U.O.C. NEUROCHIRURGIA

U.O.S.D. NEURO-ONCOLOGIA

Istituto Giannina Gaslini
Ospedale Pediatrico IRCCS

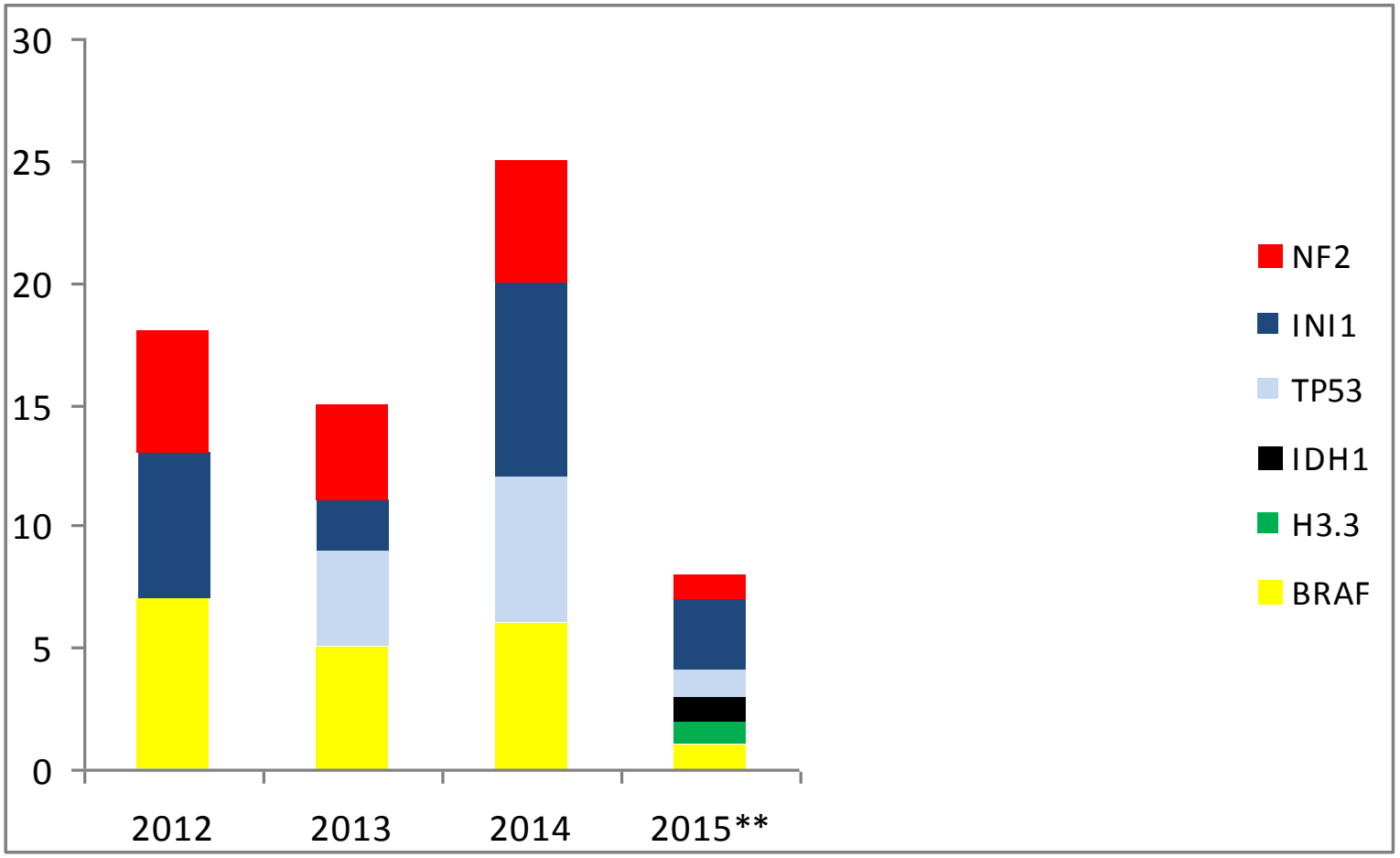
Gaslini, 21/03/2015

Diagnosi molecolare geni coinvolti nei tumori cerebrali che vengono offerti alle famiglie dal 2012 ad oggi

- ***INI1/SMARCB1*** (*Tumori rabdoidi*)
- ***NF2*** (*Neurofibromatosi tipo 2)* Orphanet (http://www.orpha.net)

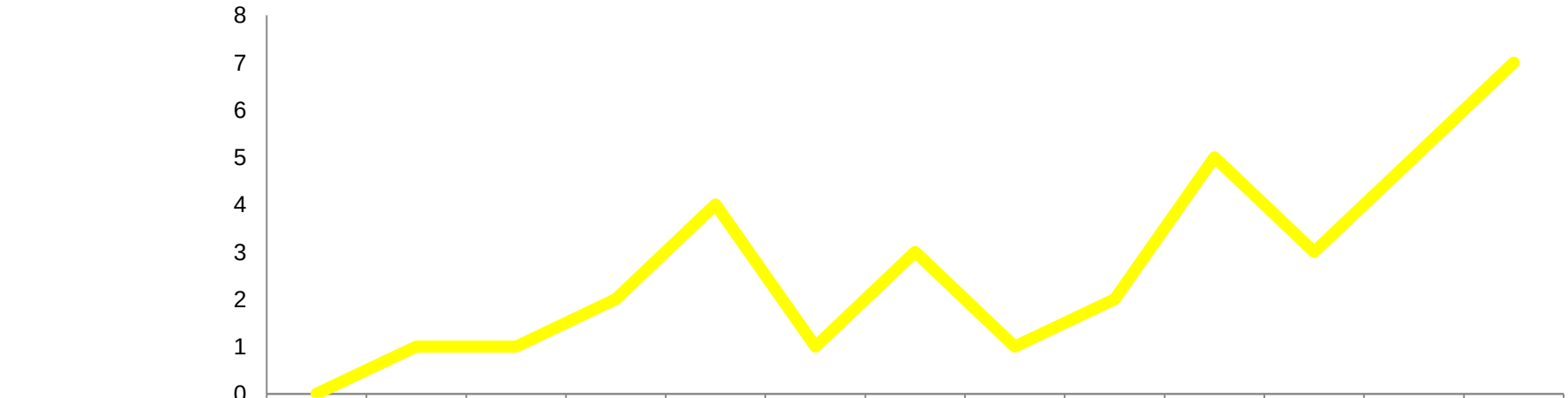
- verifica della presenza di **fusione genica** tra ***BRAF*** e ***KIAA1549*** *(Astrocitomi pilocitici e Low Grade Glioma)*
- mutazione **V600E** di ***BRAF*** *(LGG ed anche in supporto della scelta terapeutica in alcuni casi di High Grade Glioma)*
- ***TP53, H3.3 e IDH1*** *(High Grade Glioma e nei casi di diagnosi differenziale)*

Diagnosi molecolari effettuate



Pubblicistica 2002-2014

Totale 35



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Pubblicazioni totali	0	1	1	2	4	1	3	1	2	5	3	5	7

Pubblicazioni del 2014

Mascelli S, Severino M, Raso A, Nozza P, Tassano E, Morana G, De Marco P, Merello E, Milanaccio C, Pavanello M, Rossi A, Cama A, Garrè ML and Capra V. Constitutional chromosomal events at 22q11 and 15q26 in a child with a pilocytic astrocytoma of the spinal cord. Mol Cytogenet. 2014 May 15;7:31. IF: 2,36

Mascelli S. A reliable assay for rapidly defining transplacental metastasis using quantitative PCR. Methods Mol Biol. 2014;1160:125-31.

