



Pannello in pasta vitrea Domus del Chirurgo Rimini

Rimini Centro Congressi SGR
venerdì 21 ottobre 2011

ore 14:00 / 19:00

Carcinoma del colon-retto

La medicina che cambia:
l'approccio multidisciplinare
al trattamento delle metastasi
epatiche nell'era della target therapy

Personalizzazione della terapia nei tumori del colon retto metastatico: il ruolo della biologia molecolare

Dr. Wainer Zoli

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DEI TUMORI

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale di Forlì

TERAPIA “TARGET” NEL CARCINOMA COLONRETTALE METASTATICO

I farmaci citotossici convenzionali costituiscono le terapie più frequentemente utilizzate nel carcinoma del colon

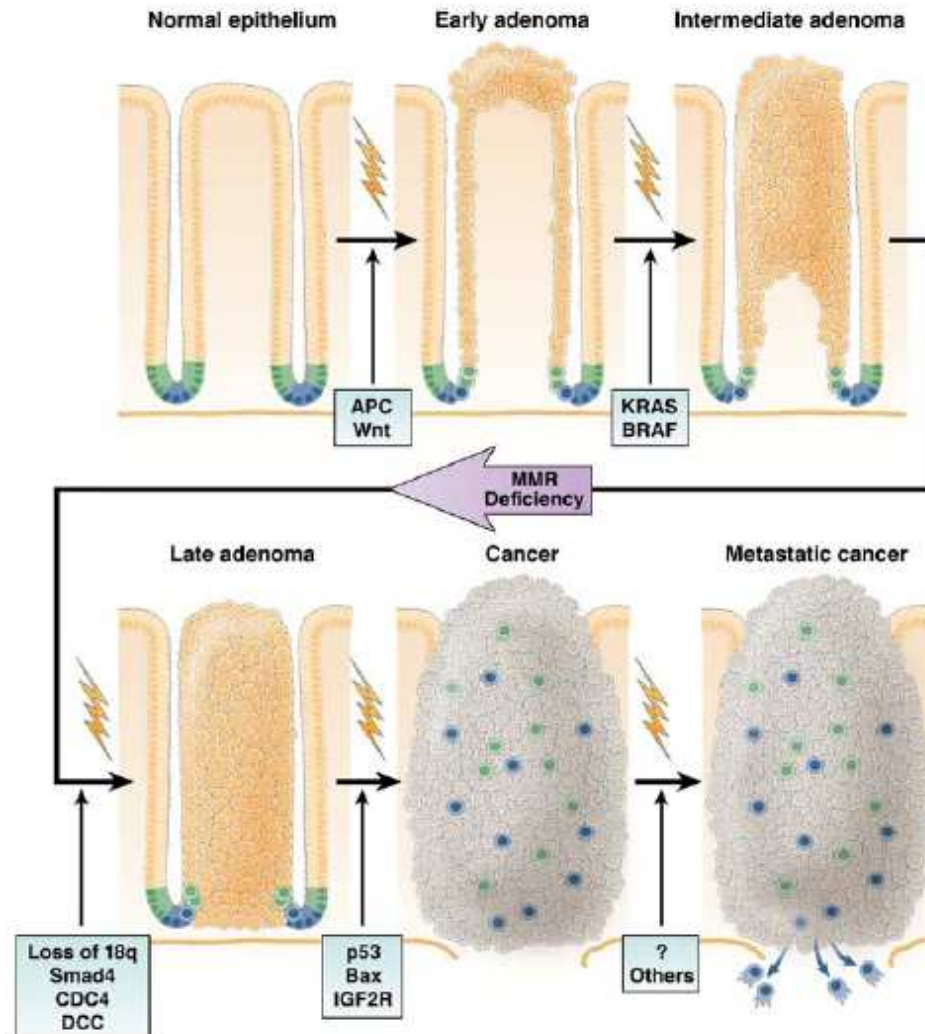
Nel trattamento della malattia colon rettale metastatica si stanno però consolidando altre strategie terapeutiche basate sull'uso di farmaci, a specifico bersaglio molecolare, finalizzati a:

Inibire il recettore per l' EGFR con anticorpi monoclonali (cetuximab and panitumumab)

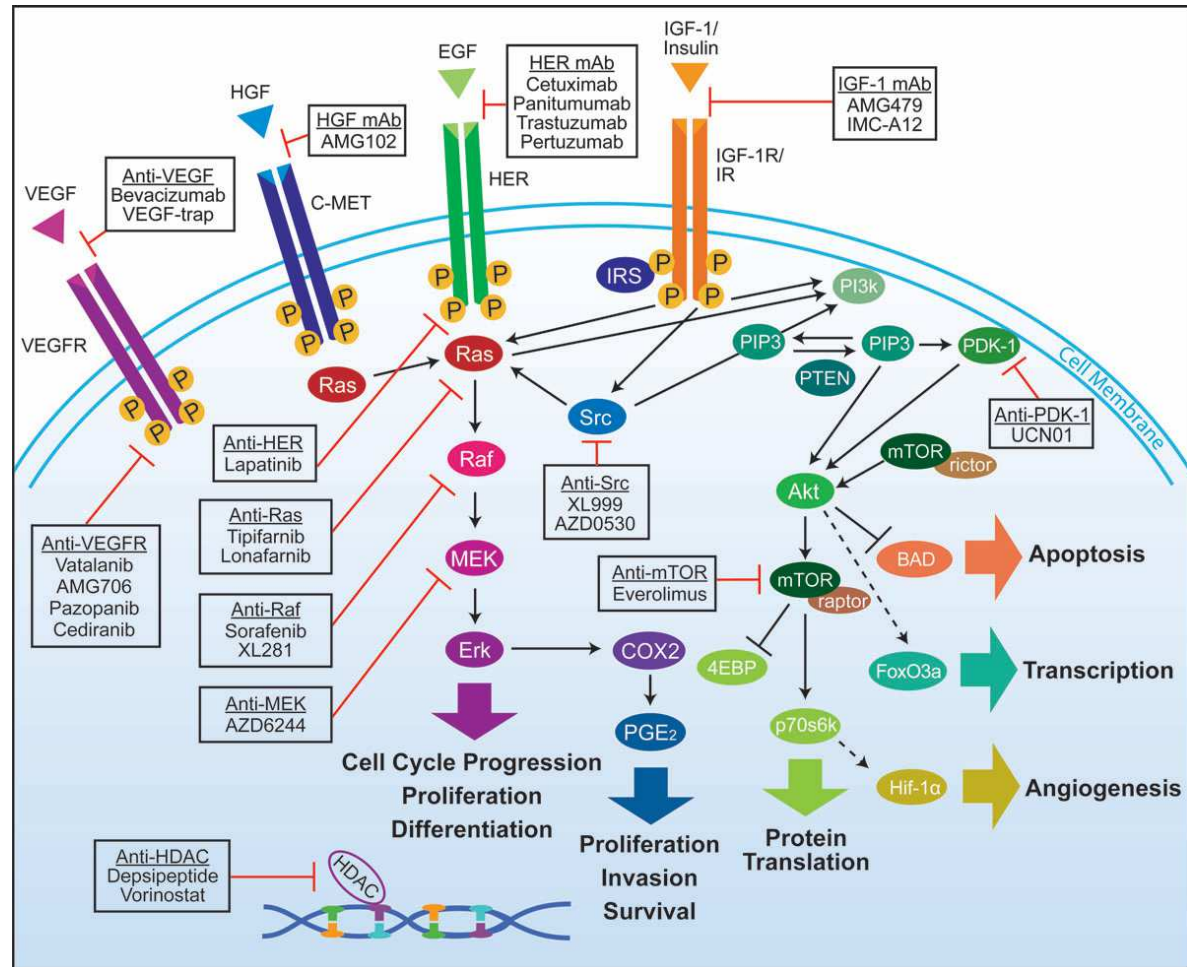
Bloccare l'angiogenesi con anticorpi anti VEGFR (bevacizumab).

Genetic alterations in colorectal cancer

Specific mutations, epigenetic changes, and defects in chromosomal stability or DNA repair, promote disease progression and malignant behaviors.

