

22 YEARS  
MEMORIAL

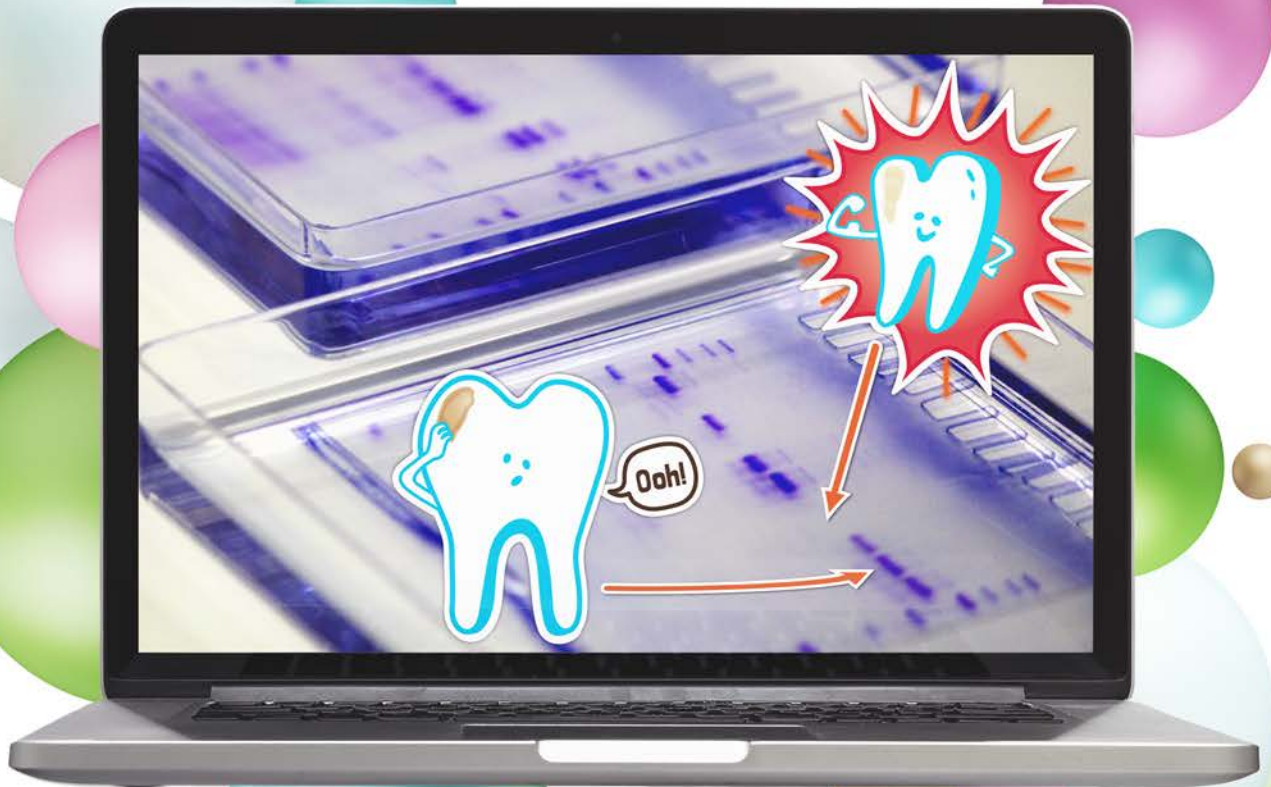


**CELEBRATING 'MRUFD'**  
and the **'POWER OF GIVING'**

**MELBOURNE RESEARCH UNIT FOR FACIAL DISORDERS**

**2003 - 2025**

*'Helping Children Smile'*



**THE 'MRUFD LAB'**  
**2003 - 2023**

*2022 Website Archive*

# A memorial to the MRUFD Laboratory (2003 – 2023)

The **MRUFD Laboratory** (Hubbard Group) was established at the University of Melbourne in 2003 by **career biochemist Mike Hubbard (Professorial Fellow, Oral and Facial Science)** and lab manager, **biochemist Jon Mangum**. After initial hosting at **Melbourne Dental School**, the **Hubbard Group** relocated to the **Department of Pharmacology and Therapeutics**, facilitating strong interactions between basic and applied biomedical science. Between 2003 and 2023, the research team attracted substantial funding, trained numerous students, and published many **innovative findings**. At **basic science** level, the standout highlight was a **100-year breakthrough about the molecular foundations of chalky enamel** which opened the door to **medical prevention** of chalky molars/Molar Hypomin (read more). **Translationally**, highlights were the publication of two online educational resources with unique research foundations (**D3G, Chalky Teeth Campaign**), a world-first **children's storybook** about chalky molars, and a **patent for detecting chalky enamel**. In 2022, Mike received the **Alan Docking Science Award (IADR, ANZ division)** for work undertaken with the MRUFD team.

For more information about **MRUFD Lab members**, see The **MRUFD Story booklet**

An archive of the **MRUFD Laboratory website** (ca. 2022) follows on Page 6.