Donatella Vecchio, Antonio Daga, Elisa Carra, Daniela Marubbi, Gabriella Baio, Carlo E. Neumaier, Stefano Vagge, Renzo Corvò, Maria Pia Brisigotti, Jean Lous Ravetti, Annalisa Zunino, Alessandro Poggi, Alessandro Raso, Samantha Mascelli and Guido Frosina. Predictability, efficacy and safety of radio-sensitization of glioma stem cells by the ATM-inhibitor KU-60019. International Journal of Cancer 2014 Jul 15;135(2):479-91. IF: 6,2

Donatella Vecchio, Antonio Daga, Elisa Carra, Daniela Marubbi, Alessandro Raso, Samantha Mascelli, Paolo Nozza, Maria Luisa Garrè, Francesca Pitto, Jean Louis Ravetti, Stefano Vagge, Renzo Corvò, Aldo Profumo, Gabriella Baio, Diana Marcello and Guido Frosina. Pharmacokinetics, pharmacodynamics and efficacy on pediatric tumors of the glioma radiosensitizer KU60019. Int J Cancer. 2014 Aug 4. doi: 10.1002/ijc.29121. IF: 6,2

Pio L, Milanaccio C, Mascelli S, Raso A, Nozza P, Sementa AR, Cama A, Buffa P, Avanzini S, Vannati M, Capra V, Lanino E, Rossi A, Morana G, Magnano GM, Severino M, Garrè ML. Congenital multifocal rhabdoid tumor: a case with peculiar biological behavior and different response to treatment according to location (central nervous system and kidney). Cancer Genet. 2014 Sep;207(9):441-4. IF: 1,915

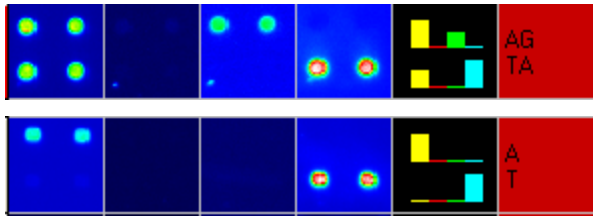
Raso A, Biassoni R. Twenty years of qPCR: a mature technology?" Methods Mol Biol. 2014;1160:1-3.

Prato G, Mancardi MM, Baglietto MG, Janis S, Vercellino N, Rossi A, Consales A, Raso A, Garrè ML. Congenital segmental lymphedema in tuberous sclerosis complex with associated subependymal giant cell astrocytomas treated with Mammalian target of rapamycin inhibitors. J Child Neurol. 2014 Sep;29(9):NP54-7 . IF: 1,8

Lavori in fase di sottomissione/revisione

Samantha Mascelli, Maria Luisa Garrè, Katrin Sak, Kairit Joost, Armando Cama, Valeria Capra, Paolo Nozza and Alessandro Raso. **"Microsatellite instability in a radiation-induced anaplastic astrocytoma harbouring *IDH1* mutation".** *Pediatric Blood and Cancer.* ***IF: 2,56***

Caratterizzazione molecolare dell'unico tumore (Astrocitoma anaplastico) radio-indotto con mutazione sul gene *IDH1*.



Mutazione in eterozigosi di hMLH1

WT

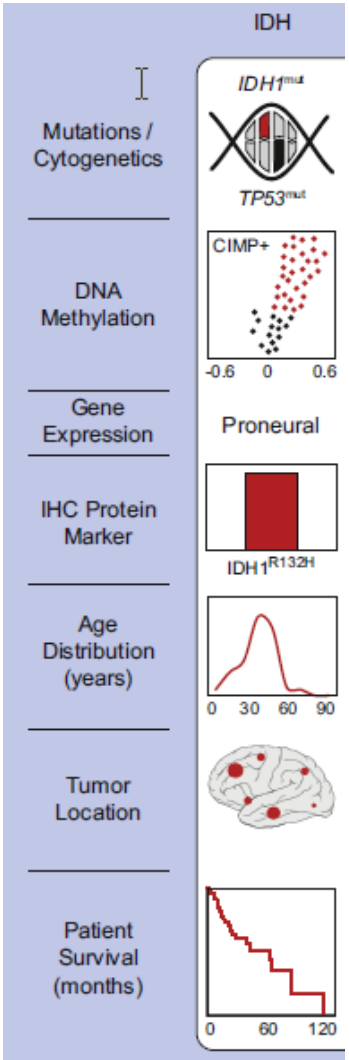
Sample ID	Surg·Age (year)/sex	Histology	WHO	site·of·lesion	IDH1· (p.R132H)	IDH2· (p.R172)	TP53	EGFR	PTEN	RB1	hMLH1	PMS2	hMSH2	hMSH6	H3F3A
HGG3	19,68/M	AA	III	Hemisphere	R132H	wt	p.R175H	wt	wt	wt	p.K618delK	wt	wt	wt	wt

J Neurooncol (2012) 109:477–484
DOI 10.1007/s11060-012-0925-1

LABORATORY INVESTIGATION

Analysis of NADP+-dependent isocitrate dehydrogenase-1/2 gene mutations in pediatric brain tumors: report of a secondary anaplastic astrocytoma carrying the *IDH1* mutation

Samantha Mascelli · Alessandro Raso · Roberto Biassoni · Mariasavina Severino · Katrin Sak · Kairit Joost · Claudia Milanaccio · Salvina Barra · Filippo Grillo-Ruggieri · Irene Vanni · Alessandro Consales · Armando Cama · Valeria Capra · Paolo Nozza · Maria Luisa Garrè



"The Arg72 TP53 may predict shorter survival in not totally resected low grade glioma in children."

British Journal of Cancer. **IF: 4.8**

In collaborazione con:

- Asper Biotechnology, Ltd, Tartu, Estonia
- Epidemiology and Biostatistics Unit, G. Gaslini Institute (Dott.ssa A. Pistorio).
- Molecular Medicine Unit, G. Gaslini Institute (Dott. R. Biassoni).
- Pathology Unit, G. Gaslini Institute (Dr. P. Nozza)
- Pre-Clinical working group, SIOP. Heidelberg group (Dr. S. Pfister)
- Computational Biology research group in Florence, "Careggi" University-Hospital (Dott. A. Magi).
- Pathologique et Neuropathologie, Hôpital de la Timone, Marseille, Francia (Prof Dominique Figuarella-Branger)
- Haematology/Oncology, The Hospital for Sick Children, Toronto, Canada (Prof Uri Tabori).

Dipartimento Testa-Collo, U.O.C. Neurochirurgia, Istituto Giannina Gaslini, Genova-Italia

SIOP-LGG preclinical working group
October 2nd and 3rd, Cassis

Genetic markers of early recurrence in LGGs

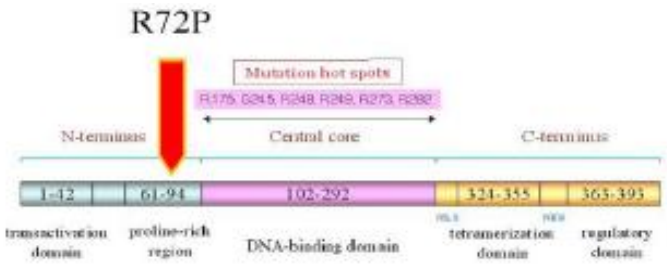
Alessandro Raso & Samantha Mascelli,

on behalf of the Neuro-Oncology group of Istituto Giannina Gaslini Genoa-Italy.

