THE REWARDS AND CHALLENGES OF CONSTRUCTING PATIENT REGISTRIES IN MEXICO: LEARNED LESSONS FROM THREE NATIONAL REGISTRIES

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PATIENT REGISTRIES

- Patient registries are organized systems that collect, store and analyze information about individuals living with a particular disease or condition.

- They are useful for clinical research, setting of clinical trials and improvement of patient care, and when clinical data is complemented with genomic information, they provide further opportunities for research

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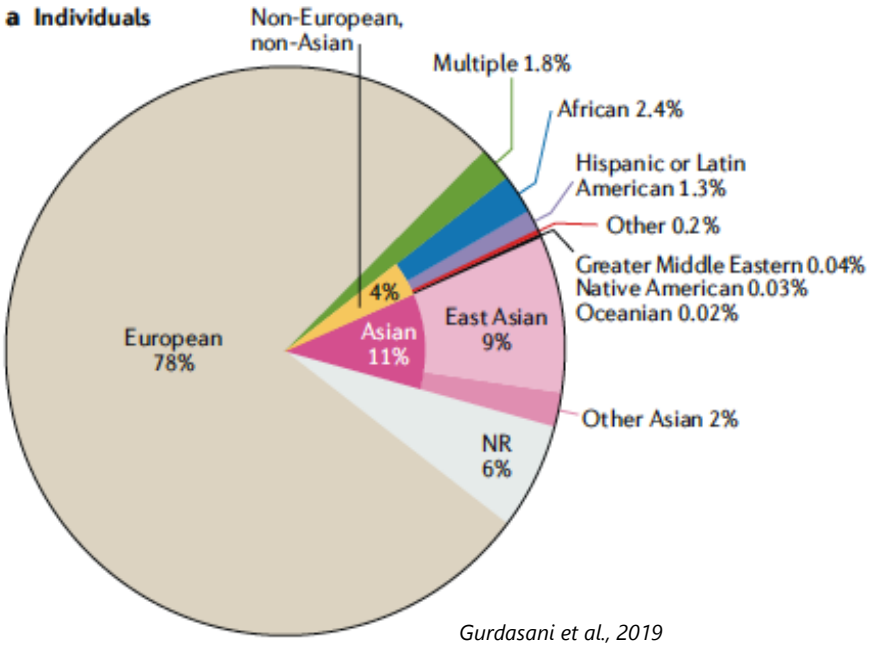
TWINS RESEARCH AUSTRALIA

Diversity in Genetic and Genomic studies



Gurdasani et al., 2019

- LATAM shows great diversity due to constant migration and differences in ecosystems that led to adaptation leaving marks in Native American genomes.
- These factors have shaped populations with diverse genetic backgrounds in which genetic variation manifests in unique effects on complex traits, including the immune system.

Electronic records in Mexico

- 73.5% of Mexico inhabitants are affiliated with either public or private health services
  - 51% are affiliated with the Instituto Mexicano del Seguro Social (IMSS)
  - 35.5% Instituto de Salud para el Bienestar (INSABI)

- 33 million people in the country remain with no health services insurance
  - 48.49% have no effective access to health services.

- NOM-024-SSA3-2012, issued in 2012, regulates the Electronic Health Record Information Systems and sets the mechanisms to record, exchange and consolidate information.

- The diversity of electronic clinical records and database storage systems greatly hinder data sharing and interaction among health institutions.

Major genomic resources in Mexico

- **Mexico City Prospective Study**
- Survey in two regions within Mexico City
  - Coyoacan (Middle – Upper class)
  - Iztapalapa (Low –Middle class)
- Medical survey with anthropometric measurements
- Exome sequencing for 150,000 people
- Recontact based on address.
- 10,000 participants were recontacted between 2015-2019
- Focus on diabetes, cardiovascular diseases and smoking outcomes
- Major publication 2022
- Lead by Oxford University and UNAM

- **MexBiobank**
- Based on samples from the National Health Survey 2000
- Generated genotyped data for 6,000 individual across the country.
- 40,000 samples
- General health survey
- No recontact
- Autoimmune diseases were not included
- Mental health surveys were not included
- Preprint published 2022
- Lead by LANGEBIO, Irapuato, Mexico

Challenges

- Recontact participants for further stages of research
- Decentralization of data adquicition, most patient studies are centered in Mexico City in the National Institutes of Health.
- Collaboration engagement with the medical community.
- Lack of trust towards the scientific community (INEGI survey on Perception on science and technology, 2017).

DEEPLY PHENOTYPED REGISTRIES

- Comprehensive medical history survey
- Ethics and consent contemplate the option to be recontacted for follow-up surveys or analysis.
- Ethics are approved for biobanking
- Metal health, cognitive assessments and lifestyle surveys are included
- Nation wide recruitment perspective.
- Public engagement through continuous communication with participants

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LUPUS RGMX
Registro Mexicano de Lupus

MEXICAN TWIN REGISTRY

- Launched in 2019
- Supported by the National Multiple Births Association
- Data collection through RedCap
- Recruitment of participants:
  - On site in annual Twin Festivals (suspended during COVID)
  - Through social media and traditional media campaigns
- Public engagement activities during Twin Festivals and Social Media Campaigns

MEXICAN TWIN REGISTRY

- Surveys selected to match the Australian and United Kingdom Twins Registries to enable comparative analysis.
- Focus on mental health and cognitive development.
- CONACYT funding to biobank swap samples from 250 twin pairs. Including functional magnetic resonance.
    - 100 pairs have been bio-banked

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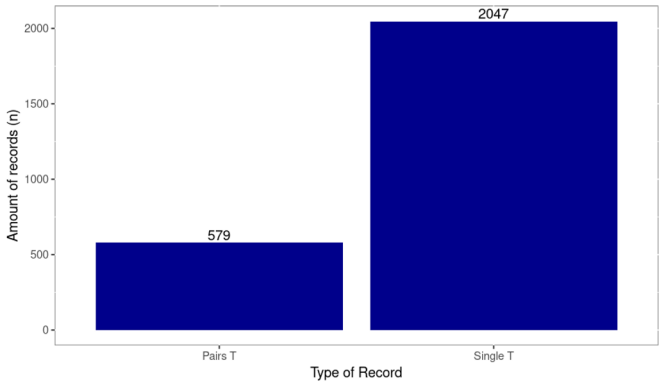
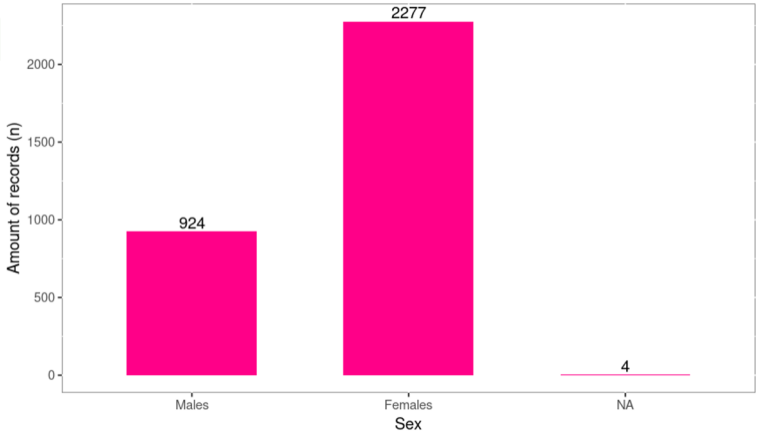
Total by July 2022

