Searching for Type 1 Diabetes Before It Starts: Screening Autoantibodies (Aab) on Organ Donors for Research

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Introduction

- Prior to 2009 no existing program to systemically screen organ donors for type 1 diabetes (T1D) related autoantibody (Aab) status.
- At University of Florida, JDRF nPOD program has established an IRB-approved study demonstrates the wide-reaching and positive outcome of running research tests alongside normal donor serology tests in order to identify early signs of autoimmune diabetes prior to clinical diagnosis.
- Type 1 diabetes has 5 known autoantibodies associated with the destruction of insulin-producing cells in the pancreas, including GADA and IA-2A. Approximately 2% of all people in the United States have at least 1 of these autoantibodies present in their bodies, but have no diagnosis of type 1 diabetes[1]. When these autoantibodies are found in the blood, they serve as markers of disease activity and severity[2]. These autoantibodies can be present in the body for several years prior to disease diagnosis.
- The T1D Aab screening program has been expanded to procure these high value donors for the NIH Human Pancreas Analysis Program (HPAP).
- Gifts from autoantibody positive donors have the potential to help scientists answer fundamental questions related to the etiology and disease progression of type 1 diabetes.

Methods

- Donor serum is tested for two auto-antibodies commonly seen in early stages of type 1 diabetes; GAD Ab and IA-2 Ab. This is done using KRONUS ELISA assays.
- Customized Aab screening kits were modified from KRONUS to fit the need of screening organ donor STAT. Training and screening kits were provided to the serology labs. Donor criteria were communicated with screening partners. Test results were reported as soon as generated. When positive screenings were identified, we communicated and worked with the OPOs for procurement.
- A set of equipment including a shaker, a plate washer and a plate reader is provided to the screening partners.
- The recovery and screening serum samples then Confirmed by T1D Aab Radioimmunoassay (RIA) independently.[3]

Results

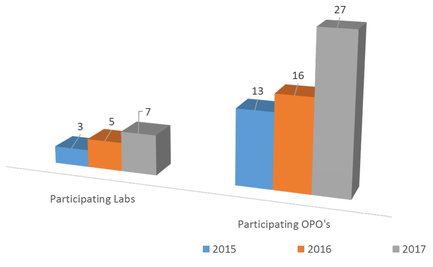

Figure 1. Screening labs and OPO participation between 2015-2017

- Tremendous amount of effort has been put in place to increase Aab screening on organ donors. We are now screening with 7 serology labs for organ donors within our criteria for T1D Aab. We have significantly increased number of participating OPOs for Aab screening from 16 in 2016 to 27 OPOs by the end of 2017. We are capturing 56% of organ donor pool in the US currently compared to 38% in 2016. The increased Aab screening effort has translated into the increased number of Aab cases procured, resulting in 16 cases in 2017 compared to 5 cases in 2016.

Results

Table 1. Number of subjects screened for Aabs performed on US organ donors, positive screens, percent positivity and number of participating OPOs

Year	# Aab Screens	Pos test	% Pos	# of Screening OPOs
2015	684	11	1.6%	13
2016	922	21	2.3%	16
2017	2036	42	2.1%	27

Table 2. Organ donor pool captured in the Aab screening program.

	2016	2017	2018 (Projected)
US Organ Donors	9971	10268	10525
Donors From Participating OPO's	3772	5715	7410
Percentage of Donors Pool Captured	38%	56%	70%

Table 3. Autoantibody screening program: Participating OPOs, Screening labs, number of organ donors in year 2016 through 2018

OPO	Testing Lab	2016	2017	2018 (Projected)
PADV	VRL, Phi	540	565	565
CAOP	VRL, LA	482	487	487
TXGC	VRL, DAL	414	381	381
TXSB	VRL, DAL	380	385	385
NEDS	VRL	338	292	292
CADN	VRL/Labs	291	308	308
NYRT	VRL,Phi	271	291	291
NJTO	VRL,Phi	183	190	190
LAOP	VRL, DAL	178	187	187
CORS	VRL, Denver	139	144	144
CASD	VRL, LA	118	118	118
UTOP	VRL, LA	110	109	109
NVLV	VRL, Denver	107	123	123
NCCM	VRL,Phi	104	101	101
CAGS	VRL, LA	78	81	81
CTOP	VRL	39	66	66
TNDS	VRL, Atl		303	303
GALL	VRL, ATL		286	286
PATF	CORE		224	224
NCNC	CORE		211	211
SCOP	VRL, ATL		166	166
OHLB	CORE		155	155
MDPC	CORE		152	152
DCTC	CORE		142	142
OHLP	CORE		124	124
OHOV	CORE		69	69
NMOP	VRL		55	55
ILIP	In house			406
MWOB	Local			245
MNOP	VRL			184
OKOP	Local			183
ALOB	VRL, ATL			170
WIUW	ILIP			150
FLUF	VRL, ATL			139
WIDN	ILIP			96
NEOR	VRL, Denver			68
IAOP	MWOB Local			54
Total		**3772**	**5715**	**7410**

Conclusions/Future Directions

- We felt the effort in expanding the Aab screening program has paid off in the number of Aab positive donors procured. Such expansion has resulted in doubling the positive Aab screens from 21 in 2016 to 42 in 2017 and translated to 16 procured cases of Aab+ donors in 2017.
- The unexpected benefit of expanding Aab screening program is the increase of finding at onset T1D donors. These are donors who were not clinically diagnosed as T1D and the patients themselves and their families were not aware they have T1D. Without knowing they are T1D, our OPO partners are not likely to identify these donors and refer them to our programs. It is only the Aab screening that brought these potential donors to our attention for procurement. These are indeed very valuable cases for the collaborative HPAP effort. Two at onset T1D cases were identified because of the Aab screening program.
- Our experience from the Aab screening program allows us to add additional criteria for donors with cause of death was related to Diabetic ketoacidosis (DKA).
- We still face challenges when trying to procure Aab+ donors. Two main obstacles including 1. donated pancreata went to transplant and 2. no research consent. Since Aab+ donors are considered at risk for T1D, it does not necessarily mean they are pre-diabetic. At times, transplant surgeons will transplant them since there is no clinical evidence to persuade them not to transplant these pancreata. We continued to expand our reach with screening partners and will further increase our capture of organ donor pool in 2018 with more Aab+ donors for HPAP program. The goal is to increase organ donor reach from 56% in 2017 to 70% by the end of 2018.

References

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Acknowledgements

- This research was performed in part using resources and/or funding provided by the NIDDK-supported Human Islet Research Network (HIRN, RRID:SCR_014393; https://hirnetwork.org; UC4DK112232-01).
- This research was also performed in part by the support from JDRF and Helmsley Chartable Trust for the Network for Pancreatic Organ donors with Diabetes (nPOD) Program
- We thank our OPO and screening lab partners for making this screening program a success.
- Sincerely thanks to the organ donors and their families for the ultimate gift they donated for research.