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GIGA-kids News & Updates

January 2019 Update

Happy New Year!

As of January 10th, 2019 there are 28 actively recruiting GIGA-kids sites. Total recruitment is presently at **N=462 participants**, including 451 cases and 11 healthy controls. We are nearing the halfway mark of our recruitment goal!

The GIGA-kids study was represented at the American Society of Nephrology Conference (ASN) in San Diego this past November. This was the third year a GIGA-kids poster was displayed as an informational poster at ASN. We include the content of the poster on the second page of the newsletter.

As always please let us know how we can best support your recruitment efforts, and do not hesitate to reach out to CUMC coordinator Olivia Balderes (ob2214@cumc.columbia.edu) with questions, concerns, or suggestions.

Please feel free to pass along this newsletter to colleagues and collaborators or share via Twitter etc.

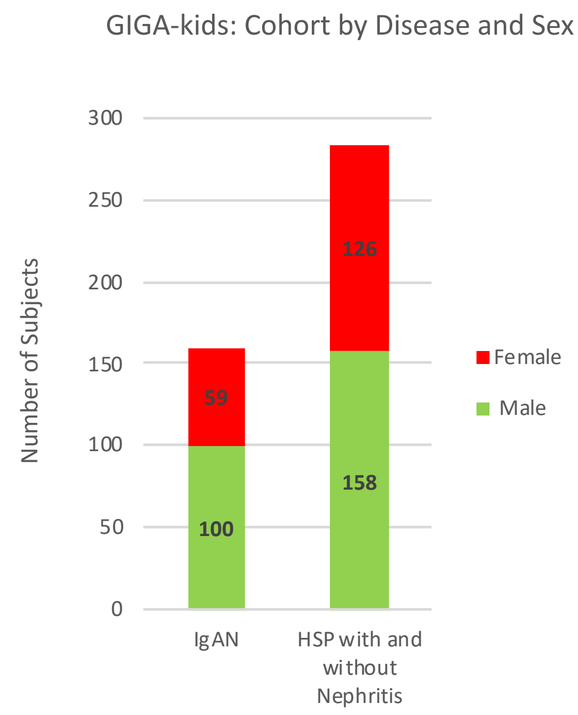

Figure 1: Overall case distribution as of January, 10th, 2019 (based on available clinical data).

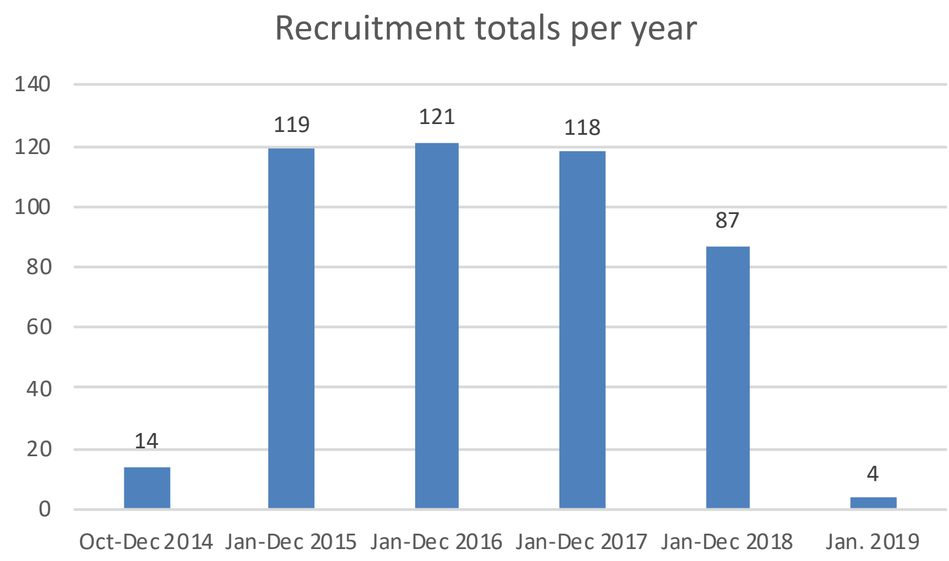

Figure 2: Cumulative annual recruitment as of January 10, 2019.

