Dipartimento Integrato Interistituzionale
DIPINT

Primo Workshop

Clinical Research and Innovation

Venerdì 4 luglio 2014 9.00 - 19.00

Aula Magna - Polo Fibonacci - Largo Pontecorvo 3, Pisa

GLIOBLASTOMA WHOLE TRANSCRIPTOME ANALYSIS: MOLECULAR MECHANISMS RELATED TO RECURRENCE FREE SURVIVAL

Antonio Giuseppe Naccarato

Division of Surgical, Molecular and Ultrastructural Pathology, Department of Translational Research and New Technologies in Medicine and Surgery

BACKGROUND

GBM is the most malignant phenotipic endpoint of DIFFUSELY INFILTRATING ASTROCITOMAS
Combination of SURGICAL RESECTION, RADIOTHERAPY and ADJUVANT CHEMOTHERAPY constitutes the STANDARD OF CARE

The invasive nature of GBM cells represents a major cause of THERAPEUTIC FAILURE

clarification of the molecular mechanisms associated with cellular migration and invasion is crucial to allow better prediction

Aim

To provide NOVEL INFORMATION on GBM behavior, with regard to the type of GENETIC CHANGES involved in length of RECURRENCE FREE SURVIVAL

MATERIALS AND METHODS

12 primary FFPE GBMs

specifically selected for different length of time of first recurrence

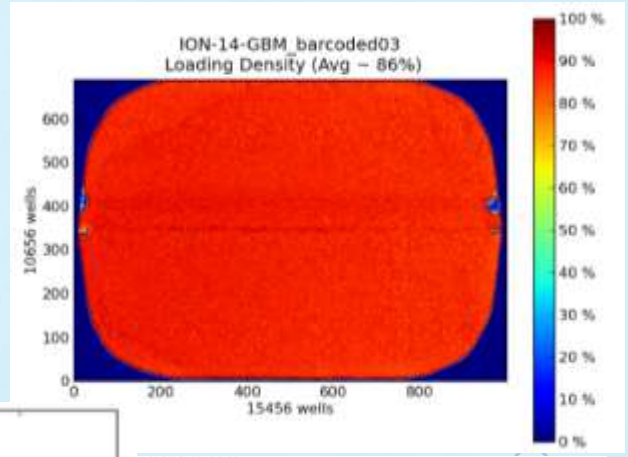
(less than 6 months-more than 25 months)

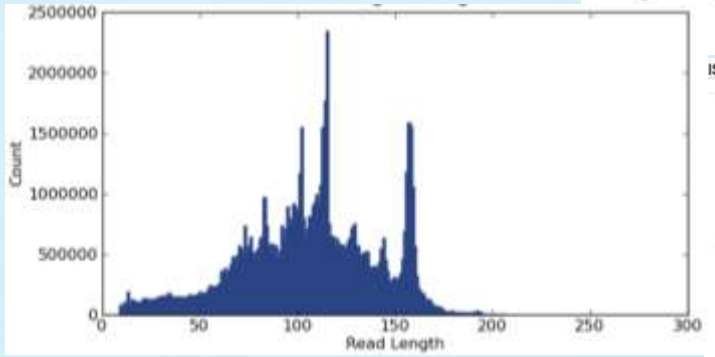
Whole-transcriptome RNA sequencing

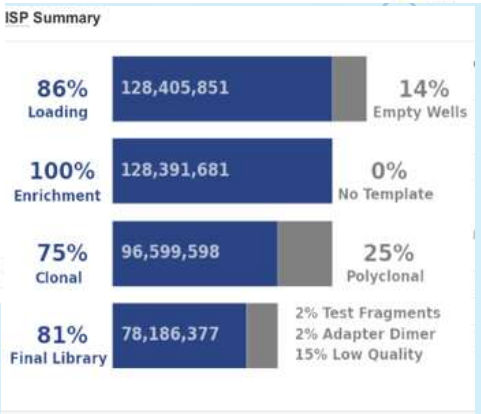
(Ion Proton System, Life Technologies)

