

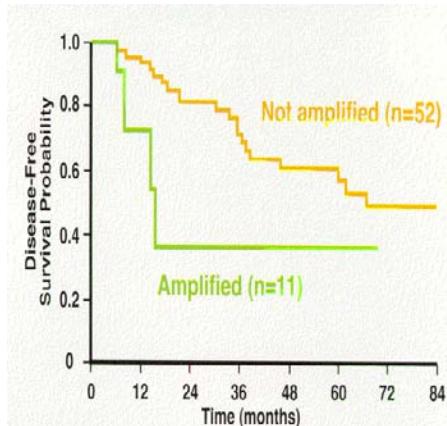
Welche Rolle spielt Her-2 in der BC-Karzinogenese *wann und wo?*

J. Rüschoff , Kassel

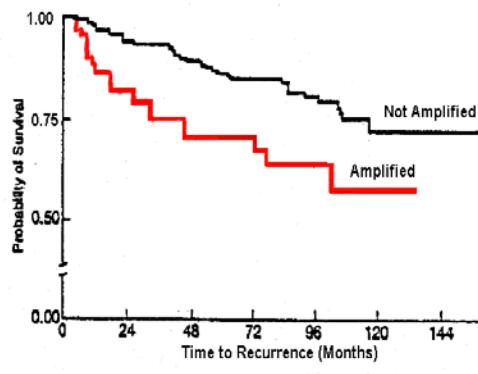
www.targos-gmbh.de

Her2 – ein „Biomarker“

Her2/neu Überexpression in 15-25% der Mammakarzinome



(Slamon 1987; bei pos. LK)



(Press 1997; bei neg. LK)

Prognostische Bedeutung

81 Studien (27,161 Pat.)

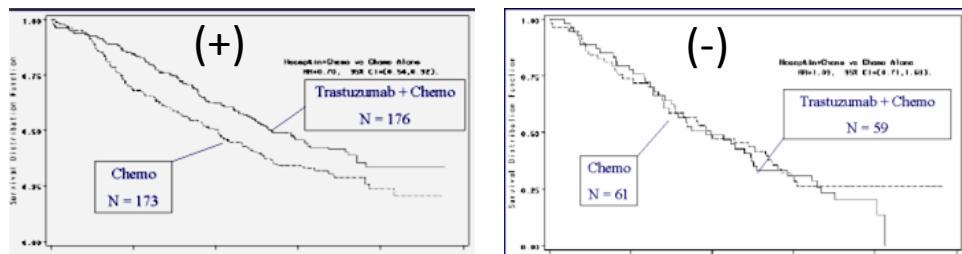
In 73/81 (90%) HER2+ BC: ungünstiger Verlauf

In 52/73 (71%) unabhängiger Prognosefaktor

(Ross et al, 2003)

Gezielte anti-Her2 Ak/Moleküle wirksam bei Her2 pos Mamma-Ca

Rezeptorüberexpression u./o. Amplifikation



(Slamon et al. NEJM 2001)

Trastuzumab bei Her2 pos BC

1989 Wirksamkeit in vitro

1993 Phase II, 1995 Phase III

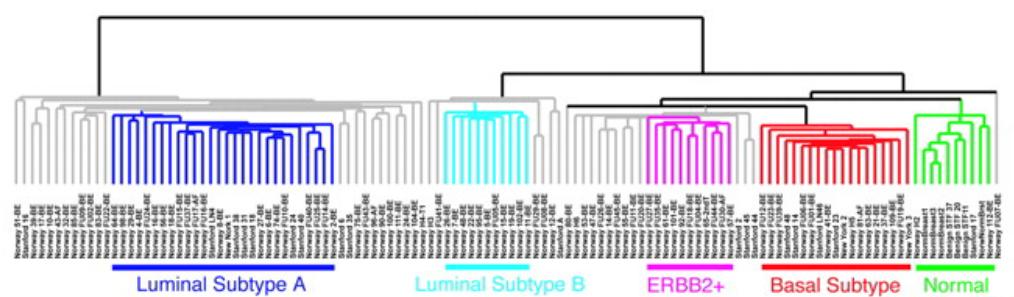
1998 FDA Zulassung metast. Mamma-Ca

2006 Zulassung in der Adjuvanz

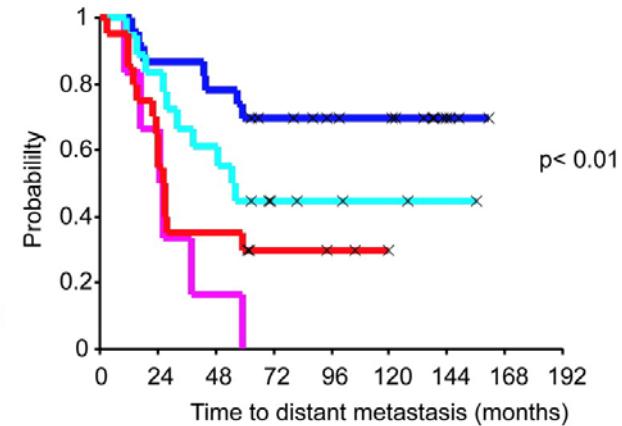
2005 St.Gallen: Her2 Testung aller BC

Her2 – Molekulare BC-Klassifikation

Gene Expression Profiling (Intrinsic Subtypes)

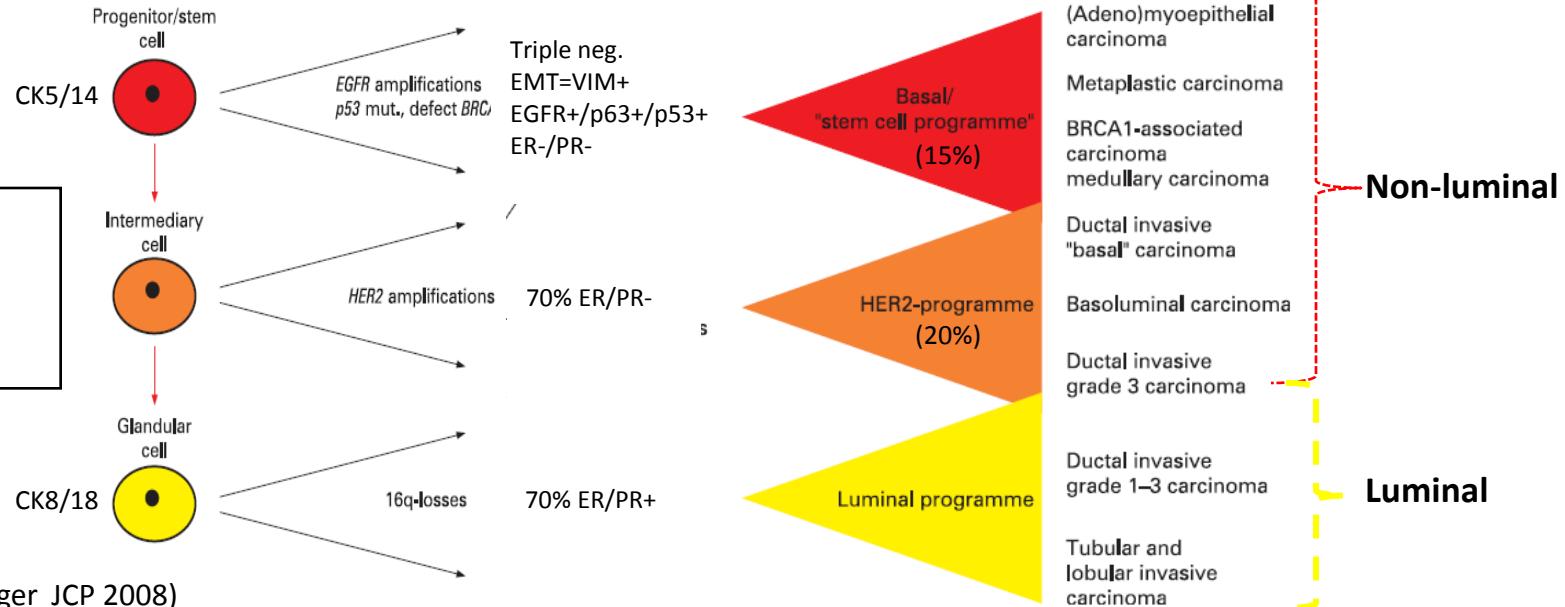


(Sorlie /Perou et al. PNAS 2003)



