Hospital A.C.Camargo

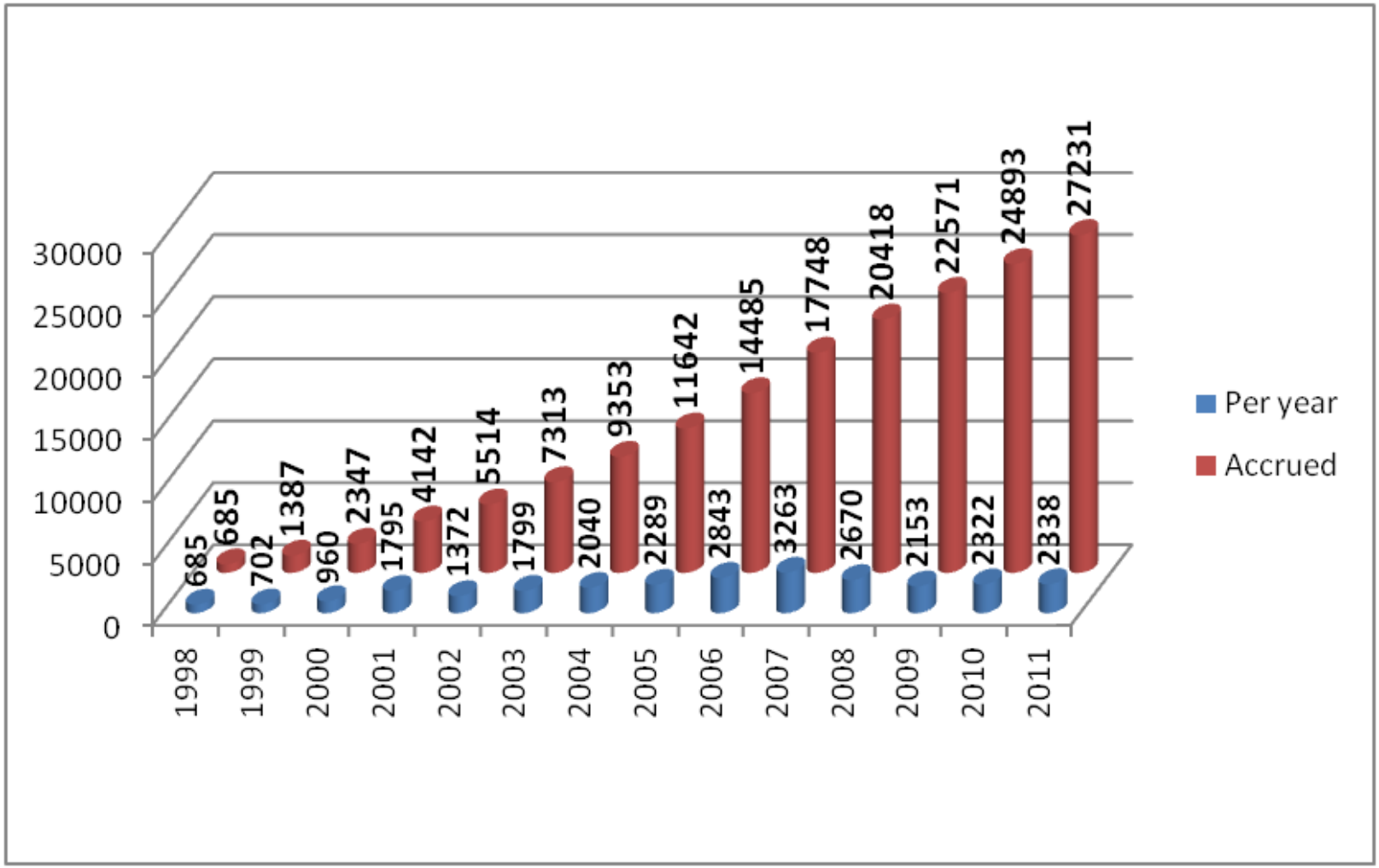
FAPESP 50 YEARS OF SCIENCE IN BRAZIL AND CHALLENGES AHEAD Week

RICARDO BRENTANI
PRESIDENT

FAPESP WEEK OCTOBER 22, 2011

Hospital A.C.Camargo

- ✓400.000 outpatient visits/year
- ✓16.000 new cancer cases/year
- ✓320 beds / 24 ICU beds
- ✓11.000 Surgeries/year
- ✓300.000 Hospital records (87-95% 5-year follow up)
- ✓1.500.000 Paraffin blocks
- ✓38,145 Paraffin blocks from 2543 autopsies
- ✓86% 5-years follow-up


30000
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14485
3263
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20418
2153
22571
2322
24893
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27231
1998
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2007
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2010
2011
Per year
Accrued

Ranking da Produção Científica do Brasil nas 48 subáreas da medicina no quinquênio 2005-2009. (1º a 16º)