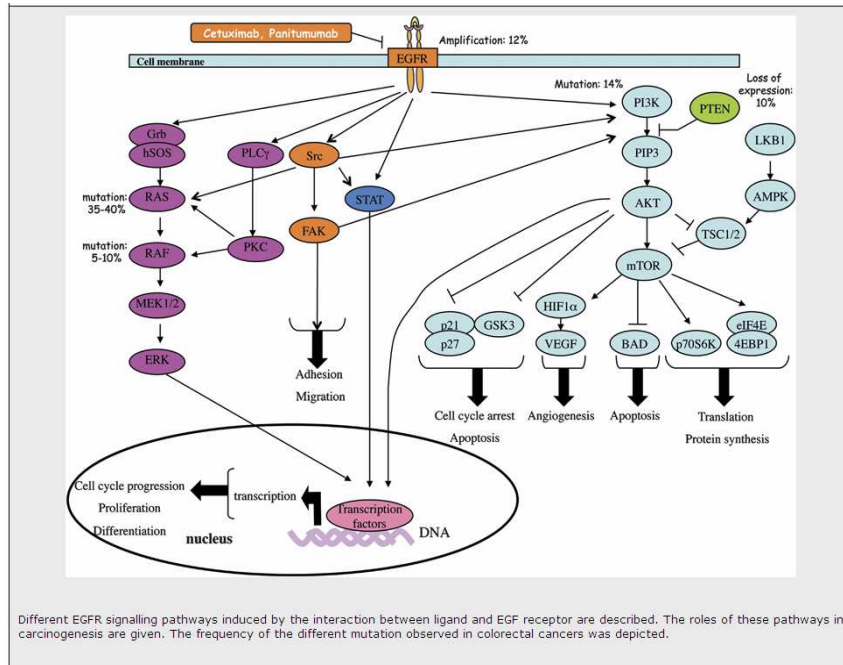


Overview of interlinked cellular signaling pathways involved in the proliferation and progression of colorectal cancer

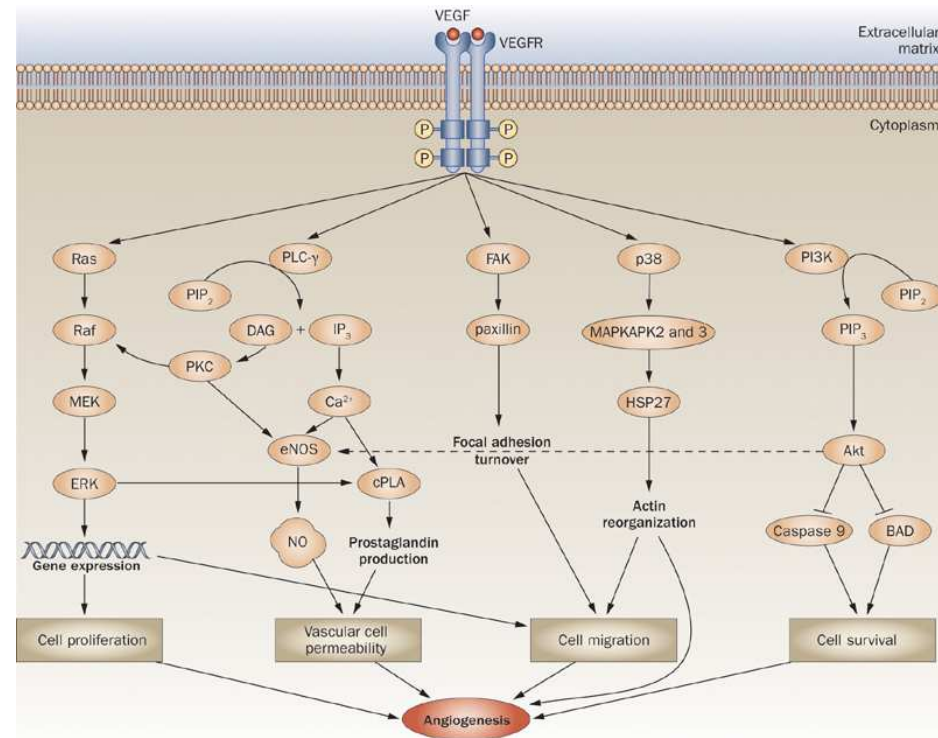


Siena S et al. J Natl Cancer Inst 2009

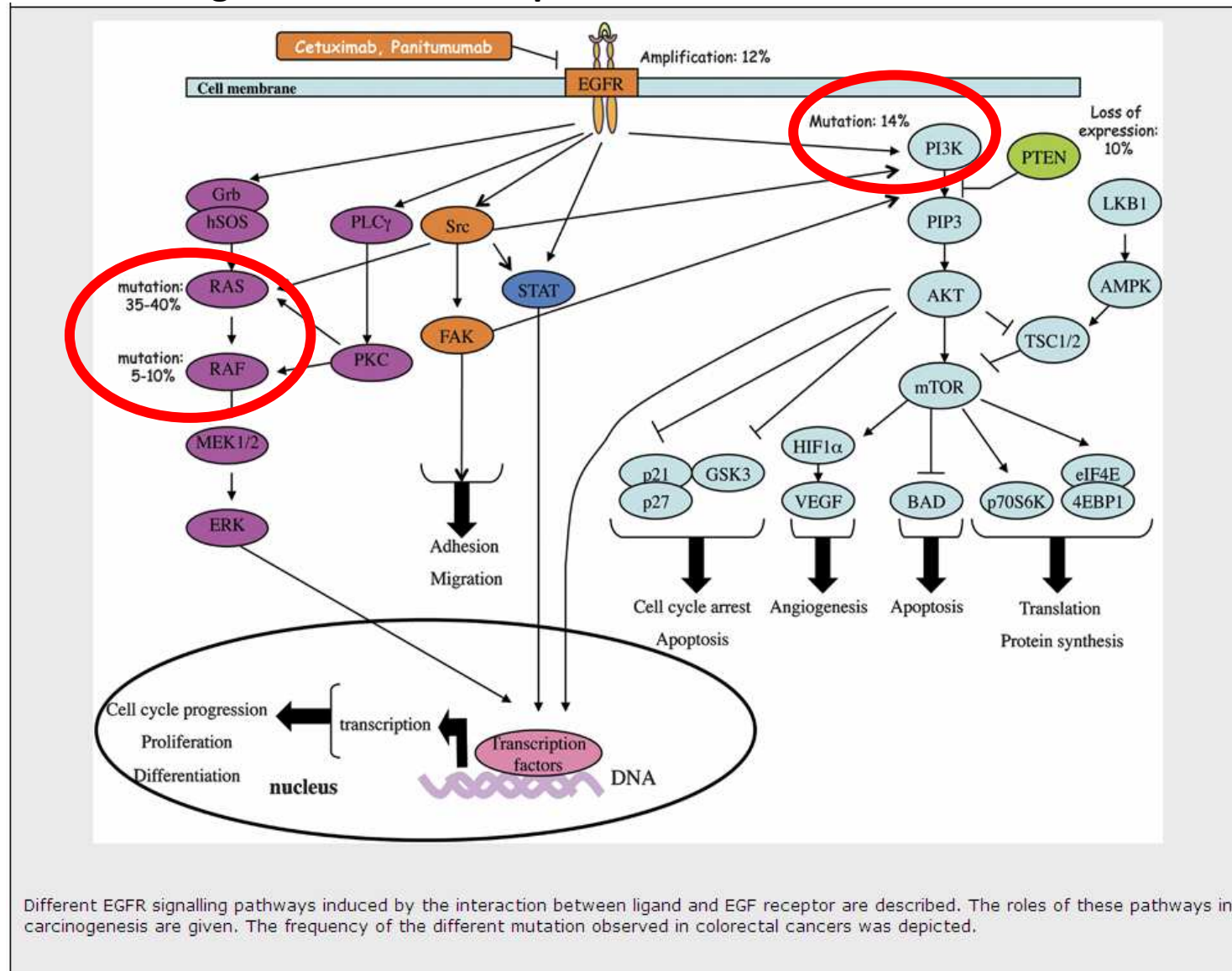
Oncogenic mutations as predictive factors in colorectal cancer



Lievre A. et al. *Oncogene* (2010) 29, 3033–3043



Oncogenic mutations as predictive factors in colorectal cancer



K-RAS

La mutazione di K-RAS è considerata un evento precoce nella tumorigenesi del carcinoma del colon.

Mutato nel 35-40% dei tumori del colon (codoni 12-13)

Fra i pazienti con tumori wildtype per KRAS, il response rate agli anti-EGFR è:

26-41% per cetuximab (normalmente in combinazione con chemioterapia)

(Lievre et al., 2006; Di Fiore et al., 2007; De Roock et al., 2008; Lievre et al., 2008)

11-17% per panitumumab (prevalentemente in monoterapia)

(Amado et al., 2008; Freeman et al., 2008),

Possibilità che altre mutazioni di questo pathway possano essere responsabili della resistenza alle terapie anti-EGFR .

Frequency of *KRAS*, *BRAF*, and *NRAS* Mutations in Colorectal Cancer

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Analizzati 2121 tumori del colon per mutazioni di *KRAS* (codoni 12 e 13) :
mutazioni identificate in 900/2121 (42.4%) dei campioni .

