

## De toepassing van MLPA in de diagnostiek van het mammacarcinoom

C.B.Moelans, UMCU  
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## MLPA bij borsttumoren

Multiplex Ligation-dependent Probe Amplification

- MLPA voor HER2 amplificatie detectie
- MLPA voor gelijktijdige kopie aantal bepaling van meerdere genen
- Polysomie 17: wel of niet?

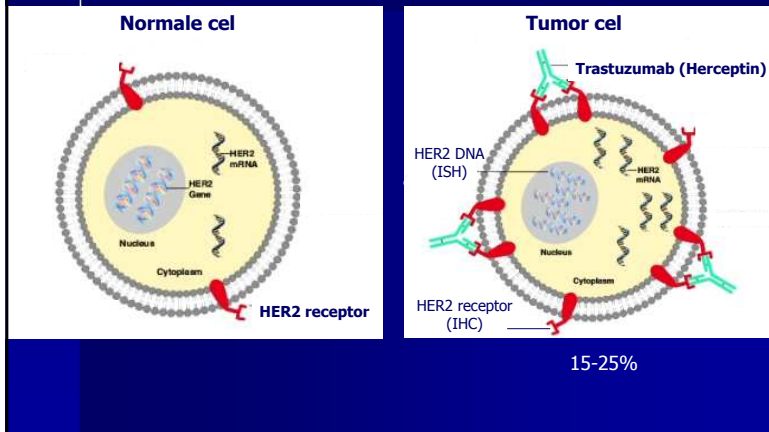
## MLPA

### HER2 amplificatie detectie

## HER2/ *neu*, c-erbB2, ERBB2

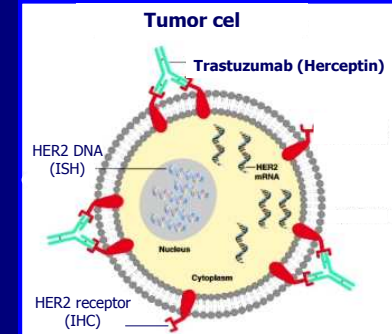
- HER2 is een groeifactor receptor (onco)gen op chromosoom 17q12-q21
- HER2 codeert voor een transmembraan eiwit P185 of erbB2 of neu
- *HER2* regelt celgroei/celdood via PI3K en MAPK pathway

## HER2 diagnostiek

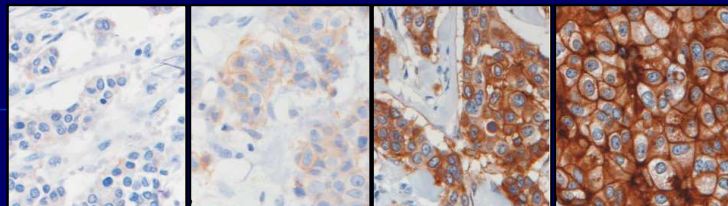


## HER2 status bepaling

- DNA niveau
  - FISH
  - CISH
  - SISH
  - MLPA (PCR)
  - Southern Blot
- RNA niveau
  - TargetPrint
  - RT-PCR
- Proteïen niveau
  - IHC (Hercep test)
  - ELISA



### IHC (Hercep test)



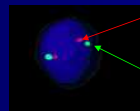
0

1+

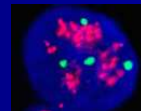
2+

3+

FISH



2 HER2 kopieën  
2 CEN17 kopieën  
HER2/CEN17 ratio <1.8  
→ Geen amplificatie



Veel HER2 kopieën  
2 CEN17 kopieën  
HER2/CEN17 ratio ≥2.2  
→ Amplificatie

## Immuunhistochemie

- Eenvoudig
- Snel
- Goedkoop

**MAAR**

Verschillende uitslagen op verschillende labs door proces variabiliteit en interpretatie verschillen

# Immuunhistochemie

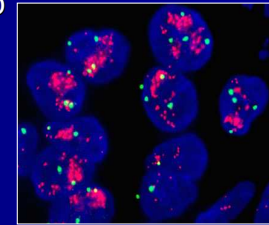
## Procesvariabiliteit

- SKML 2009: 47 labs
  - 10 ≠ antilichamen,
  - 9 ≠ voorbehandelingen,
  - 12 ≠ afwerkingsmethoden
- Fixatietijden