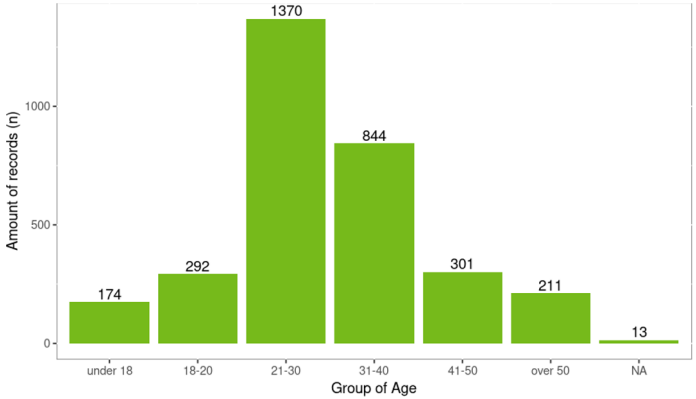
n = 3205
1158 (579 pairs)
2047 (single)



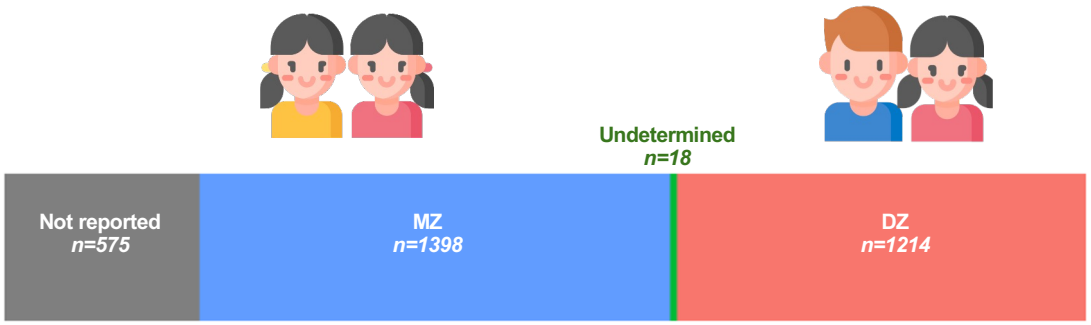
Distribution by sex



Distribution by Age



Distribution by zygosity



Coherence Rate and Heritability of Myopia and Astigmatism

Talía V. Román-López

		Twin 1	
		Yes	No
Twin 2	Yes	**Concordant**	**Discordant**
	No	**Discordant**	

$$\frac{C}{C + D}$$

n = 1399 families	**Probandwise Concordance**	
	Mz	**Dz**
Myopia	**0.74**	**0.50***
Astigmatism	**0.74**	**0.54***

** p<0.05. Tested by Likelihood ratio test*

Heritability# in Mexican Population		
Myopia	**62%**	
Astigmatism	**67%**	

#Estimated by ACE Bivariate Cholesky Modeling

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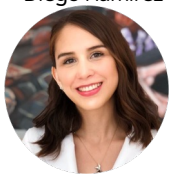

Vanessa Murillo

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CONACYT
Ciencia de Frontera, 2019
No. 6390

MEXICAN NETWORK FOR PARKINSON'S RESEARCH

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LARGE-PD
Latin American Research consortium on the GEnetics of Parkinson's Disease

- Launched in 2021
- Patient enrollment through certified Neurologists
- The shortage of Neurologists with valid certification along with their workload in the public sectors, restricts the massive extension of the registry.
- 192 registries have been recorded.
- Surveys designed to allow for cross data analysis between the Australian Parkinson's Genetics Study and the Latin American Research Consortium on the Genetics of Parkinson's Disease.
- MJFF funding to genotype 2500 patients and 2500 controls
- APDA financing allows for deep phenotyping of cognitive decay and metal health surveys of 500 patients and 500 controls.

gp2 Global Parkinson's Genetics Program

Recruitment

- 13 clinical sites in 8 regions + 2 registry sites for controls (RegGenoLab y Laboratorio de Neurogenómica Cognitiva UNAM-CU)
- 8 assistants for interview sessions online or through phone calls

Region	Start	Neurologist
B California	2021-12	Damaris Vazquez
CDMX	2022-10	Karla Salinas
CDMX	2021-12	Nadia Gandarilla
CDMX	2022-03	Sara Millán
Guanajuato	2021-11	Maritza Valadez
Jalisco	2022-01	Omar Cárdenas
Jalisco	2022-03	Teresa Pérez
Jalisco	2022-05	Moisés Rubio
Michoacán	2021-10	Eugenia Morelos
Querétaro	2021-11	Lucero Ugalde
Querétaro	2022-03	Yamil Matuk
San Luis Potosí	2022-05	Ildelfonso Rodríguez
Sinaloa	2021-10	Diana Deras

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Recruitment: Public Engagement

- 13 neulogists actively regitering patients in RedCap in 8 regions
- Sampling days calendarized throughout the year in selected sites
- Public engagement sessions (FB-live, Miércoles de ConCiencia UAQ, Club Hacienda)
- Open campaing for controls recruitment

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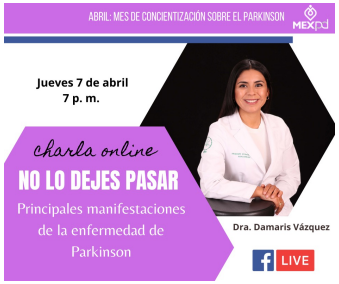

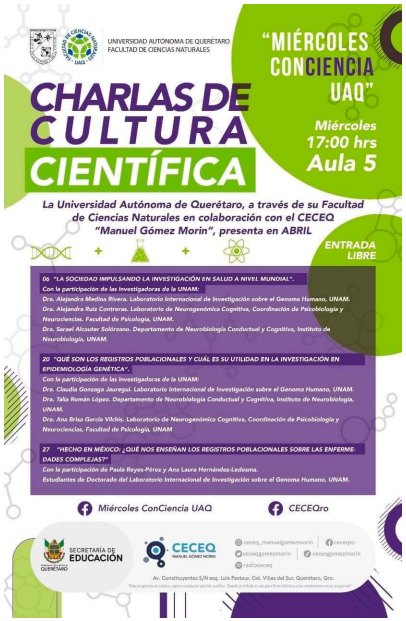

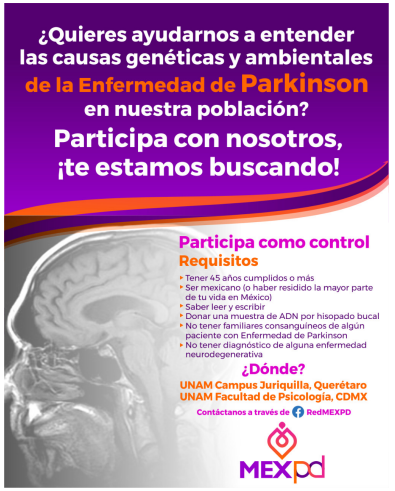

Clinical and epidemiological characterization of anxiety and depression patterns in Parkinson's patients in Mexico

