

Current Australian research

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Current EB Research Projects:

1. Clinical

- Australasian EB Registry- begun 2005; First orphan disease registry in Australia, in collaboration with Melbourne & NZ EB teams.
- Epidemiology of EB in Australasia
- Quality of Life in EB- dev of specific measure
- Cell therapy for dystrophic EB pilot study

2. Basic

- Genotype to phenotype correlations in EB simplex (keratins 5 & 14, plectin genes)
- Genotype to phenotype correlations in dystrophic EB (collagen VII gene)
- Genotype to phenotype correlations in Junctional EB (laminin 5. COL17A1 and integrin alpha 6 and beta 4 genes)
- Immunofluorescence mapping in EB

3. International Collaborative studies

- Squamous cell carcinoma pathogenesis in RDEB –with St Thomas' London and Stanford Univ
- Genotype-phenotype correlation studies with Profs Jouni Uitto, Philadelphia, USA, John McGrath, London, UK & Hiroshi Shimizu, Sapporo, Japan; Johann Bauer, Salzburg, Austria.

Previous Completed Projects

1. Establishment of a diagnostic laboratory for EB in Australia – immunofluorescence mapping and EM, based at St George Hospital.
2. Expansion of multidisciplinary EB clinic based at Sydney Children's Hospital
3. Mutation screening for KRT5 and KRT14 in EB simplex, in collaboration with Royal Brisbane Hospital
4. Prenatal diagnosis of EB from mutation studies
5. Comparison of two methods for diagnosis of EB – IFM vs EM
6. Detection of EB subtype in carrier parents after babies had died years before to enable pre-natal diagnosis.
7. Gene therapy using baculovirus to deliver collagen VII cDNA
8. Trial of mepilex and mepitel dressings for EB

Selected Publications on EB

1. Arbiser JL, Fine J-D, **Murrell DF**, Paller A, Connor S, Keogh K, Marsh E & Folkman J: Fibroblast growth factor: A missing link between collagen type VII, increased collagenase, and squamous cell carcinoma in Recessive Dystrophic Epidermolysis Bullosa. *Molecular Medicine* 4:191-5, 1998.
2. Klingberg S, Mortimore R, Parkes J, Chick JED, Clague AE, **Murrell D**, Weedon D, Glass IA: Prenatal diagnosis of dominant dystrophic epidermolysis bullosa by collagen VII molecular analysis. *Prenat Diagn* 20(8): 618-622, 2000.
3. Cummins RE, Klingberg S, Wesley J, Rogers M, Zhao Y, **Murrell DF**: Keratin 14 point mutations at codon 119 of helix 1A resulting in different Epidermolysis Bullosa Simplex phenotypes. *J Invest Dermatol* 117:1103-1107, 2001.
4. Nakano A, Pulkkinen L, **Murrell D**, Rico J, Lucky A, Garzon M, Stevens CA, Robertson S, Pfender E, Uitto J: Epidermolysis Bullosa with Congenital Pyloric Atresia: Novel Mutations in the B4 Integrin Gene (ITGB4) and Genotype/Phenotype Correlations. *Pediatric Research* 49:618-626, 2001.
5. Nakano A, Chao S-C, Pulkkinen L, **Murrell D**, Bruckner-Tuderman L, Pfender E, Uitto J: Laminin 5 Mutations in Junctional Epidermolysis Bullosa: Molecular Basis of Herlitz vs Non-Herlitz Phenotypes. *Hum Genet* 110(1):41-51, 2002.
6. Premaratne C, Klingberg S, Glass IA, Wright K **Murrell DF**: Epidermolysis bullosa simplex Dowling-Meara due to an Arg-Cys substitution in exon 1 of keratin 14. *Australas J Dermatol* 43:24-27, 2002.
7. Kemp MW, Klingberg S, Lloyd L, Marr P, Molloy T, Wang Y, Murrell GAC, **Murrell DF**: A novel 15 basepair deletion causes the removal of 5 amino acids from the highly conserved 2B rod domain in Weber-Cockayne epidermolysis bullosa simplex. *J Invest Dermatol* 124:1083-1085, 2005.
8. Yiasemides E, Walton J, Marr P, Villanueva E, **Murrell DF**: A comparative study between electron microscopy and immunofluorescence mapping in the diagnosis of epidermolysis bullosa. *Am J Dermatopathol* 28(5)Oct:387-94, 2006 . Winner of Brenan Prize at 2006 Australasian Soc of Dermatopathology Meeting.
9. Figueira EC, Challinor CJ, Coroneo MT, **Murrell DF**: Marginal Eyelid and Conjunctival Granulomas in a case of Junctional Epidermolysis Bullosa. *Clin Exp Ophthalmol* (in press).