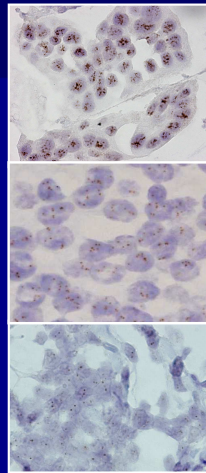
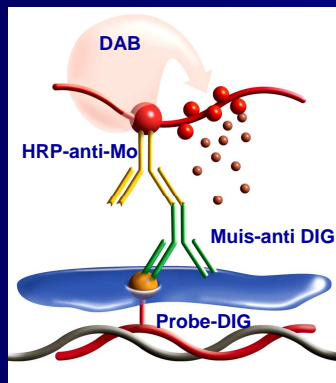
# FISH

## Kwantitatiever MAAR

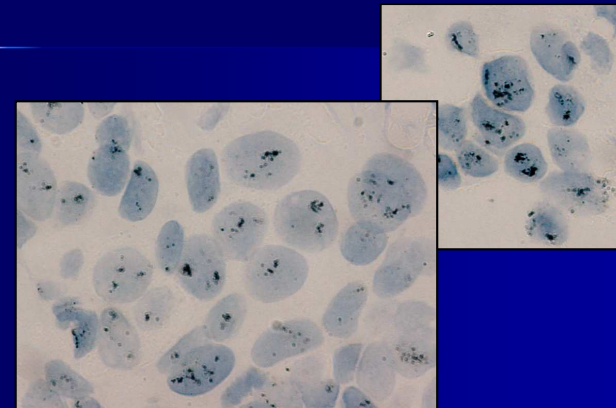
- Fluorescentie microscoop
- Slechte morfologie
- Autofluorescentie
- Fluorescentie uitdoving
- Sterke vergroting, olie
- Duur (160€/coupe)
- Tijdsrovend



# CISH



# SISH



## CISH/SISH

- Geen uitdoving → permanent bewaren
- Betere morfologie
- Geen fluorescentie microscoop
- Sneller scoresn
- Minder duur (100€/coupe)

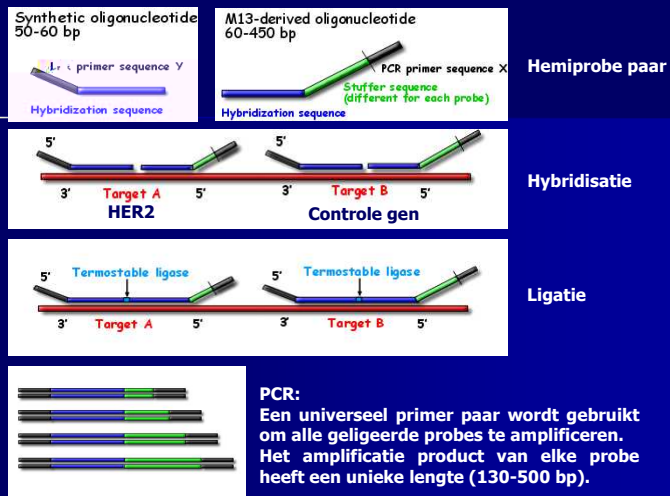
Maar:

- Geen CEP17 informatie
- Nog steeds semi-kwantitatief

## MLPA

### Multiplex Ligation-dependent Probe Amplification

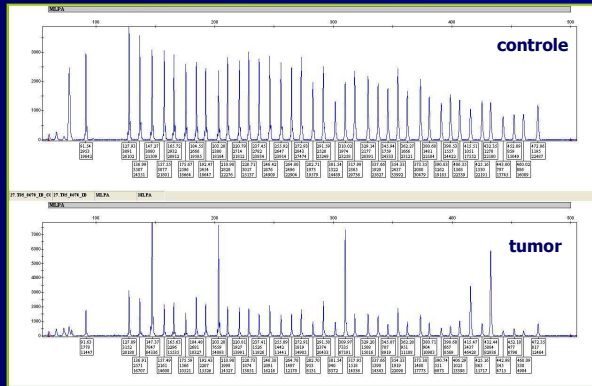
- MLPA kit (MRC Holland, Amsterdam)
- 40-50 probes gericht tegen een groot aantal genen
- 50-200 ng DNA geïsoleerd uit paraffine (of vries) materiaal
- Probe hybridisatie → Ligatie → "kwantitatieve PCR"



## MLPA

- PCR product bevat amplificatieproducten van 40-50 probes (130-500 bp)
- Capillaire elektroforese met fragment analyse (Genescan) software → piekenpatroon