In un subset di questi (513 campioni wildtype per KRAS (codoni 12 e 13), sono state ricercate eventuali mutazioni nei codoni 61 e 146 di KRAS, codone 600 di BRAF e codoni 12, 13 e 61 di NRAS.

78 campioni sono risultati mutati per *BRAF*, 19 per *KRAS* (codone 61), 17 per *KRAS* (codone 146) e 26 per *NRAS*.

In totale, 140/513 (27.3%) tumori, wildtype per KRAS (codoni 12 e 13) presentavano almeno una mutazione in un altro gene del pathway di RAS.

NRAS

Mutato in circa il 5% dei tumori del colon (codoni 12,13 e 61)

La sua mutazione sembra insorga in uno stadio avanzato di malattia

L'espressione di K-Ras stimola, nell'epitelio del colon, una iperproliferazione Mek-dependent.

N-RasG non altera le proprietà proliferative dell'epitelio ma conferisce resistenza alla apoptosi.

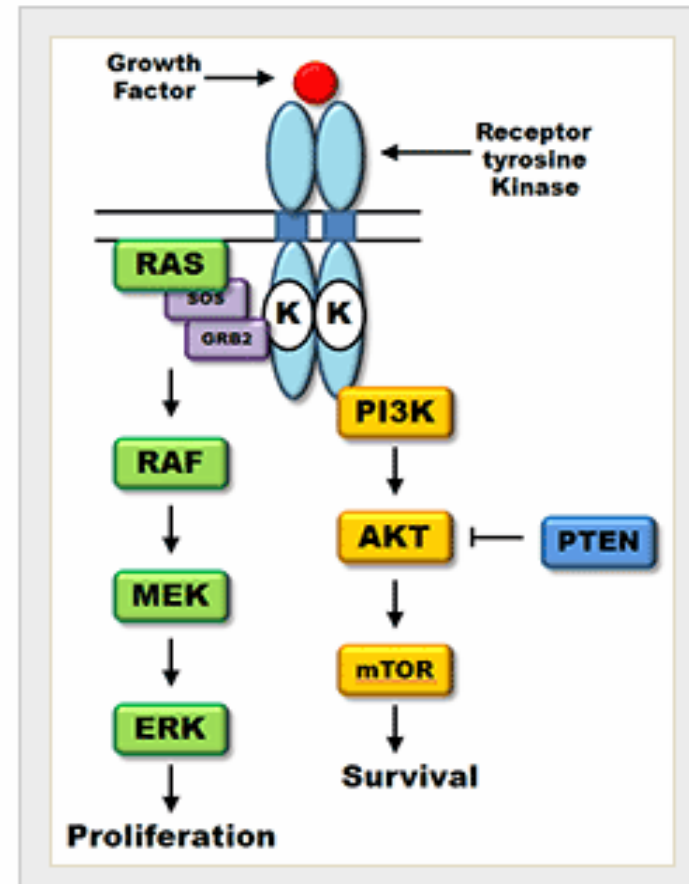
(Vogelstein B et al. *N Engl J Med* 1988;319:525–532).

Le mutazioni di NRAS sono mutualmente esclusive rispetto alle mutazioni di BRAF, KRAS e PIK3CA **(solo 5 casi)**

(Irahara N et al. *Diagn Mol Pathol*. 2010 September)

BRAF

- Mutato in circa il 10-15% dei tumori del colon-retto
- Mutazione mutualmente esclusiva con K-RAS
- Correlato a minor tempo di progressione libera da malattia e breve sopravvivenza globale
- Fattore prognostico sfavorevole, indipendentemente dalla terapia



BRAF

Summary of the studies evaluating the prognostic and predictive value of BRAF mutations on response to cetuximab or panitumumab in colorectal cancer

<i>Reference</i>	<i>Total number of patients</i>	<i>Number of KRAS WT patients</i>	<i>Number of BRAF-mutated patients (%)</i>	<i>Objective response^a (%)</i>	<i>Progression-free survival^b</i>	<i>Overall survival^b</i>
Benvenuti <i>et al.</i> (2007)	48	32	6 (12.5)	0	—	—
Cappuzzo <i>et al.</i> (2008b)	85	38	4/79 (5.1)	0	1.2 vs 4.6 months	5.4 vs 9.8 months
Di Nicolantonio <i>et al.</i> (2008)	113	79	11 (9.7)	0	Shorter $P = 0.001$	Shorter $P < 0.0001$
Loupakis <i>et al.</i> (2009b)	138	87	13 (10)	0 ($P = 0.016$)	2.6 vs 4.4 months HR = 0.59 (0.24–1.07) ($P = 0.073$)	4.1 vs 13.9 months HR = 0.51 (0.18–0.95) ($P = 0.037$)
Souglakos <i>et al.</i> (2009)	92	60	9 (10)	0	2 vs 3.9 months HR = 3.6 (1.8–7.4) ($P < 0.0005$)	HR = 4.1 (2.1–8) ($P < 0.0001$)
Laurent-Puig <i>et al.</i> (2009)	173	116	5/171 (3)	0 ($P = 0.063$)	8 vs 31 weeks ($P = 0.0005$)	6.5 vs 14.8 months ($P = 0.0004$)

Abbreviations: HR, hazard ratio; WT, wild type.

^aObjective response, progression-free and overall survival in *BRAF*-mutated patients (vs *BRAF*-non-mutated patients) among the KRAS WT subgroup of patients.

BRAF

These findings clearly show that BRAF mutations are an additional tool for the selection of patients who might be resistant to anti-EGFR antibodies and that they should be considered before considering anti-EGFR therapies for mCRC.

However, no randomized phase III study with a placebo control arm is currently available to definitively demonstrate the negative predictive value of BRAF mutations in mCRC.

Lievre A. et al. *Oncogene* (2010) 29, 3033–3043

229 tumors were analysed for KRAS/BRAF genotypes from patients treated with systemic chemotherapy

RESULTS: KRAS and BRAF mutations were present in 34.5% and 6.5% of patients, respectively.

The median overall survival (OS) for BRAF mutation-positive and KRAS 13 mutation-positive patients was 11.0 and 27.7 months, respectively, which was significantly worse than that for patients with wild-type (wt) KRAS and BRAF (40.6 months)(BRAF; HR=4.25, P<0.001, KRAS13; HR=2.03, P=0.024).

CONCLUSION: Presence of mutated BRAF is one of the most powerful prognostic factors for advanced and recurrent CRC.

Yokota T et al. *Br. J. of Cancer* (2011) 104, 856 – 862

REVIEWS IN BASIC AND CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

Robert F. Schwabe and John W. Wiley, Section Editors

Targeting PI3K Signaling as a Therapeutic Approach for Colorectal Cancer

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Recent large-scale sequencing and other genomic analyses of human colorectal tumors indicate that there are up to 80 nonsilent mutations in each tumor and that individual tumors have different mutations.

Although the mutations are many and varied, classification of common and rare mutations revealed that 38 pathways are disrupted with particular frequency; many of these pathways intersect with PI3K signaling

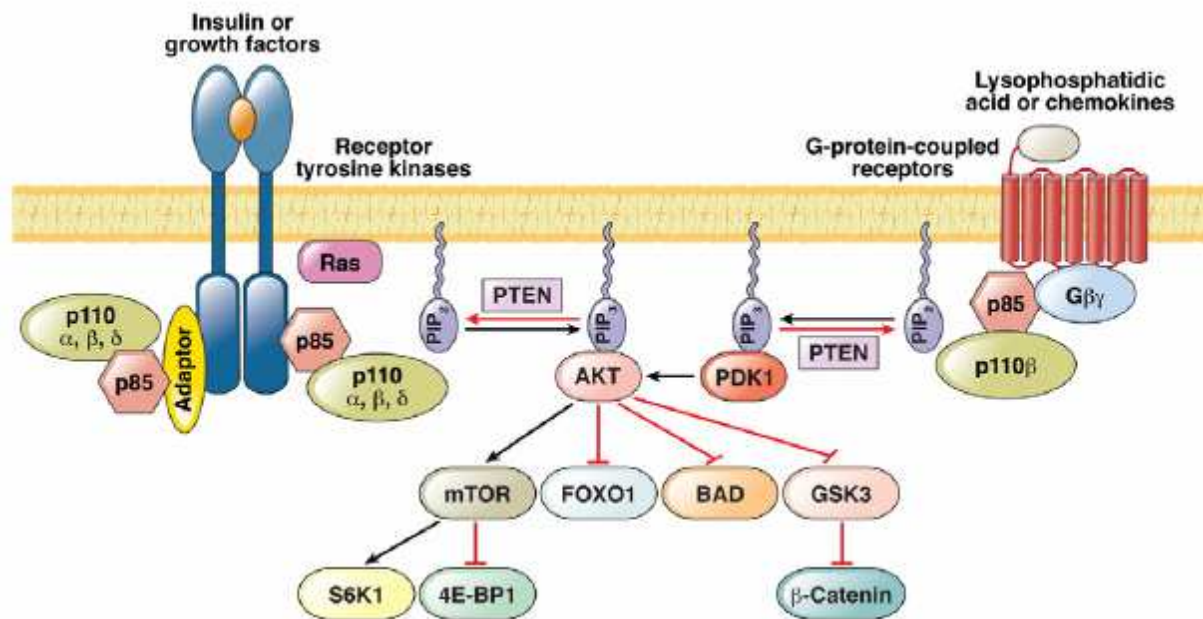
PI3KCA

- Esistono 3 classi eterodimiche di PI3Ks (I, II, e III).
- La più caratterizzata è la classe I che è suddivisa in:

classe IA PI3K e classe IB PI3K

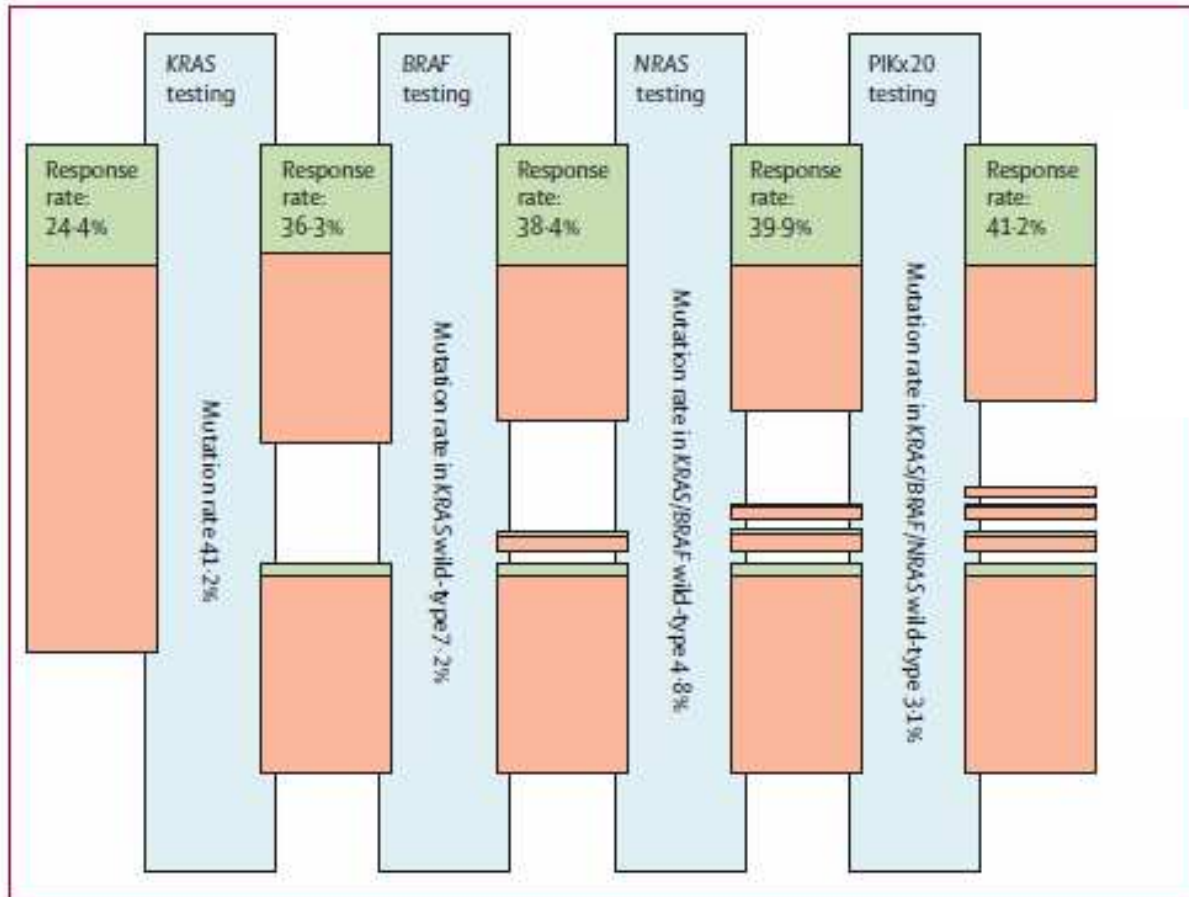
IA PI3K è costituita da una subunità regolatoria (p85) ed una catalitica (p110)

- Mutato in circa 15-30% dei tumori del colon-retto (esoni 9 e 20)
- Mutazioni più frequenti nelle donne e nel colon prossimale
- Spesso concomitante alla mutazione di k-ras e alla perdita di PTEN



Activated PI3K converts PIP2 to PIP3, which provides docking sites for signaling proteins such as AKT. Once activated, AKT phosphorylates many downstream effectors to regulate cell processes such as protein synthesis, cell survival, proliferation, and metabolism.

PTEN functionally antagonizes PI3K activity by dephosphorylating PIP3.



773 tumori del colon analizzati per frequenza di mutazioni di *KRAS*, *BRAF*, *NRAS* e *PIK3CA*

Valutata la risposta obiettiva, il PFS e l'OS, per sottogruppi molecolari, in **649 pazienti refrattari a cetuximab plus chemotherapy.**

Multivariate analysis and conditional inference trees confirmed that, if *KRAS* is not mutated, assessing *BRAF*, *NRAS*, and *PIK3CA* exon 20 mutations (in that order) gives additional information about outcome.

Objective response rates in our series were 24.4% in the unselected population, 36.3% in the *KRAS* wild-type selected population, and 41.2% in the *KRAS*, *BRAF*, *NRAS*, and *PIK3CA* exon 20 wild-type population.

PI3KCA

Effects of KRAS, BRAF, NRAS, and PIK3CA mutations on the efficacy of cetuximab plus chemotherapy in chemotherapy-refractory metastatic colorectal cancer: a retrospective consortium analysis



De Roock W et al Lancet Oncol 2010; 11: 753–62

PIK3CA exon 9 mutations had no effect

PIK3CA exon 20 mutations were associated with a worse outcome compared with wild types

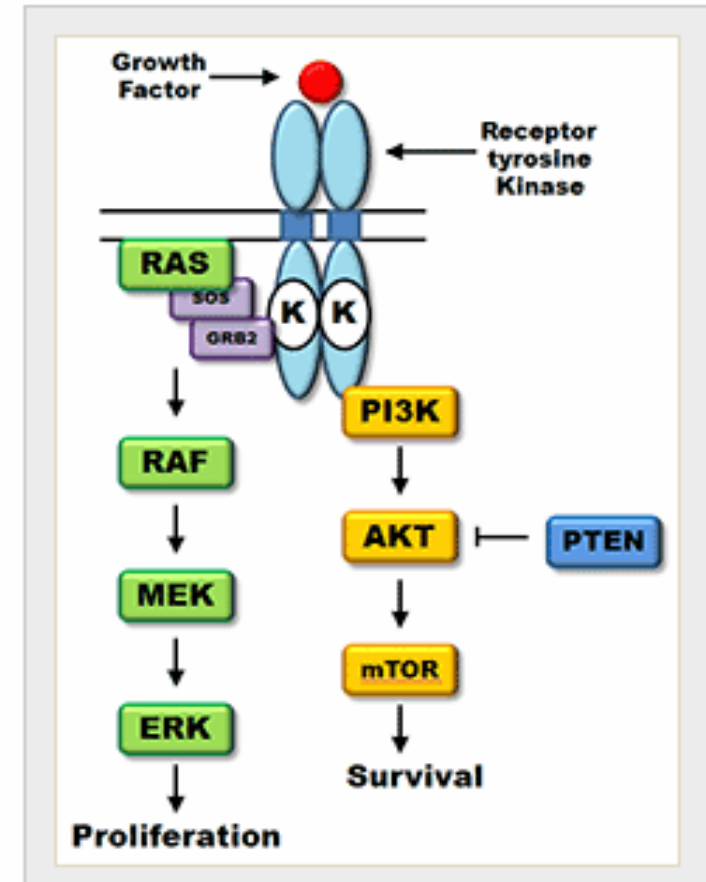
response rate of 0.0% (0/9) versus 36.8% (121/329; OR 0.00, 0.00–0.89; p=0.029),

a median PFS of 11.5 weeks versus 24 weeks (HR 2.52, 1.33–4.78; p=0.013), and

a median overall survival of 34 weeks versus 51 weeks (3.29, 1.60–6.74; p=0.0057).