10. Rubin AI, Moran K, Fine J-D, Wargon O, **Murrell DF**: Urethral Meatal Stenosis In Junctional Epidermolysis Bullosa: A Rare Complication Effectively Treated With A Novel, And Simple Modality. *Int J Dermatol* (online early 19 July 2006) in press
11. **Murrell DF**, Pasmooij AMG, Pas HH, Klingberg S, Marr K, Pfindner E, Uitto J, Collins F, Widmer R, Jonkman MF: Retrospective diagnosis of fatal BP180-deficient non-Herlitz junctional epidermolysis bullosa suggested by IF antigen mapping of parental carriers bearing enamel defects. *J Invest Dermatol* 127(7): 1772-5, 2007. Epub 2007 Mar 8.
12. Rubin AI, Moran K, Fine J-D, Wargon O, **Murrell DF**: Urethral Meatal Stenosis In Junctional Epidermolysis Bullosa: A Rare Complication Effectively Treated With A Novel, And Simple Modality. *Int J Dermatol* (online early 19 July 2006) 46:1076-1077, 2007. (Oct) doi: 10.1111/j.1365-4632.2006.03065.x
13. Dang NN, Klingberg S, Marr P, **Murrell DF**: Review of Collagen VII sequence variants found in Australasian patients with dystrophic epidermolysis bullosa reveals 9 novel *COL7A1* variants. *J Dermatol Sci* 46(3) June:169-178, 2007. Epub 2007 Apr 10. (1 citation)
14. Yiasemides E, Trisnowati N, Su J, Dang NN, Klingberg S, Marr P, Chow CW, Orchard D, Varigos G, **Murrell DF**: Clinical heterogeneity in recessive epidermolysis bullosa due to mutations in the keratin 14 gene, *KRT14*. *Clin Exp Dermatol*. Nov 2008 doi 10.1111/j.1365-2230.2008.02858.x
15. Dang NN, Klingberg S, Rubin AI, Edwards M, Borelli S, Relic J, Marr P, Tran K Turner A, **Murrell DF**: Differential expression of pyloric atresia in junctional epidermolysis bullosa with novel *ITGB4* mutations. *Acta Derm Venereol* 88(5): 438-448, 2008 (accepted with revisions Mar 08). DOI 10.2340/00015555-0484. Featured with an accompanying editorial by Leena Bruckner-Tuderman.
16. Dang NN, **Murrell DF**: Mutation analysis and characterization of *COL7A1* mutations with dystrophic epidermolysis bullosa. *Exp Dermatol*, 17; 553-568. (Impact factor 2.449; 7/39 dermatology journals).
17. Fine J-D, Eady RA, Bauer EA, Bauer J, Bruckner-Tuderman L, Heagerty A, Hintner H, Hovnanian A, Jonkman MF, Leigh I, McGrath JA, Mellerio JE, **Murrell DF**, Shimizu H, Uitto J, Vahlquist A, Woodley D, Zambruno G, Revised Consensus for Definitions of Epidermolysis Bullosa. *J Am Acad Dermatol* 58(June): 931-950, 2008 (in press Dec 2007; advance online March 2008. doi:10.1016/j.jaad.2008.02.004)