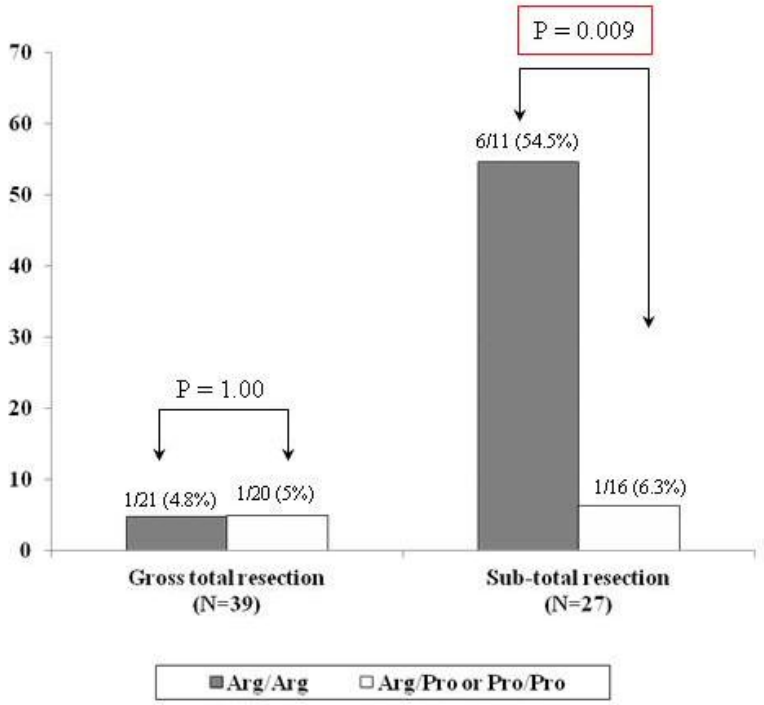
Esistono specifici marcatori molecolari predittivi per i LGGs in rapida progressione di malattia ?

p53

Guardiano del genoma



Su 66 casi Italiani



Nei pazienti in cui la resezione totale del tumore non è possibile, occorre valutare lo stato del polimorfismo (R72P) del gene *TP53.*

La variante Arg/Arg (R72P) è un fattore prognostico avverso per cui si manifestano casi di Early Progression.

Analisi estesa a 121 casi LGGs provenienti da:

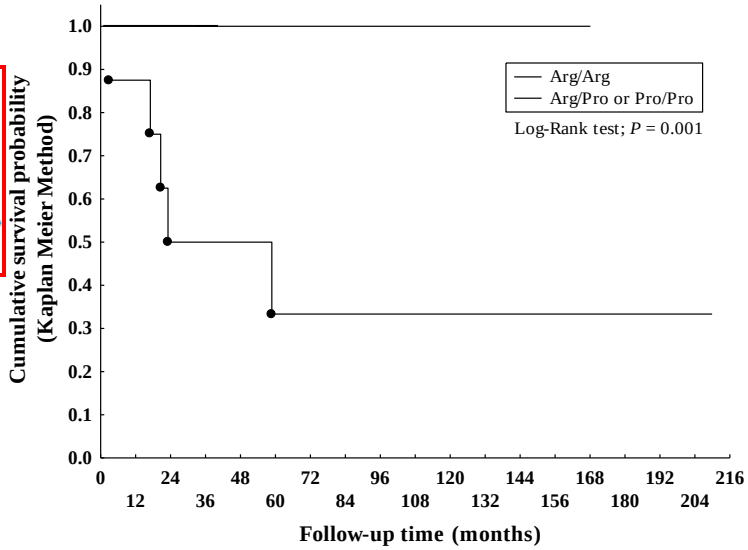
- **Pathologique et Neuropathologie, Hôpital de la Timone, Marseille, Francia (Prof Dominique Figuarella-Branger)**
- **Haematology/Oncology, The Hospital for Sick Children, Toronto, Canada (Prof Uri Tabori)**

86 casi (Italia e Francia)

Table 3: Number (and percentage) of deaths or disease progression in Low-grade gliomas in Italian and French patients

	No. of deaths disease progression (%)	IR × 1000 p-ms	P value Log-Rank
Histology mixed glial-neuronal tumors (N=31)			
R72P, *TP53* Arg/Arg (homozygous) (N=16)	3 (18.7)	2.454	0.31
Arg/Pro or Pro/Pro (N=15)	5 (33.3)	4.715	
Histology mixed glial-neuronal tumor in STR only (N=11)			
R72P, *TP53* Arg/Arg (homozygous) (N=5)	2 (40.0)	6.282	0.30
Arg/Pro or Pro/Pro (N=6)	3 (50.0)	10.341	
Histology Pilocytic astrocytomas (PA) (N=54)			
R72P, *TP53* Arg/Arg (homozygous) (N=23)	5 (21.7)	2.739	0.028
Arg/Pro or Pro/Pro (N=31)	1 (3.2)	0.367	
Histology Pilocytic astrocytomas (PA) in STR only (N=20)			
R72P, *TP53* Arg/Arg (homozygous) (N=8)	5 (62.5)	9.894	0.0015
Arg/Pro or Pro/Pro (N=12)	0 (0.0)	0.000	
Site of lesion: Supratentorial (N=43)			
R72P, *TP53* Arg/Arg (homozygous) (N=23)	5 (21.7)	2.666	0.89
Arg/Pro or Pro/Pro (N=20)	4 (20.0)	2.436	
Site of lesion: Supratentorial in STR only (N=15)			
R72P, *TP53* Arg/Arg (homozygous) (N=8)	4 (50.0)	7.954	0.22
Arg/Pro or Pro/Pro (N=10)	2 (20.0)	2.679	
Site of lesion: Infratentorial (N=43)			
R72P, *TP53* Arg/Arg (homozygous) (N=17)	3 (17.6)	2.544	0.32
Arg/Pro or Pro/Pro (N=26)	2 (7.7)	0.934	
Site of lesion: Infratentorial in STR only (N=14)			
R72P, *TP53* Arg/Arg (homozygous) (N=6)	3 (50.0)	9.152	0.19
Arg/Pro or Pro/Pro (N=8)	1 (12.5)	1.436	

PA in STR
N=20



78 casi da Toronto

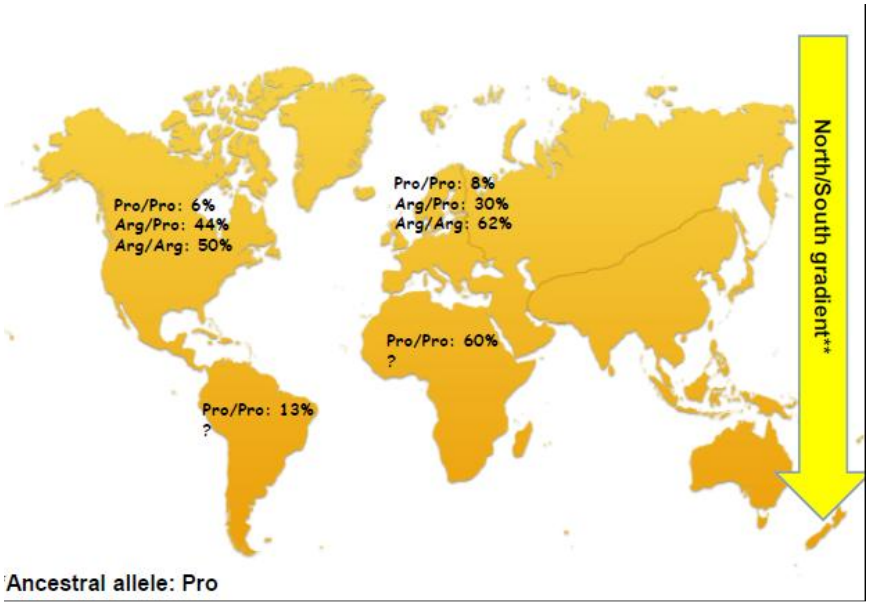
Table 3: Number (and percentage) of deaths or disease progression in Low-grade glioma patients from Toronto with selected histology and type of surgery and site of lesion.