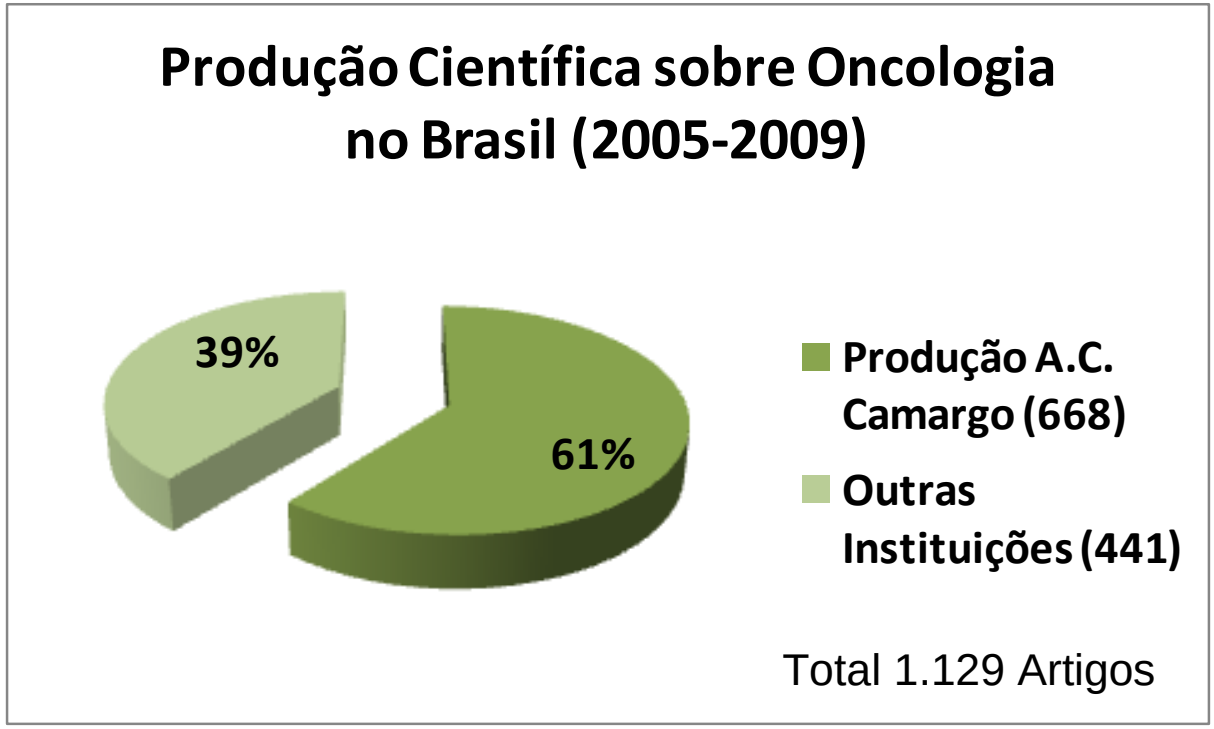
Rank	Área do conhecimento	Nº Artigos	Citação	Impacto	% Artigos no Mundo
1	Pharmacology & Pharmacy	4.203	17.048	4,06	2,86
2	Dentistry Oral Surg & Med	3.403	9888	2,91	10,41
3	Public Env & Occ Hlth	3.365	6680	1,99	4,07
4	Surgery	2.650	7113	2,68	1,99
5	Immunology	2.328	13.184	5,66	2,40
6	Tropical Med	2.147	4829	2,25	20,84
7	Endocrinology & Metabolism	1.828	8.029	4,39	2,67
8	Med Res & Experimental	1.572	5.568	3,54	2,88
9	Clinical Neurology	1.550	6.962	4,49	1,53
10	Infectious Diseases	1.456	8.483	5,83	3,30
11	Cardiac & Cardiovascular Sys	1.411	6.289	4,46	1,92
12	Physiology	1.163	4.037	3,47	2,30
13	Oncology	1.129	11.765	10,42	0,89
14	Nutrition & Dietetics	1.127	3.487	3,09	3,16
15	Pediatrics	1.099	2.737	2,49	1,81
16	Med General & Internal	1.061	1910	1,80	1,42

Fonte: ISI - Institute for Scientific Information. CD-Rom: National Science Indicators - Base Deluxe – SCI 2009, USA.

PRODUÇÃO CIENTÍFICA

Entre as 48 principais especialidades médicas, Oncologia é a de maior impacto em produção científica no Brasil (quinquênio 2005 – 2009).

Fonte: ISI – Institute for Cientific Information, CD-Rom: National Science Indicators –Base de Luxe – SCI 2009, USA



141 Artigos publicados em Revistas Internacionais até outubro de 2010.

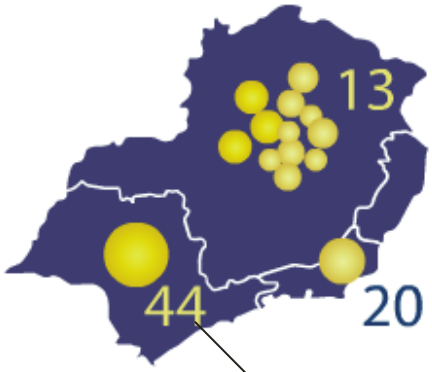
Hospital A.C.Camargo
Centro de Tratamento, Ensino e Pesquisa em Câncer

Research and Innovation Center for Cancer Research

inct
institutos nacionais
de ciência e tecnologia

Institutos - Sudeste

77 Institutos



Região Sudeste - SP

SP
RJ
MG

SP - Instituto Nacional de C&T em Metrologia das Radiações na Medicina

SP - Instituto Nacional de C&T para Mudanças Climáticas

SP - Instituto Nacional de C&T de Neurociência Translacional

SP - Instituto Nacional de C&T de Obesidade e Diabetes

SP - Instituto Nacional de C&T em Oncogenômica

SP - Instituto Nacional de C&T em Óptica e Fotônica

SP - Instituto Nacional de C&T de Políticas do Álcool e Drogas

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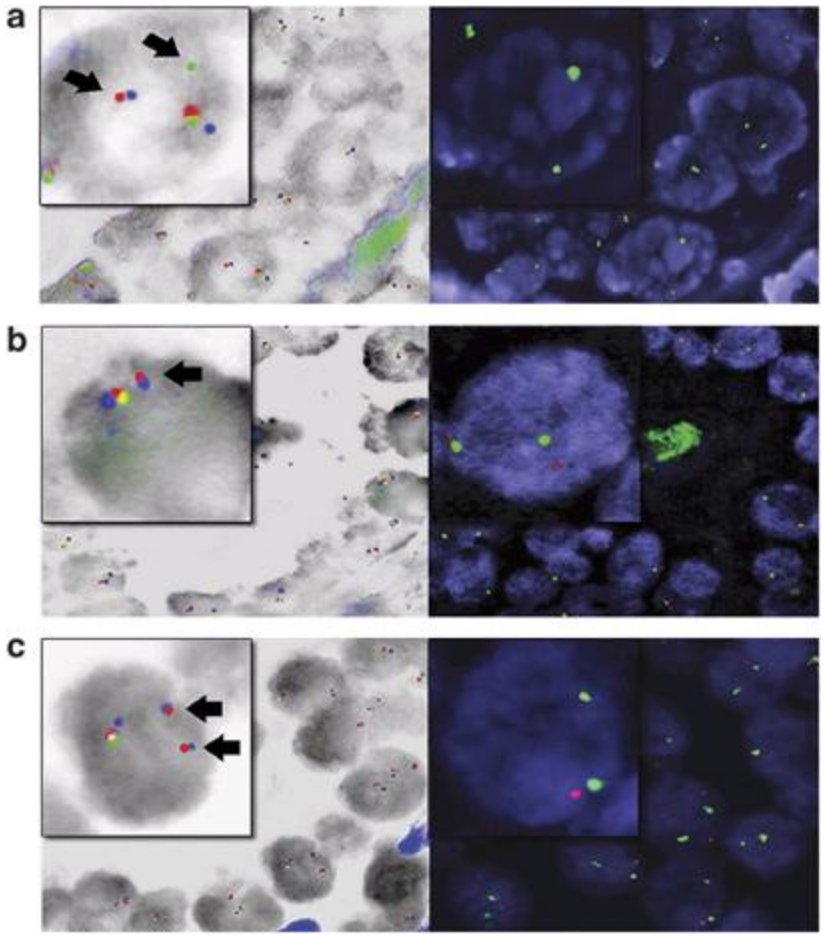


