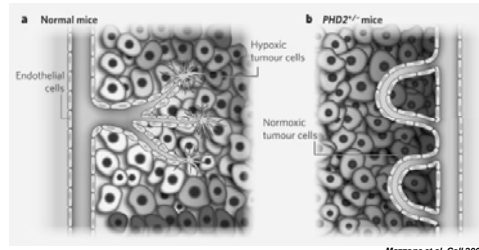


Biomarkers of Efficacy of Antiangiogenic Agents

Rafael Rosell

10th European Perspectives in Lung Cancer
Brussels 6-7 March 2009

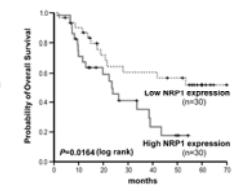
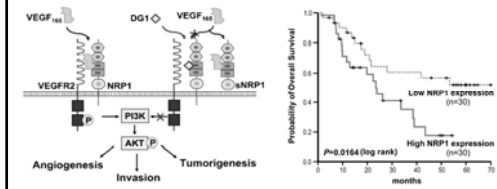
Heterozygous deficiency of PHD2 restores tumor oxygenation and inhibits metastasis via endothelial normalization



Mazzone et al. Cell 2009

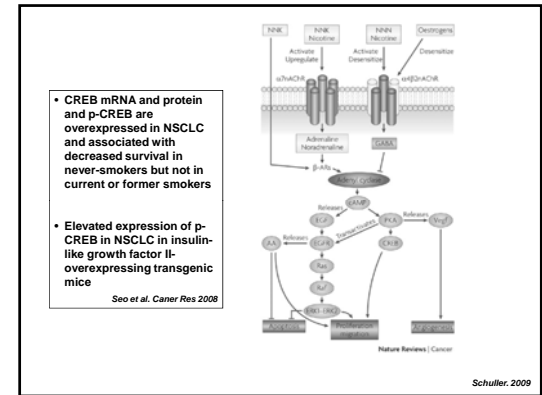
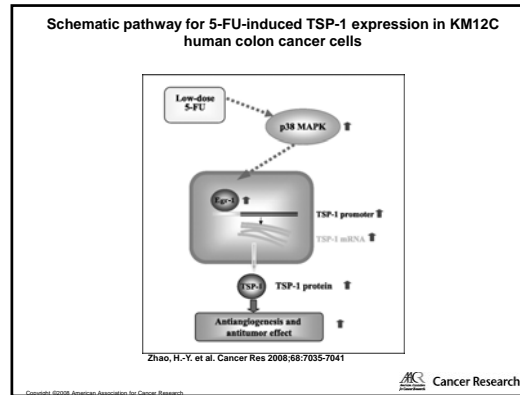
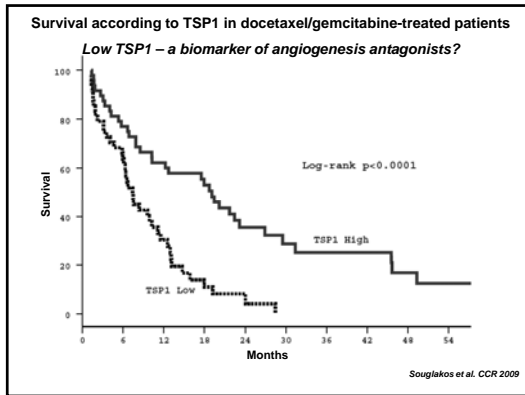
Inhibition of PHD2 could be an alternative cancer therapy

VEGF can bind NRP1 and trigger the NRP1/VEGFR2/PI3K/Akt signaling pathway



NRP1 is an angiogenesis enhancer in NSCLC and could be a potential biomarker for the selection of high-risk NSCLC patients

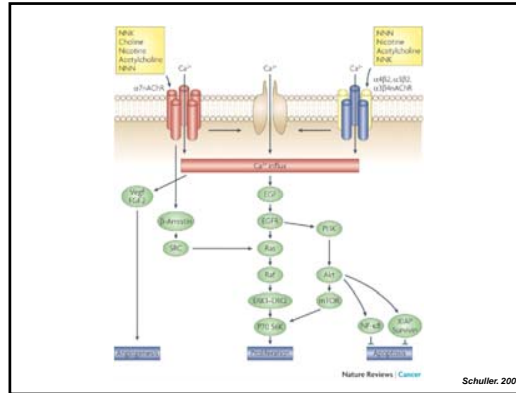
Ernstoff et al. CCR 2007



Multivariate analysis for TTP in 187 patients with EGFR mutations treated prospectively with erlotinib