13 active registry sites
in clinics in 8 states +
2 control registry sites

DNA extraction and processing

164 samples sent to Cleveland for genotyping

98 patients and 66 controls

Paula Reyes

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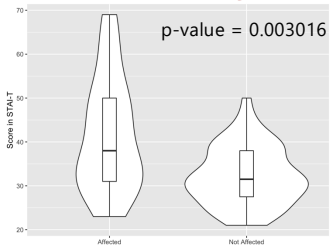
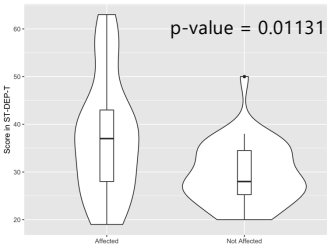
Records per instrument					
	Clinical basic data	**SCL-90R**	**PAS**	**STAI**	**ST-DEP**
Cases	142	27	27	25	23
Controls	129	17	46	45	38
Total	271	44	73	70	61

	Per sex		Age at recruitment		
	Male	**Female**	**Min**	**Max**	**Mean (SD)**
Cases	86 (56.20%)	67 (43.79%)	43	88	58.11 (9.37)
Controls	36 (27.69%)	94 (72.30%)	42	91	68.38 (9.41)

Trait-anxiety



Trait-depression



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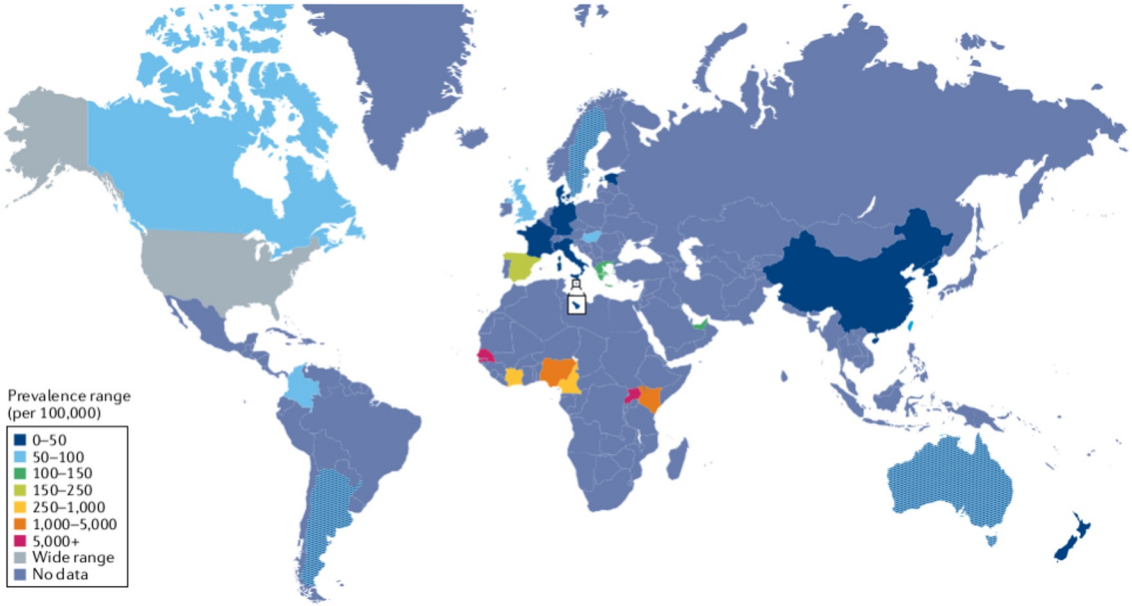
Patients, care partners and unaffected controls

LUPUS RGMX
Registro Mexicano de Lupus

Lupus

- Systemic Lupus Erythematosus (SLE) is a multi-systemic autoimmune disease with a widely heterogeneous set of clinical manifestations
- Previous studies have shown the influence of ethnicity and socioeconomic status on SLE's risk and prognosis.
- Earlier and more severe development of SLE, as well as a higher rate of mortality, has been observed in Latin American, North American Mestizos, African descendants and Native American patients



Martin, 2019; Barber et al 2021

Lupus prevalence in Mexico

- No epidemiological surveillance in place
- Affects mostly women **(9:1)** and people between the ages of **20 and 40** years old.
- Prevalence **20/100,000**.
- Incidence between **1.8 and 7.6** cases/100,000-año.

Regions	Year of study	cases / 100,000 habs
Chih, NL, Sin, Yuc y CDMX	2005	70
Nuevo León	2008-2009	40
Yucatán	2011	70
Oaxaca	2016	90

Scolnik, 2016

LUPUS RGMX
Registro Mexicano de Lupus

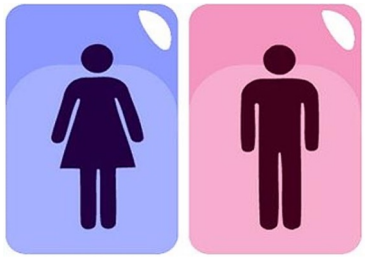
- Launched in May 2021
- Initial recruitment through social media based on self reported status and self assessment of clinical manifestations
- Close collaboration with patient communities
- 5 rheumatologists joined in the last year to recruit patients

LUPUS RGMX
Registro Mexicano de Lupus

Progress

May 2021-May 2022

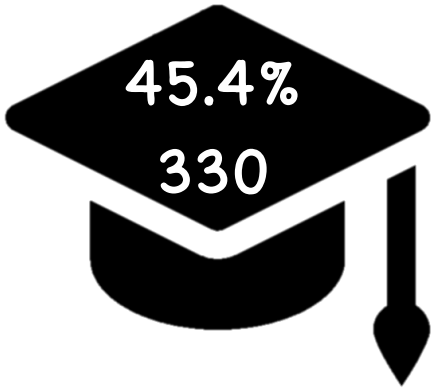
726

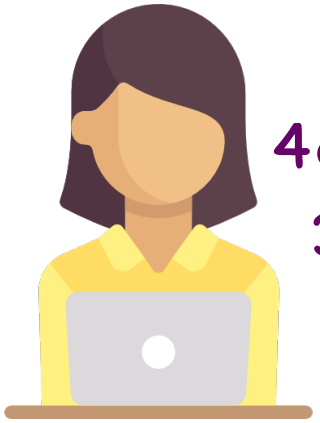


94.2%
684

5.8%
42

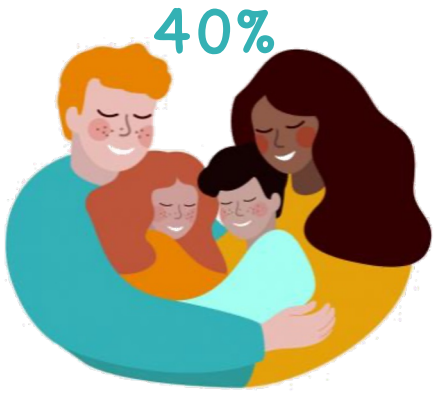
36 (±10) años
Range 18-79 años
Mostly between
29 and 44 años





