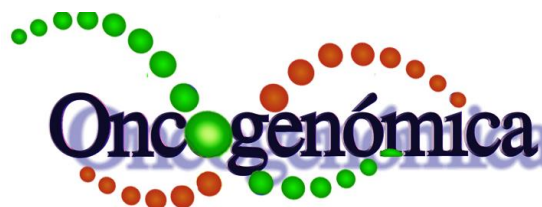


## GENOMIC-BASED MOLECULAR MARKERS IN CERVICAL CANCER FOR DISTAL PROGRESSION AND TREATMENT FAILURE

Carlos Pérez-Plasencia, PhD



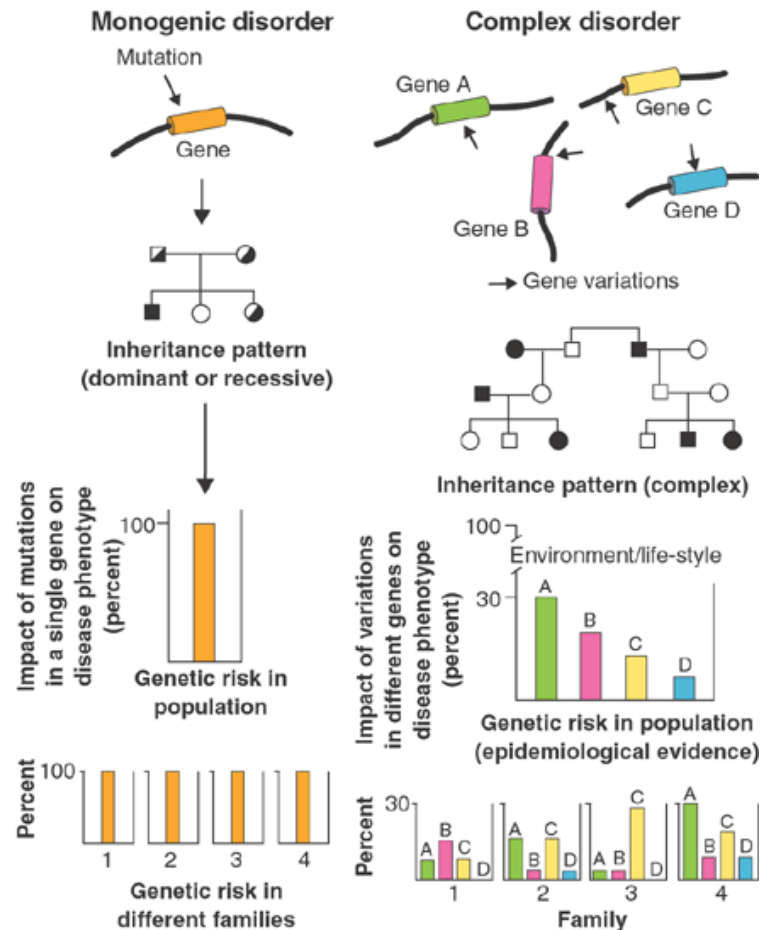
Instituto Nacional  
de Cancerología



# Gynecologic Cancer InterGroup Cervix Cancer Research Network



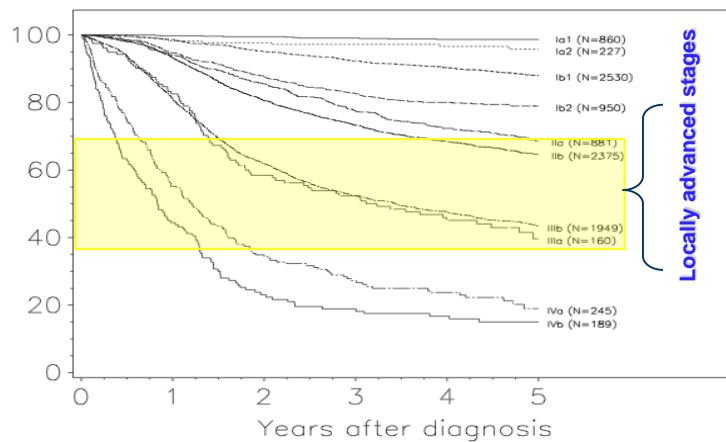
## Cancer is a Complex Disease



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## Overall Survival for Locally Advanced Cervical Cancer (LACC) Patients