	HR	95% CI	p
Gender			
Female	1 ref.		
Male	3.7	1-17.84	0.05
ECOG PS			
0	1 ref.		
1	1.67	0.19-14.53	0.64
≥2	4.65	0.46-46.44	0.19
CHRNA3			
TT	1 ref.		
CT	0.18	0.04-0.83	0.03
CC	0.21	0.04-1.16	0.07
EGFR mutation			
del 19	1 ref.		
L858R	2.31	0.57-9.25	0.23

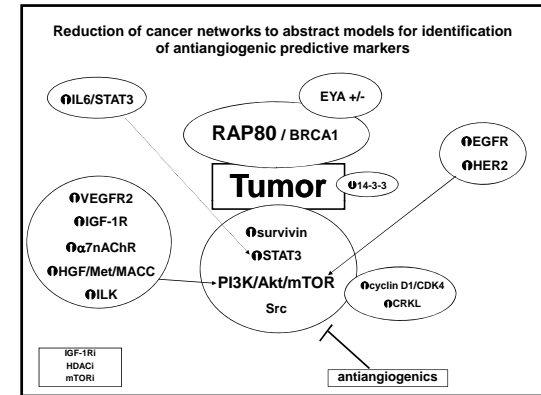
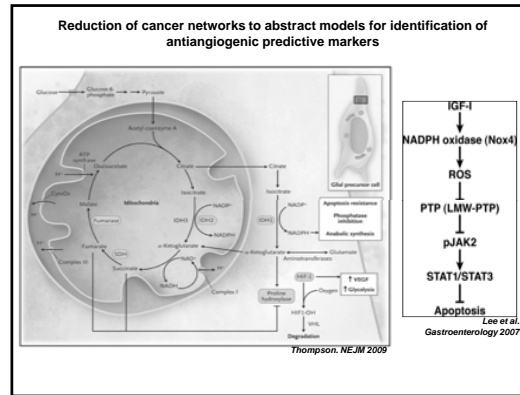
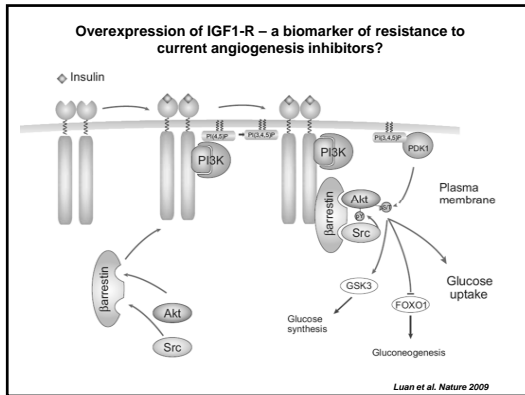
CHRNA3 TT homozygous variant – a biomarker of angiogenesis antagonists?

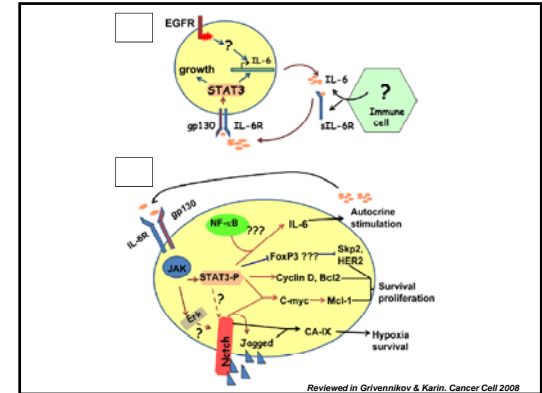
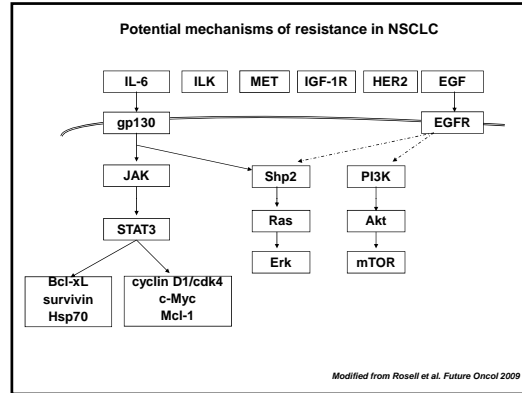
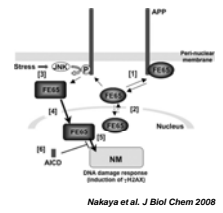
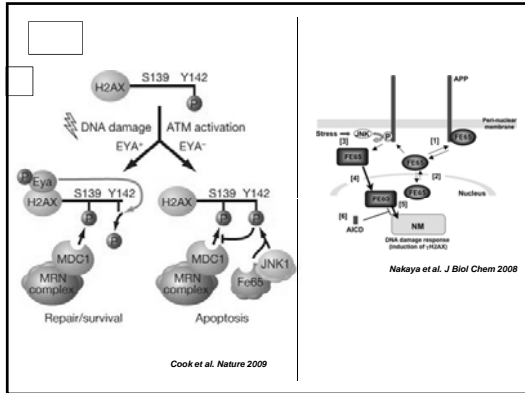


