IARC International Multicenter population based case-control study on Premenopausal BC: PRECAMA

Precama.iarc.fr

PRECAMA study - Hypothesis

- *Breast cancer phenotypes* are distinct in Latin American women (more aggressive tumors)

- *Overweight and obesity* have different effects depending on fat distribution and BC phenotypes

- *High intake of processed foods, sweetened beverage*, deficiency in micronutrient (vitamin D and folate) and sedentary behaviours are major predictors of breast cancer

Objectives

- Advance the ***prevention and management of pre-menopausal BC in Latin America (LA)*** through a better understanding of molecular, pathological and risk factor patterns

- Develop a ***multi-centric population-based case-control study on BC*** in centers across LA, with structured collection of lifestyle, clinical and pathological information, as well as biological specimens, according to strictly controlled protocols

- Characterize the subtypes of ***premenopausal BC*** on the basis of ***their molecular and pathological phenotypes***

- Through these activities**, *provide advanced training, induce a structuring effect on the BC research community in LA, and influence the public health agenda regarding the management of BC*.**

PRECAMA Study

- *Standardized protocol* for clinical and exposure data (reproductive history, lifestyle, anthropometry, diet, environment), biological specimens, and tumor sampling and analyses

- *Pilot study* on 200 cases/200 controls (Chile, Colombia, Costa Rica, Mexico)

    Population-based controls, matched to cases on age and center

- *Molecular subtypes of premenopausal BC (FHCRC, IARC)*
    - Classification into Luminal A, Luminal B, Basal like, HER2+/ER- based on IHC biomarkers
    - Analyses of tumor DNA for TP53 mutations

- *Identification of endogenous risk factors for specific subtypes of BC*

General Characteristics

	All (n=678)	Controls (n=304)	Cases (n=375)	P
Age at recruitment	41 (31-45)	40 (31-45)	41 (31-45)	*0.21*
Age at menarche	12 (11-15)	12 (11-15)	12 (11-15)	*0.95*
Pregnancy ever	592 (87%)	281 (92%)	311 (83%)	*<.0001*
Age first pregnancy	22 (17-31)	21 (17-28)	23 (17-32)	*<0.001*
Age last pregnancy	29 (22-37)	29 (22-36)	30 (23-38)	*0.014*
Parity	2 (0-4)	2 (1-4)	2 (0-3)	*<0.001*
Breastfeeding ever	367 (79%)	175 (88%)	192 (72%)	*<0.001*
Total months breastfeeding	13 (2-48)	18 (3-48)	12 (1-44)	*0.002*

n(%); or median (p10-p90).
Logistic regression adjusted for age and country

Tumor characteristics

	Chile	Colombia	Costa Rica	Mexico	Total	P53 positive[a]	Ki67 %[b]
Luminal A (ER+/PR+/HER2-)	18 (82%)	16 (64%)	9 (35%)	21 (66%)	**64 (61%)**	10 (33%)	28 (10-72)
Luminal B (ER+/PR+/HER2+)	4 (18%)	5 (20%)	2 (8%)	0 (0%)	**11 (10%)**	4 (13%)	42 (9-72)
HER2 enriched (ER-/PR-/HER2+)	0 (0%)	2 (8%)	3 (12%)	0 (0%)	**5 (5%)**	3 (10%)	31 (12-82)
Triple negative (ER-/PR-/HER2-)	0 (0%)	2 (8%)	12 (46%)	10 (31%)	**24 (23%)**	12 (40%)	72.5 (21-97)
Of which Basal-like (TN + EGFR and/or CK 5/6)	*0 (0%)*	*2 (8%)*	*11 (42%)*	*9 (28%)*	***22 (21%)***	*11 (37%)*	*73 (25-97)*
Total	22	25	26	31	104	30	36 (10-84)

IHC data on PRECAMA's tumours (FHCRC)
[a]P53 positive when >10%, 1 participant with missing data.
[b]Median (p10-p90), 1 participant with missing data.