PTEN

- Agisce come oncosoppressore antagonizzando l'effetto della PIK3CA
- Perdita della sua espressione nel 30-40% dei tumori del colon-retto
- Risultati discordanti in letteratura riguardo la sua predittività a risposte ai TKIs
- Variabilità di risultati in letteratura dovuta alle diverse metodologie utilizzate e ai diversi cut off (immunoistochimica, FISH..)



Epidermal growth factor receptor (EGFR) gene promoter methylation and cetuximab treatment in colorectal cancer patients

Scartozzi M et al. British Journal of Cancer (2011)

....under normal circumstances, EGFR expression is primarily regulated by the abundance of its m-RNA....

(Scartozzi et al, 2007; Van Cutsem et al, 2009).

This observation is of particular relevance if we consider that EGFR m-RNA expression demonstrated a possible correlation with survival during anti-EGFR treatment

(Xu et al, 1984; Merlino et al, 1985; Vallbo"hmer et al, 2005).

At least hypothetically, EGFR promoter silencing may then affect clinical outcome of patients treated with anti-EGFR strategies through the inhibition of EGFR m-RNA expression.

52 pazienti EGFR-positivi (IHC), K-RAS wildtype, con carcinoma del colon metastatico, trattati con un regime contenente irinotecan per almeno 6 w. in progressione (durante il trattamento o entro 3 mesi).

Tutti pazienti hanno ricevuto cetuximab (dose iniziale: 400 mg /m² →infusione settimanale di of 250 mg /m². Irinotecan alla dose di 180 mg /m²ogni 2 w solo o in combinazione con 5-FU e leucovorin).

30 patients (58%) showed EGFR promoter hypermethylation.

In EGFR promoter methylated and EGFR promoter unmethylated patients:

Median progression-free survival of 2.4 months in patients showing EGFR promoter methylated tumours and 7.4 months for those who had EGFR promoter unmethylated tumours ($P < 0.0001$)

Median overall survival was 6.1 months in patients showing EGFR promoter methylated tumours and 17.8 months for those who had EGFR promoter unmethylated tumours ($P < 0.0001$)

Among the 21 patients in whom both primary site and metastases were available for EGFR methylation study, EGFR methylation status of primary tumour was in accordance with that of metastasis in 16 patients (76%)

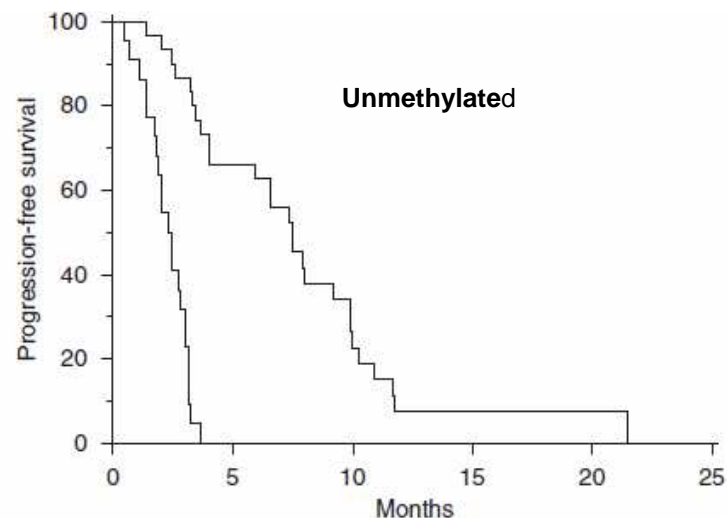


Figure 1 Kaplan–Meier curves for median progression-free survival (PFS) of colorectal cancer patients treated with irinotecan and cetuximab with EGFR promoter methylated (—) and without EGFR promoter methylated (---) tumours (2.4 vs 7.4 months, $P < 0.0001$).

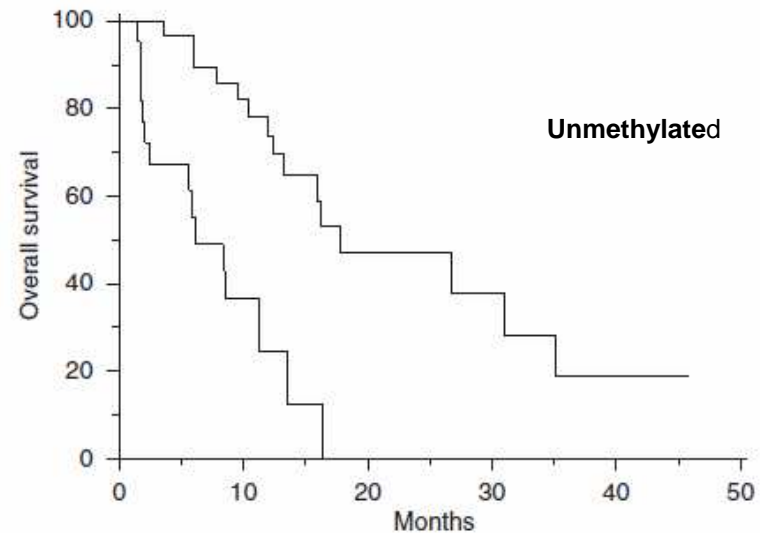


Figure 2 Kaplan–Meier curves for median overall survival (OS) of colorectal cancer patients treated with irinotecan and cetuximab with EGFR promoter methylated (—) and without EGFR promoter methylated (---) tumours (6.1 vs 17.8 months, $P < 0.0001$).

Determinazioni molecolari: sul primitivo o sulle metastasi?

Raccomandazioni AIOM-SIAPEC-IAP indicano che l'analisi di k-ras può essere fatta indifferentemente sul tessuto tumorale primitivo o sulla lesione metastatica

Concordanza delle analisi molecolari veramente del 100%?

Analisi di diversi marcatori molecolari del tessuto tumorale primitivo, metastasi linfonodale e a distanza

Case no.	EGFR IHC			EGFR FISH			K-Ras			BRAF			PTEN IHC			Clinical response
	T	LN	M	T	LN	M	T	LN	M	T	LN	M	T	LN	M	
1	+	+	+	P	A	A	WT	WT	WT	WT	WT	WT	+	+	+	-
2	+	NA	+	P	NA	D	G12A	NA	G12A	WT	NA	WT	-	NA	-	-
3	+	+	+	P	NV	P	WT	WT	G12C	WT	WT	WT	+	+	+	-
4	+	NA	+	A	NA	P	G12D	NA	G12D	WT	NA	WT	-	NA	-	-
5	+	+	+	P	P	P	G12A	G12A	G12A	WT	WT	WT	-	-	-	-
6	+	+	+	D	D	P	WT	WT	WT	WT	WT	WT	-	-	-	-
7	+	NA	+	P	NA	P	G12C	NA	WT	WT	NA	WT	-	NA	-	-
8	+	NA	+	NV	NA	NV	WT	NA	WT	NV	NA	NV	+	NA	-	-
9	+	+	+	P	P	P	G13D	G13D	G13D	WT	WT	WT	+	+	+	-
10	+	NA	+	A	NA	A	WT	NA	WT	WT	NA	WT	+	NA	+	-
11	+	+	+	A	A	P	WT	WT	WT	WT	WT	WT	+	+	+	-
12	+	NA	+	A	NA	A	WT	NA	WT	WT	NA	WT	+	NA	+	-
13	+	NA	+	A	NA	A	WT	NA	WT	WT	NA	WT	+	NA	+	-
14	+	NA	+	P	NA	P	WT	NA	WT	WT	NA	WT	+	NA	+	-
15	+	NA	+	D	NA	D	WT	NA	WT	WT	NA	WT	+	NA	+	-
16	+	NA	+	P	NA	P	G12D	NA	G12D	WT	NA	WT	+	NA	+	-
17	+	NA	+	P	NA	P	G13D	NA	WT	WT	NA	WT	+	NA	+	-
18	+	NA	+	P	NA	P	G13D	NA	G13D	WT	NA	WT	-	NA	-	-
19	+	NA	+	L	NA	L	WT	NA	WT	WT	NA	WT	+	NA	+	-
20	+	+	+	P	P	P	G12V	G12V	G12V	WT	WT	WT	+	+	+	-
21	+	NA	+	D	NA	P	WT	NA	WT	WT	NA	WT	+	NA	+	-
22	+	+	+	P	P	D	WT	WT	WT	WT	WT	WT	+	+	+	-
23	+	+	+	D	D	P	G12A	G12A	G12A	WT	WT	WT	+	+	+	-
24	+	NA	+	NV	NA	NV	NV	NA	NV	NV	NA	NV	+	NA	+	-
25	+	+	+	D	D	D	WT	WT	WT	V600E	V600E	V600E	+	+	+	NR
26	+	+	+	D	D	D	G12D	G12D	G12D	WT	WT	WT	+	+	+	-
27	+	+	+	D	P	P	G12A	G12A	G12A	WT	WT	WT	-	-	-	NR
28	+	+	+	P	NV	A	G12A	G12A	G12A	WT	WT	WT	+	-	-	NR
29	+	+	+	D	D	P	G12D	G12D	G12D	WT	WT	WT	+	+	+	NR
30	+	NA	+	A	NA	A	WT	NA	WT	WT	NA	WT	+	NA	+	PR
31	+	+	+	P	P	P	WT	WT	WT	V600E	V600E	V600E	+	-	-	NR
32	+	NA	+	D	NA	D	WT	NA	WT	WT	NA	WT	+	NA	+	NR
33	+	NA	+	A	NA	A	WT	NA	WT	WT	NA	WT	+	NA	+	PR
34	+	NA	+	P	NA	P	G12S	NA	G12S	WT	NA	WT	+	NA	+	NR
35	+	NA	+	P	NA	P	G12A	NA	G12A	WT	NA	WT	+	NA	+	NR
36	+	NA	+	P	NA	P	WT	NA	WT	WT	NA	WT	+	NA	-	NR
37	+	NA	+	D	NA	P	WT	NA	WT	WT	NA	WT	+	NA	+	-
38	+	NA	+	A	NA	A	WT	NA	WT	WT	NA	WT	-	NA	-	NR

