KEEPING IN TOUCH

June 2006

Cornelia de Lange Syndrome Association (Australasia) Inc.
Authority to Fundraise: NSW CFN 15201
Donations of $2 and over are Tax Deductible
DGR 419321 ABN 97 070 990 653

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International: www.cdlsworld.org

Online support groups: OZ/NZ online discussion group: oznz-cdls@yahoogroups.com
(register via the link on the www.cdlsaus.org homepage)

International Online Support Group: www.cdls-support.org

ANOTHER GENE FOR CdLS DISCOVERED BY ITALIAN RESEARCHERS. See inside for details.

From the Editor

As the Argent family is presently travelling Australia (CAMPING!!!), the editing has been delegated for this issue of KIT. I hope you will take advantage of opportunities as they arise to meet other CdLS families. Picnics, seminars and conferences help enormously with networking, creating friendships, and sharing information to improve the lives of our CdLS loved ones. This issue of KIT contains exciting news of another CdLS gene discovery, and more information about future meetings. Grateful thanks to our CdLS Medical Director, Dr Meredith Wilson for her explanation of this latest gene discovery.

Electronic KIT

If you would like to receive KIT by email, please send an email to jennyrollo@bigpond.com with the subject as: “Electronic KIT”.

MEMBERSHIP RENEWAL TIME!

The start of the new financial year is also the time to renew your CdLS Association membership. Please use the membership form in this issue of KIT.

CdLS CLINIC DAY

The next clinic day for adults who live in NSW/ACT is 13th September 2006. If you would like an appointment as a "new" patient, or a follow-up appointment, please contact Jenny.

BEHAVIOUR SURVEY

Thank you to all those who have sent in their behaviour surveys. Answers are presently being analysed by Dr Chris Oliver (UK), who will present carers with an individual report later in the year, and discuss results at our National conference in Queensland. Your participation in CdLS research benefits every person with CdLS.

Membership Form

CdLS Association (Australasia) Inc.

Date: _____ Enclosed is a Donation of _____

_____ I wish to become an Active Member (Membership Fees $25)

_____ I wish to become an Inactive Member _____ I wish to become an Associate Member (Professionals)

NAME:_____
Telephone:_____

Email: _____
Fax:_____

ADDRESS:
_____

State:_____ Postcode: _____ Country: _____

PERSON'S NAME WITH CdLS: _____ Birthdate: _____

I am a parent_____ : Grandparent _____ : Relative _____ : Professional (incl. Field) _____:

Other (specify) _____.

I wish to receive the KIT newsletter - yes / no

I give permission for the release of my name to other families for the purpose of mutual support: yes / no

Signature: _____

Cheques made payable to CdLSA can be sent to The Secretary, P.O. Box 20 Putney, NSW, 2112, AUSTRALIA.

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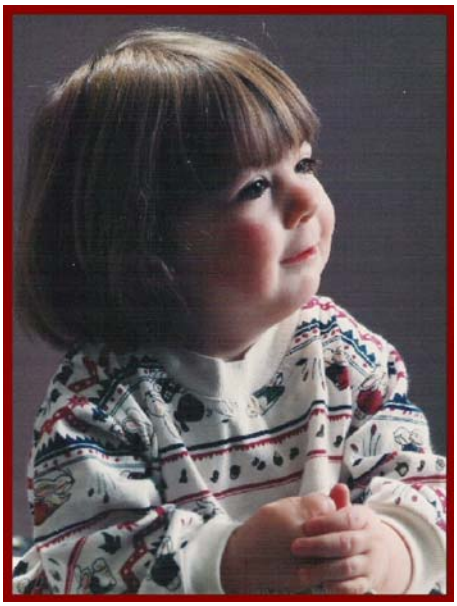
New Zealand Members only – Send $NZ to 11 Winsomere Cresc. Westmere, Auckland 2 New Zealand



Love Ella

I am delighted to announce the release of a book written by Madeleine Witham, called “Love Ella”. This is a detailed account of this mother’s experiences since the birth of Ella, who was born 11 years ago and diagnosed with CdLS. Madeleine’s experiences often mirror those of every other family dealing with CdLS. This book is highly recommended for families and professionals who care for people with disabilities.

Many of you will have met the Withams at various CdLS fundraisers and conferences. Madeleine is a past CdLS management committee member who has greatly contributed to the fundraising efforts of our group.

The book launch will be held 14th July 2006 at North Sydney. Please accept this as your invitation to join Maddi and her family. CdLS families in particular are very welcome. CdLS Australia’s Patron, Nick Farr-Jones, will be guest of honour at the launch. Please RSVP for catering purposes to Madeleine at email: mwitham@optusnet.com.au

You can read reviews, and a slice of the first chapter on the internet at www.love-ella.com Purchases can also be made through this site.