# MLPA kit (P004-A1)



# Coffalyser

- Coffalyser software vergelijkt test samples met negatieve controle samples
- Een verschil in relatieve piekoppervlakte/hoogte geeft een verandering aan in het kopie aantal van de probe target sequentie
  - Ratio HER2/controle <0.7 → loss
  - Ratio HER2/Controle <1.3 → geen amplificatie
  - Ratio HER2/Controle 1.3-2.0 → gain
  - Ratio HER2/Controle >2.0 → amplificatie

name	Chr	Start (kb)	Length (kb)	Insertion (kb)	Control Ratio	A		B		C		D	
						6-1-2010 9:40	6-1-2010 9:40	6-1-2010 9:40	6-1-2010 9:40	6-1-2010 9:40	6-1-2010 9:40	6-1-2010 9:40	
ESR1 probe 11998.L12824	11	124	1	1.0014	0.0061	0.0041	1.0048	0.8811	0.9524	0.8911			
ESR1 probe 11998.L12826	11	232	2	1.0020	0.0007	0.0055	1.0454	0.9091	0.9050	1.1169			
EGFR probe 0208.L10283	7	171	2	1.0039	0.1025	1.0188	0.9286	0.8084	0.9602	1.1749			
EGFR probe 0209.L10336	7	171	2	1.0014	0.0604	0.9284	1.0715	0.8868	0.9607	1.0007			
FGFR1 probe 0444.L03826	8	113	3	1.0021	0.0750	0.9582	0.9845	0.9734	0.9791	1.1354			
FGFR1 probe 0405.L04004	8	113	3	1.0014	0.0591	0.9524	1.0141	0.9402	1.0112	1.0029			
ADAM9 probe 11964.L12820	11	123	138	7	1.0003	0.0202	0.9695	1.0240	1.0188	0.9578	1.0042		
ERBB2 probe 11998.L12821	11	121	148	8	1.0007	0.0460	0.9695	1.0591	0.9890	0.9552	1.0244		
ERBB2 probe 12003.L12831	11	121	148	9	1.0024	0.0794	0.9847	0.9879	0.9979	0.9916	1.1397		
PROX1A probe 12004.L12830	11	133	145	10	1.0012	0.0550	1.0143	0.9824	0.9654	0.9701	1.0050		
MTOR probe 0415.L10350	11	281	11	1.0020	0.0815	0.9524	1.0255	0.9285	0.9727	1.1338			
MTOR probe 0412.L10357	11	337	12	1.0011	0.0525	0.9663	0.9223	1.0103	0.9486	1.0430			
MVC probe 0247.L0848	11	118	13	1.0104	0.1586	1.0402	0.9739	1.2146	1.0440	0.7754			
MVC probe 0072.L10169	11	24	14	1.0006	0.1257	1.0184	0.8804	0.9847	1.0066				
MVC probe 0266.L10025	11	177	15	1.0016	0.0665	0.9516	1.0250	1.0070	0.9521	0.9133			
CCND1 probe 0540.L10408	12	113	12	1.0033	0.0040	0.9807	0.9920	0.9114	0.9916	1.1608			
CCND1 probe 0585.L10746	12	113	12	1.0009	0.0804	0.9804	1.0231	0.9027	0.9569	1.1842			
CTDSP3 probe 09173.L09347	11	113	15	1.0024	0.0768	0.9672	0.9913	1.0771	1.0783	0.8980			
CTDSP3 probe 09174.L09348	11	113	15	1.0009	0.0466	0.9962	0.9952	1.0126	1.0211	0.9774			
CDH1 probe 0280.L10349	11	221	20	1.0041	0.1011	1.0320	1.0252	0.9870	0.9591	1.1402			
CDH1 probe 0240.L10337	11	221	21	1.0009	0.1529	0.9872	0.9722	1.2174	1.1126	0.9704			
TRAF4 probe 09178.L09350	11	112	22	1.0005	0.0339	0.9899	1.0264	1.0313	1.0073	0.9474			
CPS1 probe 0218.L09913	11	112	25	1.0014	0.0587	0.9688	1.0068	0.9872	1.0485	0.8949			
MEI1 probe 09953.L13205	17	121	24	1.0010	0.0600	1.0105	0.9853	1.0449	1.0318	0.8795			
ERBB2 probe 00675.L10146	17	142	25	1.0006	0.0388	0.9979	1.0546	0.9734	0.9895	0.8778			
ERBB2 probe 00685.L10149	17	142	25	1.0037	0.0850	1.0003	1.0380	0.9103	0.9993	1.1209			
ERBB2 probe 00384.L12811	17	142	25	1.0056	0.1162	0.9624	1.0081	1.1471	1.0527	0.8078			
ERBB2 probe 12014.L10315	17	142	24	1.0013	0.0409	0.9914	1.0121	0.9027	0.9569	1.1842			
CDCE4 probe 08913.L13204	17	142	196	20	1.0024	0.0773	0.9453	1.0883	0.9898	0.9987	1.0091		
TOP2A probe 11968.L13177	17	121	30	1.0009	0.0700	0.9668	0.9967	0.9850	0.9240	0.9450			
TOP2A probe 12004.L12828	17	121	30	1.0010	0.0500	1.0119	1.0037	0.9566	0.9553	1.0774			
TOP2A probe 11968.L12822	17	121	32	1.0002	0.0244	0.9862	1.0182	0.9842	1.0108	1.0122			
MMP7 probe 03354.L08311	17	121	31	1.0034	0.0054	0.9641	1.0219	0.9284	0.9412	1.1615			
BIRC5 probe 0217.L10340	17	121	36	1.0004	0.0589	0.9688	0.9948	0.9870	0.9485	0.8949			
BIRC5 probe 03189.L10249	17	121	35	1.0035	0.0044	0.9825	1.0107	0.9834	0.9886	1.1463			
BIRC5 probe 02023.L11038	17	121	36	1.0005	0.0448	0.9665	1.0128	0.9409	0.9444	1.0774			
CENPF probe 09176.L09344	17	121	37	1.0037	0.0975	0.9920	0.9550	1.1443	1.0555	0.9875			
CENPF probe 0381.L10248	17	121	36	1.0003	0.0263	0.9627	1.0236	1.0248	1.0002	0.9681			
CENPF probe 10256.L10712	17	121	37	1.0011	0.0249	0.9471	1.0249	1.1376	1.0053	1.0120			
Probe 08054.L09059	17	121	38	1.0033	0.1122	1.0014	1.0941	1.1130	0.9994	0.9237			
Probe 02760.L0707	17	121	41	1.0002	0.0662	0.9662	1.0016	0.9445	0.9749	1.0074			
Probe 00204.L09501	17	121	42	1.0022	0.0742	0.9861	0.9969	1.0733	0.9858	0.9297			
Reference probe 00603.L00500	17	121	43	1.0010	0.0465	0.9633	1.0141	0.9338	0.9749	1.0074			
Reference probe 10223.L10704	17	121	44	1.0004	0.0847	0.9444	0.9823	1.0690	1.0623	0.8400			
Reference probe 02018.L10010	17	121	45	1.0003	0.0243	0.9443	0.9946	1.0243	0.9188	0.9509			
Reference probe 10224.L10705	17	121	46	1.0004	0.0316	0.9641	0.9821	1.0148	0.9520				
Reference probe 0007.L10016	17	121	47	1.0002	0.0484	0.9443	0.9448	0.9448	1.1047				
Reference probe 11350.L12075	17	121	48	1.0014	0.0588	0.9697	1.0326	0.9241	0.9725	1.0790			
Reference probe 00078.L10065	17	121	49	1.0002	0.0226	1.0284	0.9752	1.0089	1.0006	0.9999			
Reference probe 00079.L10065	17	121	49	1.0004	0.0404	1.0440	0.9604	1.0006	0.9606	1.0006			

