokine expression. R Logan, R Gibson, D Keefe & S Sonis. Australian Dental Research Foundation Inc. (ADRF) \$3000

Most Recent Publications 2006-2007:

Book Contributions

1. Keefe DMK & Logan RM. (2007), Oral complications of Cancer and its treatment. in: *Palliative Medicine*, D Walsh et al. (Eds) Elsevier. (in press).
2. Keefe, DMK, Bowen JM & Gibson RJ.(2007) The use of Project Teams in preclinical development, Chapter in: *Preclinical Development Handbook*. Ed: S. C. Gad. Wiley. (in press)
3. Gibson RJ, Bowen JM & Keefe, DMK. (2007) The use of animal models in preclinical development, Chapter in: *Preclinical Development Handbook*. Ed: S. C. Gad. Wiley. (in press)

Invited Editorials

4. Keefe DMK. (2007) Supportive care silos: time to forge cross-links, using mucositis as an example. Invited Editorial. *Current Opinions in Supportive and Palliative Care* (in press).
5. Keefe DMK. (2006) Mucositis Guidelines: what have they achieved, and where to from here? Invited Editorial. *Supportive Care in Cancer* 14(6)489-491

Refereed Journal Articles

6. Keefe DMK (2007), Intestinal Mucositis: mechanism and management. invited review article for *Current Opinions in Oncology* (in press).
7. Jones A, Wilson I & Keefe DM. (2007). Developing a process of continuous quality improvement in medical school assessment: lessons from one school. *Focus on Health Professional Education*.(in press).
8. Joshi R, Olver O, Keefe D, Marafioti T, & Smith K (2007). A Phase I study to assess the safety and activity of topical Lovastatin (FP252S) for the prevention of chemotherapy-induced alopecia. *Supportive Care in Cancer*. 2007 (in press)
9. Keefe DM, Rassias G, O'Neil L, & Gibson RJ (2007). Severe mucositis: how can nutrition help? *Current Opinions in Nutrition and Metabolic Care*. (in press)

10. Bowen JM, Stringer AM, Gibson RJ, Yeoh ASJ, Hannum S, & Keefe DMK, (2007). VSL#3 probiotic treatment reduces chemotherapy-induced diarrhoea and weight loss, *Cancer Biology and Therapy* (in press).
11. Bowen JM, Gibson RJ, Stringer AM, Logan RM, Tsykin A, & Keefe DMK, (2007). Gene expression analysis of multiple gastrointestinal regions following cytotoxic chemotherapy by oligonucleotide microarrays, *International Journal of Cancer* (in press).
12. Stringer, A.M., Gibson, R.J., Logan, R.M., Bowen, J.M., Yeoh, A.S.J., & Keefe, D.M.K., (2007). Chemotherapy-induced mucositis: the role of gastrointestinal microflora and mucins in the luminal environment *Journal of Supportive Oncology* (in press)
13. Logan RM, Stringer AM, Bowen JM, Yeoh ASJ, Gibson RG, Sonis ST & Keefe, DM. (2007) The role of pro-inflammatory cytokines in cancer treatment-induced alimentary mucositis: pathobiology, animal models and cytotoxic drugs. *Cancer Treatment Reviews*. (in press)
14. Duggan P and Keefe DM. (2007). A survey of paid term-time employment in undergraduate medical students at the University of Adelaide. Focus on Health Professional Education.(in press)
15. Keefe, DM, Schubert MM, Elting LS, Sonis ST, Epstein JB, Raber-Durlacher JE, Migliorati C McGuire DB, Hutchins RD & Peterson DE. (2007) Updated Clinical Practice Guidelines for the Prevention and Treatment of Mucositis. *Cancer* (in press)
16. Gibson RJ, Bowen JM, Alvarez E, Finnie JW, & Keefe DMK (2007). Establishment of a single dose Irinotecan model of gastrointestinal mucositis. *Chemotherapy* (in press).
17. Gibson RJ, Bowen JM, Logan RM, Stringer AM & Keefe DM, (2007) Velafermin improves gastrointestinal mucositis following Irinotecan treatment in tumour-bearing DA rats *Cancer Biology & Therapy*. 6(4): epub ahead of print
18. Stringer AM, Gibson RJ, Logan RM, Bowen JM, Yeoh ASJ, Burns J, Finnie JW, Keefe DMK. (2007) Chemotherapy-induced diarrhoea is associated with changes in the luminal environment in the DA rat. *Experimental Biology and Medicine*. 232: 96-106
19. Bowen JM, Gibson RJ, Stinger AM, Chan TW, Prabowo A, Cummins AG and Keefe DM. (2007) The role of p53 in irinotecan-induced intestinal cell death and mucosal damage. *Anti-Cancer Drugs* 18(2): 197-210
20. Bowen JM, Gibson RJ, Cummins AG, Tsykin A, & Keefe, DMK.(2007) Irinotecan changes gene expression in the small intestine in the rat with breast cancer. *Cancer Chemotherapy & Pharmacology* 59(3): 337-348
21. Logan RM, Gibson RJ, Sonis ST & Keefe DM. (2007) Nuclear Factor κ B (Nf κ B) And Cyclooxygenase-2 (Cox-2) Expression In The Oral Mucosa Following Cancer Chemotherapy. *Oral Oncology* 43(4) 395-401
22. Keefe DMK (2006). Mucositis Management in Cancer Patients. *Supportive Cancer Therapy* 3(3):154-157.
23. Keefe DMK. (2006) Supportive Care in Colon Cancer (Commentary). *Supportive Cancer Therapy* 3(3): 171-172.
24. Keefe DM & Gibson RJ. (2006) The combination of oral and small intestinal mucositis, paediatrics and biomarkers: a particularly tricky problem! *Cancer Biology & Therapy* 5 (10)1282-4

