2013 Research Update

National Centre for Inherited Metabolic Disorders

Peer reviewed publications 2013
Knerr I, Blessing H, Seyferth S, Watling RJ, Chaudhri MA. Evaluation of plasma trace element and mineral status in children and adolescents with phenylketonuria using data from inductively-coupled-plasma atomic emission and mass spectrometric analysis. Ann Nutr Metab. 2013;63(1-2):168-73.
Knerr I, Coss KP, Doran PP, Hughes J, Wareham N, Burling K, **Treacy EP**. Leptin levels in children and adults with classic galactosaemia. J Inherit Metab Dis Rep. 2013;9:125-31.
Grünert SC, Müllerleile S, De Silva L, Barth M, Walter M, Walter K, Meissner T, Lindner M, Ensenauer R, Santer R, Bodamer OA, Baumgartner MR, Brunner-Krainz M, Karall D, Haase C, **Knerr I**, Marquardt T, Steinfeld R, Beblo S, Koch HG, Konstantopoulou V, Scholl-Bürgi S, van Teeffelen-Heithoff A, Suormala T, Sperl W, Kraus JP, Superti-Furga A, Schwab KO, Sass JO. Propionic acidemia: clinical course and outcome in 55 paediatric and adolescent patients. Orphanet J Rare Dis. 2013 Jan 10;8:6. doi: 10.1186/1750-1172-8-6.
De Franco E, Shaw-Smith C, Flanagan SE, Shepherd MH; International NDM Consortium incl. **Knerr I**, Hattersley AT, Ellard S. GATA6 mutations cause a broad phenotypic spectrum of diabetes from pancreatic agenesis to adult-onset diabetes without exocrine insufficiency. Diabetes. 2013 Mar;62(3):993-7.
Coss KP, Doran PP, Owoeye C, Codd MB, Hamid N, Mayne PD, **Crushell E, Knerr I, Monavari AA**, **Treacy EP**. Classical Galactosaemia in Ireland: incidence, complications and outcomes of treatment. J Inherit Metab Dis. 2013 Jan;36(1):21-7.
Treacy EP. Invited Review for Irish Medical Times 'Clinical Times'. Rare Diseases in Ireland and the European context, what are the plans? March 1st edition 2013
L Morrissey, C Tiernan, D Lambert, E O'Reilly, **EP Treacy.** Hereditary Metabolic Diseases (HMDs) in adult practice in Ireland, a preliminary assessment. Ir. J Med Sciences, 2013, (182), 4: 565-571
Van Erven B, Gubbels CS, van Golde RJ, Dunselman GA, Derhaag JG, de Wert, Geraedts JP, Bosch AM, **Treacy EP,** Berry GT, Welt CK, Rubio-Gozalbo ME. Fertility preservation in female classic galactosaemia patients. Orphanet J Rare Dis, 2013, June; 16;8:107. doi: 10.1186/1750-1172-8-107
O'Gorman P, Benjamin D, Gethins M, Khan S, **Treacy EP**. Gaucher's disease in the Irish population. British Journal of Haematology. Key Opinions in Medicine, Vol 4 (1), February 2013 (pages 1-5).
Coss KP, Hawkes CP, Adamczyk B, Stockmann H, **Crushell E**, Saldova R, **Knerr I, Monavari AA**, Rudd PM and **Treacy EP**. IgG *N*-glycan abnormalities in children with Galactosaemia. J of Proteome Research, 2014: 13 (2): 385-94