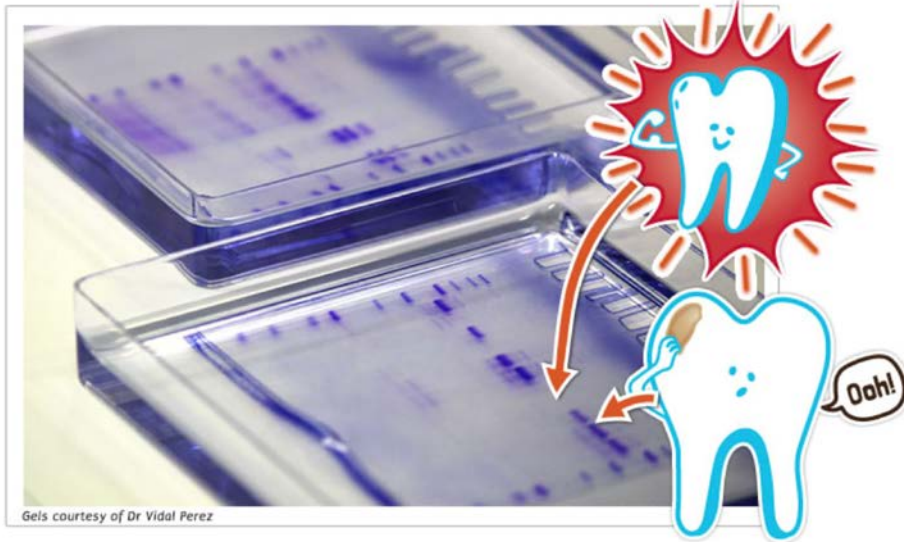
## Origins of MRUFD's research portfolio

Initially, the MRUFD Lab worked to extend **three pioneering research avenues** established independently by Mike Hubbard's research group in New Zealand (Otago University, 1990–2002). These 3 topics – which involved different facets of **calcium handling in enamel cells** and a technological foundation in **proteomics** (see website archive below) – in turn leveraged Mike's earlier postdoctoral studies in the USA (National Cancer Institute, NIH, 1984-86) and Scotland (University of Dundee, 1987-89) where he worked on two complementary aspects of **cell signalling (calcium signalling, protein phosphorylation)**. Before that crucial overseas experience in basic **biomedical science**, Mike did a **PhD in biochemistry** (Otago Uni), investigating proton transport in the medically-important yeast **Candida albicans**, along with some side studies on the famous calcium-signalling protein **calmodulin**. Mike's earliest research, which he undertook as a dental student, investigated dental enamel formation and decay. Amazingly, 30 years later, those award-winning studies (**IADR Hatton Award**, Chicago, 1980) proved to be a serendipitous foundation for MRUFD's investigations into chalky enamel. See the influential publications spanning Mike's career – before, during and after MRUFD – **here**.

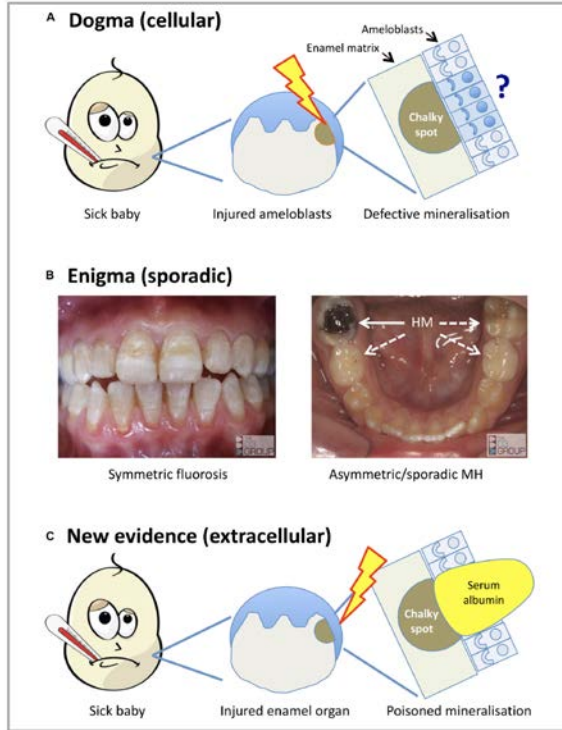
## 'Helping Children Smile' – Converting basic science into social good

MRUFD's translational mission – encapsured by the *'Helping Children Smile'* tagline – imposed a special context on the MRUFD Lab, both in terms of research undertaken, people trained, and our support for scientifically robust education. We hope the following images convey a sense of how well this challenging mission worked out, thanks to wonderful commitment from all concerned.