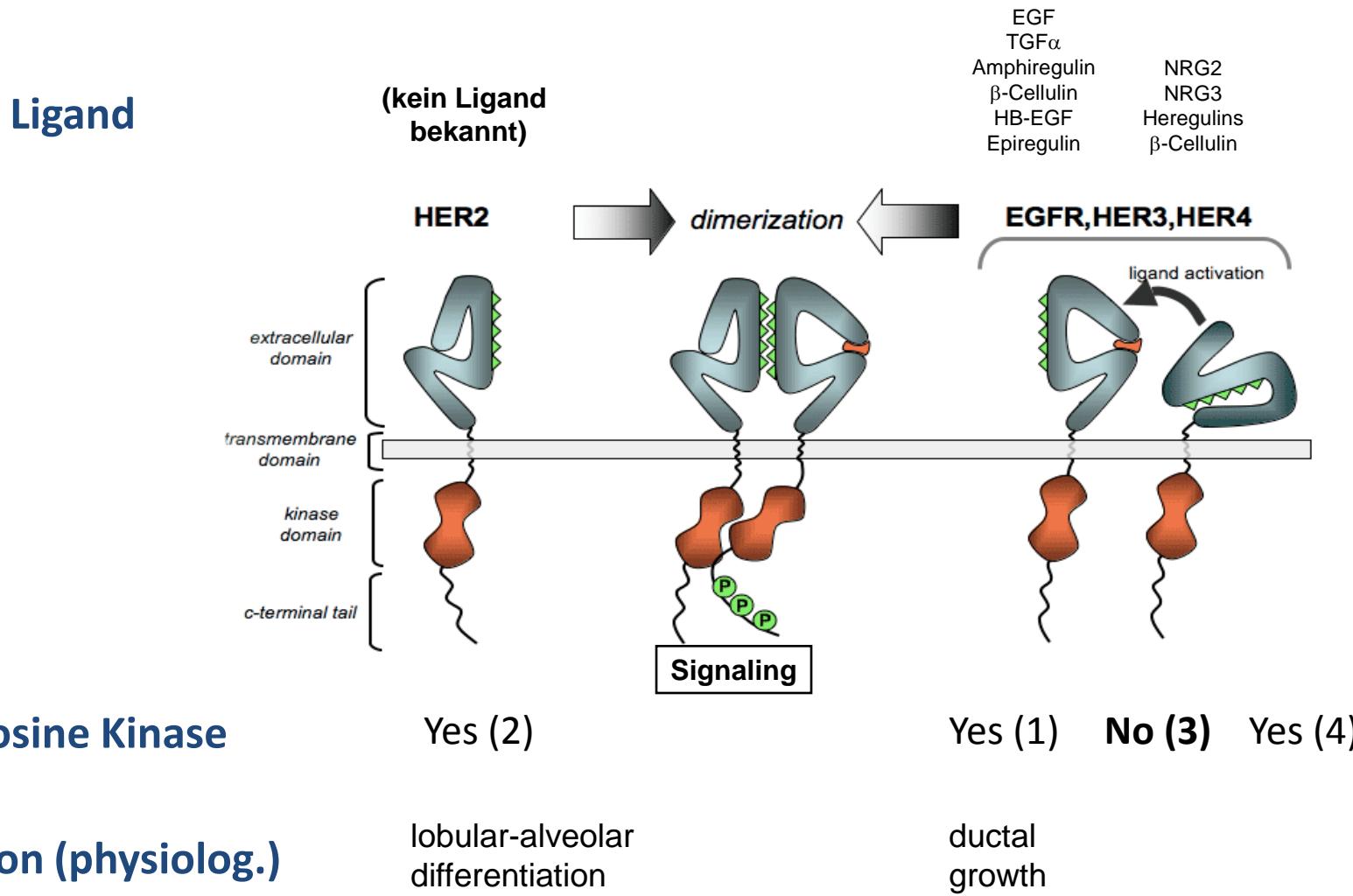
p < 0.01

Molekulare BC Klassifikation



(Korschning/Boecker/Bürger JCP 2008)

Her-/ErbB- Rezeptor Familie

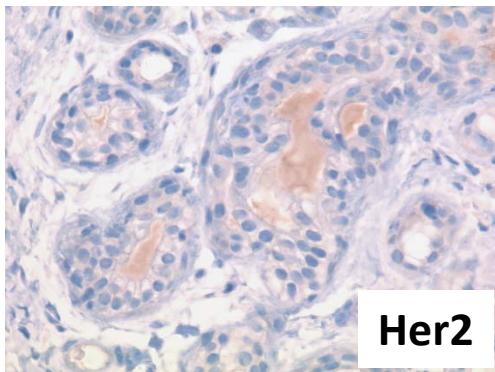
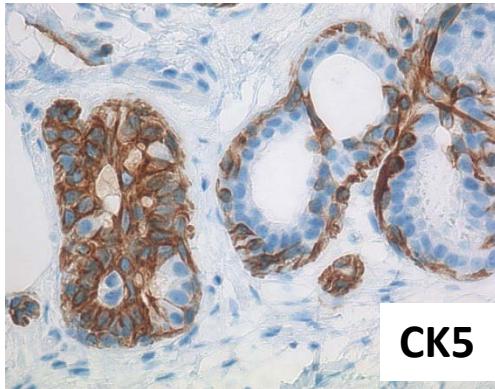


Her2 & Karzinogenese

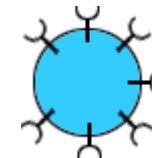
HER-2 - was ist 'Normal' vs. 'Überexpression' ?



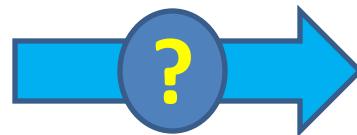
normal expression
20.000 - 50.000



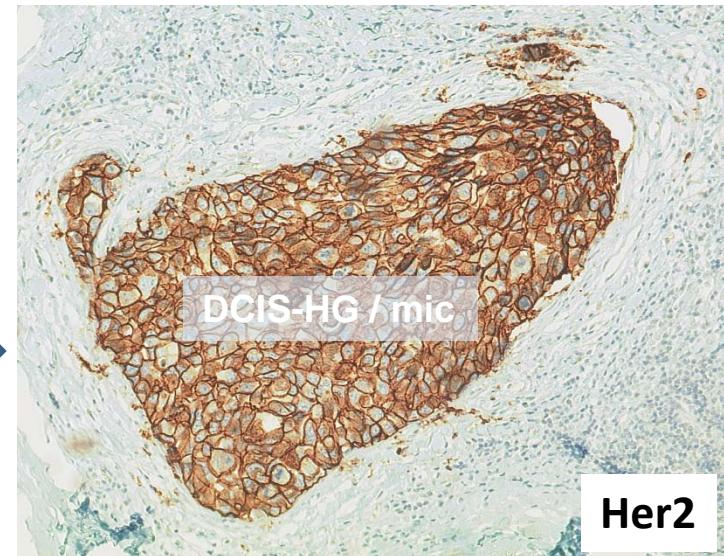
(receptors / cell)



