R-spondin3 is associated with basal-progenitor behavior in normal and tumor mammary cells

Supplementary Tables

Supplementary Table S1. Samples of malignant and benign breast lesions used for RSPO3 expression analysis by IHC

Diagnosis	RSPO3			
		Non- neoplastic breast tissue		
	Neoplasia	Lobular structure	Ductal structure	Stroma
DCInNOS	Negative	Absent	Luminal columnar cells ++/+++	Negative
DCInNOS	+++	Mioepithelial and basal columnar cells +++	Basal cell +++	Lymphocytes +++
DCInNOS	+	Absent	Absent	lymphocytes +
DCInNOS	++/+++	Absent	Absent	Negative
DCInNOS	Negative	Absent	Luminal and basal columnar cells +++	Negative
DCInNOS	Negative	Absent	Absent	Negative
DCInNOS	+++	Mioepithelial cells +++	Luminal and Basal columnar cells +++	Fibroblast +++ Lymphocytes +++
DCIS + DCInNOS	++	Absent	Absent	Absent
DCInNOS	+	Absent	Absent	Negative
DCInNOS	Negative	Absent	Basal columnar cells +++	Negative
DCInNOS	++	Absent	Absent	Negative
DCInNOS	++	Absent	Luminal and basal columnar cells +++	Negative
DCInNOS	+/++	Absent	Luminal and basal columnar cells +++	Negative
DCInNOS	+++	Absent	Absent	Negative
DCInf. mucinous	+	Mioepithelial and basal columnar cells +++	Luminal and basal columnar cells +++	Lymphocytes +++
LCIS +LCInf.	++	Hyperplasia Mioepithelial cells +++	Basal columnar cells +++	Negative
LCIS + Inf.	++/+++	Mioepithelial cells ++	Luminal and basal columnar cells ++	Negative
LCInf.	Negative	Absent	Luminal and basal columnar cells ++	Negative
Dysplasia fibrous	Absent	Mioepithelial and basal columnar cells +++	Luminal and basal columnar cells +++	Lymphocytes +++
Dysplasia fibrous	Absent	Mioepithelial ++ and basal columnar cells +++	Absent	Negative
Dysplasia fibrous-cystic	Absent	Hyperplasia Mioepithelial cells +++	Basal columnar cells +++ Mioepithelial cells +++	Negative
DCIS: ductal carcinoma *in situ*; DCInf. NOS: ductal carcinoma infiltrative not otherwise specified; LCIS: lobular carcinoma *in situ*; LCInf.: lobular carcinoma infiltrative. Positive: (+) mild, (++) moderate and (+++) intense.				

Supplementary Table S2. Comparative analysis of RSPO3 expression and cancer stages by IHC using a breast cancer tissue micro-array

Cancer stage	RSPO3					
	Negative		Positive		Total	
	n	%	n	%	n	%
"Early"(0-IIIA)	20	31.2	44	68.8	64	100
IIIB- IV	2	20.0	8	80.0	10	100
Total	22	29.7	52	41.9	74	100

Stage is expressed as a number on a scale of 0 through IV. Fisher test, p value=0,713. Non-statistically significant association was obtained.

Supplementary Table S3. Comparative analysis of RSPO3 and clinically relevant biomarkers (ER, PR, and Her2) expression levels by IHC using a breast cancer tissue micro-array

| | RSPO3 | | | | | | | |
| | Negative | | Low | | Strong | | Total | |
Biomarker profile	n	%	n	%	n	%	n	%
PR (-) ER (-) Her2 (-)	4	40.0	4	40.0	2	20.0	10	100
PR (+) ER (+) Her2 (+)	4	21.1	7	36.8	8	42.1	19	100
PR (-) ER (-) Her2 (+)	8	30.8	11	42.3	7	26.9	26	100
PR (+) ER (+) Her2 (-)	4	40.0	5	50.0	1	10.0	10	100
PR (-) ER (+) Her2 (-)	1	33.3	2	66.7	0	0.0	3	100
PR (+) ER (-) Her2 (+)	0	0.0	0	0.0	1	100.0	1	100
PR (-) ER (+) Her2 (+)	1	20.0	2	40.0	2	40.0	5	100
PR (+) ER (+) Her2 (-)	0	0.0	0	0.0	0	0.0	0	0
Total	22	29.7	31	41.9	21	28.4	74	100

Supplementary Table S4. Comparative analysis of RSPO3 and Ki67 expression by IHC using a breast cancer tissue micro-array

Ki67	RSPO3					
	Negative		Positive		Total	
	n	%	n	%	n	%
Negative	6	33.3	12	66.6	18	100
Positive	16	28.6	40	71.4	56	100
Total	22	29.7	52	70.3	74	100

Non-statistically significant association was obtained; Chi-squared test; p=0.770.