Research and publications

Current clinical trials at CUH | Key publications

At CUH we are always looking to improve both the quality of care and the treatment options available to all our patients. We are actively involved in both academic and clinical research, funded independently and in conjunction with our partners in the pharmaceutical industry.

Current clinical trials at CUH:

Fabry Disease

Protalix F20 (BALANCE)

A randomised, double blind, active control study of the safety and efficacy of PRX-102 compared to Agalsidase beta on renal function in patients with Fabry disease previously treated with agalsidase beta.

Current status: recruitment closed

Clinical trials.gov NCT02795676

Protalix F30

An open label study of the safety and efficacy of PRX-102 in patients with Fabry disease currently treated with Replagal

Current status: recruitment closed

Clinical trials.gov NCT03018730

Protalix F50

A Phase 3, Open Label, Switch Over Study to Assess the Safety, Efficacy and Pharmacokinetics of pegunigalsidase alfa (PRX-102) 2 mg/kg Administered by Intravenous

Infusion Every 4 Weeks for 52 weeks in Patients with Fabry Disease Currently Treated with Enzyme Replacement Therapy: Fabrazyme® (agalsidase beta) or Replagal™ (agalsidase alfa).

Current status: recruitment closed

Clinical trials.gov NCT03180840

Protalix F51

Open Label extension Study to Assess the Safety, Efficacy and Pharmacokinetics of pegunigalsidase alfa (PRX-102) 2 mg/kg Administered by Intravenous Infusion Every 4 Weeks for 52 weeks in Patients with Fabry Disease.

Current status: open to participants of F50

Clinical trials.gov NCT03614234

Protalix F60

Open label extension study to evaluate the long term safety and efficacy of pegunigalsidase alfa (PRX-102) in patients with Fabry disease.

Current status: open to participants of F30/F20

Clinical trials.gov NCT03566017

Gaucher disease

LEAP (Sanofi Genzyme)

A 52-week two-part, open-label, multicenter, multinational study of the safety, tolerability, pharmacokinetics, pharmacodynamics, and exploratory efficacy of GZ/SAR402671 in combination with Cerezyme in adult patients with Gaucher disease Type 3 (LEAP)

Current status: open

Clinical trials.gov NCT02843035

Pompe disease

COMET (Sanofi Genzyme)

A phase 3 randomised multicentre multinational double blinded study comparing the efficacy and safety of repeated biweekly infusions of neoGAA (GZ402666) and alglucosidase alfa in treatment-naïve patients with late onset Pompe disease.

Current status: closed to recruitment

Clinical trials .gov NCT02782741

PROPEL (Amicus therapeutics)

ATB200-03: A Phase 3 Double-Blind Randomized Study To Assess The Efficacy And Safety of Intravenous ATB200 Co-Administered With Oral AT2221 In Adult Subjects With Late-Onset Pompe Disease Compared With Alglucosidase Alfa/Placebo.

Current status: open

Clinical trials.gov NCT03729362

Other research:

International, multicentre, long term observational database studies

- FOS & HOS (Fabry & Hunter Outcome surveys - Shire) NCT03289065
- Genzyme registries (Gaucher NCT00358943, Fabry NCT00196742 & Pompe NCT00231400)
- Elisafe - registry for patients receiving therapy with Cerdelga (eliglustat) – Sanofi Genzyme
- Follow me –registry for patients receiving therapy with Galafold (migalastat) – Amicus therapeutics
- LAL-D registry - registry for patients with lysosomal acid lipase deficiency (LAL-D)/ cholesterol ester storage disease (CESD) NCT01633489

Current status: open

Predictive measures to stratify clinical outcomes in children and adults with Gaucher disease and responses to specific therapies -a study to classify Gaucher disease.

Current status: open

Clinical trials.gov NCT03240653

Rapsodi

Rapsodi is a pioneering study that uses the internet to find new ways to diagnose Parkinson's earlier and develop life changing treatments. You have been invited to join the study because you may carry the GBA gene associated with the condition. The latest research has identified a link between the GBA gene and a slightly higher risk of developing Parkinson's much later in life. Rapsodi aims to identify certain early symptoms that appear many years before the movement problems associated with Parkinson's.