| Stage | Patients (n) | Mean age (yr) | Overall survival (%) at |         |         |         |         | Hazards ratio <sup>a</sup> (95% CI) |
|-------|--------------|---------------|-------------------------|---------|---------|---------|---------|-------------------------------------|
|       |              |               | 1 year                  | 2 years | 3 years | 4 years | 5 years |                                     |
| Ia1   | 860          | 44.3          | 99.8                    | 99.5    | 99.1    | 98.7    | 98.7    | 0.1 (0.1–0.2)                       |
| Ia2   | 227          | 45.5          | 98.2                    | 97.7    | 97.2    | 96.7    | 95.9    | 0.3 (0.1–0.5)                       |
| Ib1   | 2530         | 48.3          | 98.7                    | 95.1    | 92.3    | 90.4    | 88.0    | Reference                           |
| Ib2   | 950          | 47.4          | 94.8                    | 87.8    | 82.6    | 79.9    | 78.8    |                                     |
| IIa   | 881          | 56.5          | 94.1                    | 85.6    | 77.6    | 72.3    | 68.8    | 2.4 (2.1–2.8)                       |
| IIb   | 2375         | 54.1          | 93.3                    | 80.7    | 73.4    | 68.5    | 64.7    | 2.9 (2.6–3.3)                       |
| IIIa  | 160          | 60.1          | 82.8                    | 58.8    | 52.6    | 45.3    | 40.4    | 5.2 (4.0–6.6)                       |
| IIIb  | 1949         | 56.4          | 81.5                    | 62.2    | 52.6    | 47.6    | 43.3    | 5.7 (5.0–6.4)                       |
| IVa   | 245          | 60.0          | 56.1                    | 35.6    | 27.9    | 24.1    | 19.5    | 12.6 (10.5–15.1)                    |
| IVb   | 189          | 56.6          | 45.8                    | 23.9    | 19.6    | 17.2    | 15.0    | 19.2 (15.8–23.4)                    |

**Carcinoma of the cervix uteri: patients treated in 1996-98.  
Survival by FIGO stage, n=10366**

*Int J Gynaecol Obstet, 2003;  
83(suppl1):41-78*

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## Aim of the Study

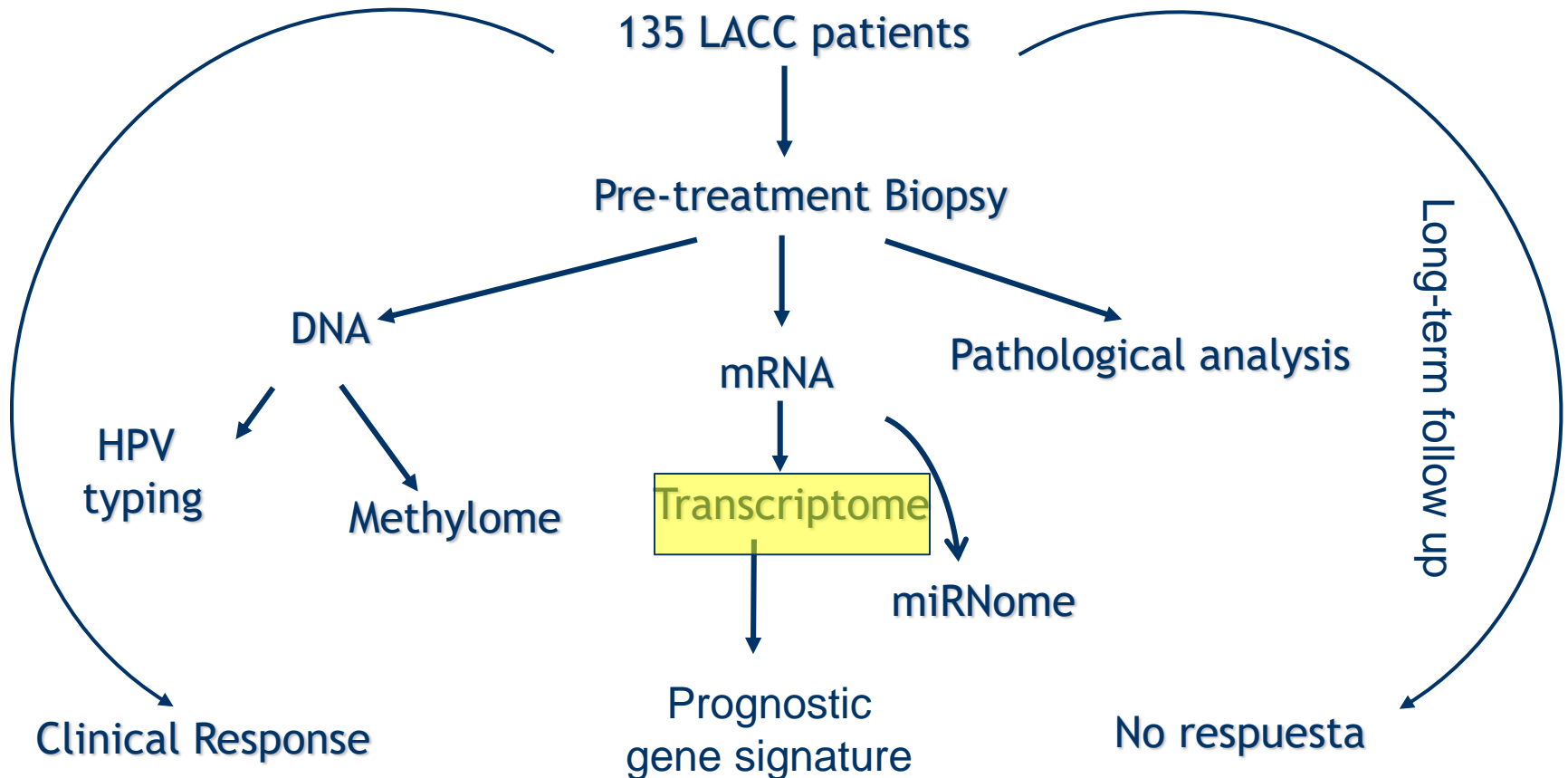
By means of Transcriptome analysis to search for a prognostic gene signature able to discriminate patients who do not respond to the conventional treatment employed to treat LACC