Differential gene transcription analysis

Gene fusion transcripts





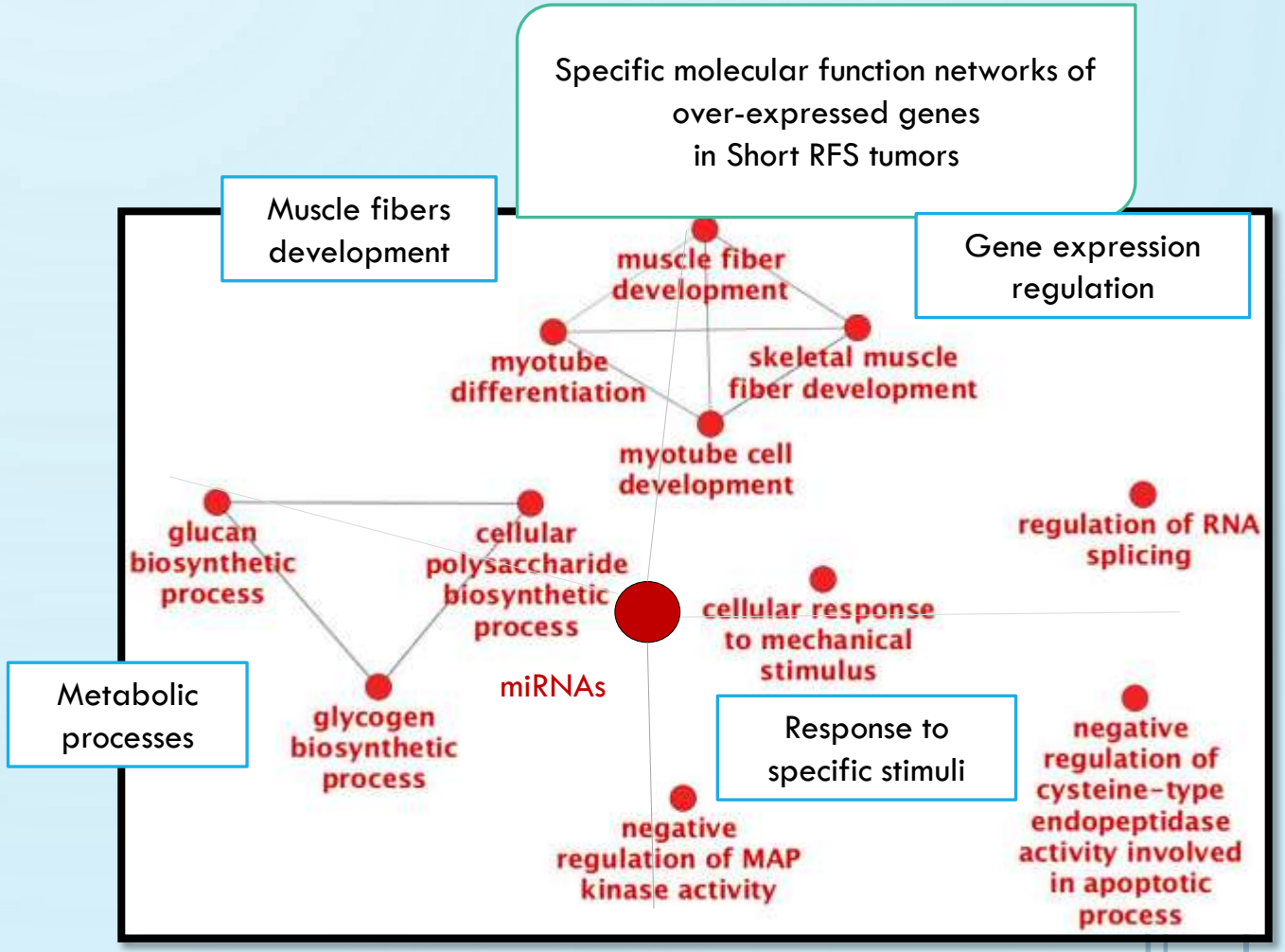


RESULTS 1/3

Statistical SIGNIFICANT DIFFERENTIAL EXPRESSION of 83 genes allowed to distinguish THREE DISTINCT GROUPS