06-182.3 ESR1	1.51	0.97
06-182.3 ESR1	1.45	1.13
06-182.3 ESR1	1.31	1.02
07-055.2 EGFR	1.05	1.05
07-055.2 EGFR	1.05	1.17
07-055.2 EGFR	1.15	1.14
08-0338.4 EGFR1	0.97	0.99
08-0338.4 EGFR1	0.98	1.08
08-039.0 ADAM9	1.26	1.21
08-042.3 IKKKB	1.01	1.06
08-042.3 IKKKB	0.95	0.89
08-071.1 PRDM14	1.1	0.89
08-128.8 MYC	1.46	1.46
08-128.8 MYC	1.14	1.05
08-128.8 MYC	1.13	1.32
11-069.2 CCND1	1.04	1.05
11-069.2 CCND1	0.7	0.86
11-069.2 CCND1	1.01	1.13
11-078.9.1.1 TORF30	1.05	1.05
11-078.9.1.1 TORF30	1.13	1.08
16-367.4 CDH1	0.83	0.74
16-367.4 CDH1	1.09	0.84
16-367.4 CDH1	1.11	0.84
17-023.1 TRAF4	1.13	0.62
17-023.1 TRAF4	1.03	0.65
17-023.1 TRAF4	1.11	0.75
17-023.1 TRAF4	0.89	0.75
17-035.1 ERBB2	8.28	10.3
17-035.1 ERBB2	9.12	9.2
17-035.1 ERBB2	9.2	9.2
17-035.1 ERBB2	10.41	9.2
17-035.1 ERBB2	6.99	8.59
17-035.1 ERBB2	10.05	9.10
17-035.1 ERBB2	10.69	9.11
17-035.1 ERBB2	11.7	11.2
17-035.1 ERBB2	11.76	11.6
17-035.1 ERBB2	11.55	11.10
19-035.0 CCNE1	1.11	1.11
19-035.0 CCNE1	1.04	0.97
19-035.0 CCNE1	1	1.03
23-054.1 RAB34	0.97	1.15
e	0.97	1.15
e	1.01	0.95
e	0.91	0.95
e	1.15	1.15
e	0.99	1.29
e	0.88	0.74
e	1.12	1.12
e	0.96	1.08