Yoshimoto et al, Britsh Journal Cance, 97,678, 2007

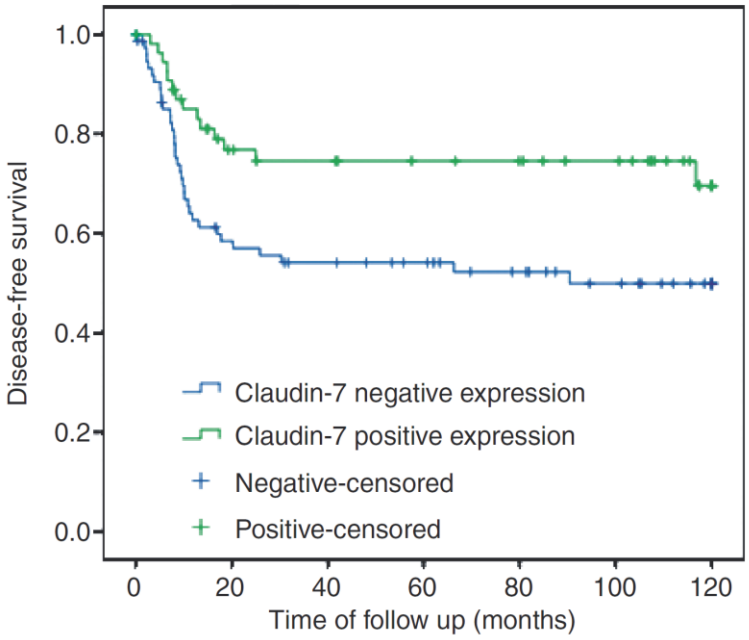


Figure 2. Survival curve of oral squamous cell carcinoma patients with either positive claudin-7 expression or negative expression. The disease-free 10-year survival rate for patients with positive (green line) claudin-7 expression and negative (blue line) expression was 69.9% and 49.9%, respectively.

Silvia Vanessa Lourenço, et.al, Histopathology 2010

Table 1. HCGP and CGAP transcript sequence generation and clustering

ORESTES submitted to GenBank	823,121 sequences
CGAP EST submitted to GenBank	1,214,358 sequences
TOTAL EST submitted to GenBank	2,037,479 sequences
Total clusters	32,129 clusters
Total clusters with known genes	22,152 clusters
Clusters without known genes	9,977 clusters
Clusters without known genes but with coding potential	1,285 clusters
Estimated total genes based on HCGP and CGAP data	23,437 genes

Brentani H. et al, Proc Natl Acad Sci U S A; 100(23):13418-13423,2003

Array Production:

With Bioinformatics, we can design "project-oriented" arrays,

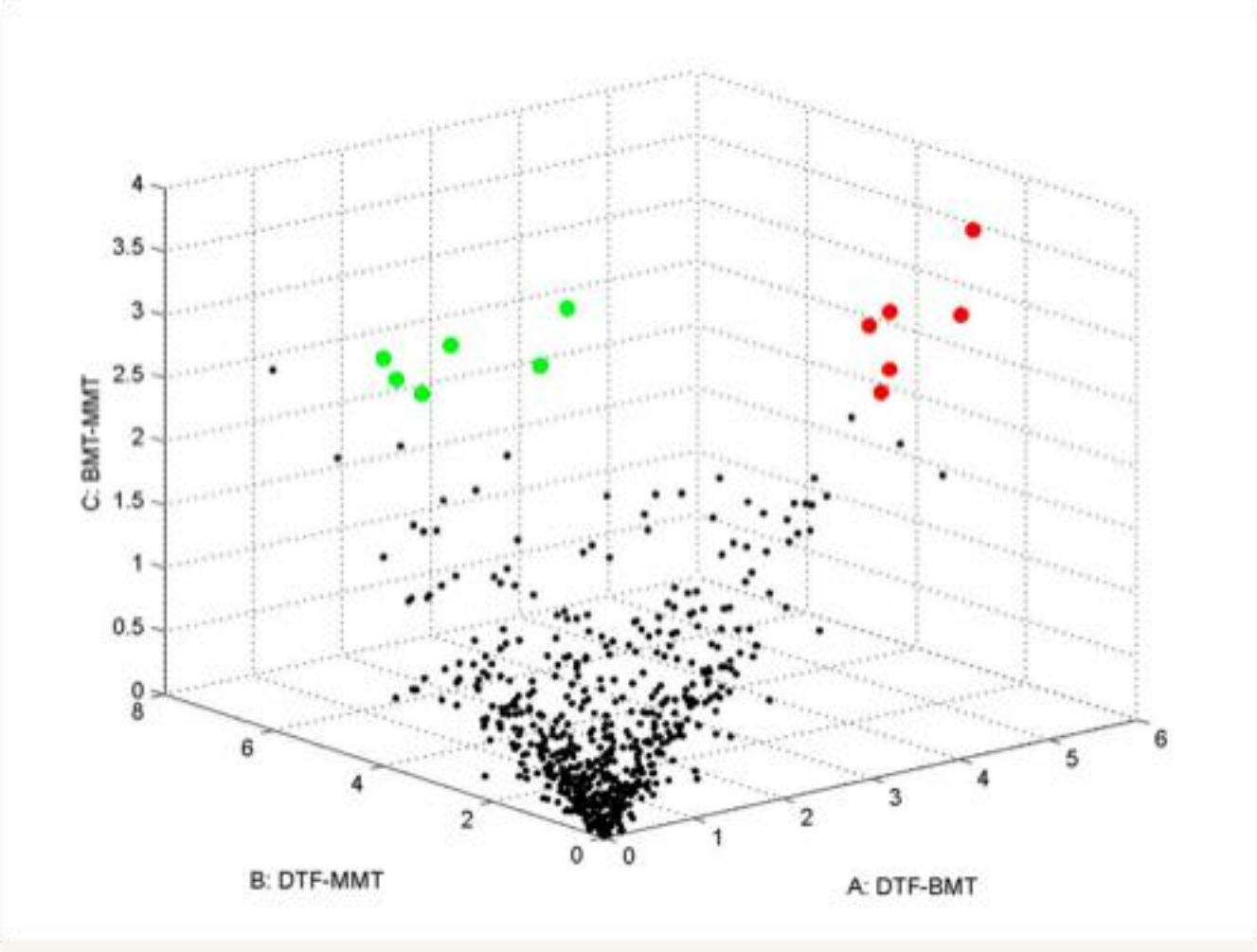
Exploitation of ORESTES clone collection.