Teaching kids how dental students can learn to do biochemistry that makes a difference



## Making complicated biochemistry understandable by the masses



### Pathogenesis of Molar Hypomineralisation: Hypomineralised 6-Year Molars Contain Traces of Fetal Serum Albumin

Rebecca Williams<sup>1,2</sup>, Vidal A. Perez<sup>1,2</sup>, Jonathan E. Mangum<sup>1</sup> and Michael J. Hubbard<sup>1,2,4,5\*</sup>

### Pathogenesis of Molar Hypomineralisation: Aged Albumin Demarcates Chalky Regions of Hypomineralised Enamel

Vidal A. Perez<sup>2</sup>, Jonathan E. Mangum<sup>1</sup> and Michael J. Hubbard<sup>1,2,4,5\*</sup>

### A Breakthrough in Understanding the Pathogenesis of Molar Hypomineralisation: The Mineralisation-Poisoning Model

Michael J. Hubbard<sup>1,2,3,4\*</sup>, Jonathan E. Mangum<sup>1</sup>, Vidal A. Perez<sup>2,3</sup> and Rebecca Williams<sup>1,4</sup>



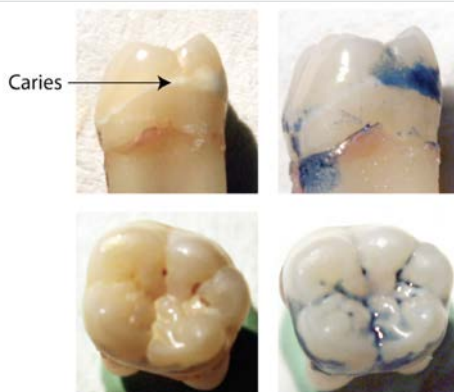
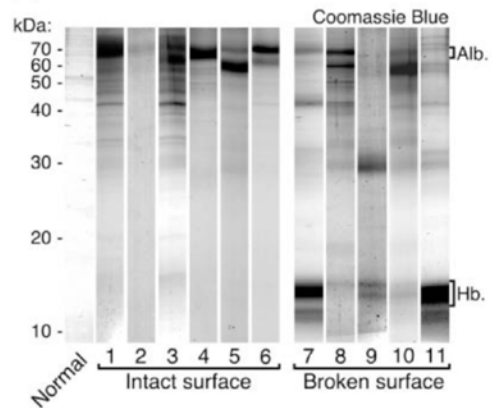
## Converting basic biochemistry into a patented tool for chalky enamel detection

### RESEARCH REPORTS

Biological

#### Surface Integrity Governs the Proteome of Hypomineralized Enamel

J.E. Mangum<sup>1</sup>, F.A. Crombie<sup>2</sup>,  
N. Kilpatrick<sup>3</sup>, D.J. Manton<sup>2</sup>,  
and M.J. Hubbard<sup>1,4\*</sup>



#### (12) **United States Patent** Hubbard et al.

(54) **KIT AND METHOD FOR DETECTING POROUS DENTAL HYDROXYAPATITE**

(71) Applicant: **Incise Technologies Pty Ltd**,  
Melbourne, Victoria (AU)

(72) Inventors: **Michael James Hubbard**, Melbourne (AU); **Jonathan Edward Mangum**, Melbourne (AU)

(73) Assignee: **INCISIVE TECHNOLOGIES PTY LTD**, Melbourne (AU)

## Research Projects

- [Enamel cell biology – how is bulk calcium handled safely?](#)
- [Chalky teeth - can they be prevented?](#)
- [Calbindins - what do they do?](#)
- [ERp29 – what does it do?](#)

# MRUFD laboratory: proteomics and calcium biology

## Research Overview

This research laboratory of the Melbourne Research Unit for Facial Disorders, is a central component of our translational research and education enterprise based at the Royal Children's Hospital (hosted by [Department of Paediatrics](#), Melbourne Medical School, 2003-2018). An overview of this pioneering translational context can be gained from the following websites.

- [Melbourne Research Unit for Facial Disorders \(MRUFD\)](#)
- [The D3 Group](#) for Developmental Dental Defects
- [Chalky Teeth Campaign](#)
- [Proteomics & Metabolomics Victoria](#) (PMV)
- [Incisive Technologies](#)



[Professor Mike Hubbard](#)  
mike.hubbard@unimelb.edu.au



Luke has chalky teeth (see [TV bulletin](#)), and Vidal's research ([Kids](#), [family](#) and [scientist](#)) ultimately aims to prevent this [common](#) and [costly](#) problem. Image copyright The D3 Group

## Research Projects

- [Enamel cell biology – how is bulk calcium handled safely?](#)
- [Chalky teeth - can they be prevented?](#)
- [Calbindins - what do they do?](#)
- [ERp29 – what does it do?](#)

# Our Biology

## Cell Signalling

The mechanisms used to relay messages within cells are of intense biomedical interest. Complex signalling pathways underlie normal development and health of cells. Many diseases are associated with cell-signalling anomalies. Numerous drugs target the principal signalling effectors, calcium and protein phosphorylation.

