

The Human Trisome Project - Latin America Network

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Introduction

- Down syndrome (DS) is the most common autosomal chromosomal abnormality and a leading cause of intellectual and developmental disability.
- The Human Trisome Project (HTP, NCT02864108) is a comprehensive natural history study of DS in the USA, including deep annotation of clinical metadata, cognitive phenotyping, a biobank with diverse biospecimens, and multi-omics datasets.
- HTP has enrolled >1150 participants, with more than 750 having T21, representing 47 US states and 8 other countries.
- HTP does not yet capture the substantial diversity of the Latino community with DS worldwide, nor the potential differences in their developmental and clinical profiles.

Methods

- The HTP includes collection of clinical metadata, cognitive phenotyping, a multidimensional biobank, and -omics datasets.
- Our polyglottal and multicultural team launched the HTP - Latin America (LATAM) Network to conduct research activities in Mexico, Colombia, Venezuela, Brazil, Bolivia, Argentina, and Chile.
- In weekly virtual conferences we discuss research activity implementation logistics, coordinate data collection and analysis, and are working toward establishing harmonized protocols and online data-sharing platforms.
- We implemented a four-day in-person training workshop for HTP research activities in Colorado, USA in November 2023.
- We conducted a preliminary analysis of epidemiologic changes in 53 co-occurring conditions across various systems using data from existing site databases.

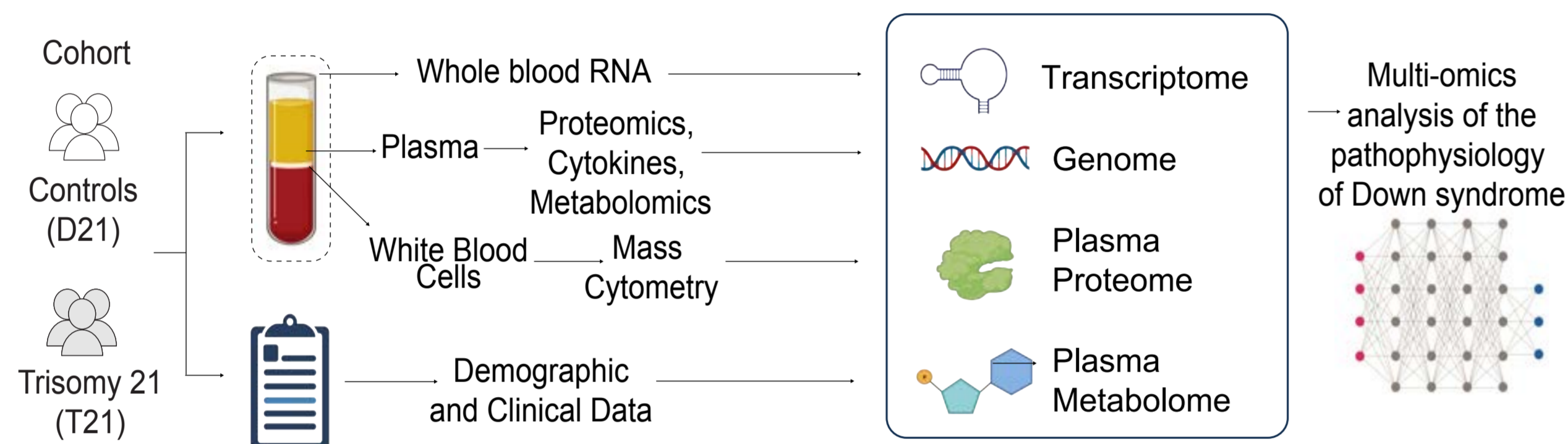


Fig. 1 | The Human Trisome Project. Research participants with trisomy 21 (T21) and euploid controls (D21) recruited into the HTP are characterized through matched multi-omics analysis of blood samples and annotation of clinical data.



Fig. 2 | The HTP - LATAM Network Overview. The HTP - LATAM network consists of sites in Colorado, Mexico, Colombia, Venezuela, Brazil, Bolivia, Chile, and Argentina. Venezuela and Bolivia would be supported through crossstraining activities and remote conferences facilitated by the Argentina and Colombia sites, respectively.

Results

Meet Our Team



Fig. 3 | The HTP - LATAM Network Site Leaders. Each site in Latin America provides great expertise through decades of managing large DS clinics in their respective localities, while also contributing populations of great racial, ethnic, socio-economic, and cultural diversity.

Results

Four-Day HTP Training Workshop

- 11 team members representing 7 Latin American countries attended the workshop
- Sites identified personnel, equipment, and facilities needed and found no major obstacles to research activities.



Fig. 4 | The HTP - LATAM training workshop. Delegates from each of the HTP - LATAM network sites trained in HTP activities.