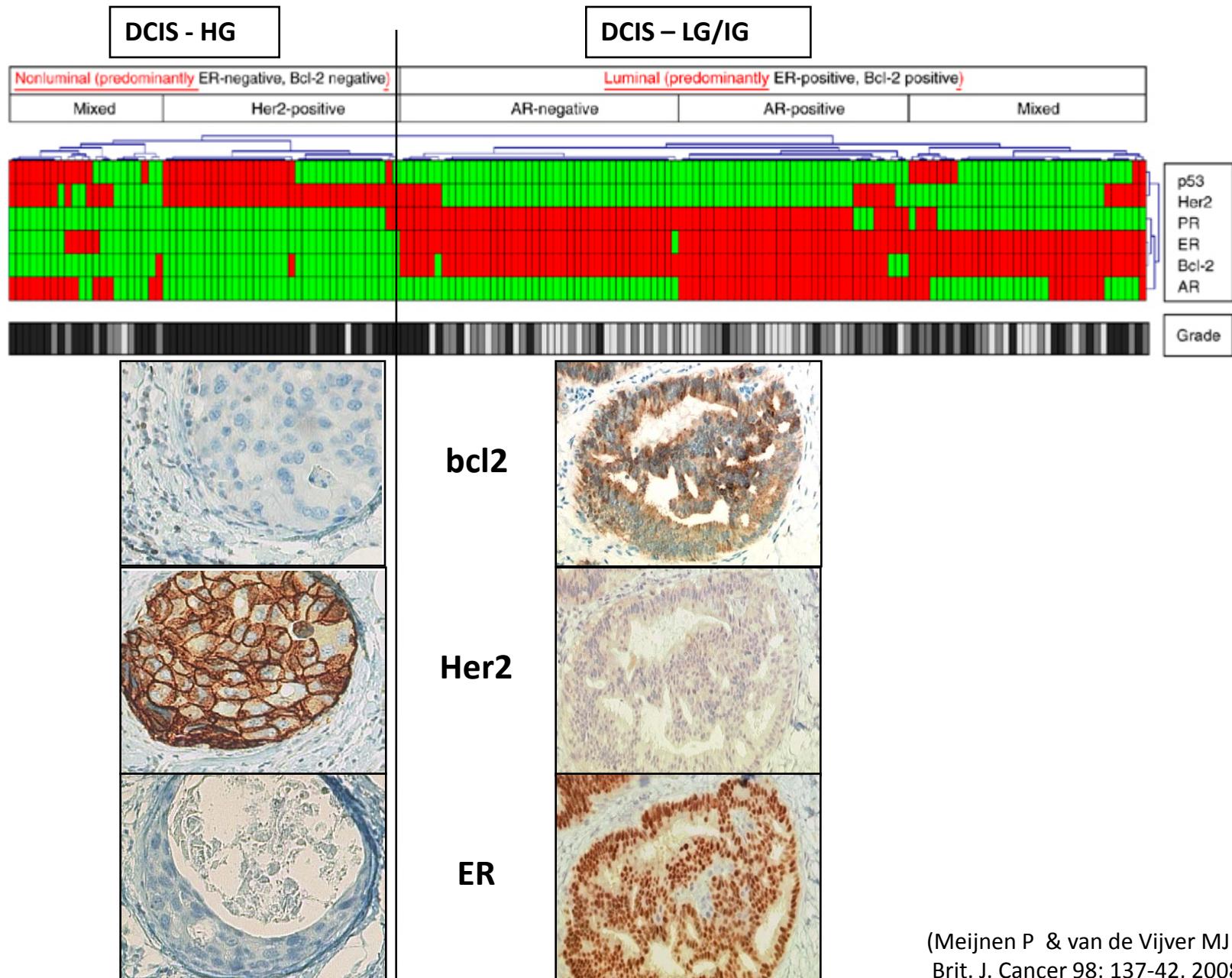
Overexpression
200.000 - 3.000.000



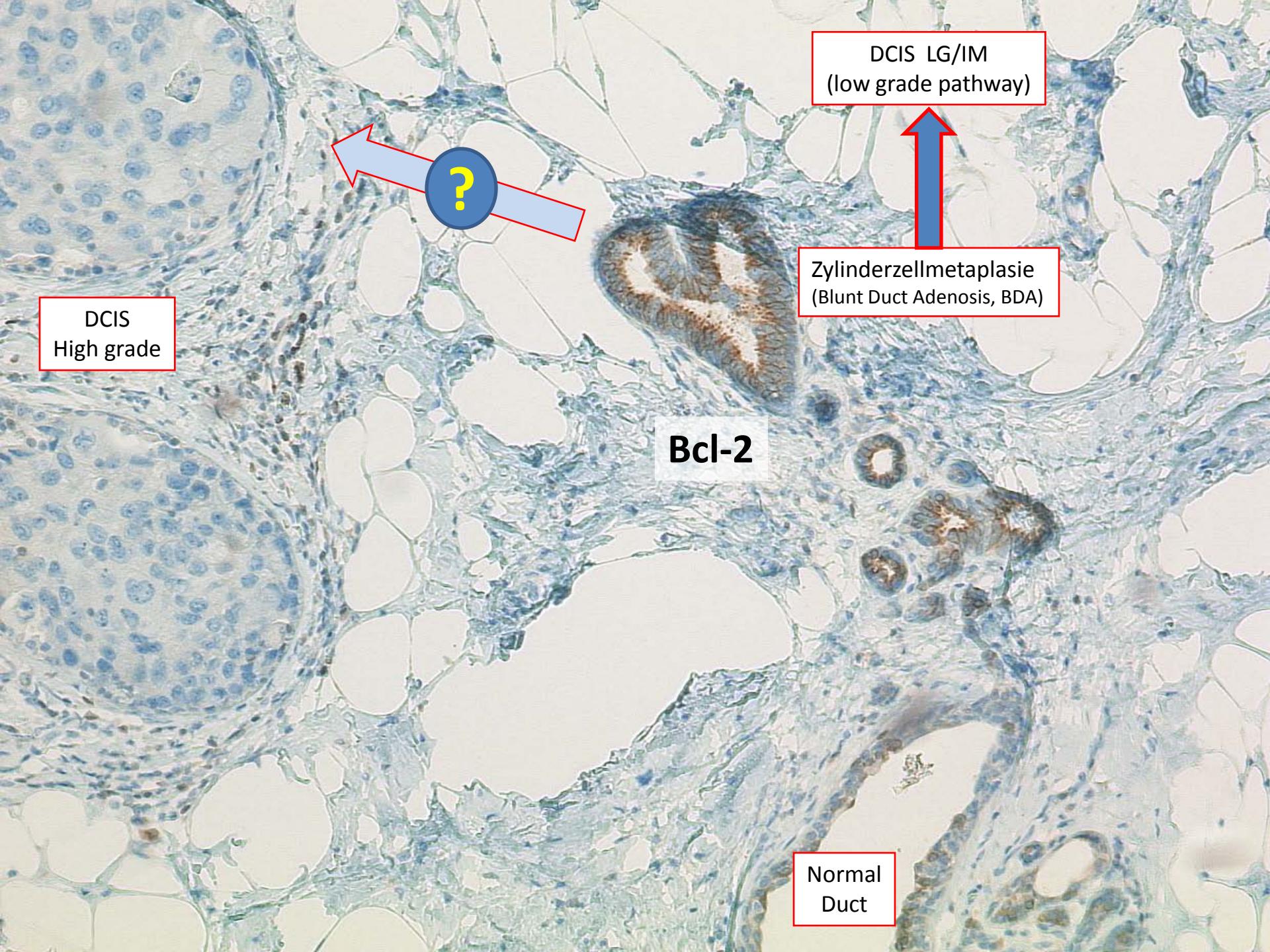
Wann?
Wo?