## Calcium biology

Calcium has many roles inside and outside cells necessitating strict regulation at different concentrations in various locations. Calcium signals are transmitted through cells as transient increases of calcium which normally is kept at a very low concentration in the cytosol (cellular fluid). Cellular toxicity arises if these calcium elevations are too large or frequent (calcium cytotoxicity). It is clear that excess calcium can lead to cell death but disease-related disruptions of calcium signalling are not well understood. How calcium is transported in bulk across epithelia without causing cytotoxicity is a key area requiring pathomechanistic elucidation.

## Dental enamel cells

We initiated investigations of calcium handling in enamel cells questioning how they make such a highly-calcified product (tooth enamel is 40% calcium) without suffering the cytotoxic effects of excess intracellular calcium. Of broader biomedical value, this research model comprises epithelial cells that have an informatively elongate morphology and undergo functionally-distinct phases of development linked to production of a hypermineralized extracellular matrix. Dentally, these cells are also central to the understanding of enamel mineralization and associated developmental defects.

For more information - see "[Why Enamel Cells](#)" (PDF, 324 KB)

## Current research focus

(follow links to see allied Projects and Publications)

- **Calcium handling** and avoidance of calcium cytotoxicity during mineralization of enamel
- Cause, treatment and prevention of **enamel defects**, particularly "chalky molars" (Molar Hypomineralisation)
- Function of **calbindins** (calcium-binding proteins) in health and disease
- Role of **ERp29** (a novel protein in the Endoplasmic Reticulum) in ER pathobiology

### Research Projects

- [Enamel cell biology – how is bulk calcium handled safely?](#)
- [Chalky teeth - can they be prevented?](#)
- [Calbindins - what do they do?](#)
- [ERp29 – what does it do?](#)

## Our Research Technologies

### Molecular and cellular biology

We are using a broad range of experimental approaches from the DNA level (eg cDNA cloning, qPCR) through protein (eg 2-D gels, recombinant protein engineering), cellular (eg confocal and transmission electron microscopy) and physiological levels (eg knockout mouse characterisation).

### Proteomics and protein biochemistry

Our speciality is microscale protein biochemistry, a challenging area necessitated by the scarcity of enamel cells. Approaches include mass spectrometry, Edman analysis, amino acid composition, gel electrophoresis and the purification, biophysical and functional analysis of proteins.

An online database ([ToothPrint](#)) of dental proteins in rat has been established.

### Hard tissue microanalysis

We phenotypically characterise mouse, rat and human teeth using a variety of approaches including polarised light and scanning electron microscopy, histology, micro-CT and microradiography, microhardness and quantitative fracture analysis.

## Our Translational Research & Education

### Oral and facial sciences

Our laboratory serves as a research hub for the [Melbourne Research Unit for Facial Disorders](#), a medico-dental translational network based at Royal Children's Hospital of Melbourne.

By hosting students and practitioners from medical and dental fields, we blend their clinical understanding with our basic science expertise to provide a strong translational platform for cross-disciplinary research and training. Learn more [here](#).

### Developmental Dental Defects (D3s, “chalky teeth”)

To provide a much-needed hub for research and education about Developmental Dental Defects (DDD = D3s), we instigated a world-first, cross-sector, translational network (The D3 Group; D3G). Research from our lab and elsewhere (“[Tooth science](#)”) has been embedded throughout [D3G's online education resource](#), supporting a public awareness campaign about the need for research into the prevention of the commonest type of “[chalky teeth](#)” ([Molar Hypomineralisation](#)). Learn more [here](#).

### Proteomics and metabolomics

To amalgamate proteomic and metabolomic interests in Victoria, we instigated a pioneering cross-sector network (Proteomics and Metabolomics Victoria; [pmv.org.au](#)). Learn more [here](#).

### Commercialisation

We have developed a novel detector for porous hydroxyapatite that has potential applications in preventive and restorative dentistry. This invention has been patented (in [USA](#) and 7 other major jurisdictions) and spun out to a startup company (Incisive Technologies) for commercialisation. Learn more [here](#).

### Research Projects

- [Enamel cell biology – how is bulk calcium handled safely?](#)
- [Chalky teeth - can they be prevented?](#)
- [Calbindins - what do they do?](#)
- [ERp29 – what does it do?](#)

## Staff



[Professor Mike Hubbard,](#)  
MRUFD Director of Research,  
Professorial Fellow in Oral & Facial Sciences



[Dr Jon Mangum,](#)  
MRUFD Deputy Director of Research

## Research Outcomes

Please see research publications and translational outputs under each Project:

[Calcium handling](#)

[Enamel defects](#)

[Calbindins](#)

[ERp29](#)

## Research Projects

- [Enamel cell biology – how is bulk calcium handled safely?](#)
- [Chalky teeth - can they be prevented?](#)
- [Calbindins - what do they do?](#)
- [ERp29 – what does it do?](#)