International Agency for Research on Cancer
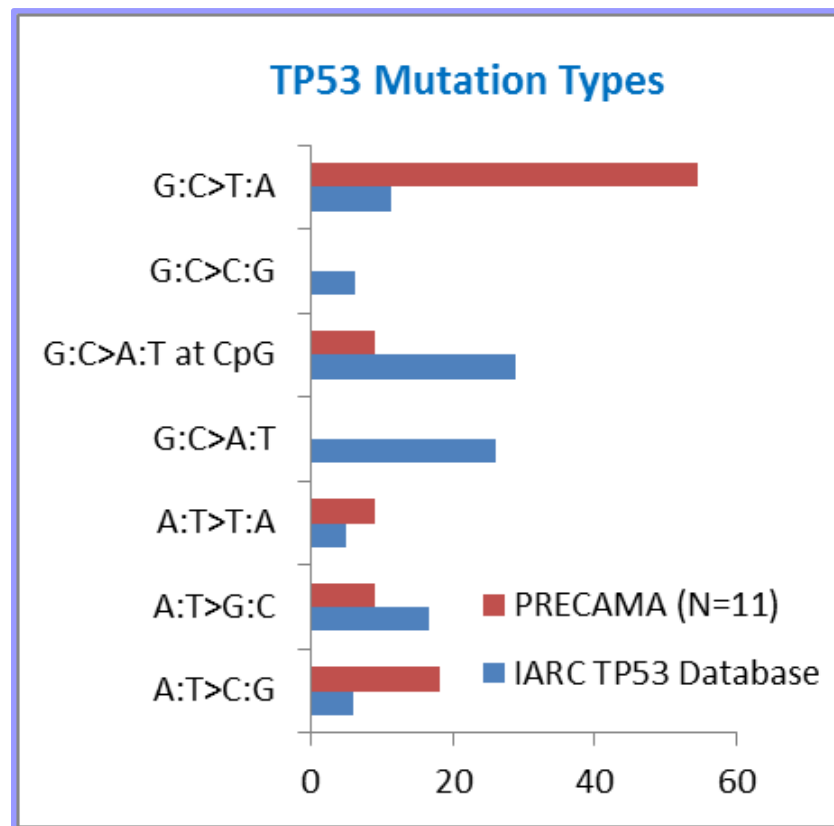World Health Organization

Standardization of Pathology and IHC biomarker testing across centers

- Meetings: Liberia, Costa Rica, 5-6 November 2013
                Mexico City, Mexico, 17-18 July 2014

- Aims: - Ensure standardization of PRECAMA study methods
          - Develop standard protocols for:
              tissue sample processing
              IHC reagents, assay and interpretation
              pathology review criteria
        - Improve local facilities' diagnostic capabilities

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Targeted sequencing

- The tested breast cancer genes (PIK3CA, TP53, NOTCH1, AKT1, RB1, CDH1, ERBB2, PTEN) mutated at frequencies similar to that reported in other populations (COSMIC database)

- The type of mutations found in the TP53 gene were different from what is reported in other populations (IARC TP53 database), with a high proportion of G>T transversions.
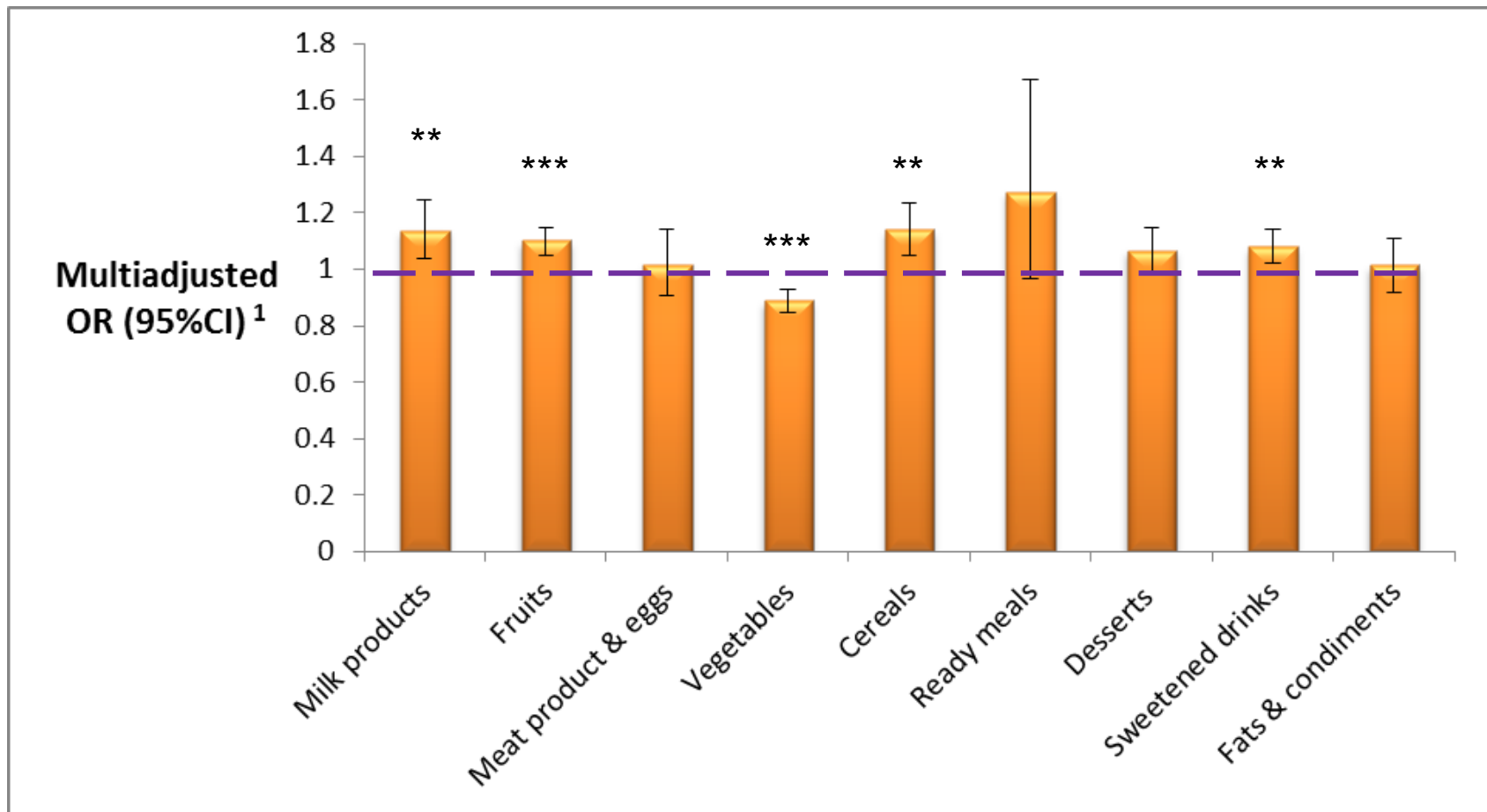
TP53 Mutation Types