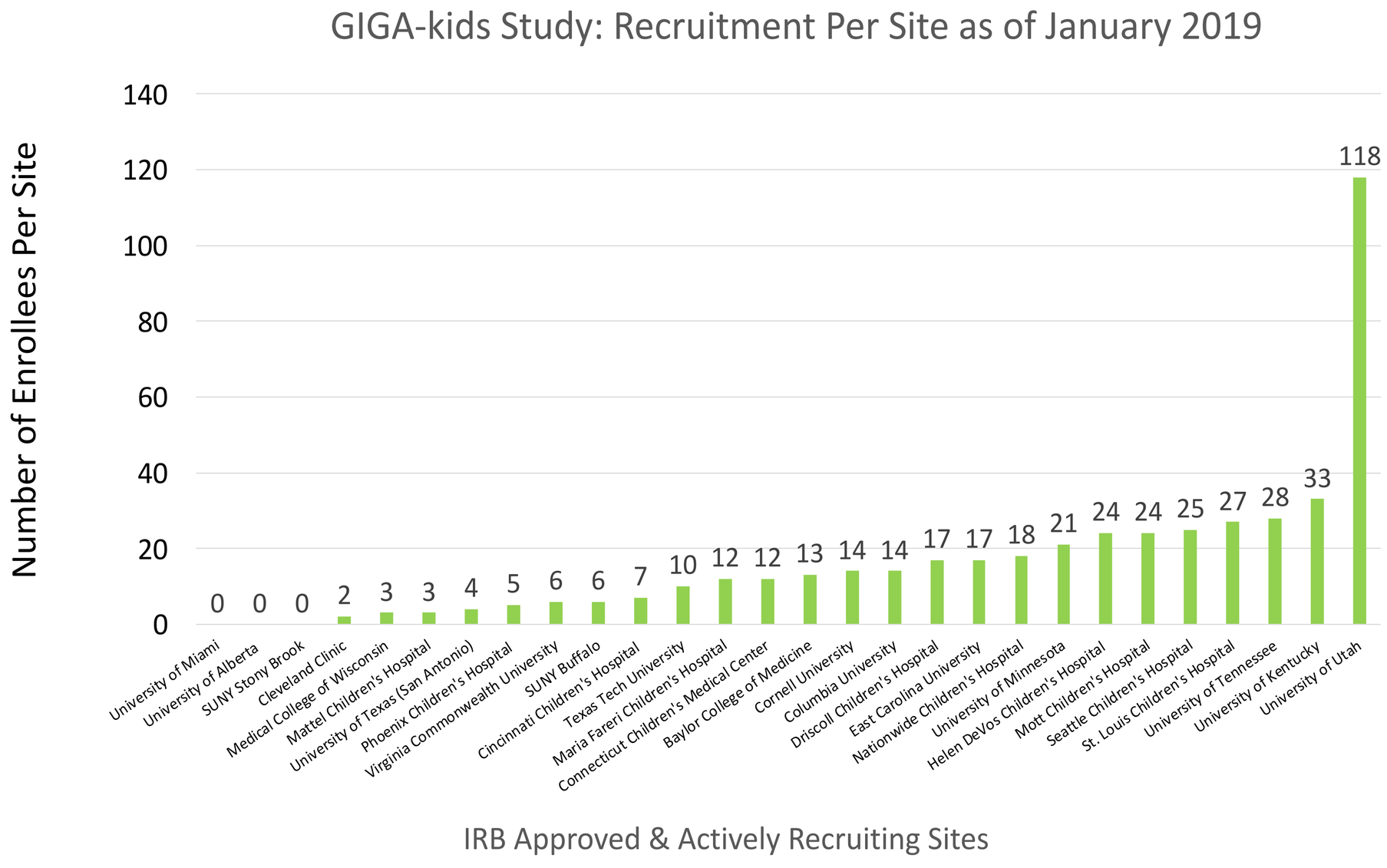

Figure 3: Cumulative Recruitment per site; October 2014 to January 2019.

Revamped Report Cards

After some consideration we have made changes to the GIGA report card criteria – specifically the data completion section, to better clarify availability of key data points. Olivia will be sending these updated report cards out in the New Year.

Additionally, we are widening the window for reporting data points to 3 months preceding/following recruitment (if lab test dates are distinct from Date of Recruitment, this can be reported in the "Notes" section). This may mean revisiting EHRs for some participants, especially those whose CRFs are missing the following data points: Height, Weight, Serum Cr, and uPCR at the time of Biopsy and Recruitment – Olivia will indicate participant specific missingness in site report cards later this month.

A note on OpenClinica: OC allows for a centralized dataset, which can be amended and updated as new information comes in. If your site does not currently have an OC account, please make sure to start the process of requesting one as soon as possible, by emailing both Olivia Balderes and Corinna Bowers. If, in the past, your site sent hard-copy CRFs for GIGA participants, please make sure there are corresponding OC profiles for these individuals. (Olivia will also make sure to indicate which individuals are missing OC profiles when I send out the site specific report cards.)