Curent status: open

For further information please go to https://rapsodistudy.com/en

Research interests

We work closely with Professor Cox's team in the university department of medicine:

Professor Timothy Cox - Department of Medicine, University of Cambridge

The broad aim of our scientific studies is to improve the diagnosis, monitoring and treatment of lysosomal disorders: we thus investigate the natural course and molecular pathogenesis of these diseases; we have discovered novel biomarkers and have introduced innovative treatments. As part of the latter, a gene transfer programme has been initiated; this involves pre clinical research designed to translate our recent therapeutic discoveries rapidly from the laboratory to the clinic.

Some of our current research interests include:

Biomarkers of disease

Pathogenesis of Gaucher disease

Gene therapy - with a specific interest in the Lysosomal storage disorders that cause neurological disease

Key publications

Professor Cox

Professor Timothy Cox - Department of Medicine, University of Cambridge

Mistry, P.K., Wraight, E.P. and Cox, T.M. (1996)
Delivery of proteins to macrophages: implications for treatment of Gaucher Disease. Lancet 348: 1555-1559.

Moran, MT, Schofield J., Hayman A.R., E. Young, Shi G-P and Cox T.M.(2000) Pathologic gene expression in Gaucher's disease with upregulation of cysteine proteinases including osteoclastic Cathepsin K. Blood 56: 1969-1978.

Cox, T.M. (2001) Gaucher's disease: understanding the molecular pathogenesis of sphingolipidoses. Journal of Inherited Metabolic Disease 24: (suppl.2): 97-105.Boot R.G., Verhoek M., de Cost M, Hollak CE, Maas M, Bleijtevens B., Van Breemen MJ. van Meurs M., Boven LA., Laman JD., Moran MT, Cox TM., Aerts JM (2004) Marked elevation of the chemokine CCL18/PARC in Gaucher disease: a novel surrogate marker for assessing therapeutic intervention. Blood 103: 33-39.

Deegan, PB., Moran, M-T., McFarlane, I., Schofield, JP., Boot, RG., Aerts, JMFG., and Cox, TM. (2005) Clinical evaluation of chemokine and enzymatic biomarkers of Gaucher disease. Blood Cells, Molecules and Disease 35:259-267

Cox T., Lachmann R., Hollak C., Aerts J., van Weely S., Hrebicek M., Platt F., Butters T., Dwek R., Moyses C., Gow I., Elstein D., Zimran A. (2000) A Novel Oral Treatment of Gaucher's Disease with N- butyldeoxynojirimycin (OGT 918) to decrease Substrate Biosynthesis. Lancet 355: 1481-1485

Elstein D., Hollak C., Aerts JM, van Weely S., Maas M., Cox T.M., Lachmann RH., Hrebicek M., Platt FM., Butters TD., Dwek RA, Zimran A (2004) Sustained therapeutic effects of oral miglustat (Zavesca, N- butyldeoxynojirimycin, OGT 918) in type 1 Gaucher disease. Journal of Inherited Metabolic Disease 27: 757-766.

Lachmann, RH, te Vruchte, D., Lloyd-Evans E, Reinkensmeier G, Sillence DJ, Fernandez-Guillen L., Dwek RA., Butters TD, Cox TM, Platt FM (2004) Treatment with miglustat reverses the lipid-trafficking defect in Niemann-Pick disease type C. Neurobiology of Disease 16: 654-658.

Whitfield PD., Calvin J, Hogg S, O'Driscoll E., Halsall D., Burling K., Maguire G., Wright N., Cox TM, Meikle PJ.,and Deegan, PB. (2005) Monitoring enzyme replacement therapy in Fabry disease – role of urine globotriasoylceramide. Journal of Inherited Metabolic Disease 28: 21-33.

Cachón-González M.B., Wang S.Z., Lynch A., Ziegler R., Cheng, SH & Cox, TM. (2006) Effective gene therapy in an authentic model of Tay-Sachs related diseases. Proceedings of the National Academy of Sciences (USA) 103: 10373-10378.

Cox, T.M., Platt, F.M. and Aerts, J.M.F.G. (2007)
Medicinal Use of Iminosugars Chapter 13, in:
Iminosugars from Synthesis to Therapeutic Applications
pp.295-328. Edited P. Compain & O. Martin, Wiley, Chichester, UK.