51 genes

- STR, less than 6 months (6)
  - 26 genes
- MTR, between 16 and 23 months (3)
  - 21 genes
- LTR, more than 25 months (3)



RESULTS 2/3

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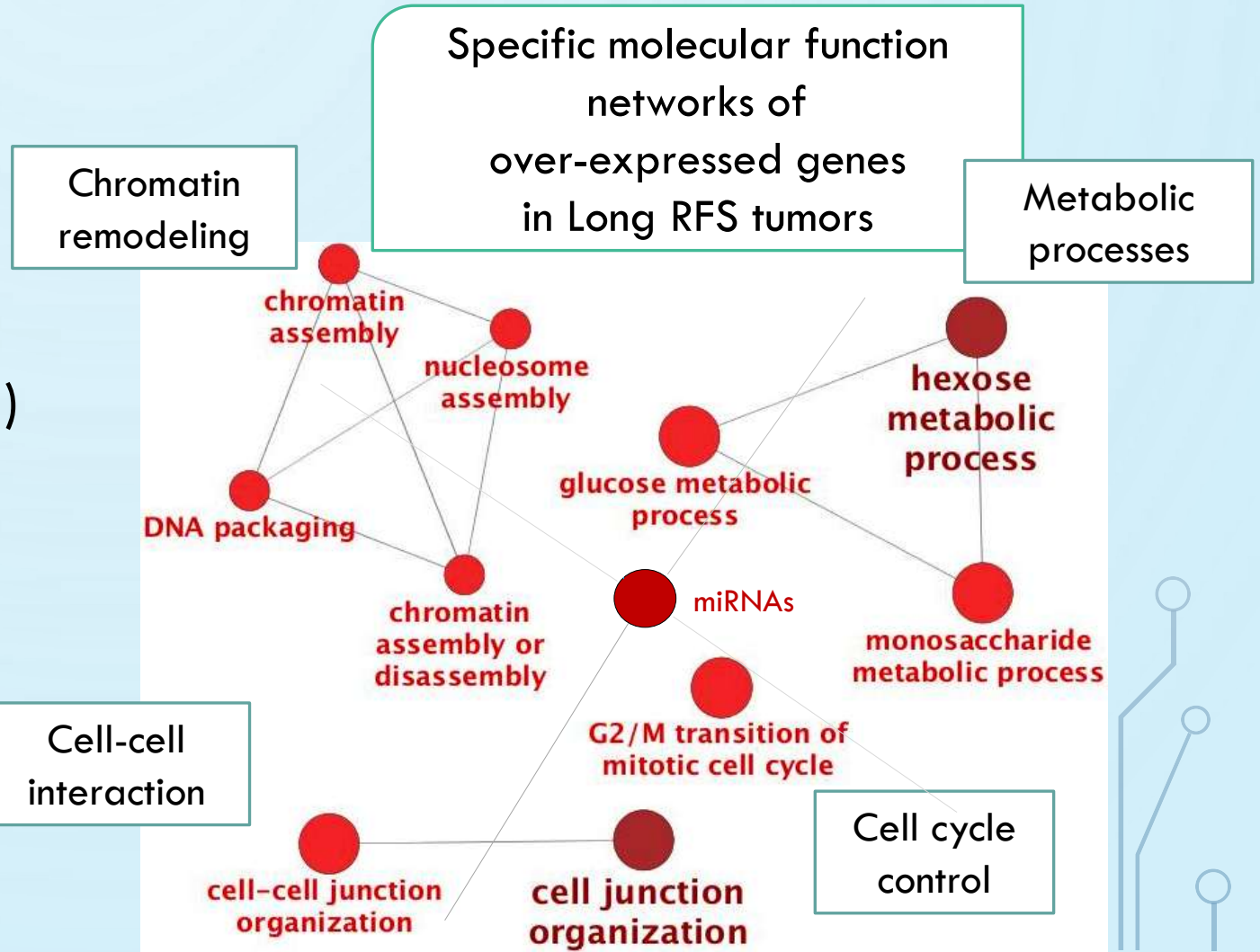