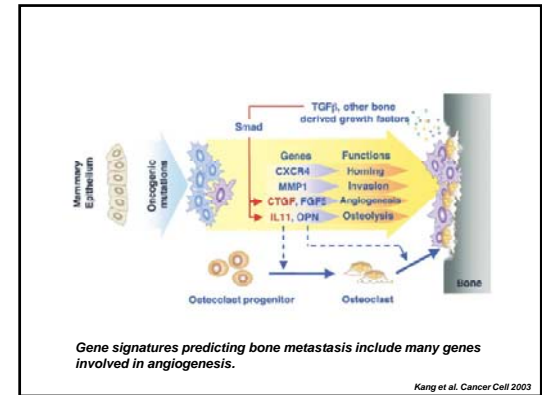
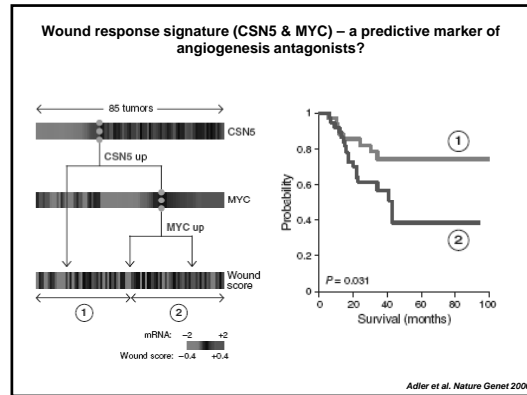
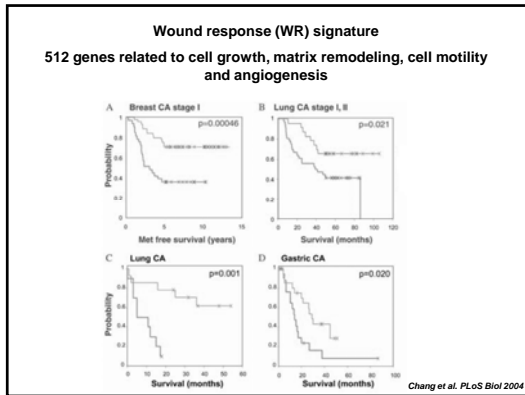
nAChR α subunit 3 (CHRNA3) SNP in PS 0 advanced NSCLC patients treated with docetaxel/cisplatin based on low ERCC1 mRNA levels

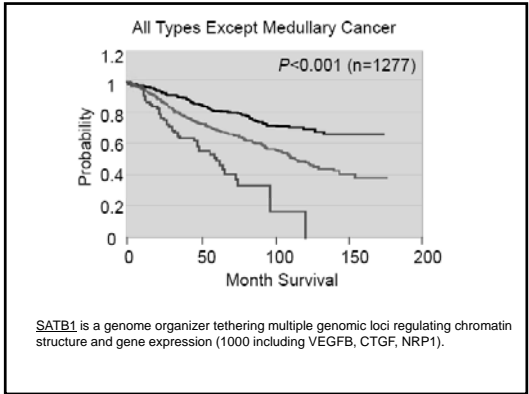
	CHRNA3			p
	CC	CT	TT	
Response				0.05
SD+PD	7 (50%)	4 (16%)	3 (50%)	
CR+PR	7 (50%)	21 (84%)	3 (50%)	
TTP	6.74 mo	12.13 mo	7.77 mo	0.05
MS	12.60 mo	18.98 mo	10.68 mo	0.41

CHRNA3 homozygosity – a biomarker of angiogenesis antagonists?









- The **integrin-linked kinase (ILK)/Akt/mTOR network** is a hallmark in several tumors of poor prognosis and drug resistance.
- Overexpression of ILK is found in melanoma, ovarian, prostate and NSCLC.
- ILK addiction is found in breast cancer.
- ILK – a therapy-predictive marker for response to mTOR inhibitors
- ILK – a therapy-predictive marker for response to BIBW2992 plus an mTOR inhibitor
- ILK – a therapy-predictive marker for resistance to erlotinib in patients with EGFR mutations