	No. of deaths/disease progression (%)	P-value
Histology—mixed glial-neuronal tumors (N=11)		
R72P, *TP53*: Arg/Arg (N=4)	1 (25.0)	1.00[a]
Arg/Pro or Pro/Pro (N=7)	2 (28.6)	
Histology—mixed glial-neuronal tumors in only STR (N=6)		
R72P, *TP53*: Arg/Arg (N=2)	1 (50.0)	1.00[a]
Arg/Pro or Pro/Pro (N=4)	2 (50.0)	
Histology—Pilocytic astrocytomas (PA) (N=62)		
R72P, *TP53*: Arg/Arg (N=35)	8 (22.9)	0.037[b]
Arg/Pro or Pro/Pro (N=27)	13 (48.1)	
Histology—Pilocytic astrocytomas (PA) in only STR (N=27)		
R72P, *TP53*: Arg/Arg (N=12)	7 (58.3)	0.71[a]
Arg/Pro or Pro/Pro (N=15)	10 (66.7)	
Histology—Pilocytic astrocytomas (PA) (N=62)		
R72P, *TP53*: Arg/Pro (*heterozygous*) (N=24)	12 (50.0)	0.033[b]
Arg/Arg or Pro/Pro (N=38)	9 (23.7)	
Site of lesion: Supratentorial (N=30)		
R72P, *TP53*: Arg/Arg (N=15)	6 (40.0)	0.71[b]
Arg/Pro or Pro/Pro (N=15)	7 (46.7)	
Site of lesion: Supratentorial in only STR (N=19)		
R72P, *TP53*: Arg/Arg (N=9)	6 (66.7)	1.00[a]
Arg/Pro or Pro/Pro (N=10)	7 (70.0)	
Site of lesion: Infratentorial (N=43)		
R72P, *TP53*: Arg/Arg (N=24)	3 (12.5)	0.038[a]
Arg/Pro or Pro/Pro (N=19)	8 (42.1)	
Site of lesion: Infratentorial in only STR (N=14)		
R72P, *TP53*: Arg/Arg (N=5)	2 (40.0)	1.00[a]
Arg/Pro or Pro/Pro (N=9)	5 (55.6)	

[a]: Fisher's Exact test; [b]: Chi-square test

Un bias nella distribuzione di R72P è stato notato

(Beckman et al. 1994).



Collaborazioni in corso:

- **Analisi del metiloma nei tumori cerebrali < 3 anni di età – 65 casi di IGG forniti**

  Pre-Clinical working group, SIOP. Heidelberg group (Dr. S. Pfister)
- **Analisi d'espressione dei miRNA nei Low Grade Gliomas – 12 casi di IGG forniti**

  Università La Sapienza, Roma (Dott.ssa Ferretti E., Prof. F.Giangaspero)
- **Analisi mutazionale del gene INI1 nei Cordomi – 15 casi da analizzare provenienti da Roma**

  Università La Sapienza, Roma (Prof. F. Giangaspero)
- **Stabilizzazione delle linee primarie di Astrocitoma Pilocitico – 10 linee di IGG fornite**

  Pre-Clinical working group, SIOP. Heidelberg group (Dr. Olaf Witt)
- **Progetto MAGIC sui Medulloblastomi – 45 casi di cui 5 casi con recidiva di IGG forniti**

  The Hospital for Sick Children, Toronto, Canada (Prof. M. Taylor)

NEURO-ONCOLOGY Prima revisione

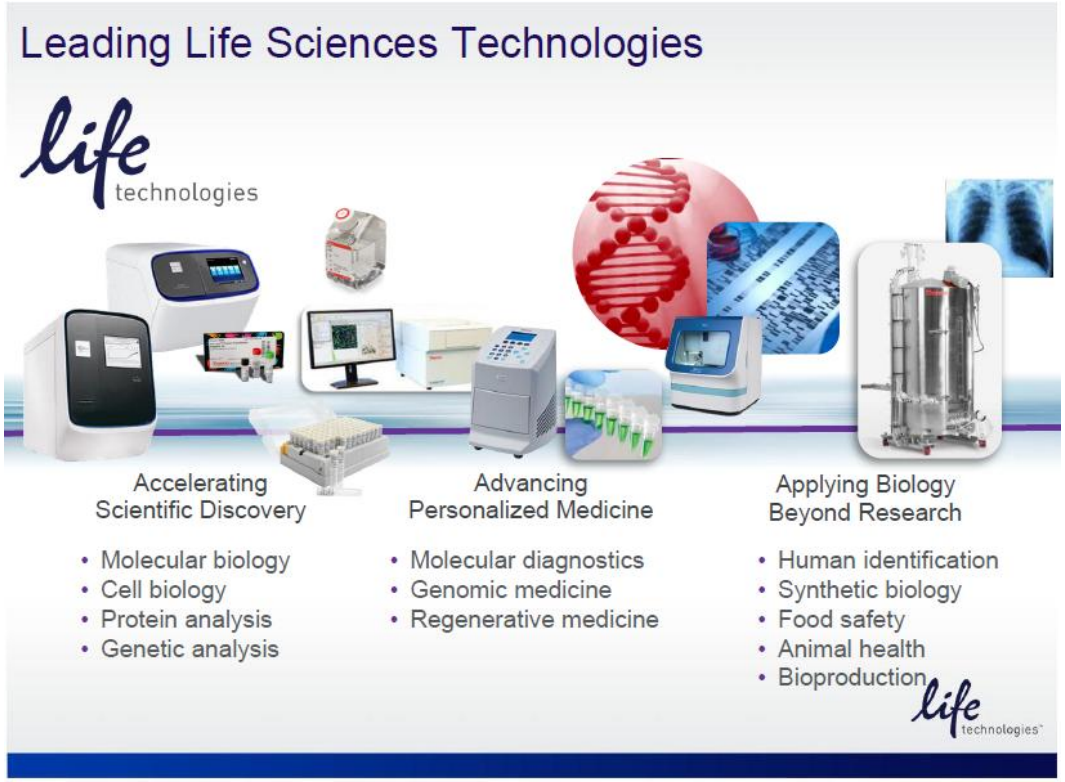
IF: 5.28

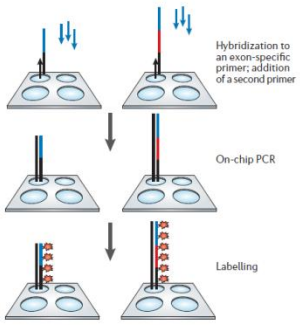
Diagnostic and prognostic value of ^{18}F-DOPA PET and ^{1}H-MR Spectroscopy in pediatric supratentorial infiltrative gliomas: a comparative study

Morana G., et al.