Ina Knerr, Eileen Treacy. Hereditary Metabolic Disorders as prototypes of treatable Rare Disorders: An Irish Perspective in an EU Context. Irish Medical Times, February 2014
Casey J, McGettigan P, Brosnahan D, Curtis E, **Treacy E**, Ennis S, Lynch SA . Atypical Alstrom syndrome with novel ALMS1 mutations precluded by current diagnostic criteria. Eur J Med Genet: 57 (2-3): 55-9.
Buraczewska, M., O'Leary, D., Walsh, O., **Monavari, A**. and **Crushell, E**. (2013) 'Parental experience of enzyme replacement therapy for Hunter syndrome', Ir Med J, 106(4), 120-2
Fitzgerald, M., **Crushell, E**. and Hickey, C. (2013) 'Cyclic vomiting syndrome masking a fatal metabolic disease', Eur J Pediatr, 172(5), 707-10
Langereis, E. J., Borgo, A., **Crushell, E**., Harmatz, P. R., van Hasselt, P. M., Jones, S. A., Kelly, P. M., Lampe, C., van der Lee, J. H., Odent, T., Sakkers, R., Scarpa, M., Schafroth, M. U., Struijs, P. A., Valayannopoulos, V., White, K. K. and Wijburg, F. A. (2013) 'Treatment of hip dysplasia in patients with mucopolysaccharidosis type I after hematopoietic stem cell transplantation: results of an international consensus procedure', Orphanet J Rare Dis, 8, 155
O'Leary OA, Hawkes CP, Cody D, **Hughes JAF**. "Atypical Wolman Disease with evidence of immune dysfunction" JIMD 2013, 36: (Supplement 2), 284
McCarron, E., McCormack, O., Cronin, T., McGowan, A., Healy, M. L., O'Rourke, D., **Crushell, E**., Ravi, N. and Reynolds, J. V. (2013) 'Management of maple syrup urine disease in the peri-operative period', Ir Med J, 106(9), 277-8
Pastores GM, Rosenbloom B, Weinreb N, Goker-Alpan O, Grabowski G, Cohn GM, Zahrieh D. A multicentre open-label treatment protocol (HGT-GCB-058) of velaglucerase alfa enzyme replacement therapy in patients with Gaucher disease type 1: safety and tolerability. Genet Med. 2013 Nov 21. doi: 10.1038/gim.2013.154
GM Pastores, DA Hughes. Eliglustat tartrate: an oral therapeutic option for Gaucher disease type 1 Clinical Investigation January 2014, Vol. 4, No. 1, Pages 45-53 , DOI 10.4155/cli.13.122 (doi:10.4155/cli.13.122

Books/chapters 2013
Knerr I, Gibson KM, Koch HG, Häberle J. Glutaminase and Glutamine Synthetase: Biochemistry, Pharmacology and Mendelian Disorder. Supplement to Chapter 85: Urea Cycle Enzymes, Scriver's Online Metabolic and Molecular Bases of Inherited Diseases (Scriver's OMMBID), Epub March 2013

Published abstracts 2013
Fitzsimons PE, Borovickova I, Trench C, Durkie M, Tops B, **Hughes J, Monavari AA**, Mayne PD. Fumarate hydratase deficiency in Ireland-the importance of carrier detection. J Inher Metab Dis (2013) 36 (S2):S221
Coss KP, Doran PP, **Knerr I,** Adamczyk B, Murray DW, Rubio-Gozalbo ME, Rudd P, **Treacy EP**. Glycosylation serum and gene biomarkers in classical Galactosaemia. J Inher Metab Dis 36, Suppl 2, S 225, 2013
Casey J, Lynam-Lennon N, McGettigan P, O'Sullivan J, McDermott M, Slattery SMC, Forde K, **Monavari AA**, **Knerr I**, **Hughes J**, Bourke B, Ennis S, Lynch SA, **Crushell E**. Recessive mutations in LARS cause a multisystem disorder with infantile liver failure, recurrent hepatopathy, anaemia and epilepsy. J Inher Metab Dis 36, Suppl 2, S 107, 2013
Knerr I, Coss KP, Doran PP, **Crushell E, Hughes J, Treacy EP.** Does leptin dysregulation contribute to long-term complications in children and adults with classical galactosaemia? Monatsschr Kinderheilkd 161, 3, 273, 2013
Recessive mutations in LARS cause a multisystem disorder with infantile liver failure, recurrent hepatopathy, anaemia and epilepsy. Jillian Casey, Niamh Lynam-Lennon, Paul McGettigan, Jacintha O' Sullivan, Michael McDermott, Slattery SMC, Forde K, **Ahmad Monavari, Ina Knerr, Joanne Hughes**, Billy Bourke, Sean Ennis, Sally Ann Lynch, **Ellen Crushell**. Journal Inherit Metab Dis, vol36suppl2.pS107 O-016
Developmental regression and congenital optic atrophy associated with OPA1 mutation. Schlunz F, O'Shea R, Lynch B, O'Keefe M, **Crushell E**. Journal Inherit Metab Dis, vol36 suppl2.pS212 P-375
Fitzsimons PE, Borovickova I, Trench C, Durkie M, Tops B, **Hughes J**, **Monavari AA**, Mayne PD. Fumarate hydratase deficiency in Ireland-the importance of carrier detection. J Inherit Metab Dis vol 36, suppl 2
Van Erven B, Gubbels CS, van Golde RJ, Dunselman GA, Derhaag JG, de Wert G, Geraedts JP, Bosch AM, **Treacy EP**, Welt CK, Berry GT, Rubio-Gozalbo ME. Fertility preservation in female classic galactosaemia patients. J Inherit Metab Dis (2013) (36), suppl 2, Abs P423

Presentations at International Conferences 2013
Prof. Treacy. European Galactosaemia Society 2013 meeting. Birmingham, March 2-3rd, 2013 **Prof. Treacy.** Co-Chair for development presentation on European Network for Galactosaemia.
Prof. Treacy. Invited speaker on 'Update on Irish Galactosaemia Research' with Karen Coss. European Galactosaemia Society 2013 meeting. Birmingham, March 2-3rd, 2013
Prof. Treacy. Invited speaker. 12th International Congress of Inborn Errors of Metabolism. Barcelona, Spain. September 3rd, 2013. Nutrition and Dietetics meeting. 'Galactose and Galactosaemia, when is enough really enough?'