Cox, T.M. (2008) Gaucher's Disease. A Model Disorder for
Therapeutic Exploration of the Lysosome, in: Mechanisms of
Disease, Edited by S.Tomlinson, A.M. Heagarty, A.P. Weetman,
R.A. Malik, 2nd edition, Cambridge University Press, pp.42-68.

Chen Y, Allegood J, Liu Ying, Wang E, Cachón-González MB,
Cox TM, Merrill A, Sullards M. (2008) Imaging MALDI Mass Spectrometry Using an

Oscillating Capillary Nebulizer Matrix Coating System and Its Application to Analysis of Lipid in Brain from a Mouse Model of Tay-Sachs/Sandhoff Disease. Analytical Chemistry e-pub 4 March

Cox, T.M. Aerts, J.M.F.G., Belmatoug, N., Capellini, M.D., vom Dahl, S., Goldblatt, J., Grabowski, G.A., Hollak, C.E.M., Hwu, P., Maas, M., Martins, A.M., Mistry, P.K., Pastores, G.M., Tylki-Szymanska, A., Yee, J. and Weinreb, N. (2008) Management of non-neuronopathic Gaucher disease with special reference to pregnancy, splenectomy, bisphosphonate therapy, use of biomarkers and bone disease monitoring. Journal of Inherited Metabolic Disease 2008 Jun;31(3):319-36. Epub 2008 May 23.

Roos, J.C.P., Lachmann, R. H.,Carpenter, R.H.S., Cox, T.M. (2008) Saccadic latency as an objective biomarker of cerebral injury in lysosomal storage disease. Lancet Neurology (submitted)

Wang, S.Z., Cachón-González, M.B., Stein, P.E., Lachmann, R.H., Woods, G., Corry, P.C., Wraith, J.E., Cox, T.M. (2008) Molecular analysis of the human HEXB gene in Juvenile Jatzkewitz-Sandhoff disease in two extended Pakistani pedigrees. Human Genetics (submitted)

Abstracts for presentation

M. B. Cachón-González, S. Wang, R. Ziegler, S. H. Cheng & T. M. Cox (2008) Functional Outcome and Survival Correlates with Time of Gene Transfer and Viral Titres in a Mouse Model of Sandhoff Disease (Boston: Am. Soc. Hum. Gene Therapy)

E.V. Pavlova, M.T. Moran, P.B. Deegan, T.M. Cox (2008) Enhanced Abundance and Processing of Cathepsin S: a potential Biomarker of Gaucher disease (Budapest: EWGGD)

E.V. Pavlova, J.E. Tindall, D.A. Hughes, A.Mehta, J.E. Wraith, T.M. Cox, and P.B. Deegan (2008) Biomarkers of Avascular Necrosis in Gaucher Disease (Budapest: EWGGD)

Deegan PB, Tindall JE, Stein PE, Mehta A, Hughes DA, Wraith JE, Waldek S, Cox TM (2008).
Osseous Complications of Gaucher Disease: a National Survey (Paris: 4th X-LSD Meeting)

M.B. Cachón-González, S.Z. Wang and T.M Cox (2007)
Combination Therapy for Tay-Sachs and Related Neurodegenerative Diseases (Bilbao: Int. Soc. Sphingolipid Res.)

Cox, T.M. (2007) Prospects for Stem-Cell and Gene Therapy for Lysosomal Storage Disorders (Porto: Treatment of Inborn Errors)

Marchesan D, Cox TM and Deegan PB (2007)
Mechanism of Uptake of Therapeutic Alpha Galactosidase A in Cells Relevant to Fabry Disease (Perrugia: Eur. Study Group Lysosomal Diseases)

M.B. Cachón-Gonzaléz, S. Z Wang, R. Ziegler, S H Cheng
and T M Cox.(2007) Successful Gene Therapy for Tay-Sachs and related Neurodegenerative Diseases (Bristol: Association of Physicians of Great Britain & Ireland)

Lachmann RH, Wright N, Parker A, Ramaswami U, Coleman M, Roos J, Bernstein R, Gillard J, Harding S, Platt FM, Wraith E, Cox TM (2006) Substrate reduction therapy in Sandhoff disease: evidence for improvement in nervous function in patients treated with miglustat (Japan: SSIEM J. Inherit. Metab. Dis)