Progetti in corso

Next Generation Sequencing





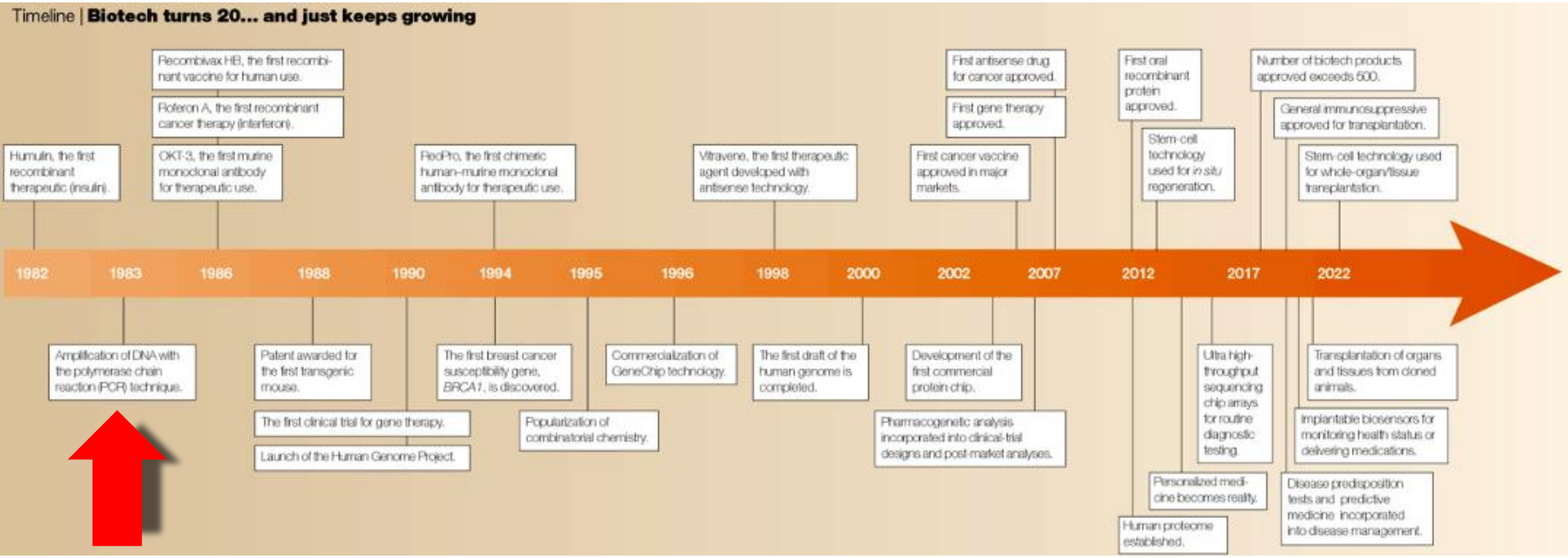
Nano-tecnologia

Reazioni che avvengono in volumi analoghi alle dimensioni cellulari

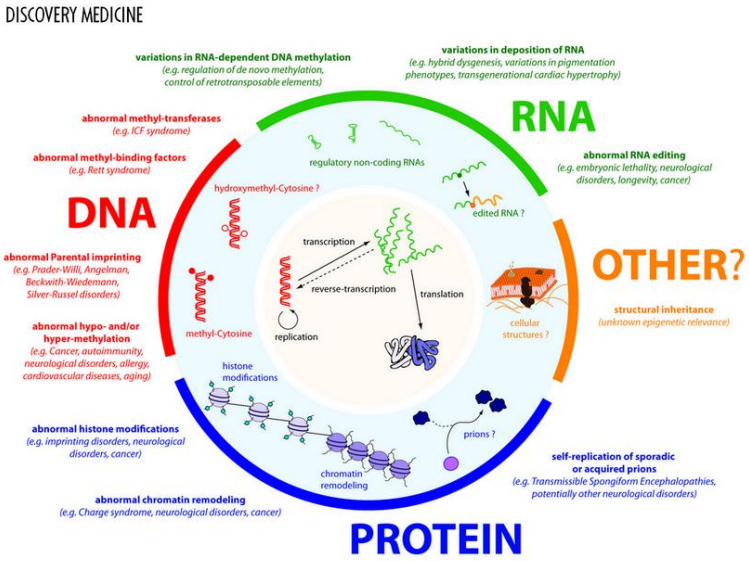
Supporto: chips di semiconduttori

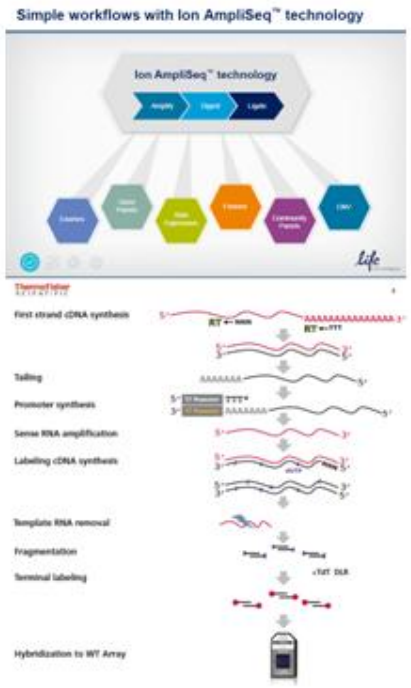
Chimiche dedicate

Timeline of biotecnology



From single molecular marker to multiomic analisys





Supporto economico

Alto expertise (preparazione-formazione)

Incremento performanche nella ricerca

Implementazione diagnostica (precisione, potenza e tempistica)

Starting to 2006 some novelties were found out...

Integrated Genomics Identifies Five Medulloblastoma Subtypes with Distinct Genetic P Signatures and Clinicopathologic

PLoS one

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Genomics Identifies Medulloblastoma Subgroups That Are Enriched for Specific Genetic Alterations

Acta Neuropathol (2012) 123:465–472
DOI 10.1007/s00401-011-0922-z

CONSENSUS PAPER

Molecular subgroups of medulloblastoma: the current consensus

Michael D. Taylor · Paul A. Northcott · Andrey Korshunov · Marc Remke · Yoon-Jae Cho · Steven C. Clifford · Charles G. Eberhart · D. Williams Parsons · Stefan Rutkowski · Amar Gajjar · David W. Ellison · Peter Lichter · Richard J. Gilbertson · Scott L. Pomeroy · Marcel Kool · Stefan M. Pfister

Acta Neuropathol
DOI 10.1007/s00401-015-1405-4

ORIGINAL PAPER

Integrated analysis of pediatric glioblastoma reveals a subset of biologically favorable tumors with associated molecular prognostic markers