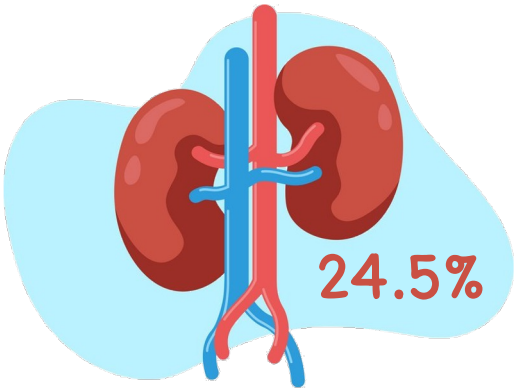
48.9%
355

27 (±10) years



Antimalaria drugs 54.9%
Glococorticoids 46.2%

IMSS 43.4%
Private 30.6%
ISSSTE 10.6%



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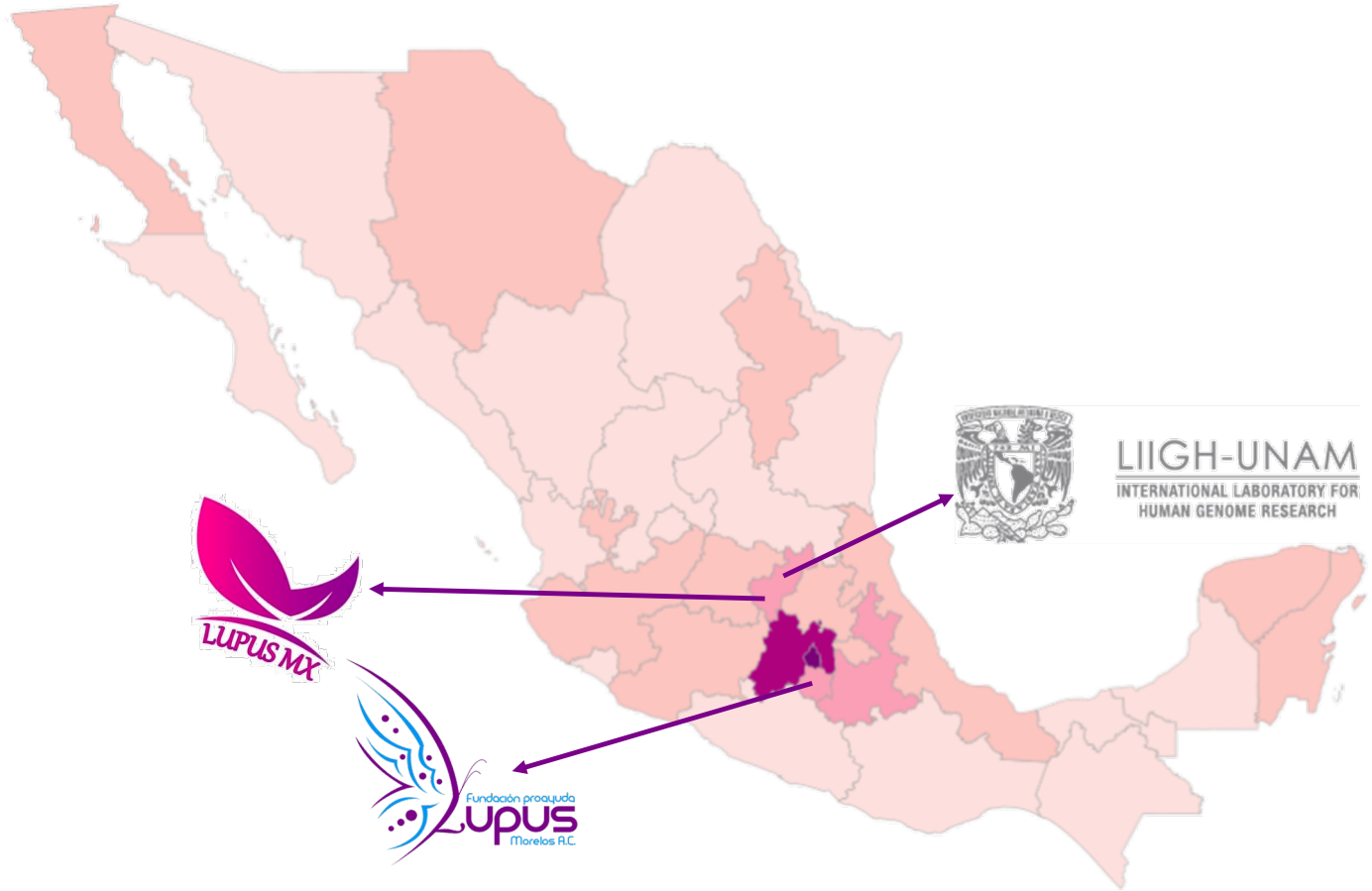