Genetics Research Update

Researchers in Italy identify a second genetic cause of Cornelia de Lange syndrome

A team of clinicians and researchers from Italy has recently published their findings of a new gene involved in CdLS. This research was published in the May 2006 issue of the journal *Nature Genetics.* The article, called **"X-linked Cornelia de Lange syndrome owing to *SMC1L1* mutations",** was from a research group based in Milan, Italy. The group was led by Dr Antonio Musio, a research scientist, and Dr Angelo Selicorni, a clinician well known to the CdLS group.

Previously, in 2004, researchers from the USA and UK had identified the first gene known to be involved in CdLS, called *NIPBL.* DNA studies show that mutations in *NIPBL*, located on chromosome 5, can be found in around 50% of individuals with CdLS. That left a lot of people for whom the cause of CdLS was unknown. Researchers knew this must be because there were other, as yet unknown gene(s), in which mutations could lead to CdLS. The question was: how to identify them?

Genes are DNA recipes, each located at a particular address on a particular chromosome. Genes code for proteins that the cell makes, each of which has a function. The insulin gene, for example, makes a protein that works as a hormone, controlling the use of glucose by our cells. Some genes, such as collagen genes, produce proteins that are used like building materials, in the structure of various tissues in our body, such as skin and ligaments. Other genes make proteins that first need to join up with other proteins, to make *complexes*. The protein complex then has a function in the cell. In those complexes, disruption of any one of the component parts could lead to a problem with the function of the whole complex.

NIPBL has a number of functions, but one function is as part of a protein complex. So one idea to follow was whether there were known genes that worked in the same complex as *NIPBL*, and whether any of these could be involved in the cause of CdLS in some people.

It was known that *NIPBL* gene has some function in chromosome cohesion (which means sticking together). Chromosomes are constantly unwinding and rewinding sections as genes are needed. Before cells multiply, chromosomes need to copy themselves, and then separate into different cells, and re-arrange themselves tidily, all of which involves control of cohesion (and lots of other things too). Chromosome cohesion problems do not usually show up on chromosome tests unless cohesion is extremely severely disrupted. One example where we can see cohesion problems with a chromosome test is a condition called Roberts syndrome. This is a very severe genetic condition which has limb abnormalities very similar to what we see in CdLS, but looks quite different otherwise.

It turns out that chromosome cohesion is controlled by a "cohesion complex", which includes at least 7 proteins, coded for by 7 different genes. Within the last 2 years, problems in two of these genes have been linked to human genetic conditions. The first was in fact *NIPBL,* reported in June 2004*,* which is involved in many individuals with CdLS*.* The other is *ESCO2*, reported in December 2005, which is involved in Roberts syndrome. However, researchers knew that *NIPBL* has *other* functions apart from its involvement in the cohesion complex –it's a gene with multiple roles. One other gene involved in producing a protein for the cohesion complex, called *SMC1L1*, is also thought to have multiple roles. So, the researchers decided to investigate this gene in 33 individuals with CdLS who did not have *NIPBL* mutations.

These 33 patients studied included one remarkable family where there were 4 affected relatives with a diagnosis of CdLS, including 2 brothers, their very mildly affected mother, and her nephew. They found mutations in the *SMC1L1* gene in all 4 individuals and one other unrelated boy. The 4 boys with mutations in *SMC1L1* all had moderate to severe mental retardation, facial features that looked like CdLS, feeding problems in childhood, and small hands. Some had reflux, and some had epilepsy as well. The mother of the two brothers really had very few differences, only slight problems with learning and some slight facial similarities. Her sister (mother of her affected nephew) and her mother were both also found to carry the same mutation in *SMC1L1* but they had no features of CdLS. The other affected boy, unrelated to that family, was the first person in his family to have a mutation in *SMC1L1* – his mother did not carry the mutation.

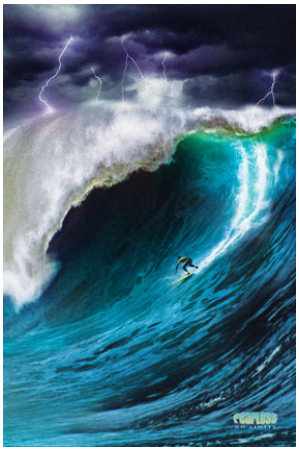
The explanation of why the boys were more severely affected and the women were only very mildly affected, or not at all, is because *SMC1L1* is an ***X-linked*** gene. This means it is located on the X chromosome. Of the total of 46 chromosomes in every cell, women have two X chromosomes (46,XX) whereas men only have one, paired with a Y chromosome (46,XY). There are hundreds of different important genes on the X chromosome. If men have a mutation (mistake) in a gene on the X, it will always cause a problem, as there is no back-up gene on the Y. Women only use one of their X chromosomes in every cell, so if they have a mutation on one X, the problem often will not show up, especially if most of their cells work from the normal copy of the X. Or if there is a condition, it will usually be much milder than it is for a male. Haemophilia is an example of another X-linked condition, which is why it usually only affects males.

