JDRF nPOD Newsletter. September 2013. Issue 18.

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REMINDER: Abstracts are due Sept 30th for the JDRF-Helmsley nPOD 6th Annual Scientific Meeting next February 23-26, 2014. Contact Mingder Yang for more information.

Donor Classification Process

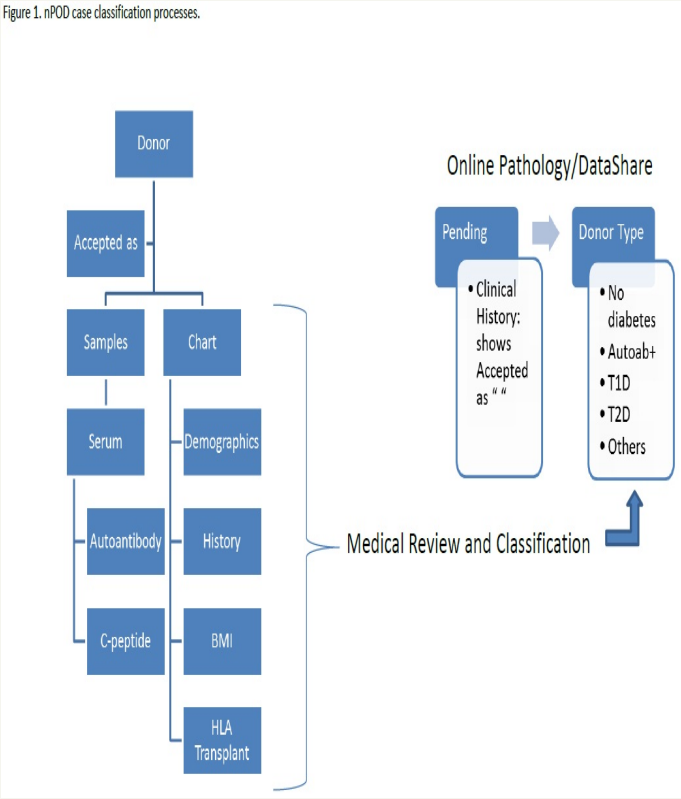
Faced with the challenges associated with the diagnosis of any disease in clinical medicine, the nPOD program has a rigorous process to provide the most precise disease diagnosis possible. While much in the way of donor information is available at the time of case acceptance, additional data (e.g., laboratory tests, medical records, family histories, etc.) often

becomes available to us after case acceptance. Given the realities we work in, from time to time, diagnoses change. Thankfully, these are rare events. A description of the nPOD donor classification is provided below and conveys reasons for which we, rarely (~3%), overturn initial classifications when additional information is received.

Classification Process: An organ donor is offered to nPOD according to inclusion and exclusion criteria as established by the nPOD Scientific Advisory Board. The "accepted as" diagnosis is assigned for each case recovered. Medical and social history is often only available through a questionnaire completed by next-of-kin during a time of great stress. The terminal medical chart is sent with each organ donor which includes key information on demographics, height, weight, medications administered during the last few days of life, and medical and social history. Hence, from the onset of every case, donor classification is largely based on a diagnosis provided by the acting organ procurement organization (OPO). Once in-house, a medical chart and laboratory review immediately occurs by way of the Administrative Core and nPOD medical consultant (Pediatric Endocrinologist). Subsequently, all cases in which there is a questionable diagnosis, are immediately discussed for the purpose of defining a definitive diagnosis.

Why would a change occur? Laboratory tests are conducted on a serum sample obtained during organ recovery for autoantibodies and c-peptide levels. Fresh tissue samples are immediately distributed to nPOD investigators, to support their project requirements, with the "accepted as" designation. Case information is entered into the nPOD database. Representative slides are also provided via the online pathology website with "Pending" as the donor type designation. The medical chart from the terminal hospitalization is reviewed by the medical consultant and nPOD coordinator for consideration of all available data before a final (i.e., definitive) diagnosis is rendered. A flow sheet developed by nPOD staff has been created integrating all criteria and steps within this process (below).

Figure 1. nPOD case classification processes.



What is the final diagnosis? Final organ donor diagnosis is more difficult than in living subjects diagnosis, given the limited medical history available and inability to conduct most diagnostic tests. The final definitive diagnosis results from the integrated review of clinical and laboratory data, and it is then entered into nPOD database. With this process, we strive to minimize revisions to diagnosis, which as noted, before have been very few. However, all nPOD investigators are urged to use DataShare, nPOD Online Pathology, or contact nPOD staff, to verify the final diagnosis. It is still possible, however, that investigators may differ in their assessment of the diagnosis. We understand and appreciate this, and consider it one of the prime reasons nPOD exists; to better understand and classify diabetes.