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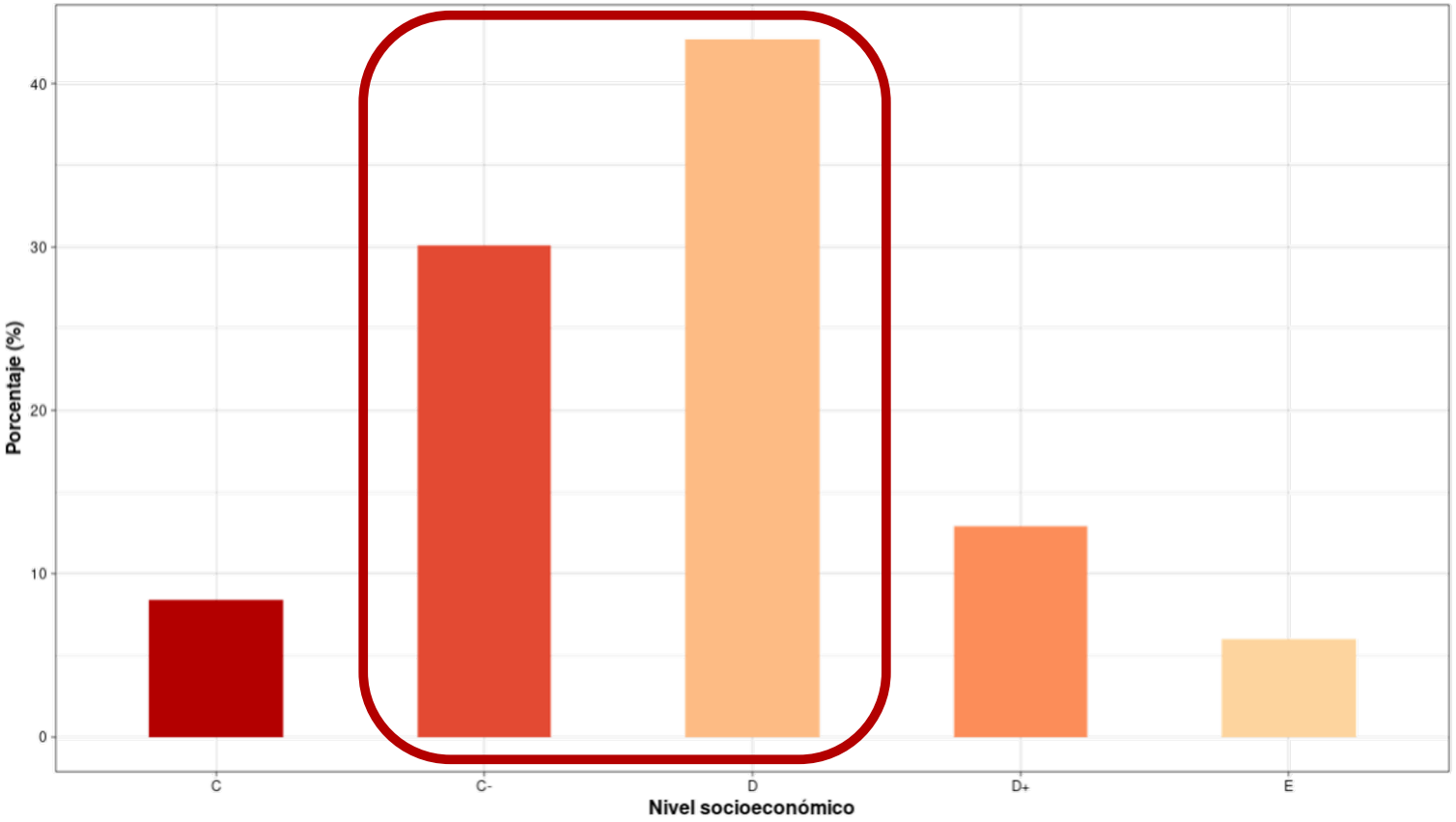
Socio economical status

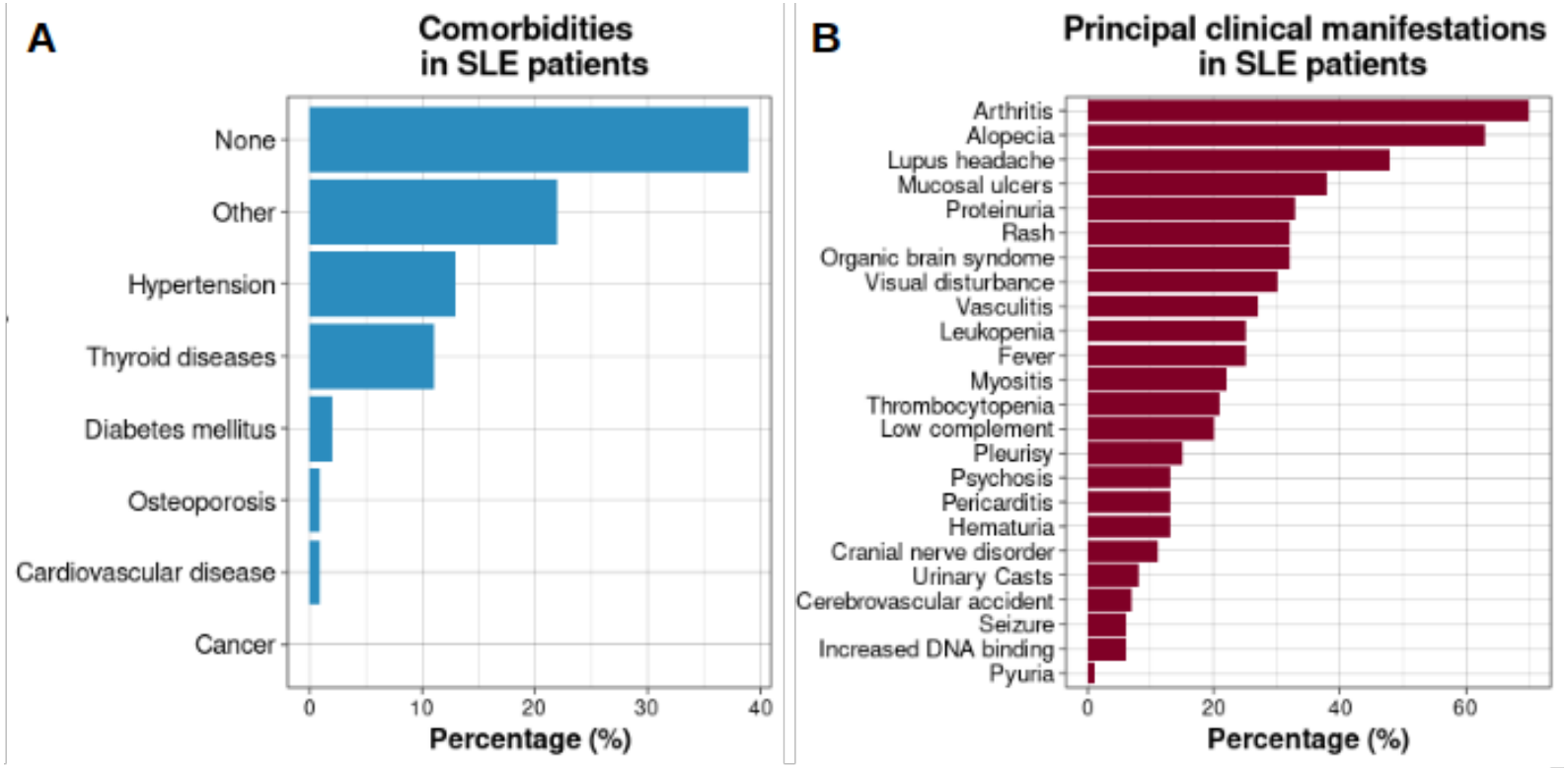


- 8,900-15,600 MXN per month
- 35-54% destined to food.
- Communication, transport, education and health