How important is this finding for CdLS? X-linked CdLS due to mutations in the X-linked *SMC1L1* gene is probably uncommon, especially compared to *NIPBL.* CdLS is not significantly more frequent overall in males than females (which it would be if *SMC1l1* was a more common cause). But X-linked CdLS due to mutations in *SMC1L1* could be the cause of CdLS in a small proportion of boys who do not have mutations in *NIPBL*. It would be particularly important to check for in any families who have more than one affected boy. As we learn more about X-linked CdLS, we may be able to recognise that there are differences in the overall appearance or features of boys with X-linked CdLS compared to others with CdLS due to mutation in *NIPBL*. *SMC1L1* might also turn out to be an important gene to check in boys whom we think look a bit like they have CdLS, but are not quite typical.

Is there another gene or even genes involved in CdLS? The answer is, almost certainly yes! Many people with CdLS, male and female, will not have mutations in either of these first two discovered genes. The next gene discovery will, we hope, be just around the corner….

Dr Meredith Wilson Clinical Geneticist Department of Clinical Genetics Children's Hospital at Westmead (Australian Representative, International CdLS Specialist Advisory Council)	 Dr Meredith Wilson

CdLS National Conference 2006



" *CdLS - Making Waves* "

Where: Hotel Watermark, Surfers Paradise

When: * Saturday 30th September 2006 – meetings, workshops
* Sunday 1st October – family fun day at theme parks or relaxing by the pool.

Plans for conference are progressing well. Registration packages will hopefully be ready for posting by the end of June. We are awaiting news of our grant applications before we can finalise the registration costs for families.

Keep looking at the CdLS Australia web site for conference updates. If you want to book your hotel room early, the hotel accommodation form is now available on the web site. All accommodation will be handled directly with the hotel.

We are delighted that the Everton Park branch of the Girl Guides will be caring for our CdLS children, babies and young siblings during conference session times on the Saturday.

Sharon Bourke, a Queensland mother of three whose two sons were born with significant disabilities will be presenting her workshop "Building Lifelong Support Strategies: Support Circles and Networks". Sharon works for the Pave the Way Project.

Pave the Way Project's work is about strengthening families' capacities by future planning and using, as one strategy, supports or allies to assist families to plan for the future, with decision making and safeguarding. This workshop will explore the importance of relationships in the lives of our sons and daughters.
One of the key roles we play as parents is providing our sons and daughters with life's opportunities. It is no different with our sons and daughters with disabilities. Where do we start? Let Sharon lead you through innovative ideas and strategies for improved quality of life for your child with CdLS.

International CdLS Conference

July 2007

Niagara Falls, Ontario

Included with this issue of KIT is a brochure describing everything you need to know about next year's International CdLS Conference hosted by Canada.

The magnificent view from the dining room of the Sheraton on the Falls.

International Conference 2007 Preview

This April I had the privilege and pleasure of spending some tourist time at Niagara Falls - the site of the CdLS Canada international conference to be held in July 2007.

I was given a tour of the hotel conference facilities & accommodation rooms; sampled the food and toured the nearby entertainment for families. The Sheraton on the Falls is a perfect venue choice for the international family conference. Its meeting rooms are spacious and easily accessed by wheelchairs, accommodation rooms are well appointed and from the point of view of a family, very reasonably priced, as charges are by the room – not per person. You can choose rooms with a view of the falls – for which you pay a little more per night – or with a view of the town – for which you pay a little less. I have to say that the views are to die for, and worth the little extra if this is within your budget. The food is adaptable for people on a soft diet, but is tasty, varied and plentiful. Most importantly, the hotel staff members are friendly and accommodating. If you need anything, just ask.

Sitting in on a committee meeting for conference, I was gobsmacked by just how much has already been finalised with 15 months to go. And impressive those plans are! Every family member has been thought of, from babies to grandparents: food, transport, entertainment and most importantly inclusion in the conference program itself. Siblings are in for the rare treat of having a full program over the course of conference.

I know how difficult it is to save or seek sponsorship for the whole family to attend, but if ever you wanted to take your children to conference, this is the one to make that special effort to attend for siblings.

The hotel complex, which overlooks the Falls, is within easy walking distance of Falls activities. Indeed, the Maid of the Mist is just across the road. When you walk out of the hotel's front door (if you can tear your eyes away from the hypnotic view!) you are able to stroll through the parks and paths or pop in to one of the many entertainment venues to suit any age group. There are bars for the over 19yr olds – Hard Rock Café, Planet Hollywood for eg. - cafés for kids, arcade games galore, shopping at reasonable prices. You name it, its there.

I look forward to meeting Canadian and International families in Niagara Falls in 2007.

Jenny Rollo
Federation Representative
CdLS Australia.

DISCLAIMER

This newsletter is not intended for diagnostic purposes or self treatment. The Cornelia de Lange Syndrome Association and its committee do not necessarily endorse or recommend any products, services, methods or literature mentioned within. Any questions about treatments should be discussed with your child's doctor.