## MLPA

- Verbeterde kwantitativiteit
- Goedkoop (40€/sample, als 5 borsttumor samples en 4 negatieve control samples in duplo/ analyse)
- Polysomie informatie
- Meer genen (probes) gelijktijdig analyseren

Maar:

- Geen morfologie
  - Heterogeniteit
  - DCIS (ductal carcinoma *in situ*)
- Tumor percentage

## MLPA-IHC-CISH

n=518

	Overeenkomst
IHC-CISH	88%
MLPA-CISH	94%
IHC-MLPA	90%

	Sensitiviteit	Specificiteit	PPV	NPV
IHC	73	92	94	97
MLPA	90	97	90	98

Cellular Oncology 2009,31:1-10

## MLPA

**Gelijktijdig bepalen van de  
amplificatie status van  
meerdere genen**

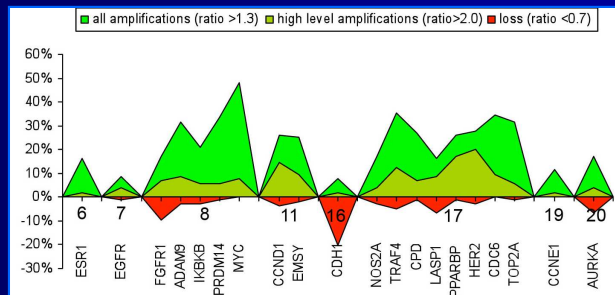
## MLPA (P078-A1)

- HER2
- TOP2A
- ESR1
- ...

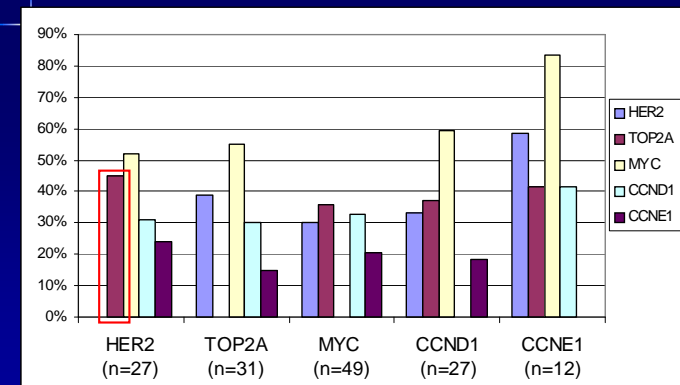
	Prognose	Predictief (Therapie Respons)	% Amplificatie bij borstkanker (range)	Functie
<b>HER2</b>	JA	Herceptin, AC, Taxanen	15-30 %	Receptor
<b>TOP2A</b>	JA	AC	5-10 %	Celdeling
<b>MYC</b>	JA	Herceptin, Tamoxifen	9-15 % (1-94)	Celdeling
<b>CCND1</b>	JA	Tamoxifen	15 % (0-27)	Celdeling
<b>CCNE1</b>	JA	Tamoxifen, Aromatase Inhibitoren	6 %	Celdeling
<b>ESR1</b>	controversieel	Tamoxifen	20.6 % (0-10?)	Receptor
<b>EMSY</b>	JA	-	13 %	DNA herstel
<b>FGFR1</b>	JA	-	8.7 %	Receptor
<b>EGFR</b>	JA	Tamoxifen Gefitinib	5-10 % (7-65)	Receptor
<b>CDH1</b>	JA	-	Loss: 15% IDC, 83% ILC	Metastase