Prof. Treacy. Poster presentations: 12th International Congress of Inborn Errors of Metabolism. Barcelona, Spain. September 3rd – 7th, 2013.
Prof. Treacy. Invited guest speaker: Portuguese Society of Inherited Metabolic Diseases. Post-graduate education day on Galactosaemia. The utility of old (galactose metabolites) and new IgG *N*-glycans and others) biomarkers in monitoring efficacy of dietetic treatment.
Prof. Treacy. The European Galactosaemia Network (EGN): an effort towards harmonizing patient treatment (with Dr. Estela Rubio-Gozalbo).
Brona Fletcher. Evaluation of the effectiveness of a Multidisciplinary Mucopolysaccharidosis clinic in the National Centre for Inherited Metabolic Disorders. Poster presentation, Connect for Care III, The European LSD Nurses Meeting, Brussels, 14th – 15th October 2013
Knerr I, Coss KP, Doran PP, **Crushell E, Hughes J**, **Treacy EP**. Does leptin dysregulation contribute to long-term complications in children and adults with classical galactosaemia? Oral presentation, APS, 27th annual meeting, Fulda/Germany, March 2013
Coss KP, Doran PP, **Knerr I,** Adamczyk B, Murray DW, Rubio-Gozalbo ME, Rudd P, **Treacy EP**. Glycosylation serum and gene biomarkers in classical Galactosaemia. J Inher Metab Dis 2013, 36, Suppl 2, S 225. Poster presentation, International Congress of Inborn Errors of Metabolism, Barcelona, 3rd - 6th September 2013
Jillian Casey, Niamh Lynam-Lennon, Paul McGettigan, Jacintha O' Sullivan, Michael McDermott, **Ahmad Monavari, Ina Knerr, Joanne Hughes**, Billy Bourke, Sean Ennis, Sally Ann Lynch, **Ellen Crushell**. Exome sequencing implicates LARS in a multisystem disorder with infantile liver failure, recurrent hepatopathy, anaemia and epilepsy. Oral presentation at British Inherited Metabolic Disease Group annual meeting, London, July 4th & 5th 2013. Award: Dr Casey won Best Oral presentation for this presentation.
Jillian Casey, Niamh Lynam-Lennon, Paul McGettigan, Jacintha O' Sullivan, Michael McDermott, Slattery SMC, Forde K, **Ahmad Monavari, Ina Knerr, Joanne Hughes**, Billy Bourke, Sean Ennis, Sally Ann Lynch, **Ellen Crushell**. Recessive mutations in LARS cause a multisystem disorder with infantile liver failure, recurrent hepatopathy, anaemia and epilepsy. Oral presentation at the 12th international Congress of Inborn errors of Metabolism (ICIEM) Barcelona 3-6th Sept 2013. Ref: J Inher Metab Dis, vol36suppl2.pS107 O-016
Schlunz F, O'Shea R, Lynch B, O'Keefe M, **Crushell E**. Developmental regression and congenital optic atrophy associated with OPA1 mutation. Poster presentation at the 12th international Congress of Inborn errors of Metabolism (ICIEM) Barcelona 3rd -6th Sept 2013. Ref: J Inher Metab Dis, vol36 suppl2.pS212 P-375
Fitzsimons PE, Borovickova I, Trench C, Durkie M, Tops B, **Hughes J, Monavari AA**, Mayne PD. Fumarate hydratase deficiency in Ireland-the importance of carrier detection. International Congress of Inborn Errors of Metabolism, Barcelona, 3rd – 6th September 2013
Atypical presentation of juvenile GM1 gangliosidosis. O'Byrne J, Forman E, **Crushell E**, King MD. Poster Presentation, British Paediatric Neurology Association annual meeting, Manchester 23rd – 25th Jan 2013