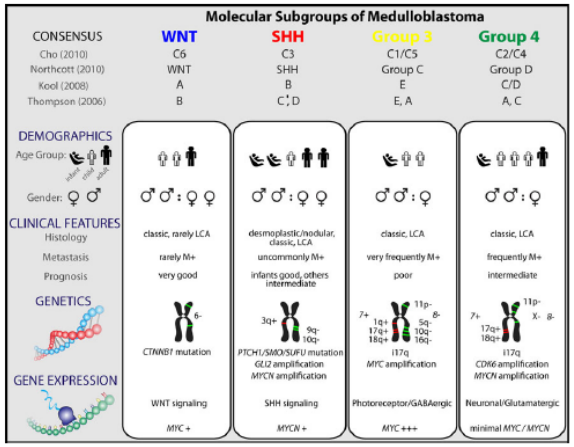
Andrey Korshunov · Marina Ryzhova · Volker Hovestadt · Sebastian Bender · Dominik Sturm · David Capper · Jochen Meyer · Daniel Schrimpf · Marcel Kool · Paul A. Northcott · Olga Zheludkova · Till Milde · Olaf Witt · Andreas E. Kulozik · Guido Reifenberger · Nada Jabado · Arie Perry · Peter Lichter · Andreas von Deimling · Stefan M. Pfister · David T. W. Jones

ARTICLES

nature genetics

Whole-genome sequencing identifies genetic alterations in pediatric low-grade gliomas

Jinghui Zhang[1], Gang Wu[1], Claudia P Miller[2], Ruth G Tatevossian[3], James D Dalton[3], Bo Tang[3], Wilda Orisme[3], Chandanamali Punchihewa[3], Matthew Parker[3], Ibrahim Qaddoumi[4], Fredrick A Boop[5], Charles Lu[6], Cyriac Kandoth[6], Li Ding[7], Ryan Lee[2], Robert Huether[1], Xiang Chen[1], Erin Hedlund[1], Panduka Nagahawatte[1], Michael Rusch[1], Kristy Boggs[8], Jinjun Cheng[8], Jared Becksfort[1], Jing Ma[3], Guangchun Song[9], Xiaojia Li[8], Lei Wei[3], Jianmin Wang[8], Shaila Shurtleff[8], John Easton[8], David Zhao[1], Robert S Fulton[6], Lucinda L Fulton[6], David J Dooling[6], Bhavin Vadodaria[3], Heather L Mulder[8], Chunlao Tang[1], Korri Ochoa[6], Charles G Mullighan[2], Amar Gajjar[4], Richard Kriwacki[10], Denise Sheer[11], Richard J Gilbertson[2], Elaine R Mardis[6], Richard K Wilson[6], James R Downing[3], Suzanne J Baker[2] & David W Ellison[3] for the St. Jude Children's Research Hospital–Washington University Pediatric Cancer Genome Project



Acta Neuropathol (2014) 128:573–581

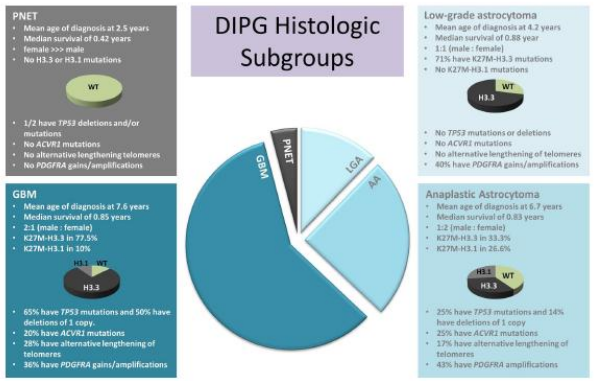
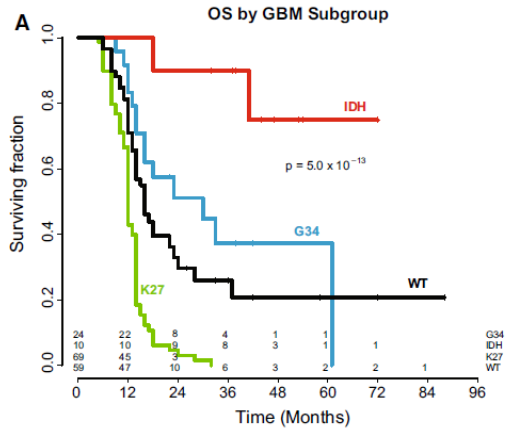


Fig. 3 DIPG histologic subgroups have some unique clinical and molecular features including mean age of diagnosis, sex, H3.3 and H3.1 mutations, *TP53* mutations and deletions, *ACVR1* mutations, *PDGFRA* gains/amplifications and alternative lengthening of telomeres (ALT)



Identificazione di marcatori molecolari utili alla stadiazione dei pazienti ed indicatori per l'utilizzo di nuove terapie

Table 1. Molecular markers of pediatric brain tumors

Tumor types	Histopathological Diagnosis	Subgroup	WHO Grades	Molecular Markers		
				Genes	Chromosomes	Immunohistochemistry
Astrocytic tumor	Pilocytic astrocytoma	cerebellar/optic/brain stem	I	*KIAA1549-BRAF* fusion	7q34 gain	
		cerebral/diencephalic	I	*BRAF* mut		
	Diffuse astrocytoma	Adult*	II	*IDH1/IDH2* mut, *TP53* mut		IDH1R132H
		Pediatric	II	*BRAF* mut		
	Pleomorphic xanthoastrocytoma		II	*BRAF* mut	9p loss	
	Glioblastoma	Adult*	IV	*CDKN2A* HD, *TP53* mut, *RB1* mut, *PTEN* mut, *EGFR* amp	Trisomy 7, Monosomy 10, 9p loss	
		Pediatric, DIPG	IV	*H3F3A* mut, *ATRX* mut, *DAXX* mut, *ADAM3A* HD, *PDGFRA* amp/mut		ATRX, DAXX
Neuronal tumor	Ganglioglioma		I	*BRAF* mut	Trisomy 7	
Ependymal tumor	Ependymoma	Posterior fossa Group A	II-III		1q gain	LAMA2
	Ependymoma	Posterior fossa Group B	II		6q loss, 22q loss, 9q gain, 15q gain, 18q gain	NELL2
Embryonal tumor	Medulloblastoma	Wnt	IV	*CTNNB1* mut, *MLL2/MLL3* mut, SMARCA4 mut, DDX3X mut	Monosomy 6	CTNNB1, DKK1
		Shh	IV	*PTCH1* mut, *SUFU* mut, *GLI* amp, *MYCN* amp	9q del, chromothripsis (*TP53* germline mut)	SFRP1, GAB1, GLI1
		Group 3	IV	SMARCA4 mut, *MYC* amp	i17q, 5q loss, 10q loss, 1q gain	NPR3
		Group 4	IV	KDM6A mut	i17q	KCNA1
	PNET		IV	*IDH1* mut, *CDKN2A* HD, *PDGFRA* amp	1q gain, 19p gain	
	ETANTR		IV	miRNA372-373 amp	19q13.42 amp	
	AT/RT		IV	*SMARCB1* mut, *SMARCA4* mut	22q loss	SMARCB1 loss
Germinal cell tumor	Germinoma			*KIT* mut	i12p, Trisomy X	KIT

The table is meant to provide an overview and for this purpose only the most typical findings for each tumor type are listed. For gene nomenclature, see text. PNET, Primitive neuroectodermal tumor; ETANTR, Embryonal tumor with abundant neuropil and true rosettes; AT/RT, Atypical teratoid/rhabdoid tumor; DIPG, Diffuse intrinsic pontine glioma. *Although adult tumors are not described in the text, they are included in the table for comparison to pediatric tumors. For more details on molecular markers in adult tumors, see Riemenschneider *et al.* Acta Neuropathol 120:567–584, 2010). Abbreviations: mut, mutation; HD, homozygous deletion; amp, amplification; i17q, isochromosome 17q; i12p, isochromosome 12p;