06-193.3 ERB1	1.55	0.97
06-193.4 ERB1	1.46	1.13
06-193.5 ERB1	1.91	1.06
07-955.2 EGFR	0.93	1.06
07-955.3 EGFR	1.06	1.17
07-955.2 EGFR	1.16	1.14
08-0338.4 FGFR1	0.87	0.80
08-0338.4 FGFR1	0.93	1.03
08-039.0 ADAM9	1.26	1.21
08-042.3 IKKB	1.02	0.96
08-042.3 IKKB	0.96	0.80
08-071.1 PRDM14	1.11	0.89
08-128.8 MYC	0.86	1.36
08-128.8 MYC	1.14	1.63
08-128.8 MYC	1.3	1.57
11-089.2 CCND1	1.04	1.03
11-089.2 CCND1	0.7	0.85
11-089.2 CCND1	1.03	1.15
11-075.9 C11ORF30	1.05	1.09
11-075.9 C11ORF30	1.13	1.08
16-067.4 CDH1	0.85	0.74
16-067.4 CDH1	1.07	0.94
16-067.4 CDH1	1.11	0.99
17-023.1 NOS2A	1.13	0.95
17-024.1 TRAF4	1.03	2.68
17-025.8 CPD	1.1	0.98
17-034.3 VSP1	0.90	0.75
17-034.3 MED1	0.98	0.93
17-035.1 ERBB2	5.12	3.72
17-035.1 ERBB2	9.2	3.50
17-035.1 ERBB2	10.41	3.23
17-035.1 ERBB2	6.29	3.52
17-035.1 ERBB2	10.95	3.10
17-035.7 CDC6	1.42	1.11
17-035.3 TOP2A	1.7	1.04
17-035.3 TOP2A	1.25	1.15
17-035.8 TOP2A	1.56	1.19
19-035.0 CCNE1	1.11	0.87
19-035.0 CCNE1	1.05	0.93
19-035.0 CCNE1	1	0.97
20-054.4 AURKA	0.83	1.16
c	0.97	1.13
c	1.01	0.95
c	1.11	1.19
c	1.13	0.91
c	0.93	1.29
c	0.86	0.74
c	1.12	0.94
c	0.96	1.08

## MLPA: P078-A1



## Co-amplificaties



## BCIRG 006 trial

N=3222

AC → T  
**AC → TH** (verhoogde cardiotoxiciteit: 2x zoveel patiënten (2,3%)!  
TCH

"BCIRG-006 demonstrates that the incremental benefit conferred by AC that is known for HER2-positive breast cancers is restricted to TOP2A co-amplified malignancies which constitute a subset (35%) of these cancers"

BCIRG 006, Slamon D, SABCs 2009

## MLPA

### Polysomie 17

## Polysomie 17: Herceptin?

- Extra kopieën van chromosoom 17 leidend tot extra kopieën van HER2
- Indien polysomie 17: geen/slechtere respons op Herceptin

**MAAR >>>**

### Polysomie 17: controversieel:

1. Hofmann M, Stoss O, Gaiser T, et al.  
Central ERBB2 IHC and FISH analysis in a trastuzumab (Herceptin(R)) Phase II monotherapy study: assessment of test sensitivity and impact of chromosome 17 polysomy. *J Clin Pathol* 2007; **1**: 89–94.
2. Kaufman PA, Broadwater G, Lezon-Geyda K, et al.  
CALGB 150002: correlation of ERBB2 and chromosome 17 (ch17) copy number with trastuzumab (T) efficacy in CALGB 9840, paclitaxel (P) with or without T in ERBB2+ and ERBB2– metastatic breast cancer (MBC). *J Clin Oncol* 2007; **25**: 1009.
3. Risio M, Casorzo L, Redana S, Montemurro F.  
ERBB2 gene–amplified breast cancers with monosomy of chromosome 17 are poorly responsive to trastuzumab–based treatment. *Oncol Rep* 2005; **13**: 305–09.
4. Reinholz M, Jenkins RB, Hillman D, et al.  
The clinical significance of polysomy 17 in the ERBB2+ N9831 intergroup adjuvant trastuzumab trial. *Breast Cancer Res Treat* 2007; **106** (supp 1): 11.