# Enamel cell biology – how is bulk calcium handled safely?

## Project Co-leader

[Professor Mike Hubbard](#)

mike.hubbard@unimelb.edu.au

## Project Details

Calcium plays numerous key roles in cells from their birth through to their death. Consequently there is much medical interest in manipulating calcium-dependent activities, for example to help keep damaged cells alive in neurodegenerative diseases or hastening the death of renegade cells in cancer. Enamel-forming cells hold interest in this regard as a calcium-savvy cell type that handles a lot of calcium (for mineralisation of dental enamel) without succumbing to the potentially cytotoxic effects of excessive intracellular calcium. To learn how enamel cells survive such a calcium onslaught, we developed microscale proteomic approaches and characterised enamel epithelial cells from developing teeth in neonatal rats and mice. This information was used to investigate the mechanistic basis of calcium transport across enamel cells. **Our findings contradicted the classical “calcium ferry” dogma and led to development of a new paradigm for transcellular calcium transport that we’ve named “calcium transcytosis”.** Increasingly it appears this organelle-based mechanism could be more generally applicable across biology. This advance in turn necessitates a reevaluation of the biological roles of calbindins (see [Calbindin Project](#)).

## Researchers

[Dr Jon Mangum](#), Project co-leader

## Research Publications

- Nurbaeva MK, Eckstein M, Devotta A, Saint-Jeannet JP, Yule DI, Hubbard MJ, Lacruz RS: Evidence That Calcium Entry Into Calcium-Transporting Dental Enamel Cells Is Regulated by Cholecystokinin, Acetylcholine and ATP. *Front Physiol.* 2018; 9, 801. (PMID: [30013487](#))
- Kirkham J, Brookes SJ, Diekwisch TGH, Margolis HC, Berdal A, Hubbard MJ. Enamel Research: Priorities and Future Directions. *Front Physiol.* 2017; 8, 513. (PMID: [28775693](#))
- Mangum JE, Kon JC, Hubbard MJ. Proteomic Analysis of Dental Tissue Microsamples. *Methods Mol Biol.* 2017: 1537, 461-479. (PMID: [27924612](#))
- Nurbaeva MK, Eckstein M, Concepcion AR, Smith CE, Srikanth S, Paine ML, Gwack Y, Hubbard MJ, Feske S, Lacruz RS. Dental enamel cells express functional SOCE channels. *Sci Rep* 2015; 5: 15803; doi: 10.1038/srep15803 (PMID: [26515404](#))
- Lacruz RS, Smith CE, Kurtz I, Hubbard MJ, Paine ML. New Paradigms on the Transport Functions of Maturation-stage Ameloblasts. *J Dent Res.* 2013 Feb;92(2):122-9. (PMID: [23242231](#))
- Lacruz, RS, Smith CE, Bringas P, Chen YB, Smith SM, Snead ML, Kurtz I, Hacia JG, Hubbard MJ, Paine ML. (2012) Identification of novel candidate genes involved in mineralization of dental enamel by genome-wide transcript profiling. *J. Cell Physiol.* 227, 2264-2275 (PMID: [21809343](#))
- Hubbard MJ, McHugh NJ, Mangum JE. (2011) Exclusion of all three calbindins from a calcium-ferry role in rat enamel cells. *Eur. J. Oral Sci.* 119 (Suppl. 1), 112-119 (PMID: [22243236](#))

### Research Projects

- [Enamel cell biology – how is bulk calcium handled safely?](#)
- [Chalky teeth - can they be prevented?](#)
- [Calbindins - what do they do?](#)
- [ERp29 – what does it do?](#)

Lacruz RS, Smith CE, Chen Y, Hubbard MJ, Hacia JG, Paine ML. (2011) Gene expression analysis of early and late maturation stage rat enamel organ. *Eur. J. Oral Sci.* (119 (Suppl. 1), 149-157 (PMID: [21809343](#))

Mangum JE, Kon JC, Hubbard MJ. (2010) Proteomic analysis of dental tissue microsamples. *Methods Mol. Biol.* 666, 309-325 (PMID: [20717792](#))

Mangum JE, Veith PD, Reynolds EC, Hubbard MJ. (2006) Towards second-generation proteome analysis of murine enamel-forming cells. *Eur. J. Oral Sci.* 114, 259-265 (PMID: [16674695](#))

Turnbull CI, Looi K, Mangum JE, Meyer M, Sayer RJ, Hubbard MJ. (2004) Calbindin-independence of calcium transport in developing teeth contradicts the calcium-ferry dogma. *J. Biol. Chem.* 279, 55850-55854 (PMID: [15494408](#))

Hubbard MJ, Kon JC. (2002) Proteomic analysis of dental tissues. *J. Chromatogr. B*, 771, 211-220 (PMID: [12016000](#))

Franklin IK, Winz RA, Hubbard MJ. (2001) Endoplasmic reticulum Ca<sup>2+</sup>-ATPase pump is up-regulated in calcium-transporting dental enamel cells: A non-housekeeping role for SERCA2b. *Biochem. J.*, 358, 217-224 (PMID: [11485570](#))

