CDKL5-Ireland: Family Awareness day

organised by Trinity College Institute of Neuroscience and CDKL5 Ireland

On behalf CDKL5 Ireland, we are delighted to have the pleasure of hosting the 1st CDKL5-Ireland: Family Awareness day.

Location: Science Gallery, Trinity College Dublin.

Date: Sat 13th July 2019

Time: 12.00pm – 4.00pm

SCIENCE GALLERY

CDKL5 IRELAND

Saturday 13th July 2019,

Science Gallery, Trinity College Dublin

Who are CDKL5 IRELAND?

CDKL5 Ireland is a small organisation, established by the parents of children with CDKL5 deficiency disorder (CDD).

Their main objective is to provide information and support to everybody in Ireland affected by this condition.

They also aim to provide information to medical professionals, service providers and the general public in order to raise awareness of this rare disorder.

Additionally, CDKL5 Ireland raise funds for CDD related research and work in close collaboration with CDKL5 UK.

Welcome Everyone,

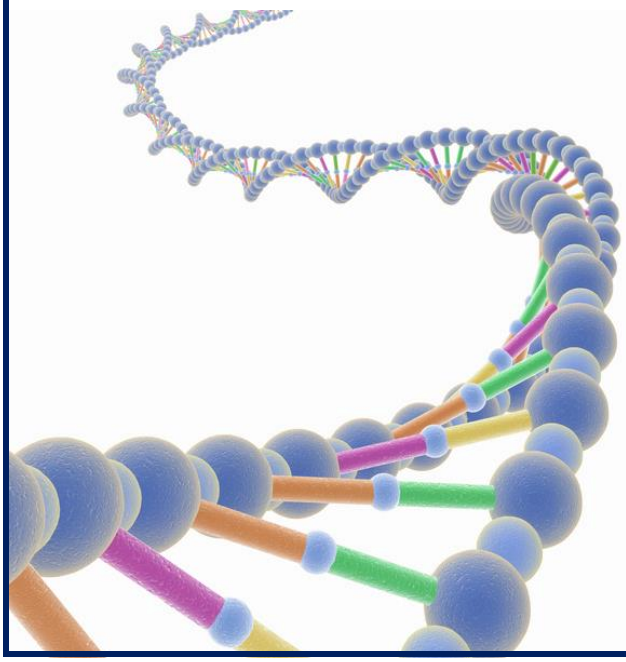
On behalf CDKL5 Ireland, we are delighted to have the pleasure of hosting the first ever CDKL5 Ireland Family Awareness Day here at the Science Gallery in Trinity College Dublin.

CDKL5 deficiency disorder is caused by mutations in the CDKL5 gene. This gene normally provides instructions for making a protein which is necessary for normal brain development and function. Mutations in this gene can cause a shortage of functional CDKL5 protein or alter its activity in neurons which disrupts brain development. It is unclear how these changes cause the specific features of CDKL5 deficiency disorder (CDD).

The CDKL5 gene is located on the X-chromosome and so the condition is inherited in an X-linked dominant pattern. CDD disorder is characterized by seizures that begin in infancy, followed by significant delays in many aspects of development. The types of seizures change with age but usually occur daily in most affected individuals and are resistant to treatment. Development is impaired in children with CDD, many have severe intellectual disability, affected speech and delayed development of gross motor skills such as standing and walking.

Medical research concerning these types of conditions is very slow paced but we hope we can all work together and strive for the day when effective treatment is available for every child born with CDKL5 DD.

CDKL5 Awareness Day Team



Agenda

CDKL5 Awareness Day	
Time	**Speaker and objectives**
13:00	Welcoming of the families followed by presentation of Agenda. How families can contribute to / benefit from research. (Dr. Massimiliano Bianchi)
13:10	Brief introduction and welcome message (Alan Connolly) Round table: Individual family stories. (Jonna Malone)
13:45	Microtubules and CDKL5: a promising path towards understanding pathogenesis of CDD. (Dr. Massimiliano Bianchi)
14:15	Project Presentation: Plasma microtubule proteins as potential biomarkers for CDKL5 Deficiency Disorder. (Dr. Omar Mamad)
14.30	Working with Patients affected by CDD. (Dr. Marina Trivisano)
14:45	How the Clinical Research Facility would support the project. (Dr. Martina Hennessy)
15:00	Overview of the Clinical Aspects of CDD (Dr. Ana Mingorance and Dr. Dan Lavery)
15:15	Entertainment: Storytelling of 'Tuby' by Federica Maran and music by PJ Murphy
15:45	Reception

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CDKL5 Ireland Trustees

Alan Connolly, Chairperson

Paula Connolly, Alliance Representative

Jonna Malone, Secretary

Cathy Byrne, Treasurer

Today's Speakers

Massimiliano (Max) Bianchi, PhD

President & CEO, Ulysses Neuroscience Ltd

Adjunct Assistant Professor, School of Psychology, Trinity College Dublin

Omar Mamad, PhD

Research Fellow Trinity College Institute Of Neuroscience, Trinity College Dublin

Martina Hennessy, MB, PhD FRCP

Associate Professor, School of Medicine, Trinity College Dublin

HRB Clinical Research Facility, St James's Hospital

Director of the Wellcome Trust

Jonna Malone

Secretary of CDKL5 Ireland.