Abbreviations: A = EGFR gene amplification; D = chromosome 7 disomy; L = chromosome 7 loss; LN = lymph node metastases; M = distant metastatic sites; NA = not available; NR = non-responsive; NV = not evaluable; PR = partially responsive; P = chromosome 7 polysomy; T = primary tumour; WT = wild-type; '+' = positive expression; '-' = negative expression.

***KRAS* and *BRAF* Mutational Status in Primary Colorectal Tumors and Related Metastatic Sites: Biological and Clinical Implications**

Italiano A et al. Ann Surg Oncol (2010) 17:1429–1434

A total of 285 and 95 matched PT/metastases were available for the analysis of the *KRAS* and the *BRAF* status, respectively.

In 6 cases (2%), *KRAS* was mutated in the PT and wild type in the metastatic site, whereas in 8 cases (3%), *KRAS* was wild type in the PT and mutated in the metastatic site.

In 1 case (1.5%), *BRAF* was mutated in the PT and wild type in the metastatic site, whereas in 1 case (1.5%), *BRAF* was wild type in the PT and mutated in the metastatic site.

Conclusions. The acquisition by metastases of a *KRAS* or a *BRAF* mutation that was not present in the PT is a rare event, occurring in 5% of cases of mCRC. This is not a frequent mechanism of primary resistance to anti-EGFR treatments in mCRC.

Mutations of *KRAS* and *BRAF* in Primary and Matched Metastatic Sites of Colorectal Cancer

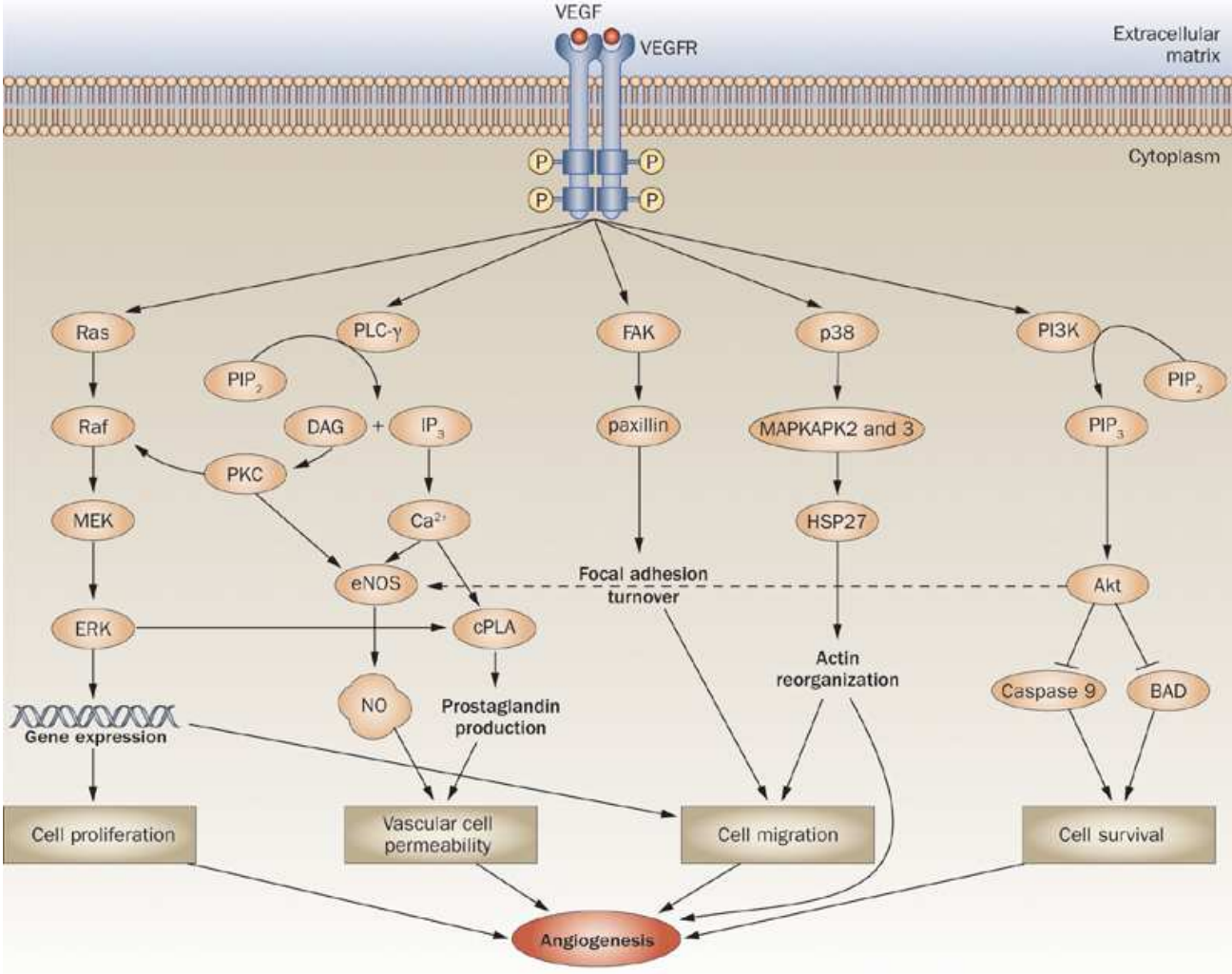
Artale s et al. J.Clin Oncol. 2008

Table 1. Molecular and Clinical Characteristics of Patients With Colorectal Cancers Harboring *KRAS* or *BRAF* Mutations

Patient No.	Primary Tumor			First Metastatic Site			Other Metastatic Site		
	Tumor Site	<i>KRAS</i>	<i>BRAF</i>	Metastasis Site	<i>KRAS</i>	<i>BRAF</i>	Metastasis Site	<i>KRAS</i>	<i>BRAF</i>
1	Colon	G12S	NA	Liver	G12S	NA			
2	Colon	G12D	WT	Liver	G12D	WT			
3	Rectum	G12D	WT	Liver	G12D	WT	Liver	G12D	WT
4	Rectum	G12D	WT	Liver	G12D	WT			
5	Colon	G13D	WT	Liver	G13D	WT			
6	Sigma-rectum	G12S	WT	Liver	WT	WT			
7	Colon	G13D	WT	Liver	G13D	WT			
8	Colon	WT	V600E	Omentum	WT	V600E			
9	Sigma-rectum	G13D	WT	Liver	G13D	WT			
10	Colon	G12C	WT	Liver	G12C	WT			
11	Colon	G12V	WT	Ovary	G12V	WT			
12	Colon	G13D	WT	Liver	G13D	WT			
13	Colon	WT	V600E	Pelvis	WT	WT			
14	Colon	WT	WT	Pancreas	G12V	WT			
15	Rectum	WT	WT	Adrenal gland	G12V	WT	Kidney	G12V	WT

Abbreviations: NA, not assessable; WT, wild type.

VEGFR : main pathways



Retrospective exploratory analysis of *VEGF* polymorphisms in the prediction of benefit from first-line FOLFIRI plus bevacizumab in metastatic colorectal cancer

Up today there are no predictive biomarkers of bevacizumab efficacy. Therefore the anti- VEGF MoAb therapy is currently approved for the treatment of mCRC in association with fluoropyrimidine based chemotherapy without any molecular selection

Methods: Genomic DNA of 111 consecutive metastatic colorectal cancer patients treated with first-line FOLFIRI plus bevacizumab was analyzed. VEGF -2578 C/A, -1498 C/T, + 405 C/G, + 936 C/T polymorphisms were analyzed.