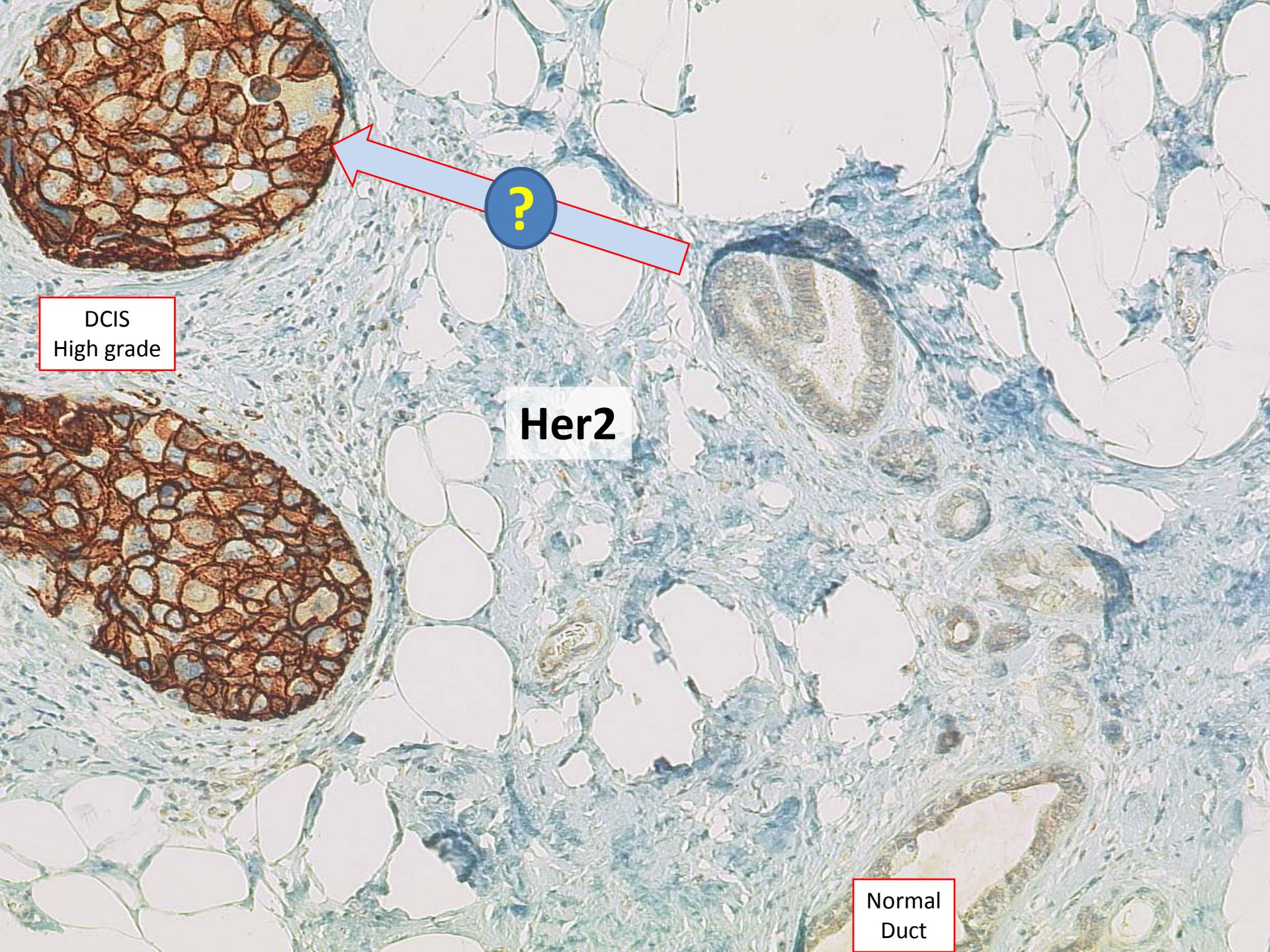


DCIS - Immuno-Profile



(Meijnen P & van de Vijver MJ
Brit. J. Cancer 98: 137-42, 2008)

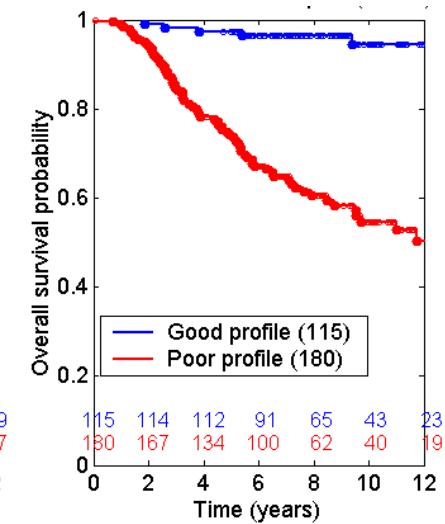
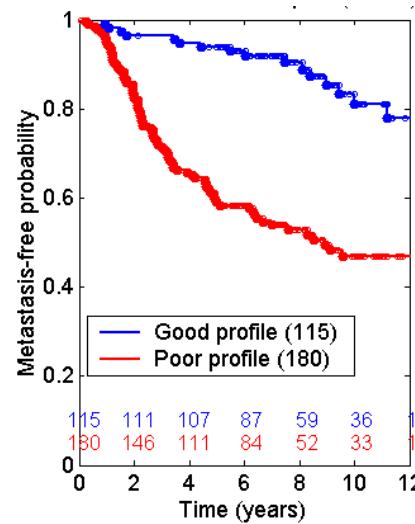
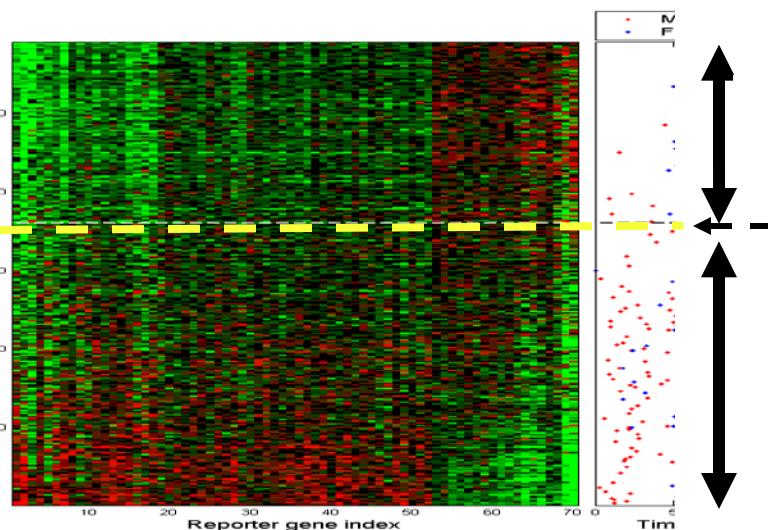