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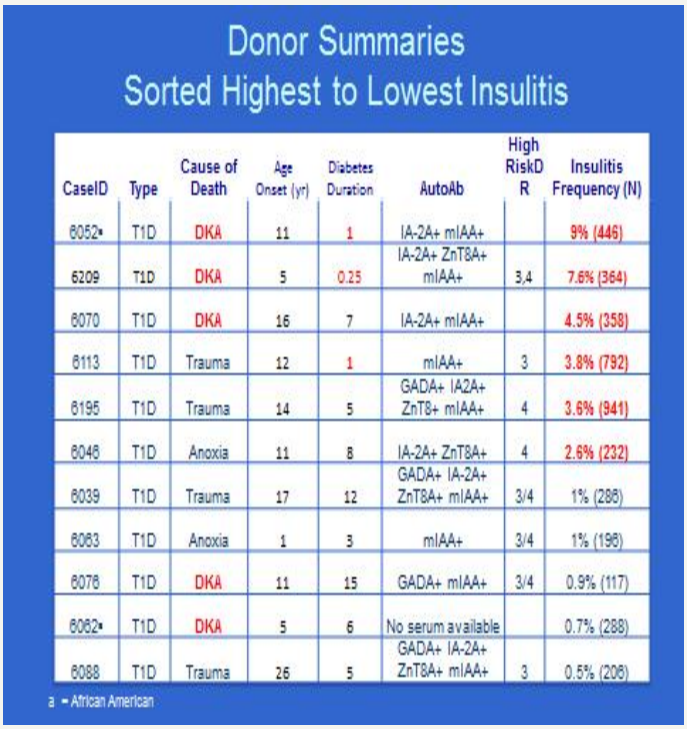
Case Update and Case Retiring

nPOD now has 19 cases with insulitis in our biorepository, including a case recovered at onset of diabetes (spring 2013). The table below highlights type 1 diabetes cases with the highest frequency of insulitis identified.



Donor Summaries
Sorted Highest to Lowest Insulitis

CaseID	Type	Cause of Death	Age Onset (yr)	Diabetes Duration	AutoAb	High RiskDR	Insulitis Frequency (N)
6052a	T1D	DKA	11	1	IA-2A+ mIAA+		9% (446)
6209	T1D	DKA	5	0.25	IA-2A+ ZnT8A+ mIAA+	3,4	7.6% (364)
6070	T1D	DKA	16	7	IA-2A+ mIAA+		4.5% (358)
6113	T1D	Trauma	12	1	mIAA+	3	3.8% (792)
6195	T1D	Trauma	14	5	GADA+ IA2A+ ZnT8+ mIAA+	4	3.6% (941)
6046	T1D	Anoxia	11	8	IA-2A+ ZnT8A+	4	2.6% (232)
6039	T1D	Trauma	17	12	GADA+ IA-2A+ ZnT8A+ mIAA+	3/4	1% (286)
6063	T1D	Anoxia	1	3	mIAA+	3/4	1% (196)
6076	T1D	DKA	11	15	GADA+ mIAA+	3/4	0.9% (117)
6062a	T1D	DKA	5	6	No serum available		0.7% (288)
6088	T1D	Trauma	26	5	GADA+ IA-2A+ ZnT8A+ mIAA+	3	0.5% (206)

a = African American

If you have questions regarding these cases, please contact us for more information.

As we have grown, we have learned much about case recovery and consequently refined our recovery instructions with our organ procurement organization partners. From time to time we receive cases that are missing important tissues or data points. nPOD will begin retiring cases where

- no medical records are available,
- no blood or serum was available due to extenuating circumstances
- elements of our core set of tissue were not recovered or are sub-optimal.

These case retirements represent less than five percent of the total nPOD collection, and will be noted in the tissue availability portion of DataShare once it is operational.

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DataShare - Sharing for the Cure

nPOD's DataShare program provides a means to improve collaboration through development of a web-based portal for data dissemination and review which is needed to accelerate discovery in the diabetes research community. This program was reviewed during the nPOD annual meeting, and is being used by the nPOD-V working group. We now invite you to review DataShare for yourself. You can also listen to the recording or download the recording of the June 19th webinar by John Kaddis. Please look through the site features such as: identifying the location of each slide and the tissue inventory for nPOD cases. If you haven't already,check our website's DataShare page to get your password and begin exploring.