Hubbard MJ, Faught MJ, Carlisle BH, Stockwell PA. (2001) ToothPrint, a proteomic database for dental tissues. *Proteomics* 1, 132-135 (PMID: [11680893](#))

Hubbard MJ. (2000) Calcium transport across the dental enamel epithelium. *Crit. Rev. Oral Biol. Med.*, 11, 437-466 (PMID: [11132765](#))

Hubbard MJ. (1998) Proteomic analysis of enamel cells from developing rat teeth. Big returns from a small tissue. *Electrophoresis*, 19, 1891-1900 (PMID: [9740049](#))

Hubbard MJ. (1998) Enamel cell biology. Towards a comprehensive biochemical understanding. *Conn. Tissue Res.*, 39, 17-32 (PMID: [11063013](#))

Hubbard MJ. (1996) Abundant calcium homeostasis machinery in rat dental enamel cells. Up-regulation of calcium store proteins during enamel hypermineralization implicates the endoplasmic reticulum in calcium transcytosis. *Eur. J. Biochem.*, 239, 611-623 (PMID: [877470](#))

Hubbard MJ. (1995) Calbindin28kDa and calmodulin are hyperabundant in rat dental enamel cells. Identification of the protein phosphatase calcineurin as a principal calmodulin target and of a secretion-related role for calbindin 28kDa. *Eur. J. Biochem.*, 230, 68-79 (PMID: [7601126](#))

## Research Projects

- [Enamel cell biology – how is bulk calcium handled safely?](#)
- [Chalky teeth - can they be prevented?](#)
- [Calbindins - what do they do?](#)
- [ERp29 – what does it do?](#)

# Chalky teeth - can they be prevented?

## Project Co-leader

[Professor Mike Hubbard](#)

[mike.hubbard@unimelb.edu.au](mailto:mike.hubbard@unimelb.edu.au)

## Project Details

Developmental defects of enamel (popularly termed “chalky teeth”) are costly to patients and society. Many of these Developmental Dental Defects (DDDs = D3s) may become preventable if a better understanding of their causes and pathologies can be gained. Recently we assembled a multidisciplinary team to investigate the commonest D3, termed Molar Hypomineralisation, which manifests as soft and porous (chalky) enamel. Worldwide, this congenital defect affects the two-year molars and/or six-year molars of 1-in-5 otherwise healthy children, causing life-long risk of toothache, tooth breakdown and decay, and perhaps tooth loss in severe cases. **Our initial proteomics investigation of chalky enamel in 2010 provided intriguing insights to the nature and possible cause of Molar Hypomineralisation, opening novel avenues for basic research and clinical developments.** This work also led to a **novel detector for porous hydroxyapatite** that has potential applications in preventive and restorative dentistry. It was first patented in 2011, and currently is undergoing commercialisation.

## Researchers

[Dr Jon Mangum](#), Project co-leader

## Research Publications

- Hubbard, MJ, Mangum, JE, Perez, VA, Williams R. A Breakthrough in Understanding the Pathogenesis of Molar Hypomineralisation: The Mineralisation-Poisoning Model, *Front. Physiol.*, 2021; 12:802833 ([open access](#))
- Hubbard, MJ, Perez, VA, Ganss, B. 100 years of chalky teeth research: From pioneering histopathology to social good. *Front Dent. Med.*, 2021; 1: 632534 ([open access](#))
- Hubbard, MJ. Molar Hypomineralization: What is the U.S. Experience (Revisited)? *Pediatr. Dent.*, 2020; 42: 414-416 (PMID: [33369549](#))
- Hubbard, MJ. Chalky teeth 100 years on: What comes next? *J. Am. Dent. Assoc.*, 2020; 151: 803-805 (PMID: [33121592](#))
- Perez, VA, Mangum, JE, Hubbard, MJ. Pathogenesis of molar hypomineralisation: Aged albumin demarcates chalky regions of hypomineralised enamel. *Front. Physiol.*, 2020; 11: 579015 (PMID: [33101060](#))
- Williams, R, Perez, VA, Mangum, JE, Hubbard, MJ. Pathogenesis of molar hypomineralisation: Hypomineralised 6-year molars contain traces of fetal serum albumin. *Front. Physiol.*, 2020; 11: 619 (PMID: [32595522](#))
- Hubbard MJ. Molar hypomineralization: What is the US experience? *J Am Dent Assoc.* 2018; 149, 329-330. (PMID: [29703275](#))
- Perez VA, Mangum JE, Hubbard MJ. Direct evidence that KLK4 is a hydroxyapatite-binding protein. *Biochem Biophys Res Commun.* 2018; 495:1896-1900. (PMID: [29229389](#))
- Kirkham, J, Brookes, SJ, Diekwisch, TGH, Margolis, HC, Berdal, A, Hubbard, MJ. Enamel Research: Priorities and Future Directions, *Front. Physiol.*, 2017; 8, 513 ([open access](#))