DNA samples from 107 patients treated with FOLFIRI alone served as historical control group.

Cox model has been performed in order to demonstrate the heterogeneity of the effect of VEGF -1498 C/T polymorphism between bevacizumab-and control group.

Retrospective exploratory analysis of *VEGF* polymorphisms in the prediction of benefit from first-line FOLFIRI plus bevacizumab in metastatic colorectal cancer

Results: In the bevacizumab-group median PFS and OS of patients carrying VEGF -1498 C/C, C/T and T/T allelic variants were, respectively, 12.8, 10.5, 7.5 months ($p = 0.0046$, log-rank test) and 27.3, 20.5, 18.6 months ($p = 0.038$, log-rank test).

VEGF -1498 T/T genotype was associated with shorter PFS (HR = 2.13, [1.41-5.10], $p = 0.0027$).

In the control group no significant association of VEGF -1498 C/T allelic variants and PFS or OS was found.

Interaction between VEGF -1498 C/T variants and treatment effect suggested that the relation of VEGF -1498 T/T genotype with shorter PFS was caused by the effect of bevacizumab ($p = 0.011$). Other investigated polymorphisms did not affect the outcome.

Conclusions: These data suggest a possible role for VEGF -1498 C/T variants in predicting the efficacy of bevacizumab in the up-front treatment of metastatic colorectal cancer patients. A prospective validating trial is currently ongoing.

Vascular endothelial growth factor polymorphisms and clinical outcome in colorectal cancer patients treated with irinotecan-based chemotherapy and bevacizumab

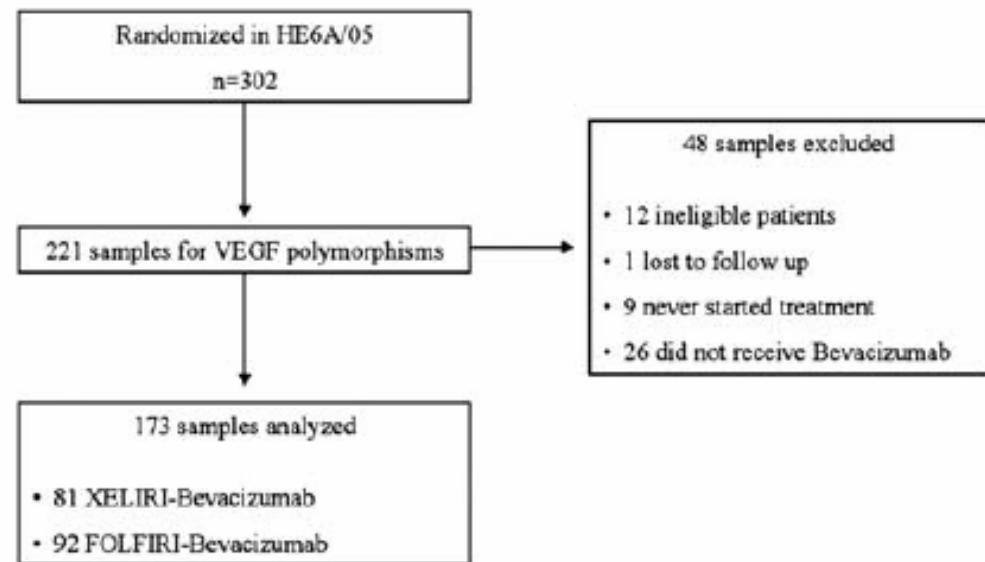
Koutras AK et al.

The Pharmacogenomics Journal (2011)

302 Patients previously untreated for metastatic disease were randomized in

Arm A (irinotecan 240mg/m² day 1, capecitabine 1000mg/m² days 1–14 and bevacizumab 7.5 mg/kg day 1, every 3 weeks; XELIRI-bevacizumab)

Arm B (irinotecan 180mg/m² day 1, leucovorin 200mg/m² day 1, 5-FU 400mg/m² bolus on day 1 followed by a 5-FU 2400mg/m² 46 h infusion, and bevacizumab 5 mg/kg day 1, every 2 weeks; FOLFIRI-bevacizumab)



Vascular endothelial growth factor polymorphisms and clinical outcome in colorectal cancer patients treated with irinotecan-based chemotherapy and bevacizumab

Koutras AK et al.

The Pharmacogenomics Journal (2011)

Genotyping was performed for selected SNPs (VEGF1154, p936, 634, 2578 and 1498). All candidate genotypes were evaluated for associations with overall survival (OS), progression-free survival (PFS) and response rate (RR). There were no significant differences with respect to the distribution of genotypes in the treatment groups.

The VEGF1154 G/G genotype was more frequent in patients not responding to treatment compared with responders (65.5 versus 39.8%, P=0.032). Furthermore, the VEGF1154 GG genotype was associated with inferior median OS compared with GA (hazards ratio=1.68; 95% confidence interval: 1.10–2.57; P=0.016)

In multivariate analysis, the VEGF1154 GG genotype remained a significant adverse factor for OS. Our results support the potential predictive ability of VEGF genotypes in patients with metastatic colorectal cancer receiving irinotecan-based chemotherapy plus bevacizumab, in terms of RR and OS. However, current results should be validated prospectively, in larger cohorts