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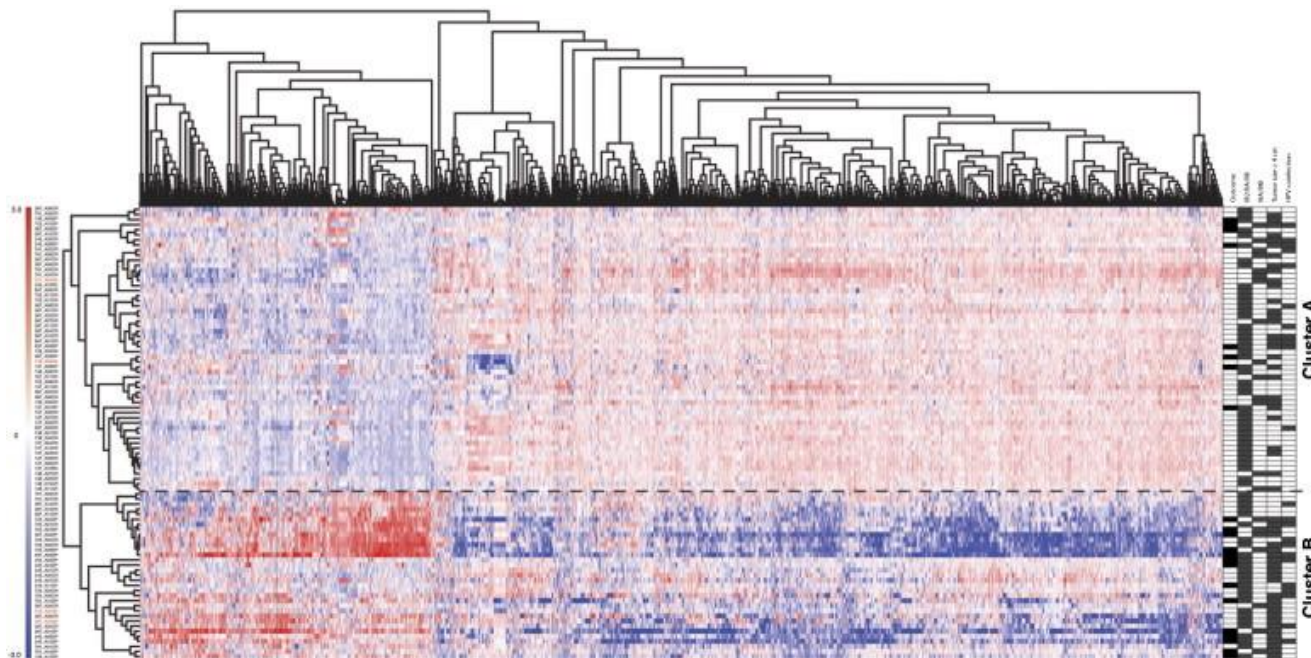
Experimental design



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Supervised two-dimensional cluster analysis of 89 CC tumor profiles.