4.8K: **Only full length genes**
Filtered for repetitive sequences
Single hit with human genome
Less than 85% homology with any other stretch of 100bp within the human genome
3' end most, but 5' from the first polyA signal
Not less than 300bp
Sequence verified
Link to external databases (NCBI, SOURCE, GO, etc)

Brentani R.R et al – Critical Reviews in Oncology Hematology 54:95-105, 2005

Some clinically relevant questions we are currently pursuing:

- Can we improve diagnosis?



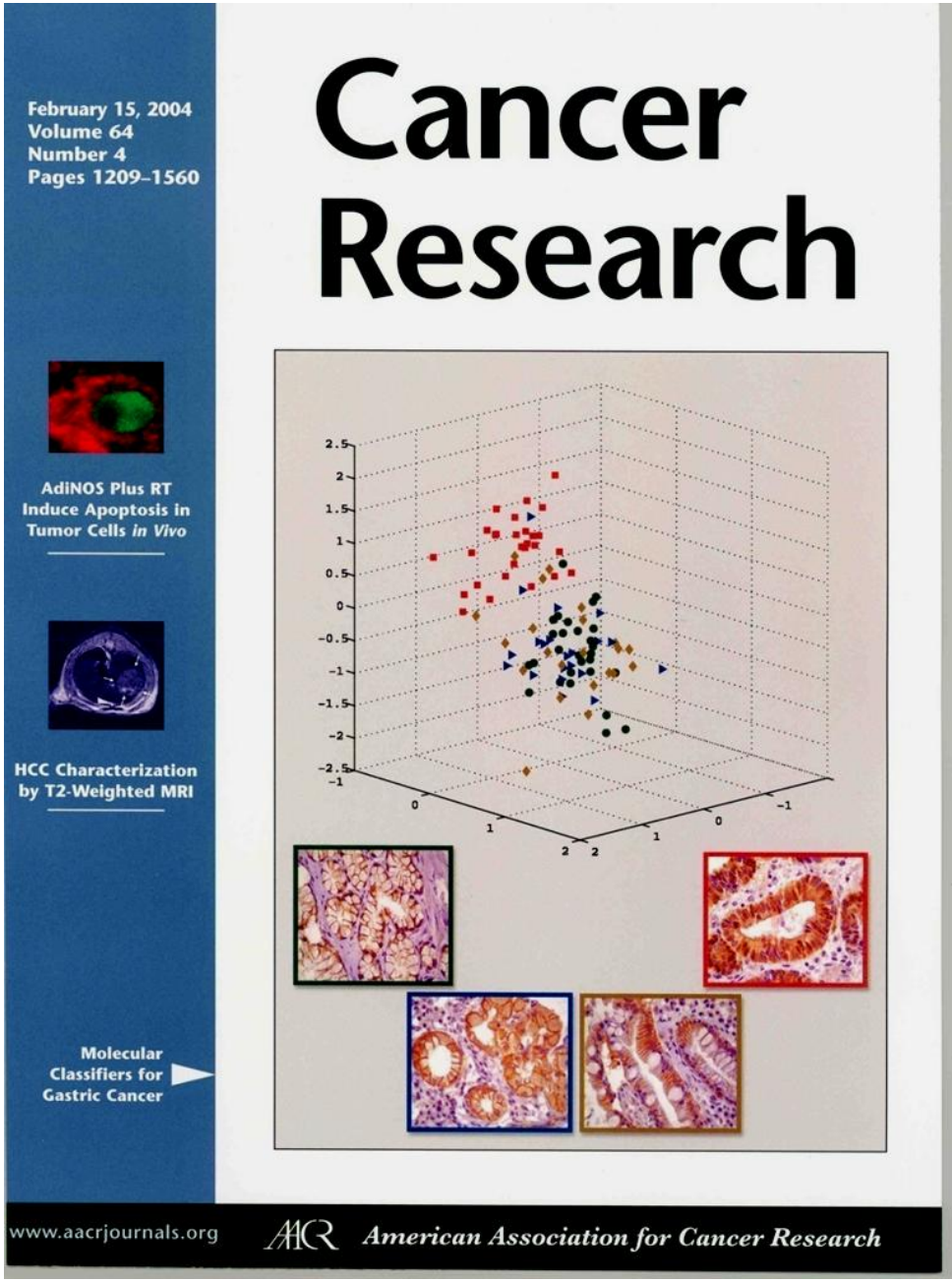
Isabella Werneck Cunha, et al; Translational Oncology (2010) 3, 23-32

- Can we improve prognosis?

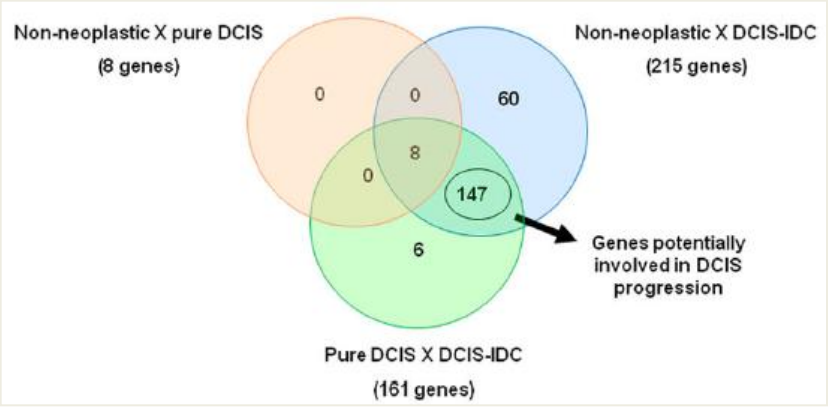
The use of Fisher's Discriminant Analysis to define predictive trios of genes for gastric cancer

About the Cover

The cover shows a molecular classifier for gastric cancer based on the expression levels of three genes in normal gastric mucosa (green frame) gastritis (blue frame), intestinal metaplasia (brown frame) and gastric adenocarcinoma (red frame). The authors describe the construction of molecular classifiers based on trios of genes that can discriminate between malignant and non-malignant samples. Importantly, some samples of intestinal metaplasia, known to be at higher risk of becoming malignant, showed signatures that resemble that of a tumor sample. For details, see the article by Meireles et al. on page 1255 of this issue.