DEPArray

Electronics

Microscopy

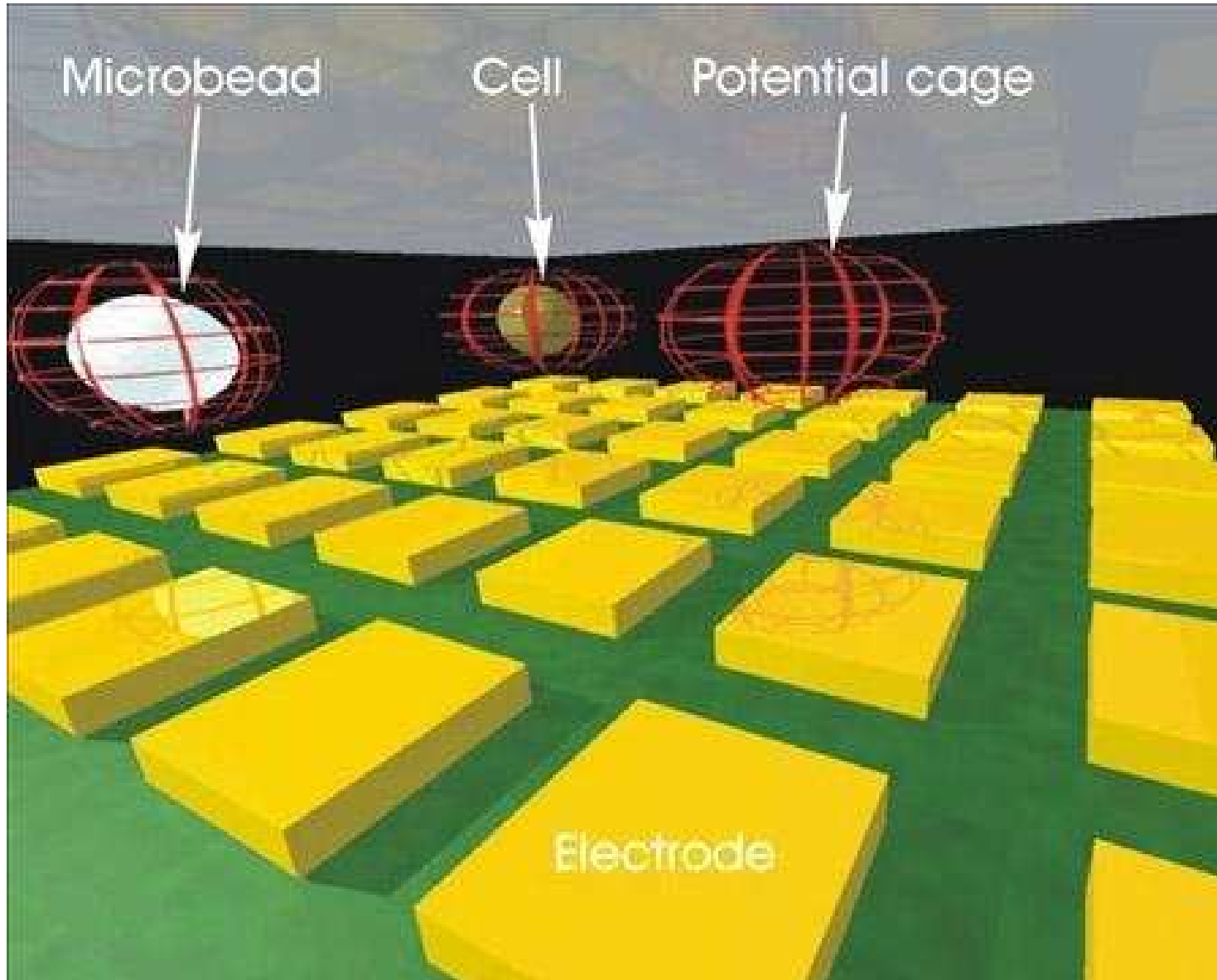
Microfluidics

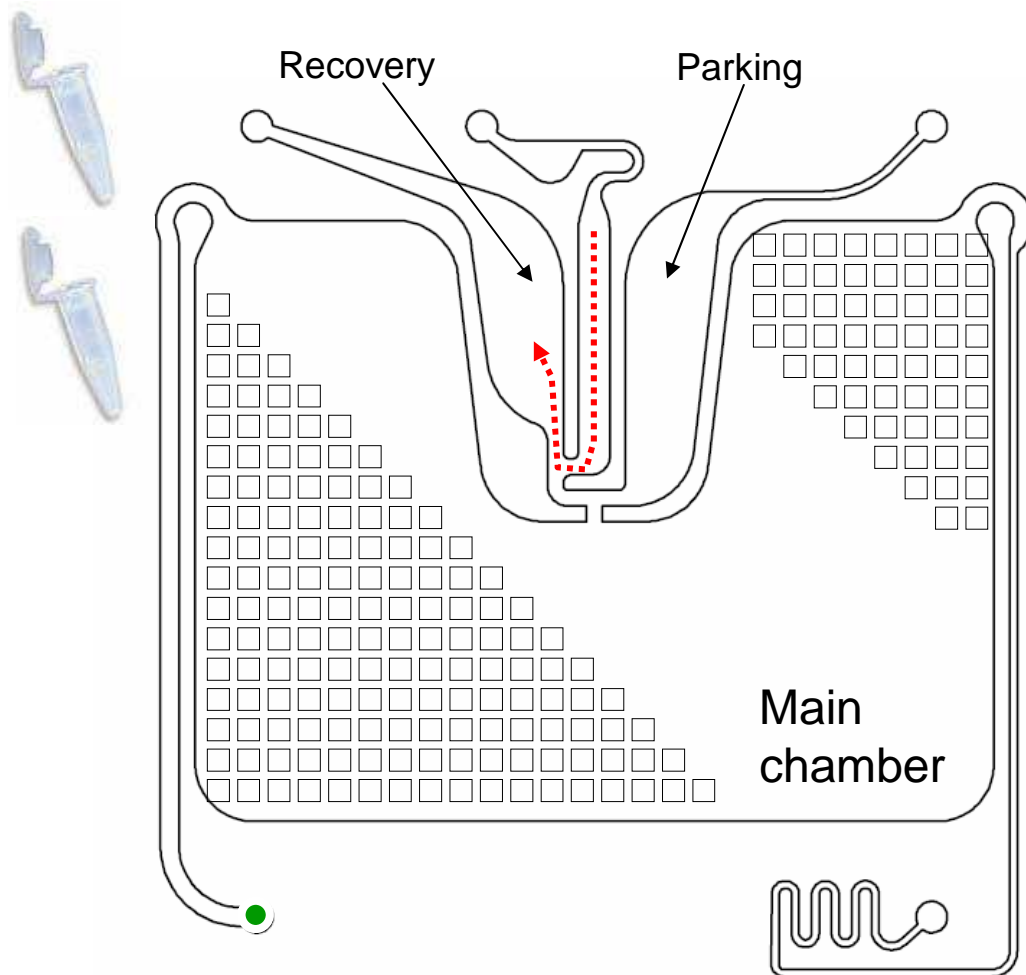
Software



DEPArray is a cell microarray for individual cell manipulation and detection

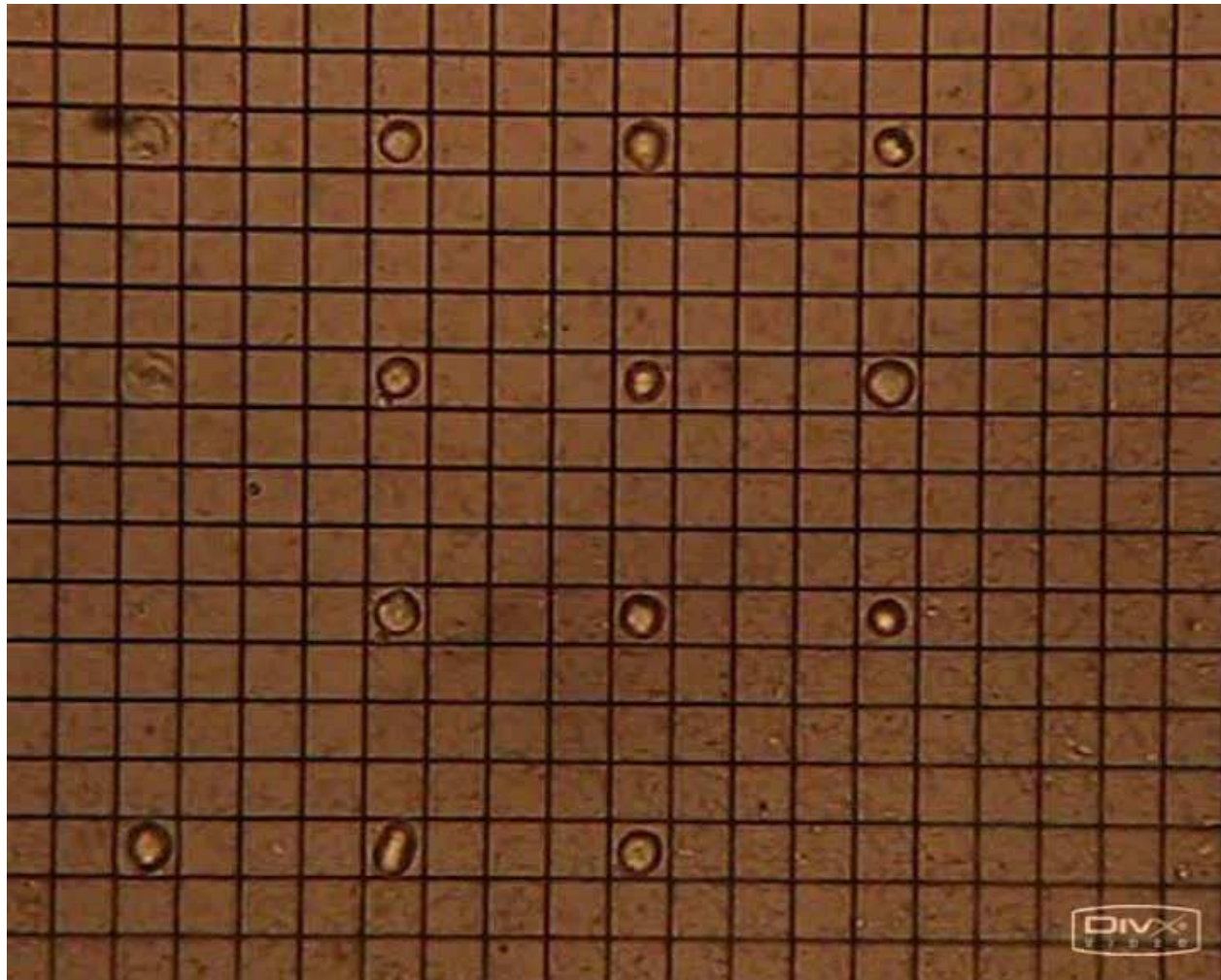
DEP Cages





1. Inject, trap and image all cells
2. Move all cells of interest into Parking chamber
3. Move separately to Recovery chamber and flush

Analisi al DEPArray



CTC: Analisi al DEPAarray

Analizzati 30 casi di tumori del colon metastatici .

Individuate CTC nel 60% dei pazienti (% superiore alla letteratura [25-30%])
(individuate circa 10 CTC x ml di sangue)

In 4 casi abbiamo tentato il confronto fra stato mutazionale di k-ras nel primitivo e CTC: concordanza del 50%.

Analizzati 14 casi di k polmone metastatici per presenza di CTC: Individuate CTC nel 50% dei pazienti (% in linea con quanto ritrovato in letteratura)

CONCLUSIONI

La ricerca di marcatori predittivi di risposta a terapie con inibitori di EGFR ha sicuramente aumentato le sue conoscenze di base portando ad un più razionalizzare l'uso di questi farmaci.

Un uso più razionale dei farmaci EGFR-targeted può consentire sia benefici clinici ai pazienti sia benefici ai costi del sistema sanitario nazionale.

Fino ad oggi non disponiamo di biomarcatori predittivi della risposta a bevacizumab .

I pazienti KRAS mutati?

Necessità di incentivare gli sforzi della ricerca di base

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