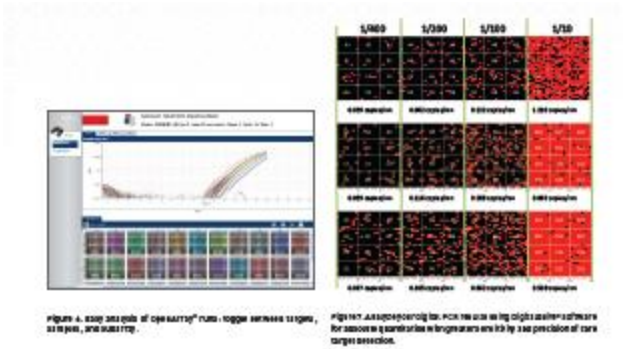
AT/RTs

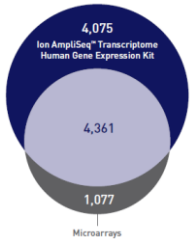
International rhabdoid, tumor group meeting; Parigi 12-14 dicembre 2013

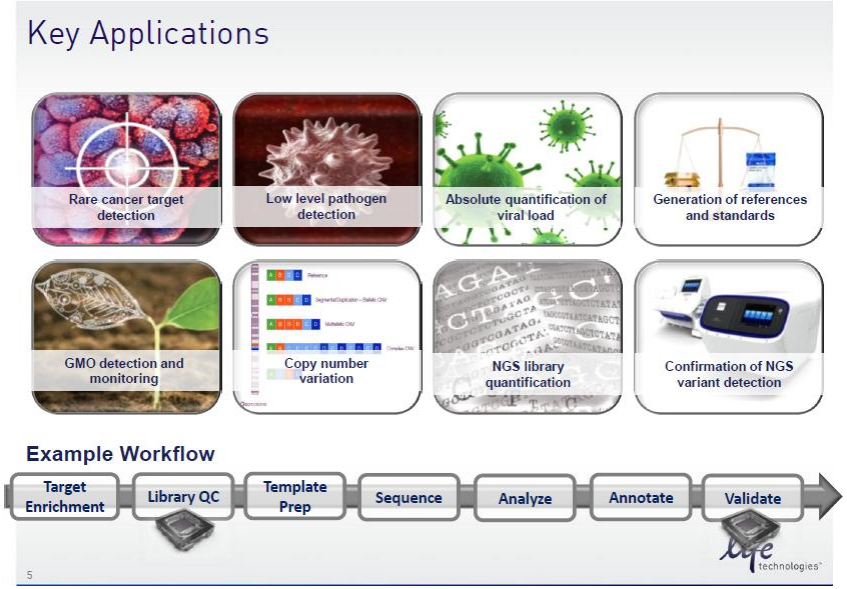
Multi-omics analysis of Atypical Teratoid Rhabdoid Tumors (AT/RTs).

>80% dei TR origina dall'inattivazione biallelica (entrambe le copie sono mutate e/o perse) del gene *SMARCB1 (INI1) nelle cellule tumorali.*

Comprehensive coverage of RefSeq- 20,802 genes targeted







Cohort 1 (discovery)

N	AT/RT	Rec	Sangue	Altra sede	
1	1	0	1	nd	
2	1	0	1	nd	
3	1	0	1	nd	
4	1	0	1	nd	
5	1	1	1	nd	
6	1	0	1	1	renale
7	1	0	1	nd	
8	0	0	1	1	renale

} 2 casi con doppia localizzazione

Cohort 2 (validation)

1	Te	1	0	0	nd	Anat Biolog., Firenze
2	Bo	1	0	0	nd	Anat Biolog., Firenze
3	De	1	0	0	nd	Anat Biolog., Firenze
4	#1	1	0	1	nd	Bambin Gesù, Roma
5	#2	1	0	1	nd	Bambin Gesù, Roma
6	#3	1	0	1	nd	Bambin Gesù, Roma
7	10/752	1	0	0	nd	Napoli
8	F L	1	0	0	nd	Padova

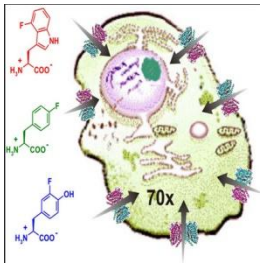
- **Esistenza di un genetic-landscape per gli AT/RT**
- **AT/RT Vs Rabdoidi Non-CNS**

Meccanismo alla base dell'*uptake* di ^{18}F-DOPA nei gliomi pediatrici: ruolo di fattore predittivo di malignità.

18F-DOPA PET: Fluorine-18-L-dihydroxyphenylalanine

Alto Grado (III, IV)
Grado II
Basso Grado (I)

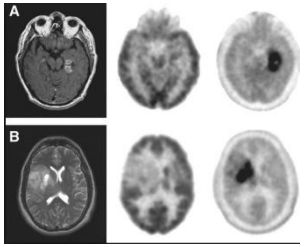
Captazione del tracciante



Systems L: LAT1 Complex

Systems ASC: ASCT1/2 Complex

System A: SNAT1



RAZIONALE

Proliferative Activity in Human Brain Tumors: Comparison of Histopathology and L-[1-^{11}C]Tyrosine PET

J Neurooncol
DOI 10.1007/s11060-012-0986-1

LABORATORY INVESTIGATION

The role of LAT1 in ^{18}F-DOPA uptake in malignant gliomas

Ryan S. Youland · Gaspar J. Kitange · Timothy E. Peterson · Deanna H. Pafundi · Judi A. Ramiscal · Jenny L. Pokorny · Caterina Giannini · Nadia N. Laack · Ian F. Parney · Val J. Lowe · Debra H. Brinkmann · Jann N. Sarkaria

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NEURO-ONCOLOGY

Prima revisione

Diagnostic and prognostic value of ^{18}F-DOPA PET and ^{1}H-MR Spectroscopy in pediatric supratentorial infiltrative gliomas: a comparative study

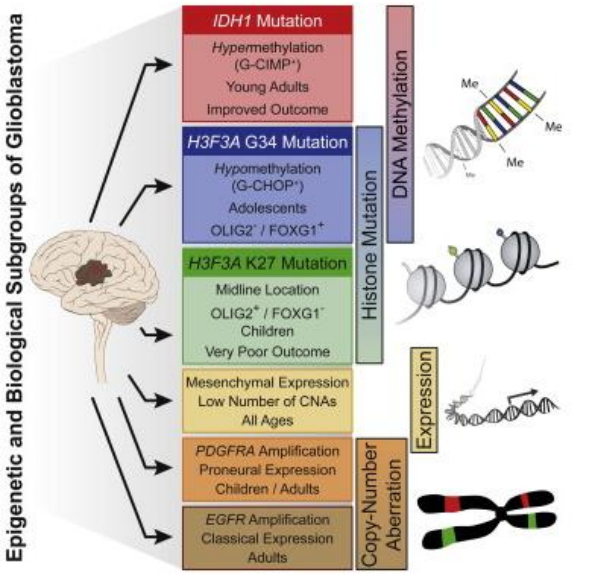
Morana G., et al.