E $5,400
D $8,900
D+ $12,300
C $15,600
C $19,900

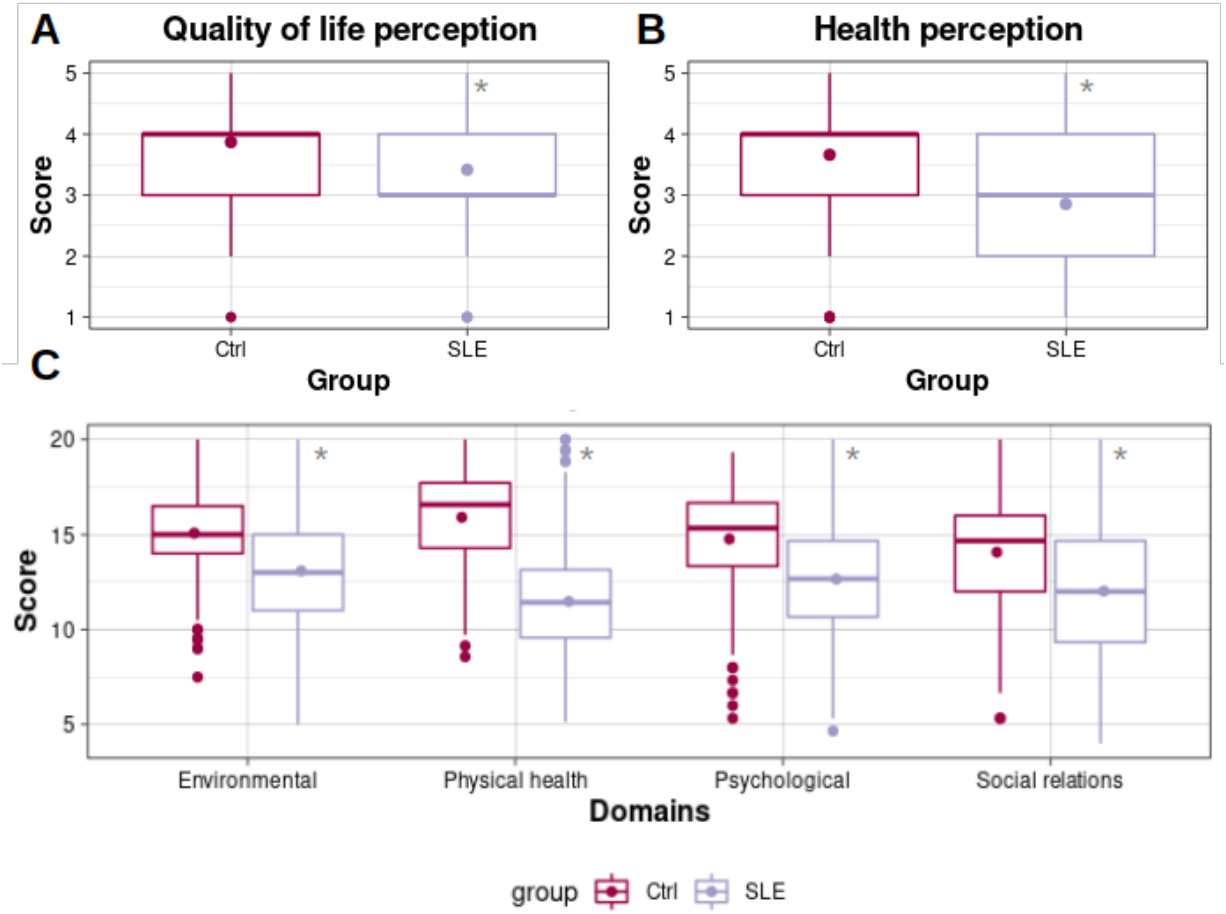
Asociación Mexicana de Agencias de Inteligencia de Mercados y Opinión Pública (AMAI).

Comorbidities and clinical manifestations



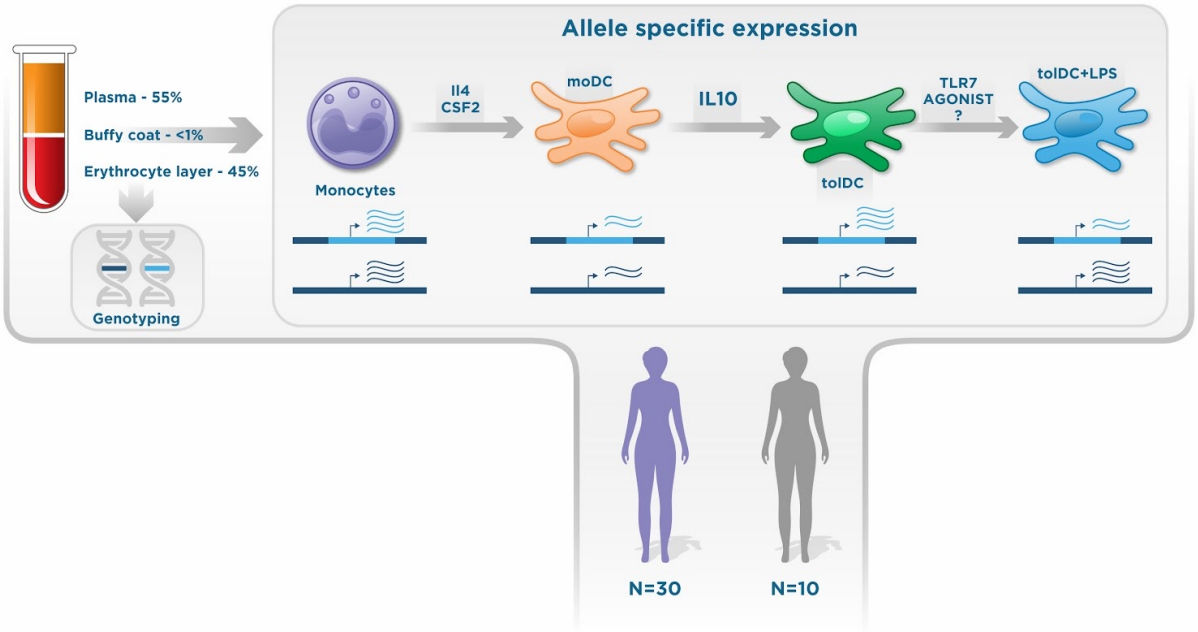
Quality of life

Control Group



León-Apodaca et al 2019.

Allele specific expression patterns in systemic lupus erythematosus during tolerogenic induction



Why?