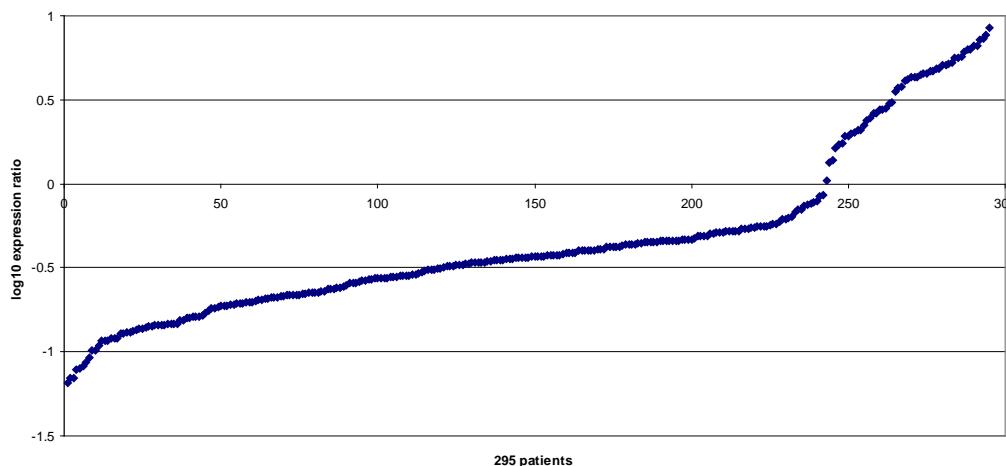
Her2 - Überexpression

Van de Vijver, NEJM 2002: 70 gene prognosis profile

295 tumors

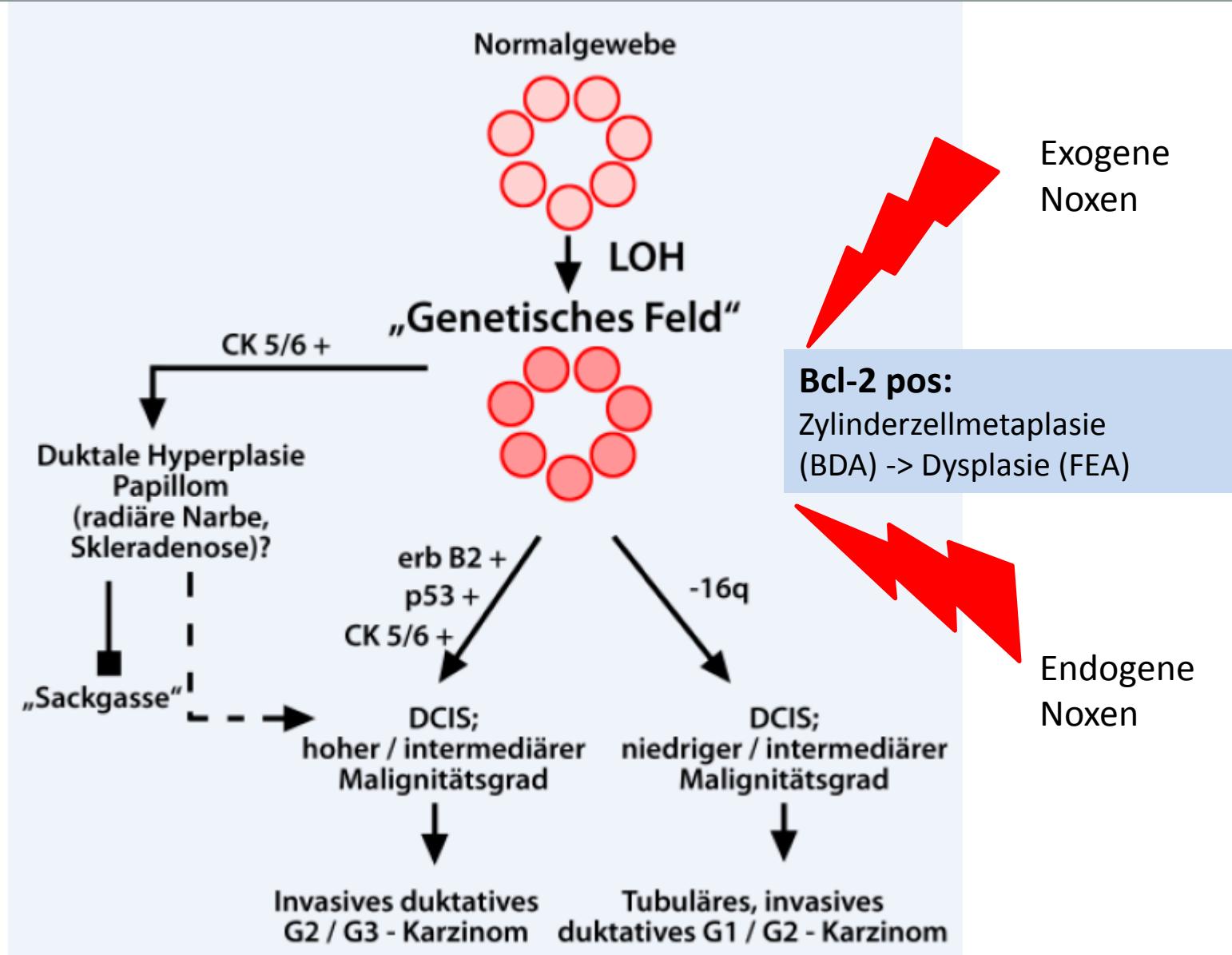


Distribution of HER2 Ratios