GM Pastores. Lysosomal storage disease, a model for diagnosis and management of rare diseases, 5th Conference of Rare Disease Day, February 26th, 2014, Rare disease Foundation, Tehran, Iran
J. Casey, P. McGettigan, **E. Crushell**, D. Slattery, A. Green, S. Ennis, S.A. Lynch. Lessons learned from Next-Gen studies in a consanguineous population. Genomic Disorders 2014: The Genomics of Rare Diseases, Cambridge, London, United Kingdom, March 2014
GM Pastores. Lysosomal storage disease, diagnosis and management update, 10th SPDM International Symposium, March 20th, 2014, Cascais, Portugal
J. Casey, P. McGettigan, **E. Crushell**, D. Slattery, A. Green, S. Ennis, S.A. Lynch. An insight into disease genes and clan structure in the Irish Traveller population. 34th Annual David W. Smith Workshop in Malformations and Morphogenesis, Mont Tremblant, Quebec, August 2013

Presentations at National Conferences 2013
Prof. Treacy. Invited Panel Member. IPPOSI sponsored meeting Feb. 28th, 2013. 'Rare Diseases without Borders', Dublin City Hall.
Prof. Treacy. Member of Organising Committee and Chairperson for Children's University Hospital, Research Day for Rare Diseases Day, 'Clinical Research in Rare Diseases. Held on March 1st, 2013
Prof. Treacy. Speaker: Research on Rare Diseases at Children's University Hospital. Oral Presentation Research Day for Rare Diseases Day, Children's University Hospital, March 1st, 2013. Knerr I, Crushell E, Hughes J, Deverell D, Mayne PD, Monavari AA, Naughten ER, Treacy EP. Four decades of newborn screening for Maple Syrup Urine Disease in the Republic of Ireland: A retrospective cohort study of the effects of early diagnosis and longitudinal metabolic control.
Prof. Treacy. Invited seminar. NIBRT (National Institute for Bioprocessing and Training). 'Galactose and Galactosaemia, the how and why', September 18th, 2013
Prof. Treacy. Invited lecture: Climb (UK Children Living with Inherited Metabolic Diseases) Dublin Conference, 21st September, 2013, Current and Future IMD Services in Ireland.
Prof. Treacy. Platform presentation: TSCUH Research Update Day, April 26th 2013. Coss KP, Doran P, Murray DW, Cotter E, Knerr I and Treacy E. "Glycomic and genomic biomarkers to monitor Classical Galactosaemia."
Prof. Treacy. Platform presentation: DAMC Young Investigators Award, May 22nd, St. Vincent's University Hospital. Coss KP, Doran P, Murray DW, Cotter E, Knerr I and Treacy E. Novel genomic biomarkers implicated in Classical Galactosaemia
Prof. Treacy. Poster presentation: MRCG, Medical Research Charities Group, Annual Conference, Rotunda Hospital, Dublin, November 12th, 2013. Coss KP, Doran PP, Cotter EJ, Knerr I, Murray DW, and Treacy EP **(**2013) "Galactosaemia, a new understanding of the pathogenesis" Medical Research Charities Group – Health Research Board, Health Research in a Changing Environment, Dublin, Ireland