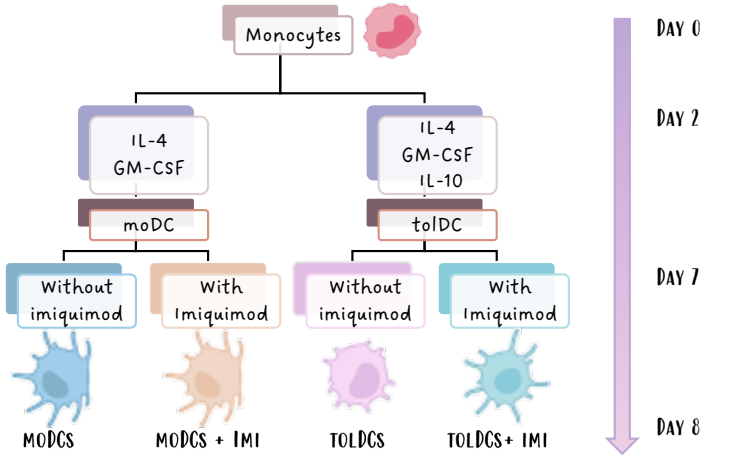
Tolerogenic dendritic cells are an immunotherapy alternative for autoimune disease

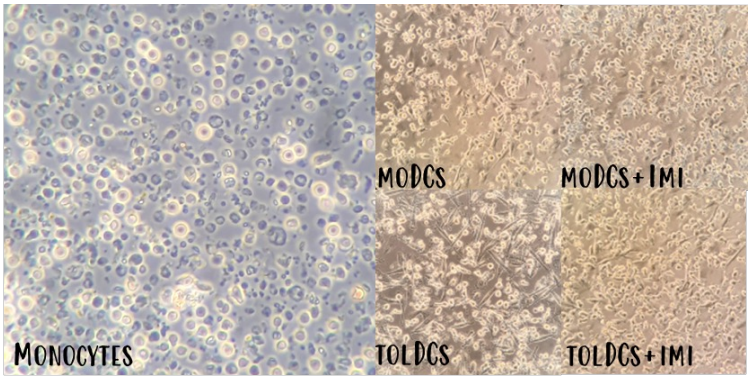
Progress:

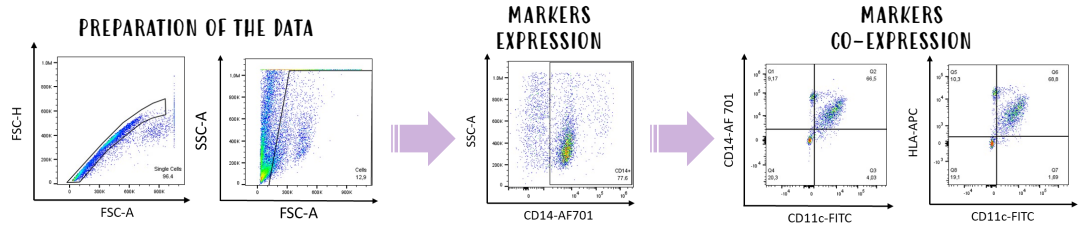
- Lupus patients: 15
- Controls: 6

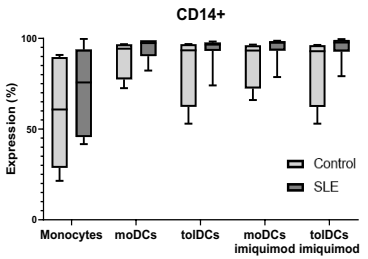
LUPUS RGMX
Registro Mexicano de Lupus

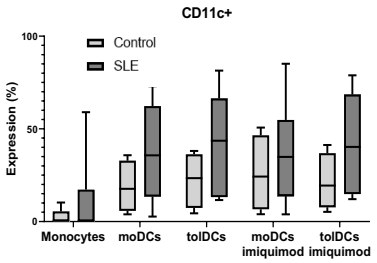
Allele especific expression in Systemic Lupus Erythematosus on immune tolerance induction.

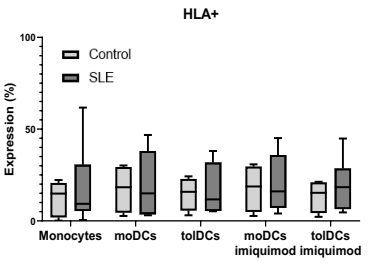


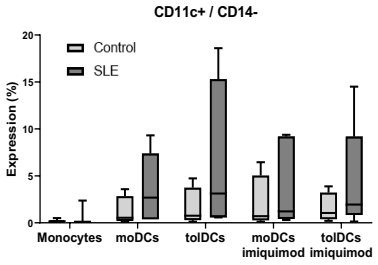


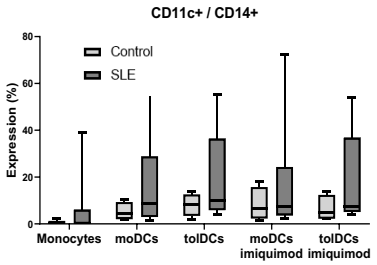


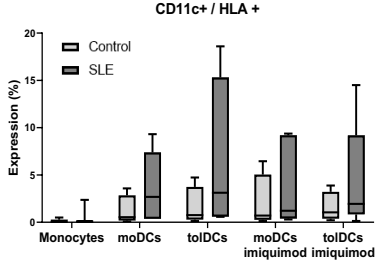












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LUPUS RGMX
Registro Mexicano de Lupus

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Pediatric Lupus

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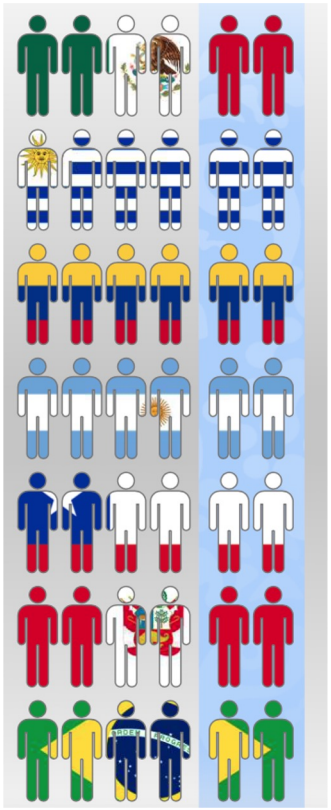
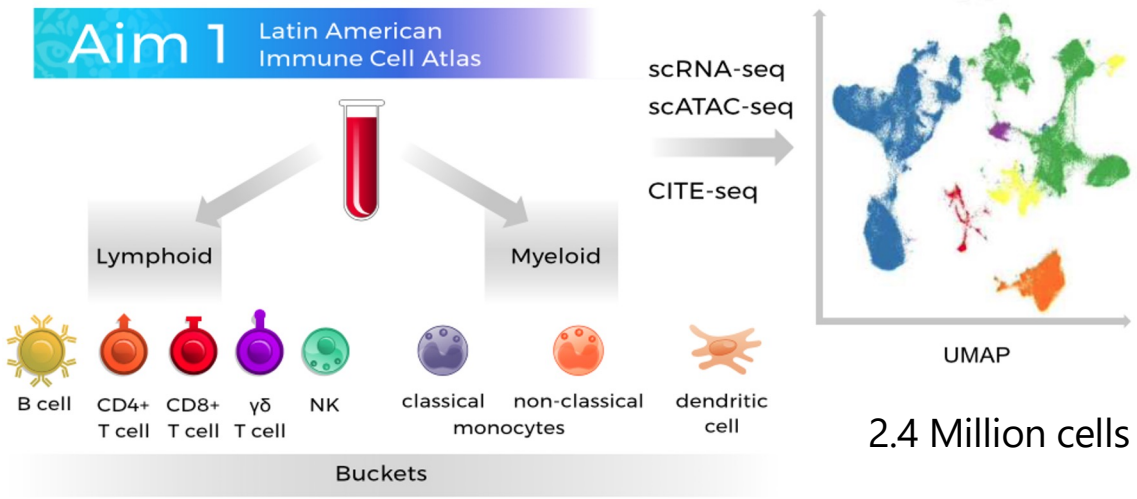
REMEXER
Red Mexicana de Enfermedades Raras