Mutation Type	
G:C>T:A	
G:C>C:G	
G:C>A:T at CpG	
G:C>A:T	
A:T>T:A	
A:T>G:C	
A:T>C:G	

PRECAMA (N=11)
IARC TP53 Database

0   20   40   60

Adiposity and Breast Cancer

	All (n=679)	Controls (n=304)	Cases (n=375)	OR (95%CI)	P[a]
Weight (kg)	66 (52-86)	69 (54-92)	64 (51-82)	**0.98 (0.96-0.99)**	**<0.001**
BMI (kg/m²)	27.0 (21.4-35.2)	28.3 (22.0-36.4)	26.1 (21.0-32.8)	0.98 (0.96-1.01)	0.135
Waist (cm)	91 (76-108)	93 (77-112)	90 (75-105)	**0.98 (0.97-0.99)**	**0.001**
Hip (cm)	104 (92-119)	105 (93-122)	102 (92-116)	**0.98 (0.97-0.99)**	**0.001**
Waist / Hip	0.88 (0.77-0.96)	0.88 (0.77-0.98)	0.88 (0.76-0.96)	0.32 (0.05-1.91)	0.211

Median (p10-p90).
[a] Logistic regression adjusted for age and country.

Dietary intake and Breast Cancer

[1] Logistic regression adjusted for age, country, education, breast feeding, age at first pregnancy, alcohol consumption, vegetables consumption, physical activity, BMI.

Cereales: includes cereales, bread, pasta, rice, corn

*P < 0.05 ; **P<0.01 ; ***P < 0.001

Physical Activity and Breast Cancer

	All (n=466)	Controls (n=198)	Cases (n=268)	OR (95%CI)	P[a]
Sleep (h)	7.6 (5.9-9)	7.6 (5.7-9.1)	7.6 (6-9)	0.96 (0.87-1.07)	0.497
Vigorous (h)	0.3 (0-2.4)	0.4 (0-2.6)	0.3 (0-2.1)	0.92 (0.83-1.02)	0.119
Moderate (h)	2.1 (0.4-6.4)	2.6 (0.7-6.3)	1.9 (0.3-6.4)	**0.90 (0.84-0.97)**	**0.004**
Sedentary (h)	13.4 (8-16.5)	13.0 (8.6-16.1)	13.8 (8-16.7)	**1.10 (1.04-1.16)**	**0.001**

Median (p10-p90).
[a] Logistic regression adjusted for age and country.

Next Steps

- On going recruitment of incident cases and population based controls

- Increase the number of recruiting sites: Brazil, Colombia (INCA Bogota)

- Determination of IHC on all tumors and tumor DNA sequencing

- Classification of BC tumors by phenotypes

- Analyses of risk factors based on questionnaires and biomarkers for specific BC phenotypes

- Follow-up of the cases
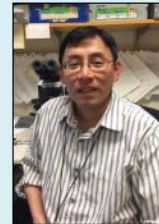
Precama Teams

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FRED HUTCH
CURES START HERE™

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Peggy Porter, MD
Principal Investigator

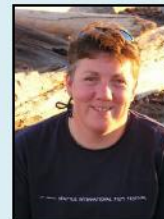**Minggang Lin, MD**
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June 2015

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Acknowledgments

- The PRECAMA teams including the epidemiologists, the pathologists, the field team nurses and health workers

- The clinicians

- The women participating in the study

- And funding from IARC, UICC, PAHO, COLCIENCIAS