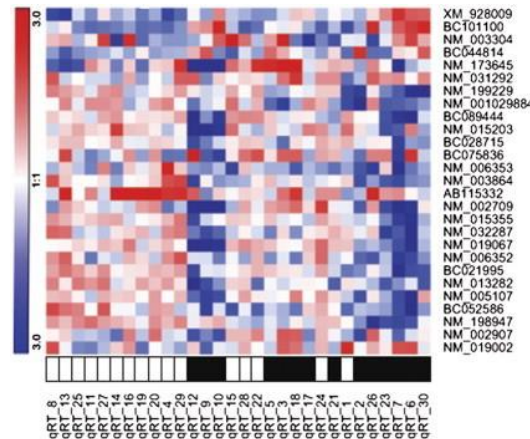
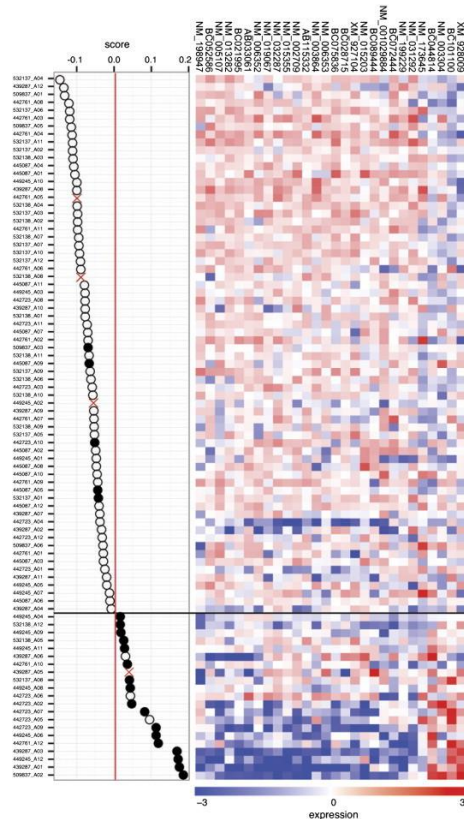


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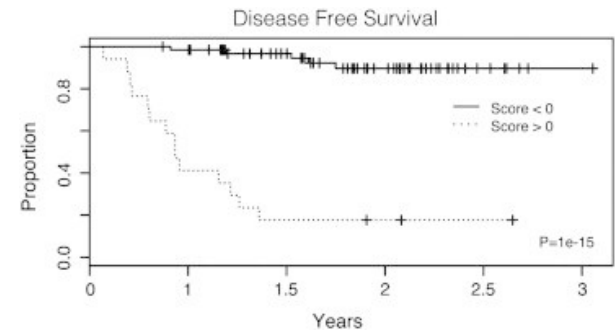


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Predictor genes are clustered based on their similarities across LACC tumors.



LOC644921  
SLC36A2  
TRCP1  
CCDC89  
DNAH6  
PUS7L  
RPE  
PLEKHG1  
FLJ39378  
RPRD2  
C10orf137  
RBBP4  
HMGH4  
SAP30  
TRIO  
PPPC1  
SUZ12  
LDOC1L  
GNL3L  
ZNF238  
SRP9  
UHRF1  
ENDGL1  
SLFN11  
FAM111B  
RECOL  
ETTA1

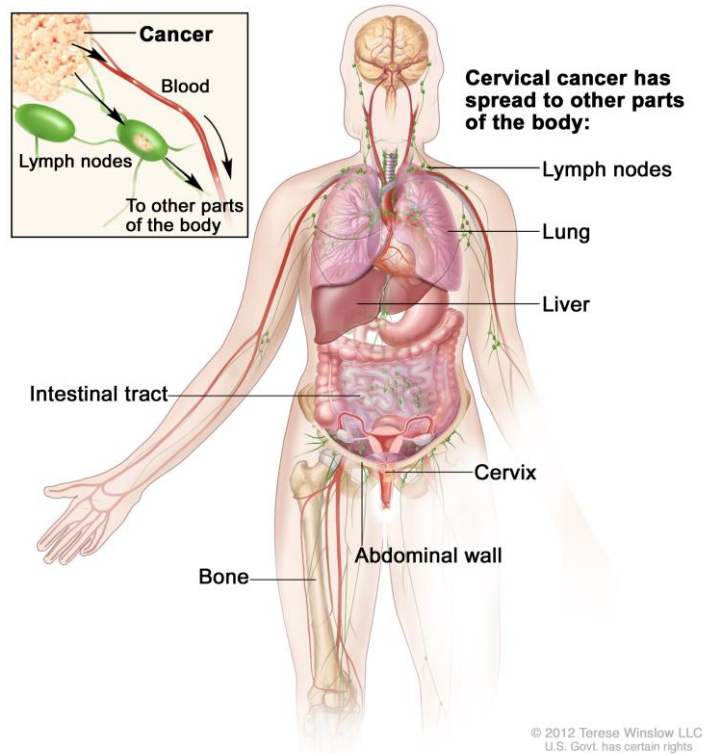


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## Metastasis pattern of Cervical Cancer