Prof. Treacy. Platform presentation: Our Lady's Children's Hospital, Crumlin. 3rd Annual Research and Audit Meeting, May 24th. Casey J, McGettigan P, Brosnahan D, Treacy EP, Ennis S, Lynch SA. Exome sequencing confirms diagnosis where previous diagnostic testing has been normal.
Coss KP, Doran PP, Knerr I, Adamcyzk B, Murray DW, Rubio-Gozalbo ME, Rudd PM, **Treacy EP**. Glycosylation serum and gene biomarkers in Classical Galactosaemia. Karen Coss, PhD student, Recipient of SSIEM student travel award
van Erven B, Gubbels CS, van Golde RJ, Dunselman GA, Derhaag JG, de Wert G, Geraedts JP, Bosch AM, **Treacy EP,** Welt CK, Berry GT, Rubio-Gozalbo ME. Fertility preservation in female classic galactosaemia patients.
Prof. Treacy. SSRA Student presentation, UCD, October 2013, Poster presentation, Odelia Lam, E Crushell, I Knerr, A Monavari, J Hughes, EP Treacy. Relative prevalence of HMDs in the Irish Traveller Community.
Prof. Treacy. Oral Platform Presentation. Irish Paediatric Association, Annual Meeting, Dublin November 9th. O'Byrne J, Treacy E, King M, Lynch SA, Sharif F. 'Unexplained global developmental delay: Guidelines for first line investigations'. Prize for best presentation in Plenary Session.
Jane Rice. The management of GSD type III: using a high CHO diet, evidence and practicalities. Invited speaker, The DMIMD – Dietary management of Inherited Metabolic disorders, 12th April 2013
Coss KP, Doran PP, Cotter EJ, **Knerr I**, Murray DW, **Treacy EP**. Galactosaemia, a new understanding of the pathogenesis. Poster presentation, Medical Research Charities Group Conference, Dublin, 12th November 2013
Knerr, I. Guest lecture "Fat-burning secrets: Clinical features of Fatty Acid Oxidation Defects" Irish Paediatric Association, Annual meeting, Dublin, 8th November 2013
Knerr I, **Crushell E, Hughes J**, Deverell D, Mayne PD, **Monavari AA**, Naughten ER, **Treacy EP**. Four decades of Newborn Screening for Maple Syrup Urine Disease (MSUD) in the Republic of Ireland: A retrospective cohort study of the effects of early diagnosis and longitudinal metabolic control. Clinical Research in Rare Disease, CUH Temple Street, 1st March 2013
Knerr I, **Treacy EP**, "Galactosaemia – Partial diet liberalisation studies. An update" Galactosaemia Support Group, Annual meeting, Dublin, 27th September 2013
S.M.C. Slattery and J. Casey, N. Lynam-Lennon, P. McGettigan, J. O' Sullivan, M. McDermott, K. Forde, M. Cotter, **A.A. Monavari, I. Knerr, J. Hughes**, B. Bourke, S. Ennis, S.A. Lynch, **E. Crushell**. Clinical phenotype associated with recessive mutations in LARS. Temple Street Children's University Hospital Research and Audit Day, Dublin, December 2013
J. Casey, P. McGettigan, D. Slattery, **E. Crushell**, S. Ennis, A. McCann, S.A. Lynch. The impact of identifying rare disease genes on patient health. National Children's Research Centre Research Symposium, Our Lady's Children's Hospital, Crumlin, Dublin, Ireland, December 2013
S.MC. Slattery and J. Casey, N. Lynam-Lennon, P. McGettigan, J. O' Sullivan, M. McDermott, K.

Forde, M. Cotter, **A.A. Monavari, I. Knerr, J. Hughes**, B. Bourke, S. Ennis, S.A. Lynch, **E. Crushell**. Clinical phenotype associated with recessive mutations in the LARS gene. Irish Paediatric Association, Dublin, November 2013 (Best presentation prize)
J. Casey, A. Green, D. Slattery, **E. Crushell**, S. Ennis, S.A. Lynch. Rare disease gene identification and its translation. Temple Street Children's University Hospital Clinical Research in Rare Disease Day, Dublin, March 2013
J. Kutty, **E. Crushell**, M. King, **J. Hughes**. Somatic Mosaicism in X-linked PDHA1 gene, a cause of developmental delay and epilepsy. Poster presentation, Irish Paediatric Association, Annual meeting, Dublin, 8th November 2013

Awards/prizes 2013
Karen Coss, PhD, SSIEM Travel award, September 2013
Dr Jim O'Byrne, Genetics trainee: Prize for best presentation in Plenary Session, Irish Paediatric Association, Annual Meeting, Dublin November 9th
S.MC. Slattery and J. Casey, N. Lynam-Lennon, P. McGettigan, J. O' Sullivan, M. McDermott, K. Forde, M. Cotter, **A.A. Monavari, I. Knerr, J. Hughes**, B. Bourke, S. Ennis, S.A. Lynch, **E. Crushell**. Clinical phenotype associated with recessive mutations in the LARS gene. Irish Paediatric Association, Dublin, November 2013. Best oral presentation prize
Jillian Casey, Niamh Lynam-Lennon, Paul McGettigan, Jacintha O' Sullivan, Michael McDermott, **Ahmad Monavari**, **Ina Knerr**, **Joanne Hughes**, Billy Bourke, Sean Ennis, Sally Ann Lynch, **Ellen Crushell**. Exome sequencing implicates LARS in a multisystem disorder with infantile liver failure, recurrent hepatopathy, anaemia and epilepsy. Oral presentation at British Inherited Metabolic Disease Group annual meeting, London. Dr Casey won Best Oral presentation award for this presentation.
Prof. Treacy. Oral Platform Presentation. Irish Paediatric Association, Annual Meeting, Dublin November 9th. O'Byrne J, Treacy E, King M, Lynch SA, Sharif F. 'Unexplained global developmental delay: Guidelines for first line investigations'. Prize for best presentation in Plenary Session.
Audits 2013
Brona Fletcher - MPS Clinic Evaluation Form
Celine Stenson, Maria O'Regan & Fiona Boyle - Audit of annual blood work in PKU patients with view to revise policy