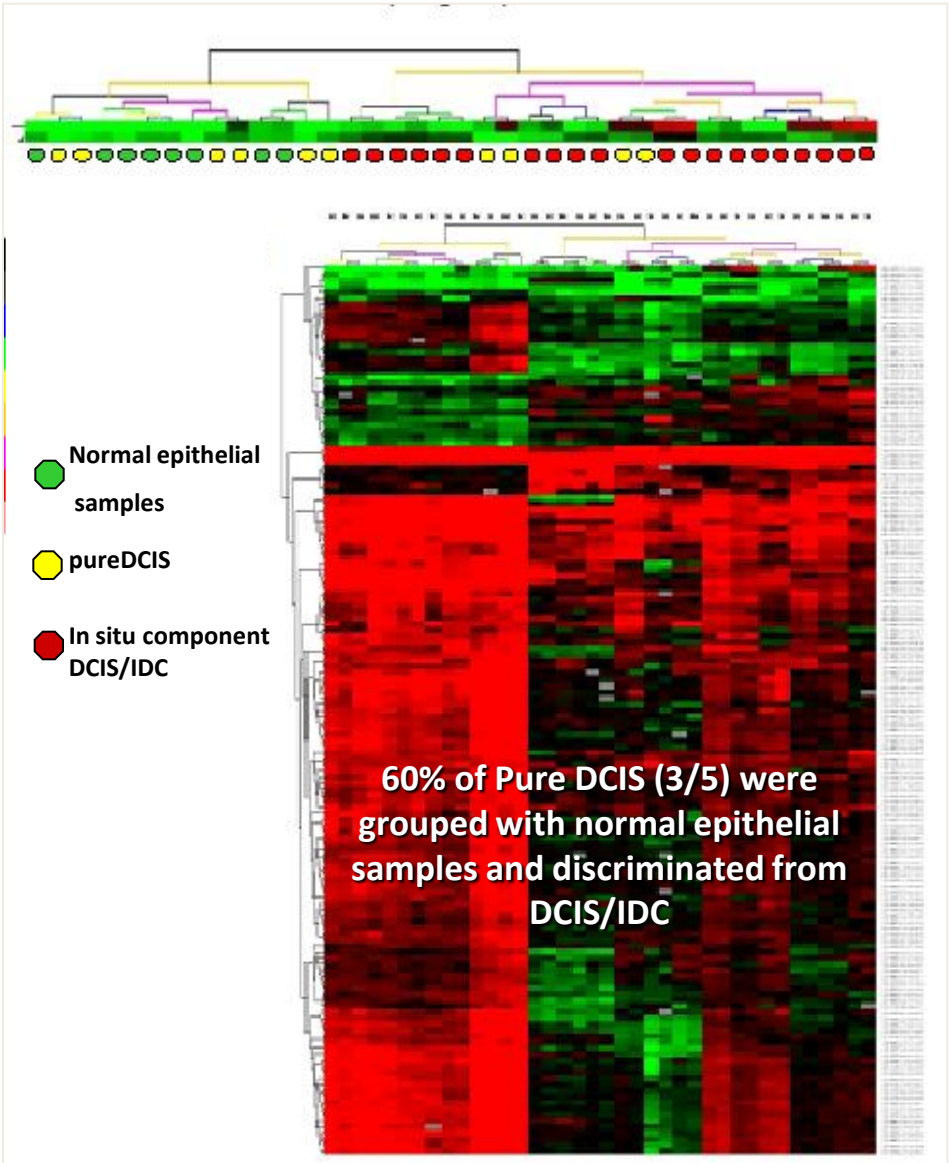
Gene expression signature for DCIS progression



147 differentially expressed genes (DEG)

Statistical significant enrichment:

- cell adhesion (represented by *C20orf42, LPXN, LKC, DGCR2, AZGP1, CHST10, ITGB2, PLEKHC1, PCDH10 and NEDD9*)
- cellular defense (represented by *CXCL9, MAPRE2* and *C3AR1*)



