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Center for Endocrinology, Diabetes, and Metabolism Research
Jacksonville
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Active and Recent Grants and Studies

Diabetes

- National Institutes of Health. Type 1 Diabetes and the Brain in Children: Metabolic Interventions (PI: N. **Mauras**). Dr. Mauras is the Co-PI and the contact PI for a five-center study that follows longitudinally a cohort of children with T1D and a group of age-matched non diabetic controls assessing structural and functional brain imaging, cognition and glycemia using continuous glucose monitors.

- National Institutes of Health. Glycemic Control and the Brain in Children with Type 1 Diabetes. (PI: N. **Mauras**). This protocol is funded with the same funds as the core grant, as a pilot study to investigate if better normalizing the blood sugars using closed loop (artificial pancreas) systems would improve some of the detected functional and cognitive brain changes being observed.

- National Institutes of Health. Final Clinical Studies for Submission of a Pre-market Approval Application to the FDA for a Bionic Pancreas that Automates Type 1 Diabetes Management. (PI: E. Damiano, Co-I: N. **Mauras**). This is a collaborative effort with Mr. Edward Damiano, inventor of the bi-hormonal (insulin and glucagon) pancreas. The work was presented at the American Diabetes Association meeting in 2019. We are in full preparation to launch the follow up pivotal trial at Nemours Jacksonville.

- National Institutes of Health. An open-label, multi-centre, randomised, single-period, parallel study to assess the efficacy, safety and utility of 6 month day-and-night automated closed-loop insulin delivery under free living conditions compared to insulin pump therapy in children and adolescents with type 1 diabetes. (R Hovorka – PI, N **Mauras** – Local PI) This study tests the safety and efficacy of a new algorithm for automated insulin delivery in children with type1 diabetes.

- Nemours Research Programs. Dietary Amino Acids and Insulin Sensitivity in Children with Type 1 Diabetes. (PI: D. **Darmaun**). Dr. **Torres-Santiago** received a career development award from the Thrasher Research Fund. Results revealed an increased number of nocturnal hypoglycemia events despite comparable measures of insulin sensitivity. A paper was published in Current Opinion in Clinical Nutrition and Metabolism in 2019.

- Nemours Research Programs Fellows Project. Can short bouts of exercise ('exercise snacks') improve body composition in adolescents with type 1 diabetes (T1D)? a feasibility study. (Fellow: R. **Hasan**, PI: D. Darmaun). This investigator-originated study investigates the impact of short bouts of resistance exercise on insulin sensitivity and glucose variability in adolescents with type 1 diabetes. A paper was accepted in Hormone Research in Paediatrics and will appear in print in 2020.

- Funded originally by Nemours Research Programs and presently by Development funds (PI: L. **Fox**). A Pilot Study of the Effect of Continuous Subcutaneous Insulin Infusion (CSII) in Adolescents with Newly Diagnosed Type 1 Diabetes on Insulin Resistance, Beta Cell Function, and the Honeymoon Period. This study evaluates how insulin pump therapy compares with multiple daily injections in affecting the time of onset and duration of the honeymoon period, a transient period of remission after the diagnosis of type 1 diabetes. The study also assesses whether differences in the honeymoon period are related to changes in insulin sensitivity and beta-cell function. Data are being analyzed.

- Leona Helmsley Charitable Trust. Type 1 Diabetes Exchange Network (T1DX). (Local PI: L. **Fox**). This is a network of clinical centers that diagnose and care for persons with type 1 diabetes. The overall objective of the network is to improve the care of individuals with type 1 diabetes by sharing best practices using a common

data repository. This multicenter, observational study collected core clinical and laboratory data on children, adolescents, and adults with type 1 diabetes. Sub-studies that are objective-directed were developed for various populations of participants within the type 1 diabetes exchange network.

- University of Florida. TrialNet Natural History Study of the Development of Type 1 Diabetes. (Local PI: L. **Fox**). TrialNet is a multicenter project aimed at learning more about how and why type 1 diabetes occurs and how to develop studies that will help researchers learn more about its prevention. Because relatives of people with type 1 diabetes have a 10- to 15-times greater risk for the disease than people with no family history, close blood relatives of people with type 1 diabetes are being screened for type 1 diabetes. Those who are positive for the screen can be entered into preventive studies already developed in TrialNet.

- Medtronic, Inc. Safety Evaluation of the Hybrid Closed Loop System in Pediatric Subjects with Type 1 Diabetes. (Local PI: L. **Fox**). The purpose of this study is to demonstrate that the Medtronic 670G Hybrid Closed Loop System is safe in children ages 2-13 years. This 670G system uses sensor data from a continuous glucose monitor to automatically adjust basal rate insulin infusion. This device has been shown to be effective in increasing the time spent with blood sugars in the target range and in decreasing overnight hypoglycemia (low blood sugars). Medtronic will use data from this trial for submission to the FDA for approval in this age group.

- Nemours Research Programs Fellows Project. Safety of Low and Very-low Carbohydrate Diets in Young Children with Type 1 Diabetes. (Former Fellow: Perez-Santiago, PI: L. **Fox**). Low and very-low carbohydrate diets are being used by families to assist with diabetes management in children with type 1 diabetes. However, the safety of these diets is unknown in this age group. The purpose of this study is to evaluate the safety of short-term (six months) low or very-low carbohydrate diets in prepubertal children ages 2 to <8 years with type 1 diabetes. The study continues to enroll after Dr. Perez-Santiago completed her training in 2019.