25. Pittman K, Olver I, Koczwara B, Karapetis C, Keefe D, Parnis F, Price T, Patterson W, & Yeend S. (2006) Gemcitabine and carboplatin in carcinoma of unknown primary site: a phase 2 Adelaide Trials and Education Collaborative (ACTEC) Trial. *British Journal of Cancer*. 95:1309-13.
26. Keefe DMK & Gibson RJ. (2006) Mucosal Injury from Targeted Anticancer Therapy. *Supportive Care in Cancer*. 15(5): 483-490.
27. Keefe DMK and Gibson RJ. (2006) Sucrose Breath Testing and Intestinal Mucositis. *Cancer Biology & Therapy* 5(9) 1196-1198
28. Yeoh, A.S.J., Gibson, R.J., Bowen, J.M., Stringer, A.M., Logan, R.M., Yeoh E, & Keefe, D.M.K. (2006) Radiation therapy-induced mucositis: Relationships between fractionated radiation, NF- κ B, Cox-1 and Cox-2, *Cancer Treatment Reviews* 32,645-651
29. Keefe D, Peterson D & Schubert M. (2006) Developing Evidence-based guidelines for the management of Alimentary Mucositis: Processes and Pitfalls. *Supportive Care in Cancer*, 14(6)492-498.
30. Peterson D, Keefe D, Hutchins R & Schubert M (2006) Alimentary Tract Mucositis in Cancer Patients: Impact of Terminology and Assessment on Research and Clinical Practice. *Supportive Care in Cancer*, 14(6)499-504.
31. von Bultzingslowen I, Brennan M, Spijkervet F, Logan R, Stringer A, Raber J & Keefe D (2006) Growth Factors and cytokines in the prevention and treatment of oral and gastrointestinal mucositis. *Supportive Care in Cancer*, 14(6)519-527.
32. Lalla R, Schubert M, Bensadoun R-J & Keefe D (2006) Anti-inflammatory Agents in the Management of Alimentary Mucositis. *Supportive Care in Cancer*, 14(6)558-565.
33. Bensadoun R-J, Schubert M, Lalla R & Keefe D (2006) Amifostine in the management of Radiation-induced and Chemotherapy-induced Alimentary mucositis. *Supportive Care in Cancer*, 14(6)566-572.
34. Keefe D, Lees J and Horvath N. (2006) Palifermin for oral mucositis in the high dose chemotherapy and stem cell transplant setting: the Royal Adelaide Hospital Experience. *Supportive Care in Cancer*, 14(6)580-582.
35. Brennan M, von Bultzingslowen I, Schubert M & Keefe D. (2006) Alimentary Mucositis: putting the guidelines into practice. *Supportive Care in Cancer*, 14(6)573-579.
36. Gibson R & Keefe D (2006) Cancer Chemotherapy-Induced Diarrhoea and Constipation: Mechanisms of Damage, Possible Prevention Strategies and Treatment of the Clinical Problem. *Supportive Care in Cancer*, 14(9)890-900.
37. Gibson R.J., Cummins A.G., Bowen J.M., Logan R.M., Healey T., & Keefe, D.M. (2006), Apoptosis occurs early in the basal layer of the oral mucosa following cancer chemotherapy, *Asia Pacific Journal of Clinical Oncology* 2:39-49.
38. Bowen, J.M., Gibson, R.J., Cummins, A.G., & Keefe, D.M.K., (2006) Intestinal mucositis: the role of the Bcl-2 family, p53 and caspases in chemotherapy-induced damage, *Supportive Care in Cancer*, 14(7)713-731.