### Research Projects

- [Enamel cell biology – how is bulk calcium handled safely?](#)
- [Chalky teeth - can they be prevented?](#)
- [Calbindins - what do they do?](#)
- [ERp29 – what does it do?](#)

- Hubbard MJ, Mangum JE, Perez VA, Nervo GJ, Hall RK. Molar Hypomineralisation: A Call to Arms for Enamel Researchers. *Front Physiol.* 2017; 8, 546. (PMID: [28824445](#))
- Mangum JE, Crombie FA, Kilpatrick N, Manton DJ, Hubbard MJ. Surface integrity governs the proteome of hypomineralized enamel. *J. Dent. Res.* 2010; 89, 1160-1165 (PMID: [20651090](#))

### Patent

- Hubbard MJ, Mangum JE. Kit and method for detecting porous dental hydroxyapatite. ([AU2011229153](#), [US10434037B2](#))

### Translational outputs

- Online education resource: [www.thed3group.org](http://www.thed3group.org)
- Children's storybook: [thed3group.org/sam-has-molar-hypomin.html](http://thed3group.org/sam-has-molar-hypomin.html)
- Public awareness campaign: [www.chalkyteeth.org](http://www.chalkyteeth.org)
- Wikipedia: [Chalky Teeth](#)

## Research Projects

- [Enamel cell biology – how is bulk calcium handled safely?](#)
- [Chalky teeth - can they be prevented?](#)
- [Calbindins - what do they do?](#)
- [ERp29 – what does it do?](#)

# Calbindins - what do they do?

## Project Co-leader

[Professor Mike Hubbard](#)

[mike.hubbard@unimelb.edu.au](mailto:mike.hubbard@unimelb.edu.au)

## Project Details

Our cells contain numerous proteins thought to bind calcium as their primary role. Many of these calcium-binding proteins play pivotal roles in cell signalling, regulation and structure, making them attractive targets for therapeutic intervention in multiple diseases including cancer and neurodegeneration. However, for such applications to be fully effective, better understanding is needed about the functions of these calcium-binding proteins at individual and collective levels. Calbindins comprise three types of calcium-binding protein (calbindin-28kDa, calbindin-9kDa, calretinin) that have long been regarded as mobile calcium buffers in the cytosol and consequently are widely investigated as potential targets in calcium transport and neurodegeneration. **Our investigations have contradicted this view and instead pointed to calbindins having a role that involves interactions with other proteins.** These findings, which lead us to contemplate an alternative role in cell signalling, hold fundamental significance for medical targeting of calbindins. These outcomes also necessitate reconsideration of the mechanisms used in transepithelial calcium transport (see [Calcium Handling](#) project).

## Researchers

[Dr Jon Mangum](#), Project co-leader

## Research Publications

- Hubbard MJ, McHugh NJ, Mangum JE. Exclusion of all three calbindins from a calcium-ferry role in rat enamel cells. *Eur J Oral Sci* 2011; 119 (Suppl. 1), 112-119 (PMID: [22243236](#))
- Turnbull CI, Looi K, Mangum JE, Meyer M, Sayer RJ, Hubbard MJ. Calbindin-independence of calcium transport in developing teeth contradicts the calcium-ferry dogma. *J Biol Chem* 2004; 279: 55850-55854. (PMID: [15494408](#))
- Sayer RJ, Turnbull CI, Hubbard MJ. Calbindin28kDa is specifically associated with extra-nuclear constituents of the dense particulate fraction. *Cell Tiss Res*. 2000; 302:171-180. (PMID: [11131128](#))
- Hubbard MJ, McHugh NJ. Calbindin28kDa and calbindin30kDa (calretinin) are substantially localised in the particulate fraction of rat brain. *FEBS Lett* 1995; 374: 333-337. (PMID: [7589565](#))
- Hubbard, M.J. Calbindin28kDa and calmodulin are hyperabundant in rat dental enamel cells. Identification of the protein phosphatase calcineurin as a principal calmodulin target and of a secretion-related role for calbindin28k Da. *Eur. J. Biochem* 1995; 230: 68-79. (PMID: [7601126](#))
- Hubbard M.J. and Carne A. Differential feeding-related regulation of ubiquitin and calbindin9kDa in rat duodenum. *Biochim. Biophys. Acta* 1994; 1200: 191-6. (PMID: [8031840](#))
- Hubbard, M.J. (1993) Rapid purification and direct microassay of calbindin9kDa utilizing its solubility in perchloric acid. *Biochem. J* 1993; 293: 223-7. (PMID: [8392333](#))

### Research Projects

- [Enamel cell biology – how is bulk calcium handled safely?](#)
- [Chalky teeth - can they be prevented?](#)
- [Calbindins - what do they do?](#)
- [ERp29 – what does it do?](#)

## ERp29 – what does it do?

### Project Co-leader

[Professor Mike Hubbard](#)

[mike.hubbard@unimelb.edu.au](mailto:mike.hubbard@unimelb.edu.au)