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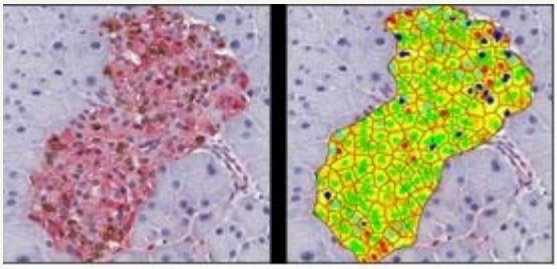
nPOD Webinar Invitation: Islet Image Analysis with Aperio and Indica Labs Software



When: Friday, October 11, 2013 11:00 AM-12:30 PM (UTC-05:00) Eastern Time (US & Canada).
Where: Webex Meeting
Dr. Kate Lillard Tunstall, PhD from Indicalab (http://indicalab.com/) is giving a webinar on Islet Image Analysis with Aperio and Indica Labs software.
By making entire tissue sections available for analysis and archiving, digital pathology has revolutionized tissue-based research. Recent improvements in fluorescent scanning open additional avenues of research by facilitating multiplex biomarker analysis across whole tissues. In this webinar, we will discuss image analysis tools that can help researchers extract meaningful information from scanned brightfield and fluorescent tissues, with a particular emphasis on metabolic research and islet biology. Topics include analysis of beta and alpha cell area, cell proliferation and apoptosis, islet measurements, adipose tissue and steatosis quantification.

Publications

Reminder: If you have a publication that relies on nPOD tissues, we want to know about it! Please fill out the Abstract & Submission form on the nPOD website.

Congratulations to the following nPOD investigators that have published since our June newsletter:
Nelson EK, Piehler B, Rauch A, Ramsay S, Holman D, Asare S, Asare A, Igra M. (2013). Ancillary study management systems: a review of needs *BMC Med Inform Decis Mak.,* 13(5). doi: 10.1186/1472-6947-13-5.
[PubMed Abstract]
Salvatoni A, Baj A, Bianchi G, Federico G, Colombo M, Toniolo A. (2013). Intrafamilial spread of enterovirus infections at the clinical onset of type 1 diabetes. *Pediatr Diabetes,* Epub ahead of print.
[PubMed Abstract]
Herold KC, Vignali DA, Cooke A, Bluestone JA. (2013). Type 1 diabetes: translating mechanistic observations into effective clinical outcomes. *Nat Rev Immunol.,* 13(4):243-56.
[PubMed Abstract]

Coppieters KT, von Herrath M. (2013). Antibody cross-reactivity and the viral aetiology of type 1 diabetes. *J Pathol.,* 230(1):1-3.
[PubMed Abstract]
Taylor-Fishwick DA, Weaver JR, Grzesik W, Chakrabarti S, Green-Mitchell S, Imai Y, Kuhn N, Nadler JL. (2013). Production and function of IL-12 in islets and beta cells. *Diabetologia.,* 56(1):126-35.
[PubMed Abstract]
Craig ME, Nair S, Stein H, Rawlinson WD. (2013). Viruses and type 1 diabetes: a new look at an old story. *Pediatr Diabetes.,* 14(3):149-58.
[PubMed Abstract]

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nPOD Welcomes New Staff

nPOD would like to welcome Marcela Gomez to the Organ Pathology and Processing Core. Marcela graduated from the University of Florida's Biological Engineering program and was active member of ASABE. She is currently a Post-Bac in the Biomedical Engineering program, and is working towards a minor in Physics. She has worked in the research field for two years working with leptin resistance and age-related obesity as well as light and gravity effects on plant growth and development. Marcela Gomez can be reached at marcelagomez@ufl.edu or by phone at (352) 273-7737.

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|Quarterly Newsletter|

nPOD is a collaborative type 1 diabetes research project funded by JDRF. We support scientific investigators by providing, without cost, rare and difficult to obtain tissues beneficial to their research. nPOD currently supports over 90 type 1 diabetes-related scientific studies at institutions around the world. Our hope is that nPOD will prove a useful resource to the community of researchers dedicated to finding a cure for type 1 diabetes. For more information, please go to www.jdrfnpod.org