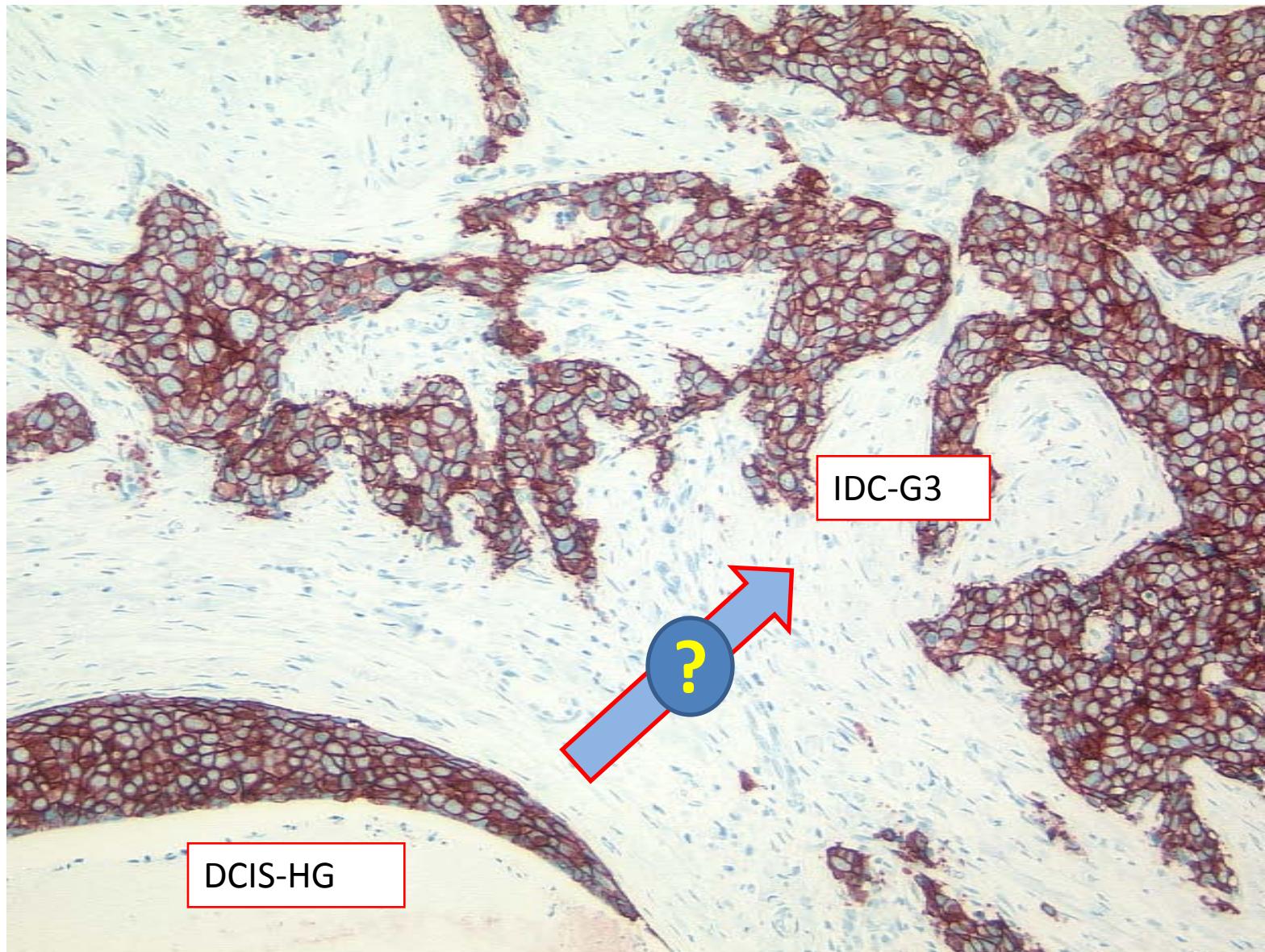


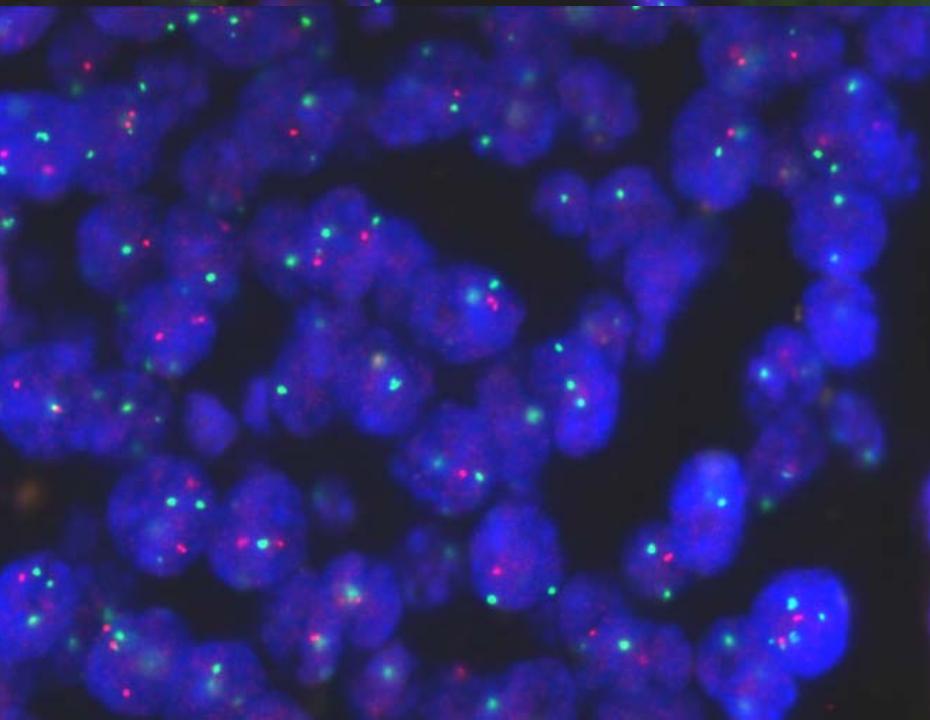
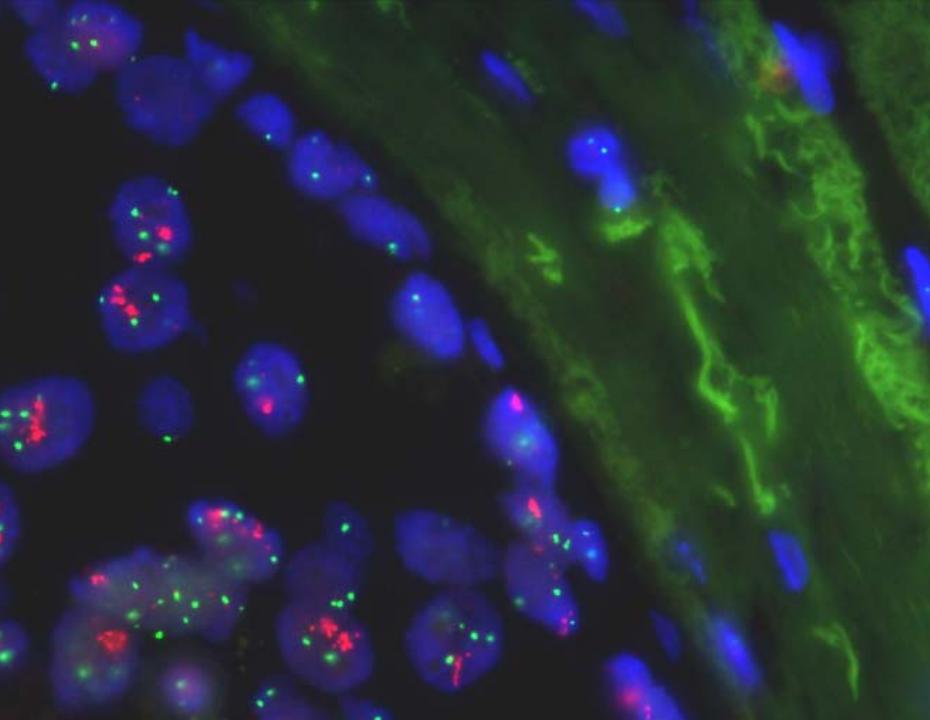
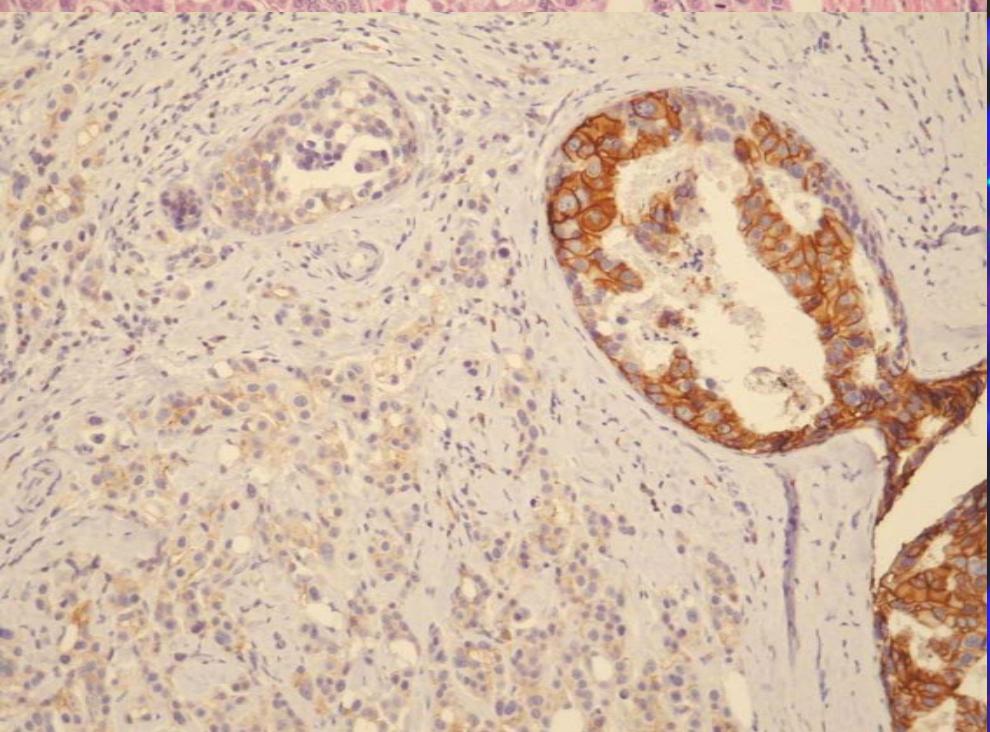
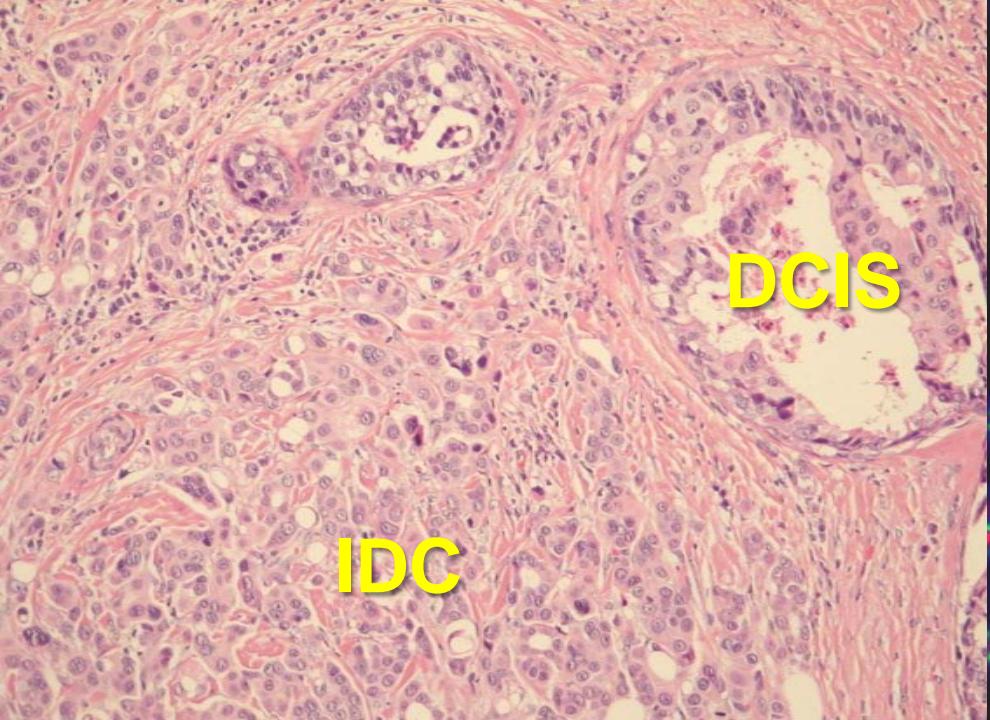
Courtesy by M.v.d.Vijver