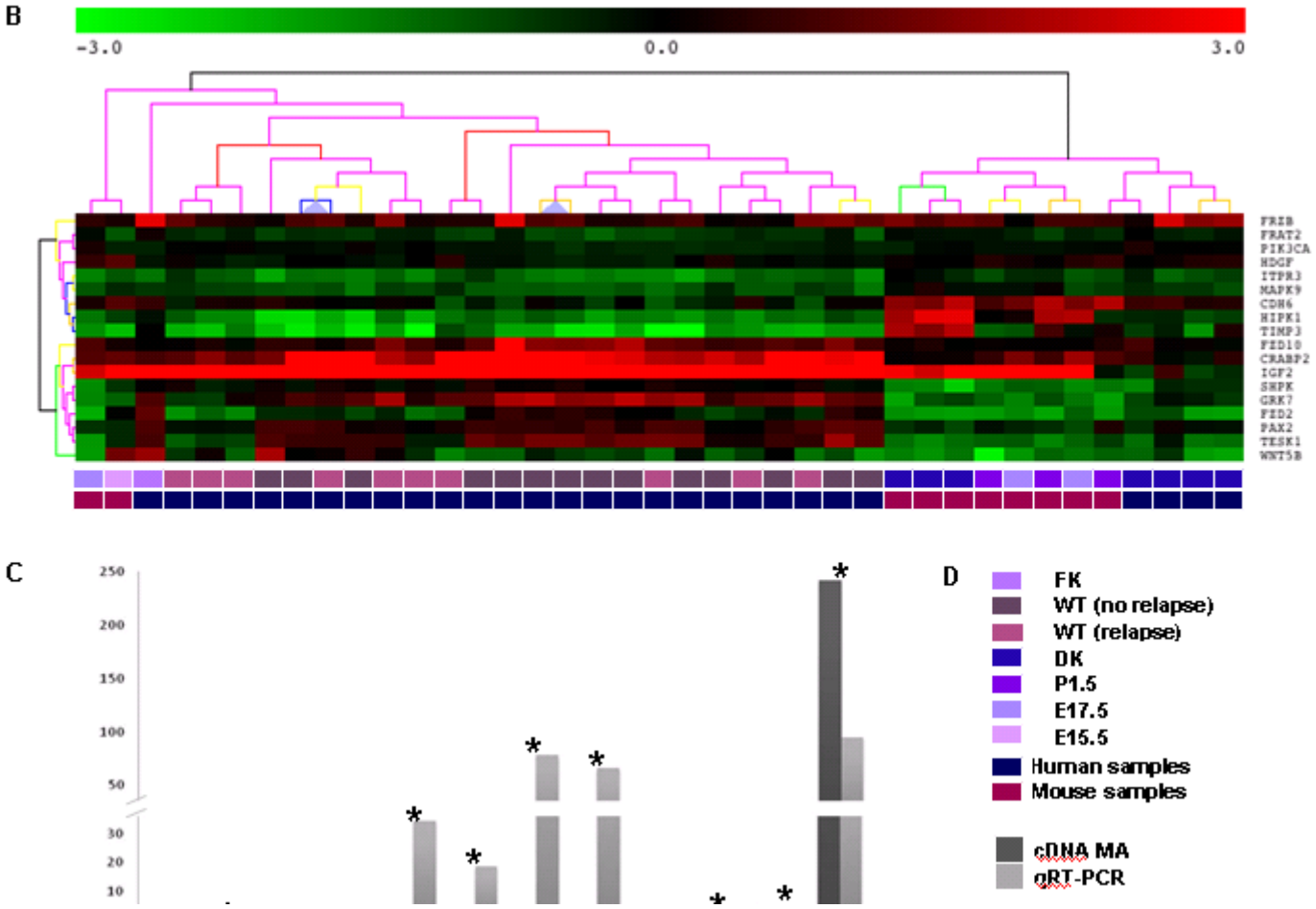
Castro *et al.*, Breast Cancer Res. 2008

- Can we investigate etiology?

Unsupervised hierarchical clustering based on the expression patterns of the 18 genes recapitulated in WT

Samples from differentiated and intermediate kidneys from humans and mice were grouped together and discriminated from the WT samples.

WT samples were grouped with the pool of human fetal kidneys and the earliest mouse embryonic kidneys

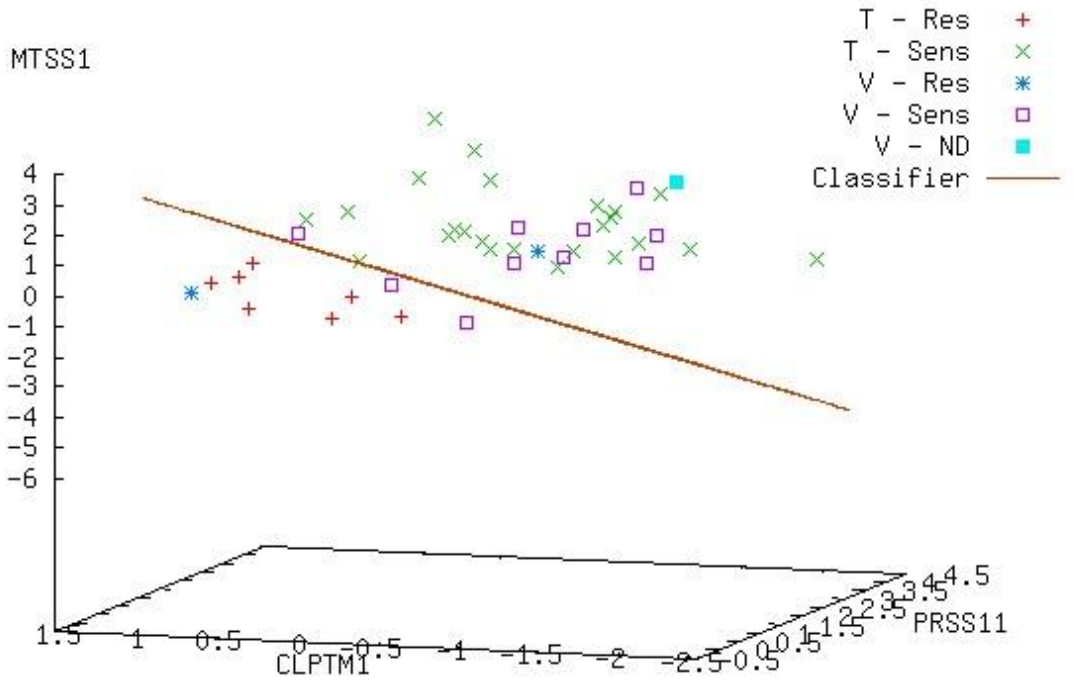


•Model for interspecific hybridization proved to be appropriate for studying human tumorigenesis and mouse embryogenesis

• Gene expression signature linked with Wnt and related signaling pathways was associated with WT onset.

•**Maschietto et al., *Cell, Death and Disease, in press***

- Can we predict response to therapy?