GIGA-kids at ASN 2018 San Diego

GIGA-kids Study: Genomics of IgA-related disorders in kids

Balderes O.[1], Bowers C.[2], Bradbury D.[1], Abitbol C.[5], Akchurin O.[6], Al-Akash S.[7], AlAbbas A.[8], BouMatar R.[9], Chishti A.[10], Davis K.[11], Erkan E.[12], Flynn J.[13], Hidalgo G.[14], Iorember F.[15], Lin F.[1], Mason S.[16], Matloff R.[17], Quiroga A.[18], Ranch D.[19], Rheault M.[20], Samsonov D.[17], Selewski D.[21], Shefali M.[22], Silva C.[16], Sreedharan R.[23], Vasylyeva T.[24], Wenderfer S.[24], Weng P.[26], Woroniecki R.[27], Xiao N.[28],Gharavi A.[1], Smoyer W.[2], Wyatt R.[3], Nelson R.[4], Kiryluk K.[1]

[1]Columbia University; [2]Nationwide Children's Hospital; [3]Univ of Tennessee; [4]Univ of Utah; [5]Univ of Miami; [6]Cornell University; [7]Driscoll Children's Hospital; [8]Univ. of Alberta; [9]Cleveland Clinic; [10]Univ of Kentucky; [11]St. Louis Children's Hospital; [12]Cincinnati Children's Hospital; [13]Seattle Children's Hospital; [14]East Carolina Univ; [15]Phoenix Children's Hospital; [16]Connecticut Children's Hospital; [17]New York Medical College; [18]Helen DeVos Children's Hospital; [19]UT San Antonio; [20]Univ of Minnesota; [21]Univ of Michigan; [22]Akron Children's Hospital; [23]Medical College of Milwaukee; [24]Texas Tech Univ; [25]Baylor Univ; [26]UCLA Mattel Children's Hospital; [27]SUNY Stony Brook; [28]Virginia Commonwealth Univ

Background & Rationale

- IgA nephropathy (IgAN) represents the leading cause of kidney failure among young adults and is the most frequent form of primary glomerulonephritis worldwide. Our genetic studies have defined IgAN as an autoimmune trait with complex genetic architecture.
- In a recent GWAS of over 20,000 adults, we have discovered several genetic variants predisposing to IgAN. Strikingly, we observed a strong inverse relationship between the burden of GWAS risk alleles and the age of disease onset (**Figure 1**).

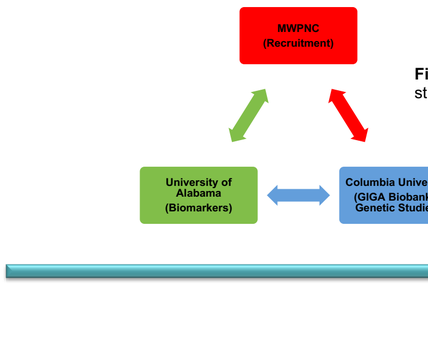

Figure 1. Number of IgAN risk alleles is inversely correlated with age at disease onset *(Kiryluk et al. Nat Gen 2014)*

- These data suggested that pediatric IgAN patients are likely enriched for genetic causes of disease, yet pediatric cohorts are not presently available for the purpose of adequately powered genetic studies.
- The genetic architecture of HSP (systemic IgA vasculitis with renal and cutaneous manifestations), is completely unknown and no large genetic cohorts presently exist.

Specific Aims and Organization

Aim 1. To recruit a cohort of 1,000+ pediatric patients with IgAN and HSP (with or without nephritis) for new genetic and biomarker studies:
a) To collect DNA, RNA and serum from 1000 children with a diagnosis of IgAN and HSP with or without nephritis.
b) To recruit 100 healthy age- and ethnicity-matched controls.

Aim 2. To perform genetic and biomarker studies in the GIGA-kids cohort:
a) To validate the existing adult GWAS loci in pediatric population.
b) To validate serum Gd-IgA1 level in pediatric IgAN and HSPN
c) To increase representation of children with these conditions in new genetic and biomarker discovery studies

Figure 2. Organizational structure of GIGA-kids

GIGA-kids Cohort

Inclusion Criteria:

- **IgA Nephropathy:** all prevalent biopsy-proven patients with disease onset before the age of 21.
- **HSP with and without nephritis:** all prevalent patients with a history of HSP regardless of renal involvement (no kidney biopsy required) with disease onset before the age of 21.
- **Healthy Controls:** age- and ethnicity-matched children (age < 21) unrelated to the cases and with no history of kidney disease or skin purpura.

Exclusion Criteria:

- Pre-existing diagnosis of autoimmune or liver disease, active HBV, HCV, or HIV infections.