Her2 – High Grade Pathway



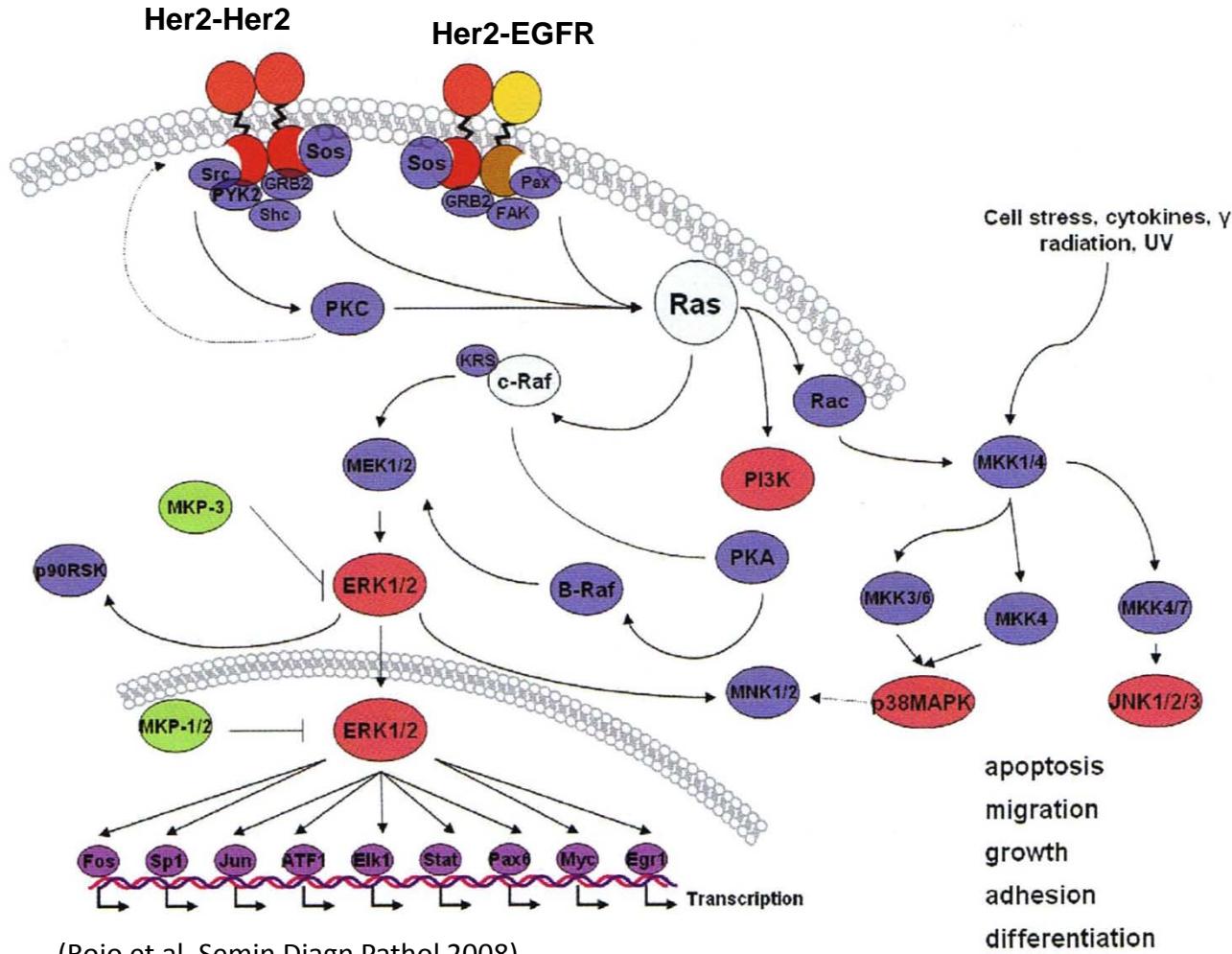
Her2 - Überexpression & Invasion



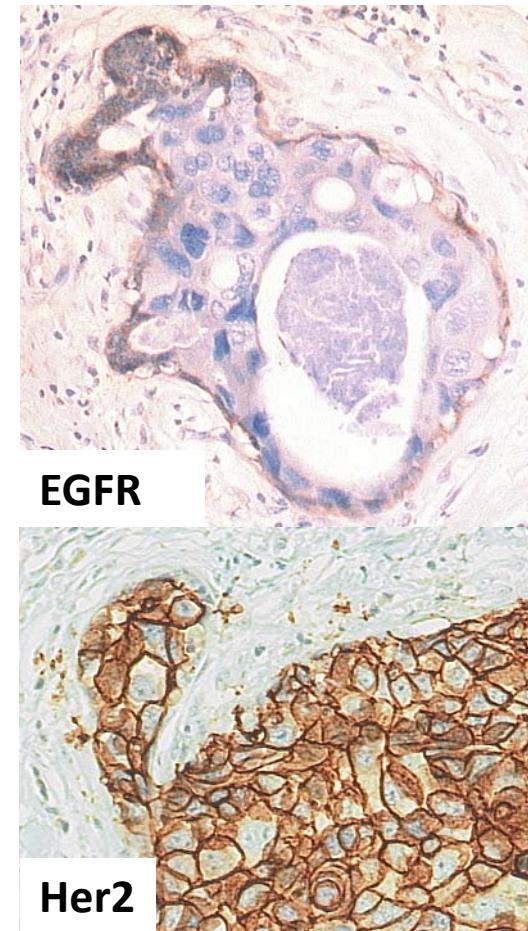


Her2-EGFR & Invasion

RAS/RAF/ERK Pathway

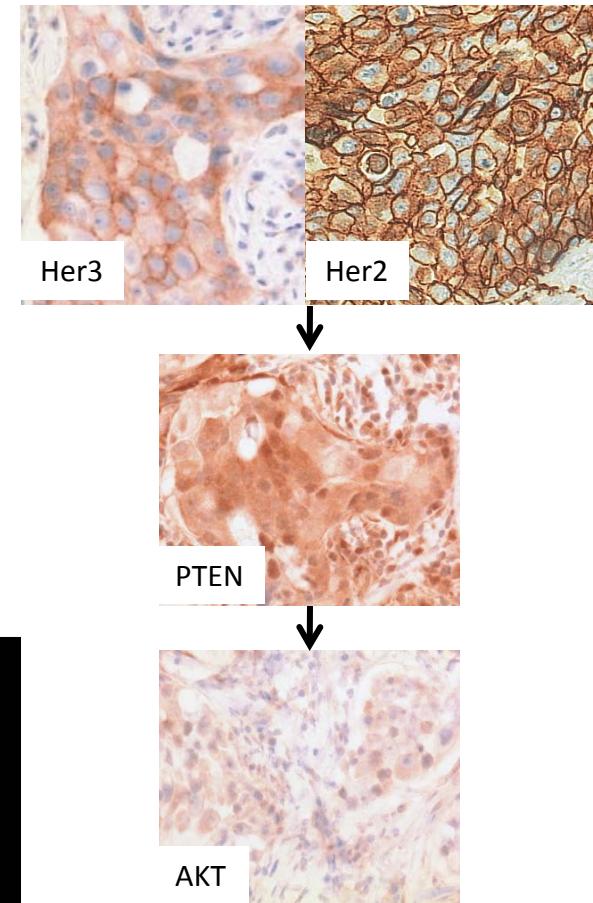
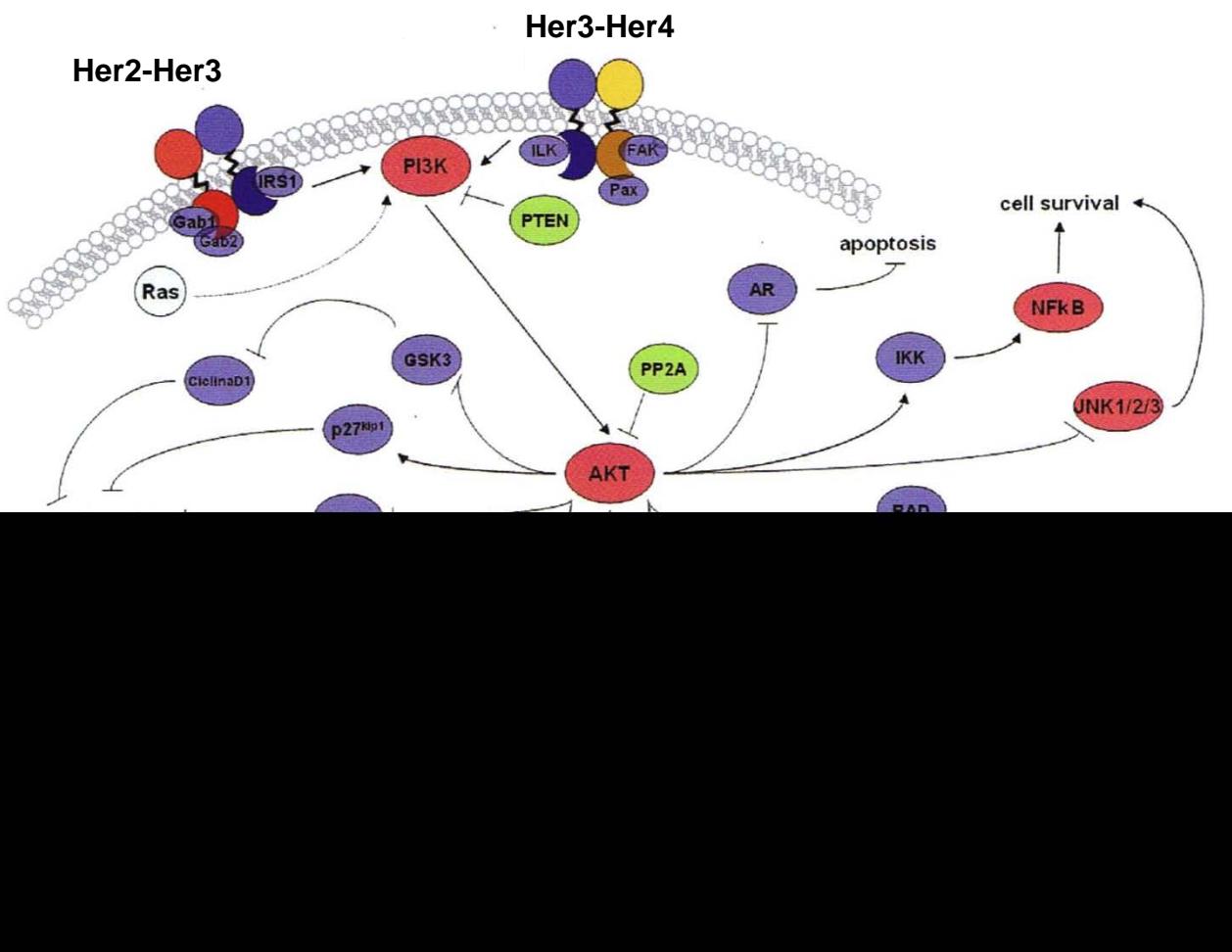


(Rojo et al. Semin Diagn Pathol 2008)



Her2-Her3 & Progression

PI3K/AKT Pathway



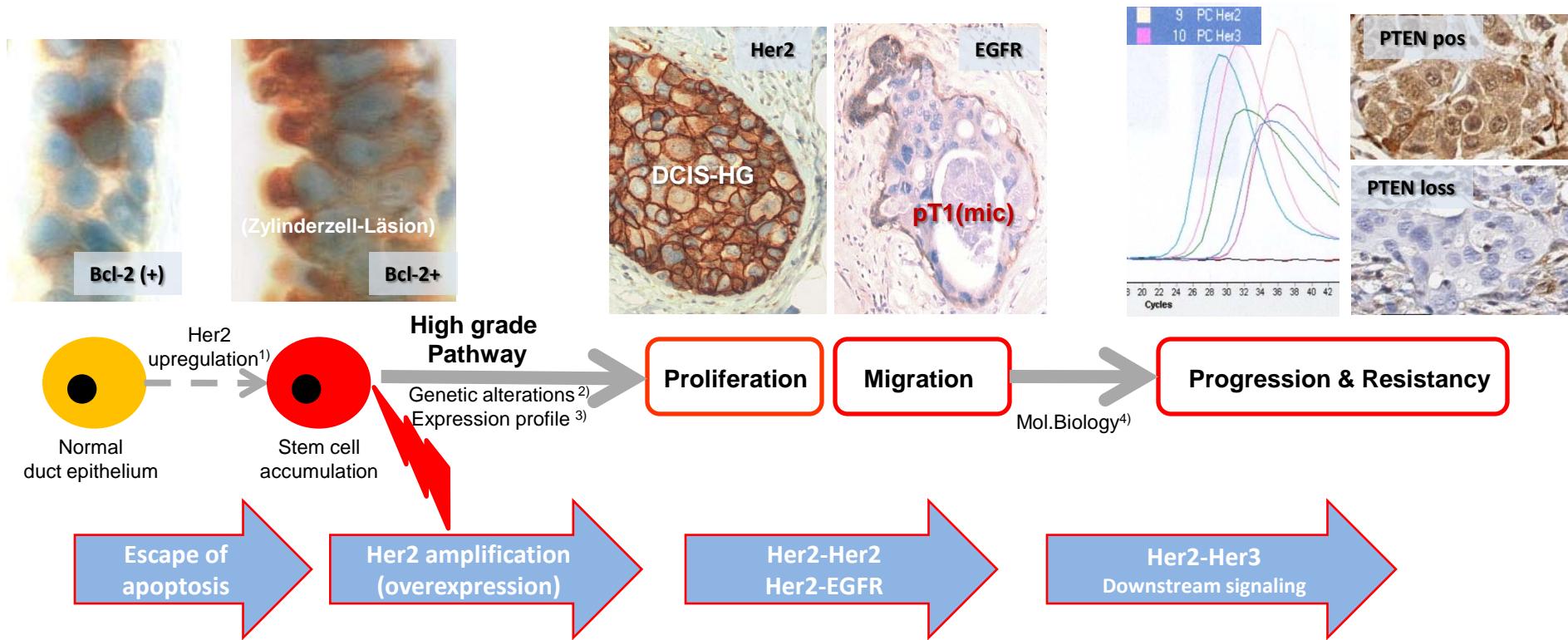
(Rojo et al. Semin Diagn Pathol 2008)

Mut	Her2+	HR+	BL
PI3K	22.7%	34.5%	8.3%
AKT1	-	1.4%	-
PTEN	-	2.3%	-

* Loss of PTEN most effective AKT activator
(Stemke-Hale / vd Vijver Cancer Res 2008)

Her2 in der BC-Karzinogenese

Wann & Wo ?



¹⁾ Korkaya et al. Oncogene 2008

²⁾ Bürger&Böcker Preneopl. of Breast 2006

³⁾ Sotiriou et al. J Nat Cancer Inst 2006

⁴⁾ Sergina et al. Nature 2007

Stemke-Hafe et al. Cancer Res 2008

Acknowledgements: Team



Kassel pathologist team



Targos team

Contact: rueschoff@patho-nordhessen.de
thomas.henkel@targos-gmbh.de

• targos
molecular pathology gmbh