Folgueira et al, Clin Cancer Res. 2005 Oct 15;11(20):7434-7443

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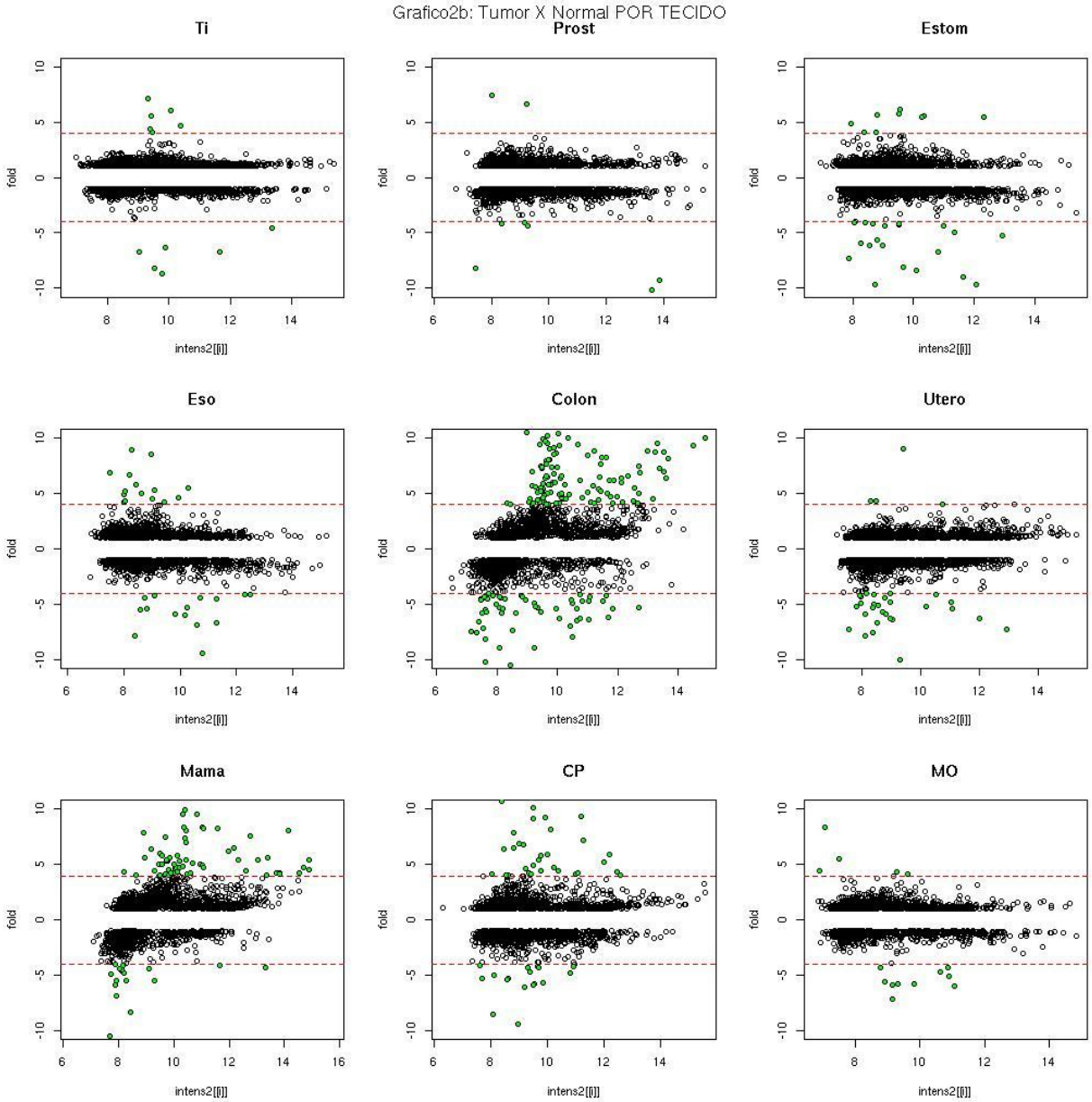
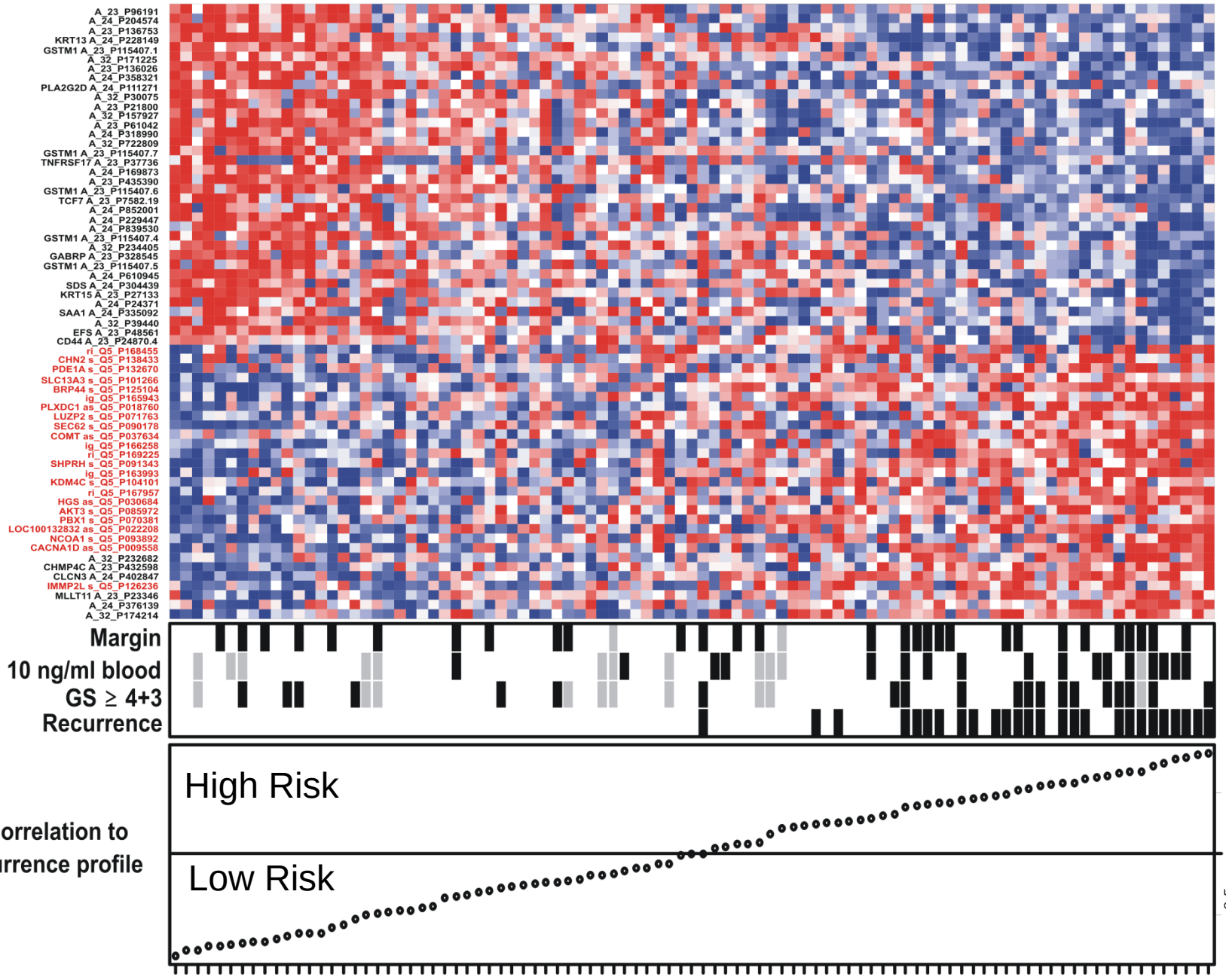