Awards relevant to EB connected with Prof DF Murrell

- 1987 Renwick Vickers Prize in Dermatology, Oxford Medical School
- 1992 Upjohn Young Investigator Award for Excellence in Dermatology Research
- 1993 Howard Hughes Postdoctoral Research Fellowship for Physicians
- 1994 N.I.H. Physician Scientist Award (K-11); 1994-1999
- 1995 Everett C. Fox Award, American Academy of Dermatology
- 1995 Bill Reed Travelling Fellowship, American Academy of Dermatology
- 2000 St George Hospital Annual Medical Competition, Best Basic Science Poster
- 2002 Supervisor for University of NSW Postgraduate PhD Scholarship Awardee, Matthew Kemp.
- 2002 Best Poster Prize, Cutaneous Biology and Endocrinology Workshop, Australasian Hair & Wool Society, Melbourne (Senior author and supervisor of Matthew Kemp)
- 2002 Best Poster Prize, St George Hospital Annual Symposium, (Senior author and supervisor of Matthew Kemp).
- 2003 Supervisor for American Academy of Dermatology Travel Awardee Dr Niken Trisnowati, for a dermatology resident or fellow from the Third World to present their research at the International Society of Dermatology meeting in Miami, USA, May 2003: project on codominant keratin mutations in EBS.
- 2003 Supervisor for Japanese Society of Dermatology Travel Awardee Matt Kemp, to present his research at the International Society of Dermatology Meeting in Miami, May 2003: project on keratin 5 novel deletion in EBS.
- 2003 Women's Dermatologic Society Career Development Award to visit Centre for Blistering Diseases, Groningen, Netherlands & present papers at International EB Symposium at Institute for Child Health, London.
- 2003 Best Poster Prize, St George Hospital Annual Symposium, (Senior author and supervisor of Dr Niken Trisnowati, project on codominant keratin 5 and 14 mutations in EBS).
- 2006 Brenan Prize, Australasian Society for Dermatopathology, for

the best research paper presented at the annual meeting, Sydney, on Comparison of IF Mapping vs EM for the Diagnosis of EB (Senior author and supervisor of Dr Eleni Yiasemides).

- 2006 Supervisor for Finalist, Dr Ningning Dang, St George Hospital Annual Symposium Clinical Research presentations: study of effect of mutations in laminin C2 gene (LAMC2) resulting in Herlitz and non-Herlitz phenotypes of JEB.
- 2007 Inaugural Young Investigator Award for Medical Student Research, St George Hospital Annual Symposium, to John Frew, 3rd year ILP student under my supervision, for Quality of Life measure specific for EB.
- 2008 Japanese Society for Investigative Dermatology Travel Scholarship, to Hellen Yan, PhD student under my supervision, to present SCC in EB project at the International Society for Investigative Dermatology meeting in Kyoto, May 2008.
- 2008 American Dermatological Association – Honorary International Membership
- 2008 Sarkany Scholarship for Mary Alice Nading, an intern at Memorial Sloan Kettering Cancer Ctr, to present a paper on How to organize a winter adventure camp for teens with severe forms of EB, at the EADV, Paris 08.
- 2008 Maria Duran Lectureship, International Society for Dermatology. (one awarded per year): What's new in the diagnosis, pathogenesis and treatment of EB.
- 2008 Young Investigator Award for Medical Student Research, St George Hospital Annual Symposium, to Yong Kho, 3rd year ILP student under my supervision, for Epidemiology of EB from the Australasian EB Registry
- 2009 Hurwitz Lecturer, Society for Pediatric Dermatology's Annual Meeting, Philadelphia

Invited Lectures on EB/ genetic blistering diseases:

European Society for Dermatological Research, Vienna, Austria, Sept 1995
Stelwagon Lecturer & Recipient of Bill Reed Travelling Fellowship
Junctional Band 6 Protein (plakophilin 1)

North American Clinical Dermatologic Society, Australian Meeting, Renaissance Hotel, Sydney.1996
Basement Membrane Diseases.

GP Education Program, St George Area: Nephrology and Urology; Sept 1998
Dermatological Manifestations of Urogenital Disease.

Dermatology Registrar Training Programme, Adelaide; Oct 1998
Diagnosis of Epidermolysis Bullosa.

Sports Medicine Trainees Education Programme, Sydney, Oct 1998
Diagnosis & Management of Dermatological Problems Encountered in Sports.