PROJECT JAGUAR

Mapping immune cell diversity across Latin America





2.4 Million cells

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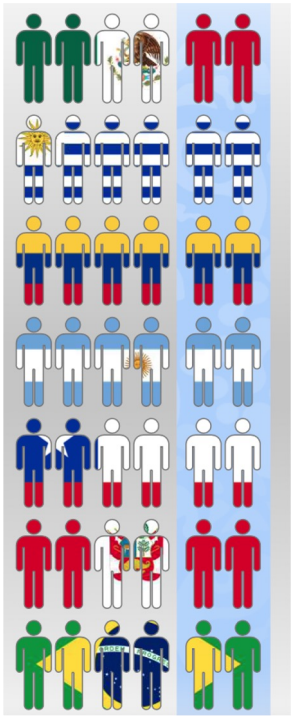
Mapping immune cell diversity across Latin America



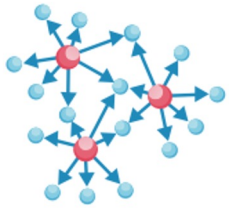
Aim 2 Regulatory Networks

Integration of Regulatory Networks

Transcriptome profile

scATAC-seq

Population specific regulatory interactions



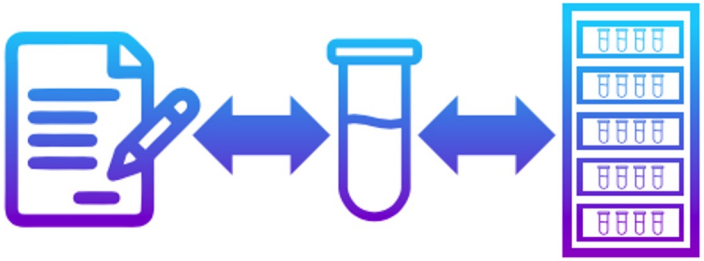
Regulatory effects of genetic variation

nnATTGCACAATnn

nnATTGTACAATnn

Aim 3 PBMC Biobank

Partnership LATAM UK



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Summary

- Launching patient registries in Mexico is a challenge but is also rewarding.
- Public engagement is key for the success of these projects.
- These resources can have great impact on research in the country and potentialize functional genomic studies in the Mexican population.
- Infrastructure can be used to help establish other registries.
- Produced data will help increase diversity in genomic samples.
- Challenge: How to access consortia data?
  - Data access for LARGE-PD is centralized in Terra.
  - LATAM institutions do not have stablished processes to pay for these type of services
  - The advantage of centralized repositories for integrative analysis will go to countries and institutions that can pay for the service (Google cloud).

THANKS!

Progress by survey

	LARGE-PD					MEX-PD							
	LARGE PD minimal set								Metal health			Cognitive fucntion	
	Datos mínimos para envío de muestra												
	Parte I	Parte II	Parte III	Genealogía	Consentimiento informado	MoCA	UPDRS		SCL-90R	PAS	IDARE	IDER	Reserva congitiva	CBS
	Datos de identificación clínica del probando, incluyendo sede y neurólogo que realiza el registro, criterios de inclusión y exclusión.	Datos del probando incluyendo edad, ancestría, síntomas motores y no motores, uso de levodopa y agonistas dopaminérgicos,.	Datos acerca de exposiciones ambientales del participante: antecedentes de residencia, fuentes de agua, consumo de sustancias; traumatismos, antecedentes laborales, exposición a pesticidas y metales pesados, uso de medicamentos.	Árbol genealógico simple de 3 generaciones donde se incluyen enfermedades conocidas en la historia familiar	Firma del documento de Consentimiento Informado	Montreal (traducción al español del Montreal Cognitive Assessment), Evalúa los siguientes dominios cognitivos: atención y concentración; funciones ejecutivas, memoria, lenguaje, habilidades visuoespaciales, razonamiento conceptual, cálculo y orientación	UPDRS-neuros, Sección del MDS-UPDRS (Official MDS Spanish Translation, 2015), correspondiente a Parte II: Aspectos Motores de las Experiencias de la Vida Diaria (M-EVD).	UPDRS-asistentes, Sección del MDS-UPDRS (Official MDS Spanish Translation, 2015), correspondiente a Parte I: Aspectos No-Motores de las Experiencias de la Vida Diaria (nM-EVD).	Inventario de Síntomas-Revisado, de Derogatis, evalúa el grado de malestar psicológico actual que experimenta una persona, en 9 dimensiones: Somatización, Obsesiones, Sensitividad Interpersonal, Depresión, Ansiedad, Hostilidad, Ansiedad Fóbica, Ideación Paranoide y Psicoticismo.	Escala de Ansiedad de Parkinson. Escala calificada por un observador o paciente de 12 ítems con tres subescalas, para la ansiedad persistente y episódica, y el comportamiento de evitación.(Parkinson Anxiety Scale, traducida al español)	Inventario de Ansiedad Rasgo-Estado (IDARE), adaptado al español, empleado para medir dos dimensiones básicas de la ansiedad: como rasgo y como estado, con 20 ítems para cada dimensión.	Inventario de Depresión Rasgo-Estado (IDERE o IDER), adaptado al español, empleado para medir dos dimensiones de la depresión: como rasgo y como estado, con 20 ítems para cada dimensión	Cognitive Reserve Index questionnaire (CRIq; versión en español), que estima la reserva cognitiva de un individuo a través de la recopilación de información sobre toda su vida adulta.	Conjunto de 8 tareas neurocognitivas para evaluar los siguientes dominios: Memoria, Razonamiento, Habilidad verbal y Concentración
Casos	**158**	**142**	**82**	**37**	**79**	**91**	**113**	**23**	**27**	**27**	**25**	**23**	**Por iniciar**	**3**
Controles	**136**	**129**	**107**	**82**	**47**	**33**	**2**	**2**	**17**	**46**	**45**	**38**	**Por iniciar**	**0**
Totales	**294**	**271**	**189**	**119**	**126**	**124**	**115**	**25**	**44**	**73**	**70**	**61**	**0**	**3**

THE STAR OF THE SHOW

When you want a more elegant approach, the dynamic presence of PANTONE Very Peri shines as the star of the show in this palette of classics and neutrals whose understated stylishness conveys a message of timeless sophistication.

AMUSEMENTS

Use this color palette when you want to tell a joyous and whimsical story. In this palette, PANTONE Very Peri injects a sense of playful freshness into the design, exuding a good-natured warmth that quickly engages the eye.