Mello, B.P., et al, Nucleic Acids Research, 2009

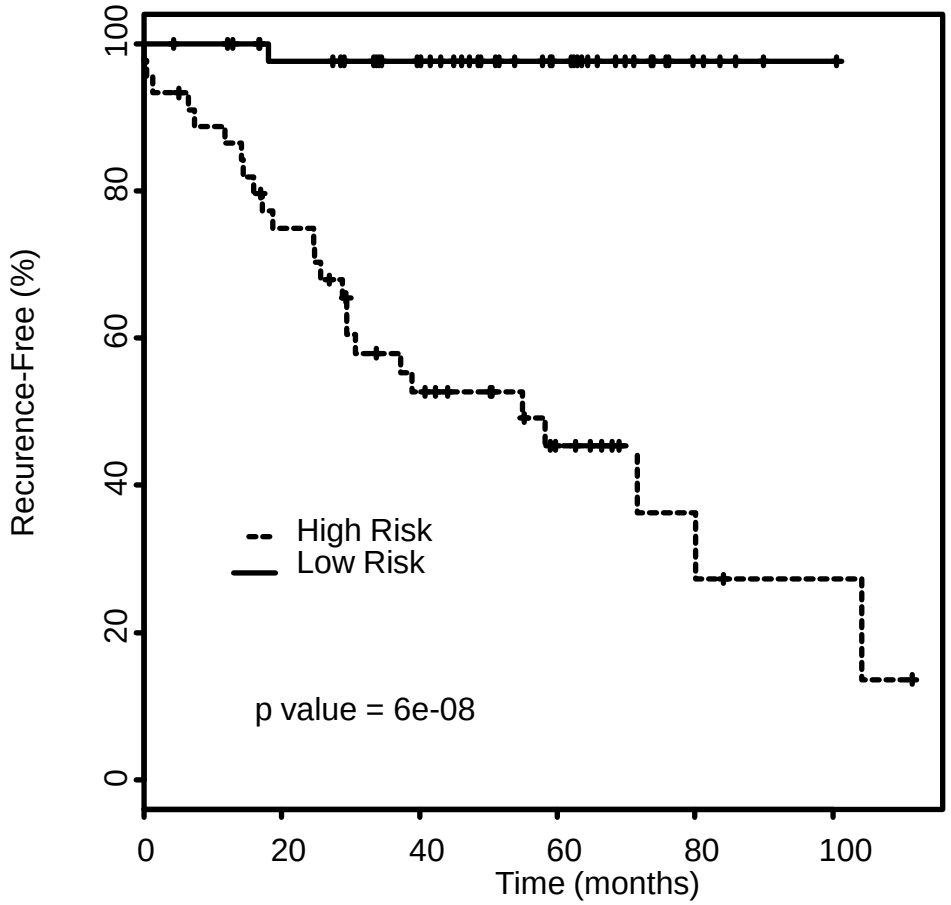
Amostras sem alteração cromossômica (CGH)
Amostras com alteração cromossômica (CGH)
Amostra sem CGH

ncRNA_Transritos intrôncicos e intergênicos

Genes codificadores de proteína



Análise de sobrevida – Alto e baixo risco baseados em expressão gênica



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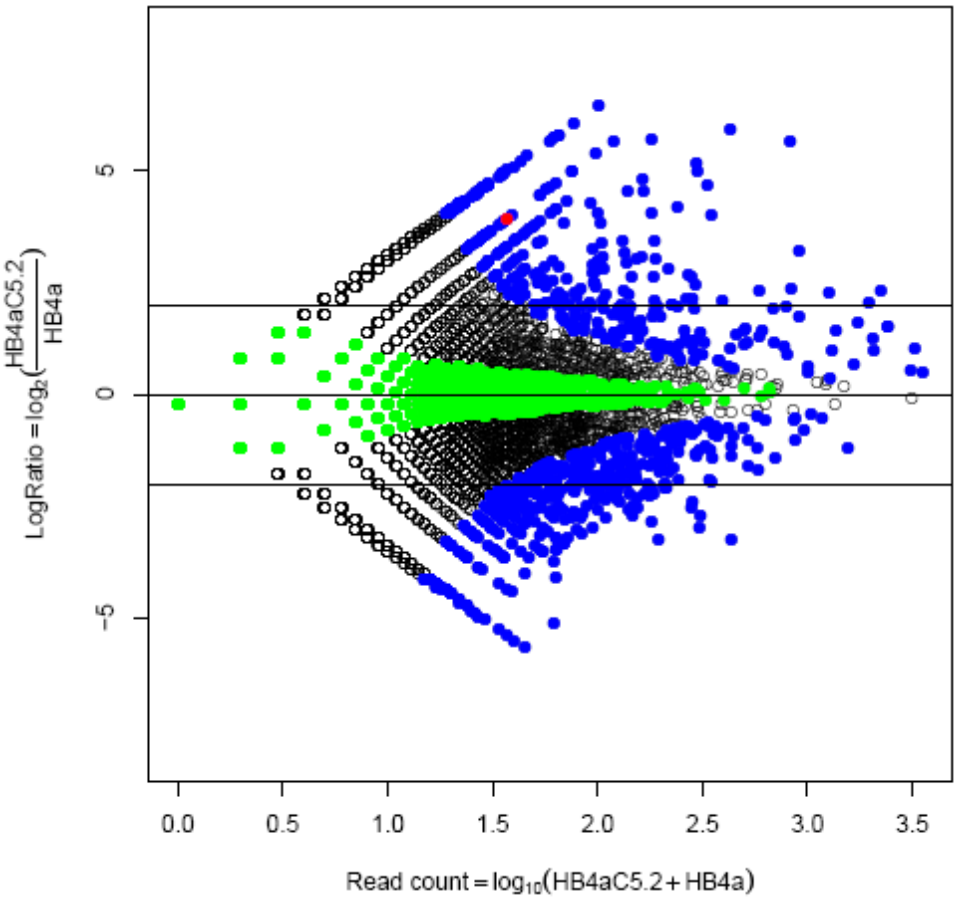

Carraro et al, PlosOne, 2011, 6 e 21022