Sydney Children's Hospital Grand Rounds, November 1999
Update on the Pathogenesis of Epidermolysis Bullosa

Surgical Grand Rounds, St George Hospital, July 2000
Dermatological Management of Non-Melanoma Skin Cancer

Sydney Children's Hospital, Genetics Dept, Sept 2000
The Genetics of Epidermolysis Bullosa

Histotechnology Group of NSW, Blackburn Bldg, Sydney University, Oct 2000
Epidermolysis Bullosa – Clinical, Genetic and Pathological Features

St George Hospital Medical Registrar Education Programme, Feb 2002
Dermatological Manifestations of Systemic Diseases

East Coast Renal Registrar Training Programme, Sydney, May 2002
Dermatology in Renal Diseases

35th Annual Australasian College of Dermatologists' Meeting, Melbourne, May 2002.
Diagnosis of Epidermolysis Bullosa in Newborns (Paediatric Dermatology Symposium)

General Practitioners' National Continuing Education Conference, Homebush, Sydney, May 2002
Skin Diseases in Children (150 registrants)

Medicine Grand Rounds, St George Hospital, Kogarah, October 2002
Genotype-Phenotype Correlations in Epidermolysis Bullosa

Sydney Genetics Fellows' Education Programme, Sydney Children's Hospital, October 2002
Update on the pathogenesis and diagnosis of Epidermolysis Bullosa.

St George Hospital Physicians Training Programme for FRACP, Sydney, February 2003
Dermatological Manifestations of Systemic Disease.

Dept of Dermatology, St Vincent's Hospital, Melbourne & Melbourne Children's, June 2003
Genotype-Phenotype Correlations in Epidermolysis Bullosa

Indonesian 7th Annual Scientific Meeting of the Indonesian Society of Dermatology and Venereology, Yogyakarta, Indonesia. July 2003:
Evidence-Based Dermatology (Plenary)
The pathogenesis of Inherited Bullous Diseases. (Plenary)

St Vincent's Hospital Annual Dermatology Meeting, Sydney, August 2003
Pathogenesis and Management of Erythropoietic Protoporphyrria

University of North Carolina, Chapel Hill, USA, Visiting Prof, Feb12th, 2004.
Genotype-Phenotype Correlation in EB
Dermatology on Three Continents

Update on therapy for skin cancers, Sheraton Mirage, Gold Coast, QLD, May 2004
Non Surgical Therapies for Basal Cell Carcinoma

Rheumatology Training Programme, Sydney, NSW ; Nov 2004
Dermatology in Rheumatology

Genetics Fellow Training Programme, Sydney, NSW; Nov 2004
Genodermatoses

The Rockefeller University, New York, July 2005
Unravelling genotype to phenotype in Epidermolysis Bullosa

Emergency Medicine Training Programme, St George Hospital, Aug 2005
Dermatological Emergencies

Department of Dermatology, Salzburg, Austria, April 24, 2006
Genotype-Phenotype Studies in Epidermolysis Bullosa.

17th ASEAN Regional Dermatology Meeting, Bali, Indonesia September 15th 2006
Recent Molecular Advances in Blistering Diseases (Plenary Session 1)
First report of IF mapping for the diagnosis of EB in Parents of deceased probands

Dept of Dermatology, Crumlin Hospital, Dublin, Ireland, October 10th, 2006
Bench to Bedside in Epidermolysis Bullosa

Australasian Society for Medical Geneticists, Sydney, February 2007
Genotype to Phenotype in Epidermolysis Bullosa

University of Santo Tomas, Manila, Philippines, Postgraduate Dermatology Course, March 15-16th, 2007 Only overseas invited speaker, 4 plenary lectures- What's New in Autoimmune Bullous Diseases, Genotype to

Phenotype in EB, Desmosome Gene Disorders, Barrier Defect in Atopic Dermatitis.

DebRA New Zealand, in conjunction with the NZ Dermatological Society, Auckland, August 2007

History of EB, Review of Research Conducted in EB in Australia; lectures on clinical management of EB

Satellite Meeting to World Congress of Dermatology, Santiago, Chile, Sept 2007

Development of a Quality of Life Measure specific to EB

Prince of Wales Hospital, Chinese University of Hong Kong, April 13th 2008
Pathogenesis of Squamous Cell Carcinoma in Epidermolysis Bullosa Invited by Prof Andrew Burd, Chair of Plastic Surgery/ Burns Unit

Visiting Professor, *University of Hokkaido, Sapporo, Japan, 19-21 May 2008*
Epidermolysis Bullosa Research in Australasia.