- Takeda. (Local L **Fox** - PI). A Multicenter, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Alogliptin Compared with Placebo in Pediatric Subjects with Type 2 Diabetes Mellitus. Alogliptin is a drug that is FDA-approved for use in adults with type 2 diabetes. This multicenter, multi-international protocol assesses the safety and effectiveness of alogliptin in children with type 2 diabetes. Data from this study will be submitted to the FDA and other similar international agencies for approval in children.

- Nemours and Wolfson Children's Hospital. Dysglycemia and Obesity: Impact on the Brain in Adolescents with Type 2 Diabetes (PI: L. **Snyder**). This is a cross-sectional study examining neurocognitive function and brain activity in resting state and during working memory and executive function tasks using BOLD fMRI during hyperinsulinemic euglycemic and hyperglycemic clamps in adolescents with type 2 diabetes compared with non-diabetic obese and lean controls.

- A Phase 3, Randomized, Double-Blind, Multinational, Placebo-Controlled Study to Evaluate Efficacy and Safety of Teplizumab (PRV-031), a Humanized, FcR Non-Binding, anti-CD3 Monoclonal Antibody, in Children and Adolescents with Newly Diagnosed Type 1 Diabetes (T1D). (PI- M **Benson**) We are in budget negotiations with the sponsor. This is a very important study with a new drug already shown to delay the development of T1D in those at risk and we will now study in new onset T1D. This is a very complex study giving this monoclonal antibody to children with new onset T1D within 6 weeks of the diagnosis of new onset diabetes mellitus. We will assess through long term follow up any impacts of the drug on endogenous insulin production through the measurement of stimulated c-peptide.

Turner Syndrome

- Genentech Foundation for Clinical Research in Endocrinology. Estrogen Dosing in Turner Syndrome: Pharmacology and Metabolism. (PI: N. **Mauras**). This work has been completed, and seminal data are now available demonstrating that transdermal estrogens are more physiologic than oral estrogens and that oral estrogens lead to the accumulation of genotoxic estrogens. This important paper was published in January 2019.

Growth

- Prolor. Safety and Dose-finding Study of Different MOD-4023 Dose Levels Compared with Daily r-hGH Therapy in Pre-pubertal Growth Hormone-deficient Children, Phase 33 study. (PI: N. **Mauras**). This drug company-sponsored trial uses a long-acting analogue of growth hormone (GH) in GH-deficient children given once a week. Studies are ongoing. 2017-2020.

- Novo Nordisk (investigator-originated). Recombinant Human Growth Hormone (GH): Effects on Metabolic Profile, Body Composition, and Skeletal Muscle Strength and Function in Prepubertal Short Boys with and without GH Deficiency. (PI: N. **Mauras**). This investigator originated study was funded by Novo after 1 year of competitive review. The study seeks to investigate the impact of GH on skeletal muscle function (strength and agility) in prepubertal boys with GH deficiency and idiopathic short stature. This study is being done in collaboration with the Kinesiology Department at the University of North Florida and Physical Therapy at Wolfson's Children's Hospital. The proposal is being run by one of our Endocrinology fellows.

- Ascendis Pharma, Inc. (Local PI: L **Fox**). fliGHt: A Multicenter, Phase 3, Open-Label, 26-Week Trial Investigating the Safety, Tolerability and Efficacy of TransCon hGH Administered Once Weekly in Children with Growth Hormone Deficiency (GHD). This pharmaceutical study also assesses the safety and efficacy of a new, long-acting form of human growth hormone (hGH) that is given once a week.

- Ascendis Pharma, Inc. (Local PI: L **Fox**). EnliGHten: A Multicenter, Phase 3, Long-term, Open-label Trial Investigating Safety and Efficacy of TransCon hGH Administered Once a Week in Children with Growth Hormone Deficiency Who Have Completed a Prior TransCon hGH Clinical Trial. This is a pharmaceutical study assessing the long-term safety and efficacy of a new, long-acting form of human growth hormone that is given once a week.

- Pfizer. (Local PI: L. **Fox**). A phase 3, randomized, multicenter, open-label, crossover study assessing subject perception of treatment burden with use of weekly growth hormone (Somatrogon) versus daily growth hormone (Genotropin®) injections in children with growth hormone deficiency. This study assesses quality-of-life and treatment burden in children with growth hormone, comparing daily growth hormone vs. a new version of growth hormone injections given weekly.

- Ascendis Pharma, Inc. Comparison of Transcon hGH, a Long-acting Human Growth Hormone with Daily hGH in a Multicenter, Phase 3, Randomized, Open-label, Active-controlled, Parallel-group, One-year Trial in Prepubertal Children with Growth Hormone Deficiency. (Local PI: L. **Snyder**). This is a pharmaceutical study comparing a new, long-acting form of human growth hormone (hGH) that is given once a week with standard, daily, hGH treatment in children with growth hormone deficiency. There have been no identified risks associated with weekly administration of TransCon hGH beyond those known to be associated with daily administered hGH.

Basic Research

- Nemours Research Programs. Method Development: Developing an In-house Assay of Tryptophan Concentration and Stable Isotope Enrichment in the Biomedical Analysis Laboratory at Nemours Children's Specialty Care, Jacksonville, FL. (PI: D. **Darmaun**). The validation of the assay is currently ongoing and samples from earlier studies will be analyzed.