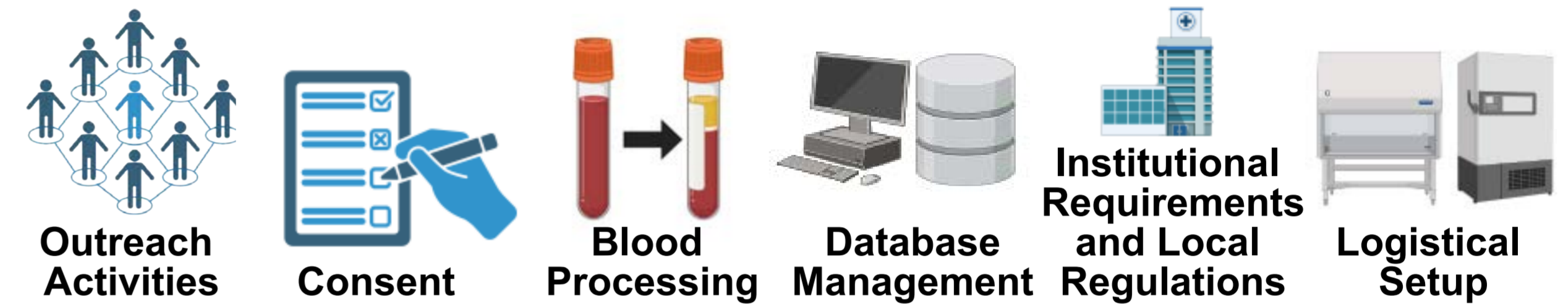


Fig. 5 | HTP Training Workshop Activities. We discussed implementation adjustments for each unique local context.

Preliminary Epidemiologic Findings

	USA (CO)	Mexico	Colombia	Brazil	Argentina	Chile
Population Total	5,810,000	129,872,000	52,000,000	214,300,000	46,044,703	19,960,889
Down syndrome Database [▽]	~6,000	150,000	62,000	178,000	40,000	20,000
	3,400	2,500	5,200	1,500	1,000	2,200
Free trisomy 21	~75%	~79%	71%	84%	92%	~84%
Translocation (any)	~2%	<1%	8%	2%	4%	~5%
Mosaic	~5%	~3%	10%	1%	3%	<1%
ASD	~35%	~9%	17%	7%	5%	~8%
VSD	~31%	~9%	13%	4%	12%	~11%
AVSD	~15%	~4%	14%	7%	14%	~9%
PDA	~22%	~22%	11%	3%	8%	~24%
Celiac disease	~10%	N/A*	N/A*	<1%	0%	~5%
Obstructive sleep apnea	53%	~45%	56%	42%	15%	~44%
Hypothyroidism	~50%	~17%	20%	8%	22%	~50%
Subclinical Hypothyroidism	~2%	~26%	20%	6%	5%	N/A*
Adenoidectomy	~51%	~6%	35%	31%	13%	~34%
Tonsillectomy	~49%	~6%	28%	28%	13%	~34%
Pediatric dyslipidemia	N/A*	~49%	16%	45%	N/A*	27%
Myopia	~13%	~28%	~28%	5%	8%	~16%
Hyperopia	12%	~9%	~25%	~23%	6%	~7%
Strabismus	~19%	~8%	~12%	~23%	1%	~17%
Astigmatism	~20%	~39%	40%	22%	8%	~16%
Neonatal jaundice/hyperbilirubinemia	N/A*	~27%	29%	40%	12%	~13%
Anemia	N/A*	~40%	31%	11%	2%	~7%
Severe neutropenia	N/A*	~11%	5%	3%	0%	~4%

Key: <10% (light green), 10-30% (medium green), >30% (dark green). *Data unavailable, [▽]Data presented in this table collected from a random sample of 100 subjects

Fig. 6 | Visual table showing the most notable co-occurring conditions in the exiting HTP - LATAM cohorts of individuals with DS, as determined by site leaders. ASD, atrial septal defect; VSD, ventricular septal defect; AVSD, atrioventricular defect; PDA, patent ductus arteriosus.

- Higher rates of ASD, VSD, hypothyroidism, celiac disease and adenoidectomy were observed in the USA cohort relative to the Latin American cohorts.
- Relative to the other HTP - Latin America sites, we observed lower rates of obstructive sleep apnea in Argentina, higher rates of anemia in Mexico and Colombia, higher rates of pediatric dyslipidemia in Mexico and Brazil, higher rates of hypothyroidism in the USA and Chile, higher rates of neonatal jaundice in Brazil, higher rates of tonsillectomy in the USA and Chile, and higher incidence of individuals with mosaic DS in Brazil.

Conclusions

The HTP - LATAM network has potential to accelerate discoveries, improve health outcomes, and increase the racial, ethnic, and socio-cultural diversity of investigations of individuals with DS.

Future Work

- Development and implementation of a common harmonized protocol.
- Comprehensive annotations of demographic information, social determinants of health, co-occurring conditions, and lifestyle factors.
- Multi-omics investigations of pathophysiology.

Acknowledgments

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