Mother to 11 year old Maia, CDD Patient

Alan Connolly

Chairperson of CDKL5 Ireland

Father of Alex aged 22, CDD Patient

Marina Trivisano, MD

Consultant Neurologist, Department of Neuroscience, Pediatric Hospital, Bambino Gesù Roma, Italy

Ana Mingorance, PhD

Chief Development Officer, Loulou Foundation

Plasma microtubule proteins as potential biomarkers for CDKL5 Deficiency Disorder.

Project Summary

CDKL5 Deficiency Disorder (CDD) is a rare brain disorder characterized by severe early-onset seizures in the first month of life, intellectual disability, motor and social impairment mainly affecting females. Currently, no therapies exist for CDD and only symptomatic pharmacological treatments are available. The use of animal models such as *Cdkl5*-null mice (lacking the *CDKL5* gene) have shown to be an invaluable tool to gather insights into the molecular alterations underlining CDD. However, there is an urgent need for minimally invasive (i.e. peripheral fluid analysis) biomarkers of translational value to monitor disease progression. Microtubules are cytoskeletal elements playing vital roles in development of brain cells, supporting the formation, maintenance and remodelling of synapses, structures through which brain cells communicate. Dysfunction in microtubule dynamics leads to altered brain development and loss of synapses. Microtubule dynamics can be analysed by measuring the post-translational modifications (PTMs) of the alpha-tubulin protein, the main building block of microtubules. We have recently discovered that alpha-tubulin PTMs can be detected in peripheral fluids, such as blood plasma and cerebrospinal fluid (CSF) in both animals and humans. Research from previous Dr. Bianchi's team shows that alterations in alpha-tubulin PTMs are evident in plasma of patients affects by neurodegenerative disorders such as Parkinson's disease (in collaboration with the Michael J Fox Foundation, MJFF). More recently, it was observed in a pilot study that behavioural alterations in *Cdkl5*-null male mice were accompanied by alpha-tubulin PTMs changes in the brain and plasma of *Cdkl5*-null mice. Importantly, those behavioural and microtubular changes were rescued by a pharmacological treatment with a specific microtubule modulator. The objective of the current project is to confirm our preliminary observations in *Cdkl5*-null male mice extending them to include also Cdkl5-heterozygous female mice since 90% of CDD patients are females. We will then translate the assay into clinical settings by measuring alpha-tubulin PTMs in plasma of CDD patients sampled from Irish, Italian and US diseased cohorts. If our hypothesis on altered plasma alpha-tubulin PTMs in CDD is correct, the results may have an immediate impact on the development of clinical diagnostic biomarkers and open new avenues for future original research, possibly leading to the discovery of innovative disease-modifying therapies.

The Team

- M. Bianchi, PhD (PI): Trinity College Institute of Neuroscience, Trinity College Dublin, Ireland.

- C. Kilstrup-Nielsen, PhD (Co-PI): Department of Biotechnology & Life Sciences, Insubria University, Italy.

- M. Trevisano, PhD (Co-PI): Rare and Complex Epilepsies, Department of Neuroscience and Neurorehabilitation, Bambino Gesù Children's Hospital, Rome, Italy.

- J.L. Neul, MD, PhD (Co-PI): Vanderbilt University Medical Center, Nashville, USA

Research Fellows

- O. Mamad, PhD: Trinity College Institute of Neuroscience, Trinity College Dublin, Ireland.

- I. Barbiero, PhD: Department of Biotechnology & Life Sciences, Insubria University, Italy.

Participants

LouLou Foundation Representatives

Dr. Daniel Lavery, Chief Scientific Officer

Dr. Ana Mingorance, Chief Development Officer

TCD and St James's Hospital Academic Team

Massimiliano Bianchi, PhD

Omar Mamad, PhD

Martina Hennessy, PhD

Aoife Dempsey

Ali Taki

Entertainment

Federica Maran

PJ Murphy

loulou FOUNDATION

Tackling CDKL5 Deficiency

the orphan disease center

Trinity College Dublin

The University of Dublin

Thank You

If you are interested in contributing or participating in next years CDKL5 Awareness Day 2020, please contact

Dr Omar Mamad mamado@tcd.ie

And

CDKL5 Ireland info@cdkl5.ie

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