## Polysomie 17: prognose?

	Number of specimens	Nottingham prognostic index	Tumour grade	Tumour histology	Tumour size	Tumour nodal status	Oestrogen receptor	Progesterone receptor	Survival
Herrington et al (1995) <sup>9</sup>	49	NR	NA	NR	NA	CI	NR	NR	NR
Persons et al (1996) <sup>12</sup>	55	NR	Y, p17	NR	Y, p17	NR	NA	NA	NR
Ichikawa et al (1996) <sup>32</sup>	106	NR*	NR	NR	NR	Y, a17	NR	NR	NR
Adeyinka et al (1999) <sup>35</sup>	16	NR	Y+	NR	NR	Y+	NR	NR	NR
McManus et al (1999) <sup>32</sup>	69	NR	Y, p17	Y, p17	NA	NA	NR	NR	NR
Botti et al (2000) <sup>35</sup>	28	NR	Y, p17	NR	NR	NA	NR	NR	NR
Visser et al (2000) <sup>32</sup>	28	NR	Y, a17	NR	NR	NR	NR	NR	NR
Tsakamoto et al (2001) <sup>32</sup>	113	NR	NR	NR	NR	Y, p17	m17/ER-	p17/PR-	NR
Fehm et al (2002) <sup>31</sup>	74	NR	NA	NR	Y, p17	NA	NA	m17/PR-	NR
Nakopoulou et al (2002) <sup>34</sup>	42	NR	NA	NA	Y	Y, m17	m17/ER-	NR	Y, m17
Watters et al (2003) <sup>35</sup>	214	Y, p17	Y, p17	NR	NR	NA	p17/ER-	NR	NA
Salido et al (2005) <sup>37</sup>	175	NR	NA	NR	NR	Y, p17	NA	NA	NR
Dal Lago et al (2006) <sup>34</sup>	893	NR	NA	NR	NA	NR	NA/ER+	NR	NR
Takehisa et al (2007) <sup>38</sup>	42	NR	Y, p17	NR	NR	NR	Y, p17	NR	NR
Hyun et al (2008) <sup>36</sup>	309	NR	Y, p17	NR	NR	NR	NR	NR	NR
Vanden Bempt et al (2008) <sup>39</sup>	226	NA	NA	NA	NA	NA	NA	NA	Trend, p17

N=number of specimens. NR=not reported in reference. CI=chromosome imbalance. NA=characteristic examined in study but not associated with chromosome 17 copy number status. Y=association exists with chromosome 17 aneuploidy (a17), polysomy (p17), or monosomy (m17) as indicated. ER= oestrogen receptor negativity, ER+=oestrogen receptor positivity, PR=progesterone receptor negativity, PR+=progesterone receptor positivity. \*No correlation with tumour stage (using TNM tumour size, nodal status, metastasis staging criteria). †Associated with polysomy of multiple chromosomes.

Table 5: Aneuploidy 17 and association with clinicopathological characteristics

Reinholz et al, Lancet Oncol 2009; 10: 267-77

## Polysomie 17: AC ?

SABCS 2008

**Chromosome 17 polysomy (Ch17) as a predictor of anthracycline response: emerging evidence from the UK NEAT adjuvant breast cancer trial.**

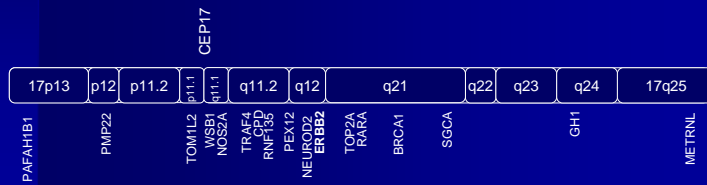
*Bartlett JMS, Munro A, Dunn JA, Hiller L, Jordan S, Twelves CJ, Cameron DA, Thomas J, Campbell F, Rea DW, Provenzano E, Pharoah P, Caldas C, Earl H, Poole CJ*

Om polysomie 17 te bepalen wordt de amplificatie van het **centromeer** (CEP17 probe) gebruikt: representatief voor het hele chromosoom

Klopt dit wel???????

# MLPA: P004-B1

- 17 chromosoom 17 probes (op 17p, 17cen en 17q)
- BRCA1, BRCA2
- HER2, ESR1, EGFR, TOP2A
- 2 of 3 probes per gen
- 15 referentie probes



# MLPA: P004-B1

- 3 WSB1 probes:  
17q11.1 (22,645,233 - 22,664,772 bp from pter),  
als alternatief voor CEP17 bij MLPA analyse
- CEP17 CISH