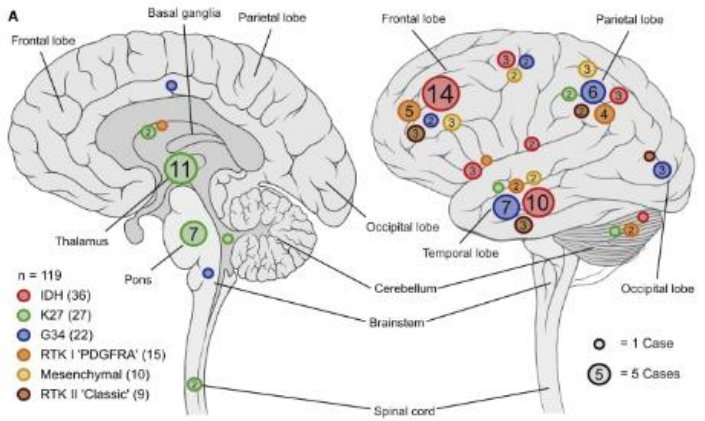
Results

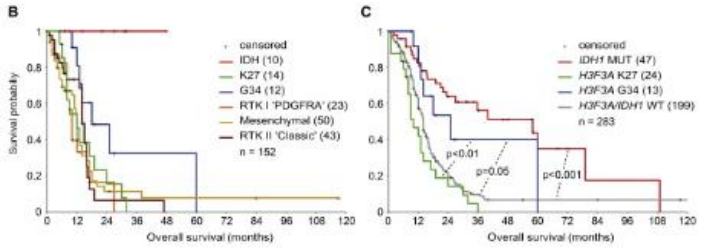
^{18}F-DOPA uptake independently correlated with progression-free survival (p≤0.05) and overall survival (p=0.04), whereas ^{1}H-MRS did not show significant association with outcome.

Conclusions

^{1}H-MRS and ^{18}F-DOPA PET provide useful complementary information for evaluating pediatric brain lesion metabolism. ^{1}H-MRS represents the method of first choice in differentiating brain gliomas from non-neoplastic lesions. ^{18}F-DOPA uptake better discriminates low- from high-grade gliomas and is an independent predictor of outcome.

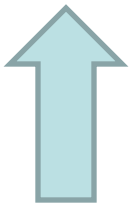






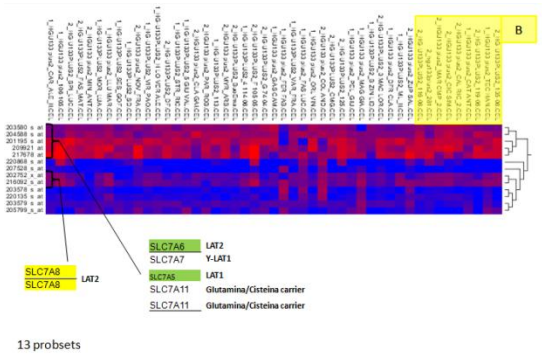
Meccanismo alla base dell'*uptake* di ^{18}F-DOPA nei gliomi pediatrici: ruolo di fattore predittivo di malignità.

Alto Grado (III, IV)
Grado II
Basso Grado (I)



Potenziali trasportatori del tracciante

RISULTATI

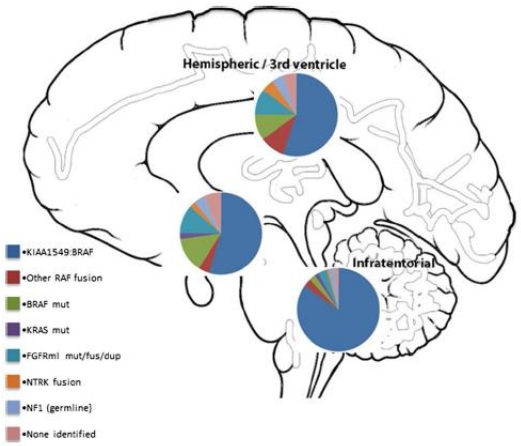


Analisi espressione su tutta la casistica >qPCR
Analisi dell immunofenotipo su paraffinato

1. **Potenziale marcatore di progressione**
2. **Potenziale Target terapeutico**

IMPLEMENTAZIONE DIAGNOSTICA con NGS

Pilocytic astrocytoma: pathology, molecular mechanisms and markers



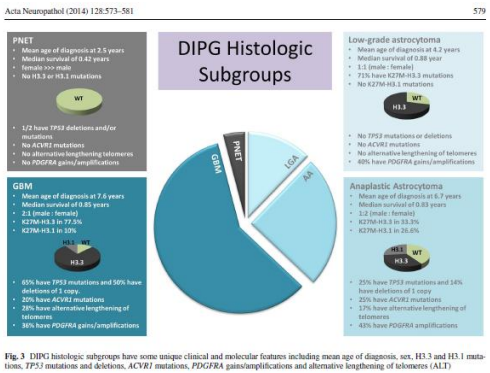


Fig. 3 DIPG histologic subgroups have some unique clinical and molecular features including mean age of diagnosis, sex, H3.3 and H3.1 mutations, *TP53* mutations and deletions, *ACVR1* mutations, *PDGFRA* gains/amplifications and alternative lengthening of telomeres (ALT)

Table 1 PA mutations, methods to detect them, and their diagnostic utility

MAPK pathway aberration	Preferred method	Alternative methods	Diagnostic utility
KIAA1549:BRAF	RNAseq	FISH (7q34 duplication); targeted RT-PCR (may miss some variants)	Highly recurrent in PA; extremely rare in other entities
Other BRAF/RAF1 fusions	RNAseq	NA (too many variants)	Recurrent in PA; extremely rare in other entities
BRAF V600E	Targeted sequencing	Anti-V600E IHC; WES; WGS; RNAseq	Recurrent in supratentorial PA; also common in GG/PXA/DNET
KRAS	Targeted sequencing (exons 2, 3)	WES; WGS; RNAseq	Rare in PA; frequency not fully established in other entities
FGFR1 mutation	Targeted sequencing (exons 12, 14)	WES; WGS; RNAseq	Recurrent in midline PA; frequency not fully established in other entities
FGFR1-ITD/fusion	RNAseq	WGS; targeted sequencing	Rare in PA; also observed in other LGG
NTRK fusions	RNAseq	NA (too many variants)	Recurrent in PA; also observed in other LGG and infant HGG
NF1	Clinical genetic testing	WGS; WES	Typically germline; closely associated with optic pathway PA

GLIAL BT	Neuroectodermal	Sclerosi Tuberosa
H3.3 (H3F3A)	NF2	TSC1
H3.1 (HIST1H3B)	SMARCB1 (INI1)	TSC2
H3.1 (HIST1H3C)		
ACVR1		
TP53		
BRAF		
IDH1		
RNF213		
PDGFRB		
TGFB1		

Codice	Descrizione	Q.tà	Prezzo List. Unitario	Sconto %	Prezzo netto unitario	Ice Hazardous
IAD75362_188	Ampliseq Custom Panel (IAD75362_188)	1	€3,857.87	0.00%	€3,857.87	D
IAD75362_197	Ampliseq Custom Panel (IAD75362_197)	1	€2,893.40	0.00%	€2,893.40	D
IAD68358_197	Ampliseq Custom Panel (IAD68358_197)	1	€725.06	0.00%	€725.06	D
IAD75572_198	Ampliseq Custom Panel (IAD75572_198)	1	€978.15	0.00%	€978.15	D
IAD75590_188	Ampliseq Custom Panel (IAD75590_188)	1	€1,669.01	0.00%	€1,669.01	D

Un sentito ringraziamento