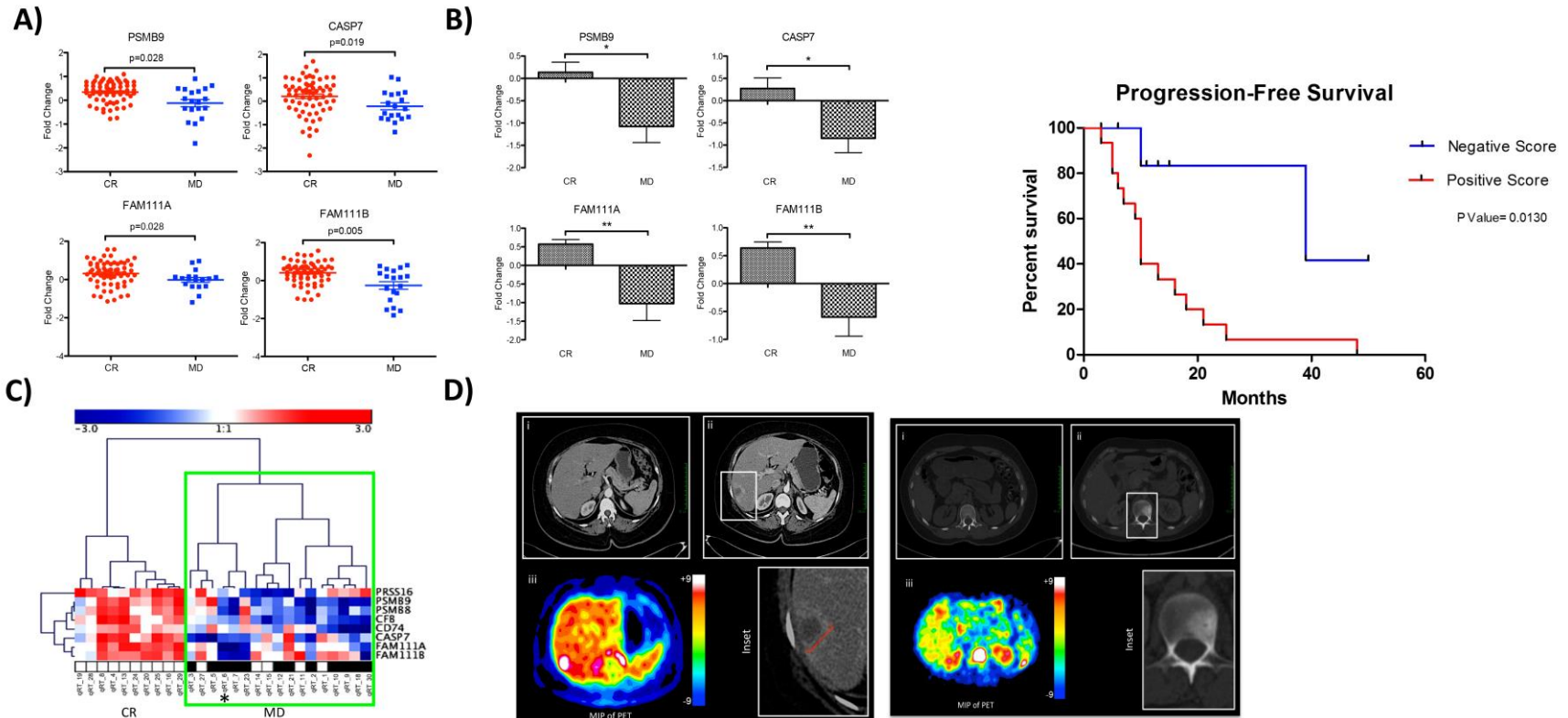
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Eight degradome related-genes are able to distinguish CCLA ptients who will develop distal progression.



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- Concluding remarks

Transcriptome analysis allowed us to identify genes with the ability to distinguish clinical responses in LACC patients.

We are extending our study to validate both gene signatures.