		WSB1 MLPA	
		Normaal	Verhoogd
CEP17 CISH	2 kopieën	82	2
	> 2 kopieën	6	14

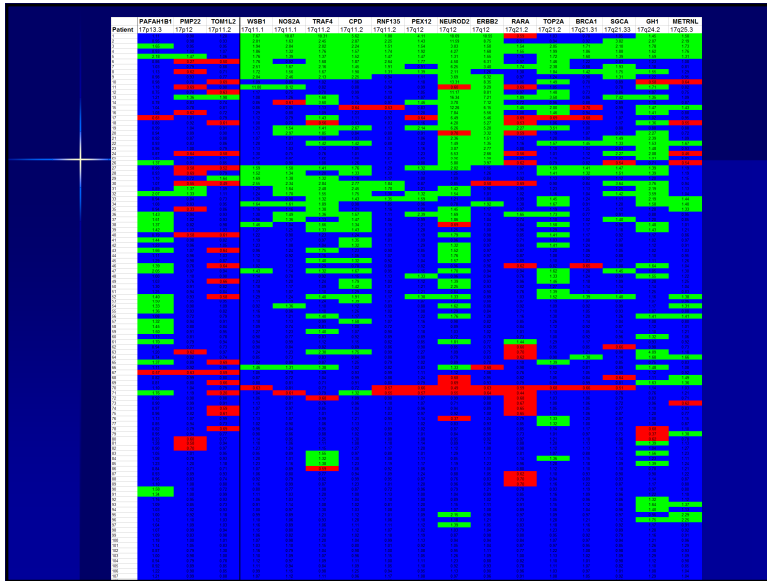
92 % concordantie

**16%**

# MLPA: P004-B1

		CEP17 CISH		WSB1 MLPA	
		2 kopieën	> 2 kopieën	Normaal	Verhoogd
HER2 status	Normaal	74	8	74	8
	Amplificatie	10	12	14	8
		<b>60%</b>		<b>50%</b>	

06-152.3 ESR1	0,99
06-152.3 ESR1	1,08
07-055.2 EGFR	0,87
07-055.2 EGFR	1,09
13-031.8 BRCA2	1,37
13-031.8 BRCA2	1,32
14-038.5 BRCA1	1,01
14-038.5 BRCA1	0,81
17-002.5 PAFAH1B1	1,08
17-015.1 PMP22	0,83
17-017.8 TOM1L2	0,95
17-022.7 WSB1	1,76
17-022.7 WSB1	1,46
17-022.7 WSB1	1,69
17-023.1 NOS2A	1,61
17-024.1 TRAF4	1,89
17-026.3 RNF135	0,98
17-026.3 RNF135	1,05
17-030.9 PEX12	0,96
17-035.0 NEUROD2	0,78
17-035.1 ERBB2	1,86
17-035.1 ERBB2	1,89
17-035.1 ERBB2	2,1
17-035.7 RARA	1,3
17-035.8 TOP2A	1,88
17-035.8 TOP2A	1,35
17-035.8 TOP2A	1,78
17-045.6 SGCA	1,2
17-059.3 GH1	1,58
17-078.6 METRN1	1,4
c	1,14
c	1,12
c	1
c	0,93
c	1,04
c	0,97
c	1,01
c	0,94
c	0,99
c	1,07
c	0,93



## P004-B1

CEP17 amplificatie (WSB1) ≠ gehele CHR17 amplificatie!

→ Bij 2/111 tumoren was heel 17q geamplificeerd, incl WSB1 en CEP17  
 → Polysomie van chromosoom 17 is erg zeldzaam

Chromosoom 17 vertoont gains en losses onafhankelijk van de centromeer status met als gevolg dat, tenminste in sommige gevallen, correctie met CEP17 probes misleidende HER2 gen status resultaten kan opleveren.

### Absence of chromosome 17 polysomy in breast cancer: analysis by CEP17 chromogenic in situ hybridization and multiplex ligation-dependent probe amplification

Cathy B. Moelans · Roel A. de Weger · Paul J. van Diest

Breast Cancer Res Treat (2009)

### Does chromosome 17 centromere copy number predict polysomy in breast cancer? A fluorescence *in situ* hybridization and microarray-based CGH analysis

Caterina Marchiò,<sup>1,2</sup> Maryou B Lambros,<sup>1</sup> Patrizia Gugliotta,<sup>2</sup> Ludovica Verdun Di Cantogno,<sup>2</sup> Cristina Botta,<sup>2</sup> Barbara Pasini,<sup>2</sup> David SP Tan,<sup>1</sup> Alan Mackay,<sup>1</sup> Kerry Fenwick,<sup>1</sup> Narinder Tamber,<sup>1</sup> Gianni Bussolati,<sup>2</sup> Alan Ashworth,<sup>1</sup> Jorge S Reis-Filho<sup>1\*</sup> and Anna Sapino<sup>2\*</sup>

J Pathol (2009)

### Clinical validation of an array CGH test for *HER2* status in breast cancer reveals that polysomy 17 is a rare event

Modern Pathology (2009)

I-Tien Yeh<sup>1</sup>, Mathew A Martin<sup>1</sup>, Ryan S Robetorye<sup>1</sup>, Aswani R Bolla<sup>1</sup>, Chris McCaskill<sup>2</sup>, Rashmi K Shah<sup>2</sup>, Mercedes E Gorre<sup>2</sup>, Mansoor S Mohammed<sup>2</sup> and Shelly R Gunn<sup>1,2</sup>

## MLPA

- Goede overeenkomst IHC, ISH
- Polysomie is erg zeldzaam
- Correctie met CEP17?
- Informatie over meer genen dan alleen HER2

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