Table 1. GIGA-kids study: case and control inclusion and exclusion criteria.

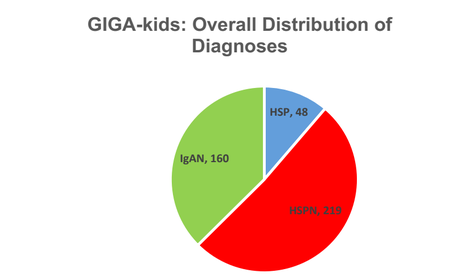

Figure 3. Breakdown of GIGA cohort by diagnosis.

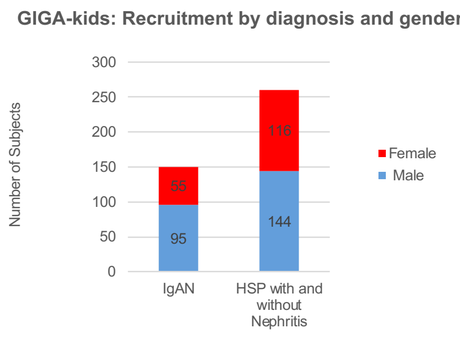

Figure 4. GIGA-kids cohort breakdown by diagnosis.

Figure 5. GIGA-kids recruitment site map.

Study Progress

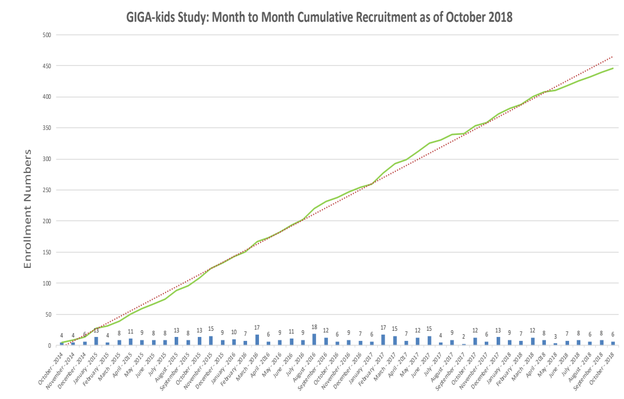

Figure 6. GIGA-kids recruitment totals by year.

.	Total Number Recruited	SNP Genotypes (1.8M MEGA chip)	Blood RNA-seq
Total	**N=446**	**N=331**	**N=352**
Diagnosis (%)			
IgAN	160 (35.9%)	122 (36.9%)	121 (34.4%)
HSP	48 (10.8%)	33 (10.0%)	36 (10.2%)
HSPN	219 (49.1%)	167 (50.5%)	178 (50.6%)
Healthy Control	10 (2.2%)	8 (2.4%)	9 (2.6%)
Uknown	9 (2.0%)	1 (0.3%)	0 (0%)
Female (%)	183 (42.0%)	141 (42.6%)	144 (40.9%)
Race (%)			
White	330 (74.0%)	241 (72.8%)	263 (74.7%)
Black	21 (4.7%)	20 (6.0%)	19 (5.4%)
Asian	16 (3.6%)	14 (4.2%)	12 (3.4%)
Other	65 (14.6%)	50 (15.1%)	45 (12.8%)
Unknown	14 (3.1%)	6 (1.8%)	5 (1.4%)

Table 2. Data generated as of September 2018

Conclusions & Future Directions

- The GIGA-kids Network consists of **28 actively recruiting sites** and 2 additional sites presently under IRB review.
- The GIGA-kids Network has recruited **430 pediatric participants** to date: **420 cases** and **10 controls**.
- Full clinical data, genomic DNA, blood RNA, and serum biospecimens are available for new genetic and biomarker studies
- The network continues to expand within the US, Canada and Europe (GIGA-Europe).

New sites are still welcome to join the network!
For more information, please visit www.gigakids.org or email ob2214@cumc.columbia.edu

Support for GIGA-kids

MWPNC MIDWEST PEDIATRIC NEPHROLOGY CONSORTIUM

IGA NEPHROPATHY FOUNDATION OF AMERICA, INC. Dedicated to finding a cure.

Figure 4: GIGA-kids Informational Poster as displayed at ASN 2019 in San Diego, CA.

Important Contact Information:

DUA/OpenClinica – Nationwide: Lisa Feurer
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IRB/MTA – CUMC: Melanie Foley
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Interested in participating in the GIGA Kids Study?

Our Coordinator for the GIGA-kids study, Olivia Balderes, can guide you through the IRB application process, and help to answer any questions you may have regarding study protocol, or recruitment.

Email: ob2214@cumc.columbia.edu
T: (212) 851 - 5216