### Project Details

The Endoplasmic Reticulum (ER) plays several critical roles in cell biology including the production of secretory proteins and the safe storage of calcium inside cells. Numerous proteins reside in the ER and so hold medical importance as potential therapeutic targets for the many diseases associated with ER dysfunction (e.g. cystic fibrosis, type 2 diabetes, cancer). However, much needs to be learned about these ER residents both in terms of their individual functions and how they work together as the ‘ER machinery’. **We discovered ERp29 during proteomic analysis of rat enamel cells, leading to the naming and first description of this ubiquitous ER resident in 1997.** The challenge since has been to figure out the functional role of ERp29, bioinformatics having offered only limited insight. In a series of pioneering studies, we’ve gathered a variety of clues that collectively point to a novel “housekeeping” role of general importance, probably as a new type of chaperone. Now linked to a broad array of physiological processes and diseases including cystic fibrosis and cancer, ERp29 holds broad potential as a medical target.

### Researchers

[Dr Jon Mangum](#), Project co-leader

### Research Publications

- Gorasia DG, Dudek NL, Safavi-Hemami H, Ayala Perez R, Schittenhelm RB, Saunders PM, Wee S, Mangum JE, Hubbard MJ, Purcell AW. A prominent role of PDIA6 in processing of misfolded proinsulin. *Biochim Biophys Acta* 2016; 1864: 715-23. (PMID: [26947243](#))
- Gorasia DG, Dudek NL, Veith PD, Shankar R, Safavi-Hermami H, Williamson NA, Reynolds EC, Hubbard MJ, Purcell AW. Pancreatic beta cells are highly susceptible to oxidative and ER stresses during the development of diabetes. *J Proteome Res* 2015; 14: 688-99. (PMID: [25412008](#))
- Suaud L, Miller K, Alvey L, Yan W, Robay A, Kebler C, Kreindler JL, Guttentag S, Hubbard MJ, Rubenstein RC. ERp29 Regulates {Delta}F508 and Wild-type Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Trafficking to the Plasma Membrane in Cystic Fibrosis (CF) and Non-CF Epithelial Cells. *J Biol Chem* 2011; 286: 21239-21253. (PMID: [21525008](#))
- Das S, Smith TD, Sarma JD, Ritzenthaler JD, Maza J, Kaplan BE, Cunningham LA, Suaud L, Hubbard MJ, Rubenstein RC, Koval, M. ERp29 restricts Connexin43 oligomerization in the endoplasmic reticulum. *Mol Biol Cell* 2009; 20: 2593-2604. (PMID: [19321666](#))
- Shnyder SD, Mangum JE, Hubbard MJ. Triplex profiling of functionally distinct chaperones (ERp29/PDI/BiP) reveals marked heterogeneity of the endoplasmic reticulum proteome in cancer. *J Proteome Res* 2008; 7: 3364-3372. (PMID: [18598068](#))
- Hermann VM, Cutfield JF, Hubbard MJ. Biophysical characterization of ERp29: evidence for a key structural role of Cysteine-125. *J Biol Chem* 2005; 280: 13529-13537. (PMID: [15572350](#))

### Research Projects

- [Enamel cell biology – how is bulk calcium handled safely?](#)
  - [Chalky teeth - can they be prevented?](#)
  - [Calbindins - what do they do?](#)
  - [ERp29 – what does it do?](#)
- Hubbard MJ, Mangum JE, McHugh NJ. Purification and biochemical characterisation of native ERp29 from rat liver. *Biochem J* 2004; 383: 589-598. (PMID: [15500441](#))
  - Macleod JC, Sayer RJ, Lucocq JM, Hubbard MJ. ERp29, a general endoplasmic reticulum marker, is highly expressed throughout the brain. *J Comp Neuro* 2004; 477: 29-42. (PMID: [15281078](#))
  - Shnyder SD, Hubbard MJ. ERp29 is a ubiquitous resident of the endoplasmic reticulum with a distinct role in secretory protein production. *J. Histochem Cytochem* 2002; 50: 557-566 (PMID: [11897809](#))
  - Hubbard MJ. Functional proteomics. The goalposts are moving. *Proteomics* 2002; 2: 1069-1078. (PMID: [12362325](#))
  - Hubbard MJ, McHugh NJ, Carne DL. Isolation of ERp29, a novel endoplasmic reticulum protein, from rat enamel cells: Evidence for a unique role in secretory-protein synthesis. *Eur J Biochem* 2000; 267: 1945-1957. (PMID: [10727933](#))
  - Hubbard MJ, McHugh NJ. Human ERp29: Isolation, primary structural characterisation and two-dimensional gel mapping. *Electrophoresis* 2000; 21: 3785-379. (PMID: [11271497](#))
  - Demmer J, Zhou CM, Hubbard MJ. (1997) Molecular cloning of ERp29, a novel and widely expressed resident of the endoplasmic reticulum. *FEBS Lett.* 1997; 402, 145-150. (PMID: [9037184](#))