Visiting Professor, *University of North Carolina, Chapel Hill, USA, August 2008:*

Cardiotrichocutaneous disorders

Visiting Professor, *Duke University Medical Centre, Durham, North Carolina, USA, August 2008*

From genotype to phenotype in Epidermolysis Bullosa

Australasian College of Dermatologists' Registrar Education Programme, August 2008

An update on the Diagnosis and Management of EB

European Academy of Dermatovenereology, Paris, September 2008
Epidermolysis bullosa – update on pathogenesis.

International Society of Dermatology, Philippine Dermatology Society Annual Meeting,

Manila, Nov 2008:

ISD's Maria Duran 2008 Lectureship: Update on the diagnosis, pathogenesis and treatment of epidermolysis bullosa. What's New in Autoimmune Bullous Diseases (plenary)

Seminars run on EB/genetic blistering disorders

American Academy of Dermatology Annual Meetings (largest dermatology meeting in the world)

1996-99: Cell Adhesion Molecules (Focus Sessions, 1.5h) 2005, 2007:

Genotype to Phenotype Correlation in EB (Focus Sessions, 1.5h) 2006-7:

Genetic Disorders of Skin Integrity (Forum, 2hrs)

Seminar on Epidermolysis Bullosa – St George Hospital, Feb 2006 for DEBRA (NSW)
Professionals Conference in EB – St George Hospital, Jun 2007 with DEBRA (Australia).

Media Interviews/Coverage re EB:

Murrell DF: *Cell Adhesion Molecules Relevant to Dermatology*: 1995 and updated annually in 1996, 1997 and 1998; National Audio Video Inc, Denver, CO.

Miniconsults in Dermatology, Volume III (1996), Volume IV (1997), Volume V (1998), Volume VI (1999), Volume VII (2000) CD Roms, **Murrell DF** (Faculty) American Academy of Dermatology, Mosby Year Book Inc.

Murrell DF/ Thew M *Dialogues in Dermatology*: Cell Adhesion Molecules. September 1998 issue. American Academy of Dermatology.

Interviewed by Rachel Friend, reporter for *A Current Affair*, Channel 9 National Network, Australia (the highest rating current affairs programme in Australia) about Epidermolysis Bullosa; Broadcast 4/2/00.

Murrell DF: Emerging therapies and gene studies for patients with Epidermolysis Bullosa; *Today Tonight*, Channel 7, (Darren Nelson) 22nd May 2003.

Murrell DF: Interview for Sun Herald medical article re Epidermolysis Bullosa by Miranda Wood. August 1st, 2004.

Murrell DF: Interview (August 2nd 2004) about the future of gene therapy for Epidermolysis Bullosa. *Today Tonight*, Channel 7 (Dr John D'Arcy) broadcast 4th August 2004.

Murrell DF: Filming of multidisciplinary Epidermolysis Bullosa clinic and care, Sydney Children's Hospital, January 2005 for Channel 9 mini-documentary for *A Current Affair*.

Murrell DF: Interview by Steven Rice for Channel 9 at Research & Education Centre, St George Hospital, regarding our research on Epidermolysis Bullosa, March & June 2005. Broadcast on *Sixty Minutes Current Affairs* on Sunday 11 June 2006. sixtyminutes.ninemsn.com.au/sixtyminutes/

What's New in Dermatological Research – featured in article about the Australasian Society for Dermatological Research by Prof Rod Sinclair, re our research on carriers of non-Herlitz Junctional EB; **The Mole, Australasian College of Dermatologists**, issue 69, winter 2006, page 5.

Interviewed by *Dermatology Times*, USA, for article on desmosome gene disorders, based on talk given at AAD in Feb 2007, published May 2007. "Genes provide clues to cardiocutaneous desmosome disorders. New

understanding may yield tools for early diagnosis, future treatment.
Dermatology Times. p 34-38.

Mention of our EB Registry set up at St George in the House of Representatives, 14th May 2008, by Tony Zappia, MP for Makin, proposing more federal funding for EB services. Hansard p 2782.

Dialogs in Dermatology – “Under the EB Umbrella” – interview on the new classification of epidermolysis bullosa with Dr Warren Heyman recorded at the AAD –Nov 2008 (circulation, one third of all US dermatologists).