RESULTS 3/3

Few gene fusion transcripts were identified

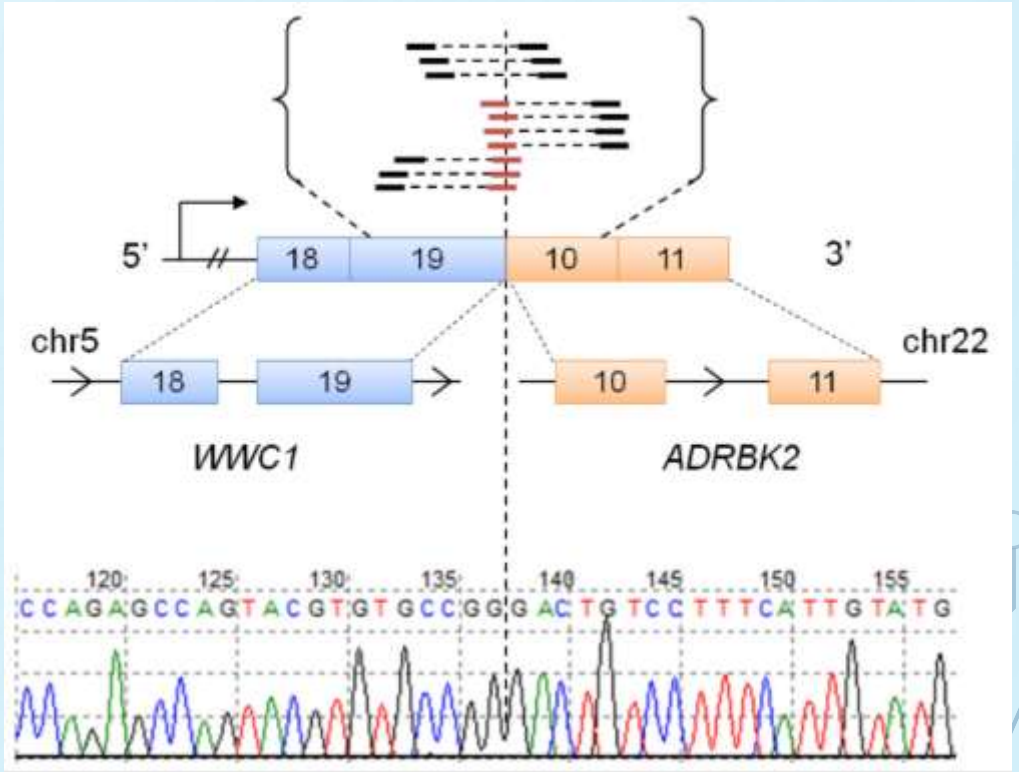
DLG2-APP, *LTR group*

SEC14L1-MAPK1,

4/6 STR and 3/3 MTR groups

HFM1-DLG2, *11/12*

CFLAR-TSR1, *12/12*



DISCUSSION 1/2

Most of the genes related to time of recurrence are involved in the epigenetic landscape of the transcriptional potential of the cell:

HISTONE expression dis-regulation

miRNA expression dis-regulation

DISCUSSION 2/2

GENE FUSIONS

are being reported for the first time

involve genes related to:

neuron cell polarity (DLG2)

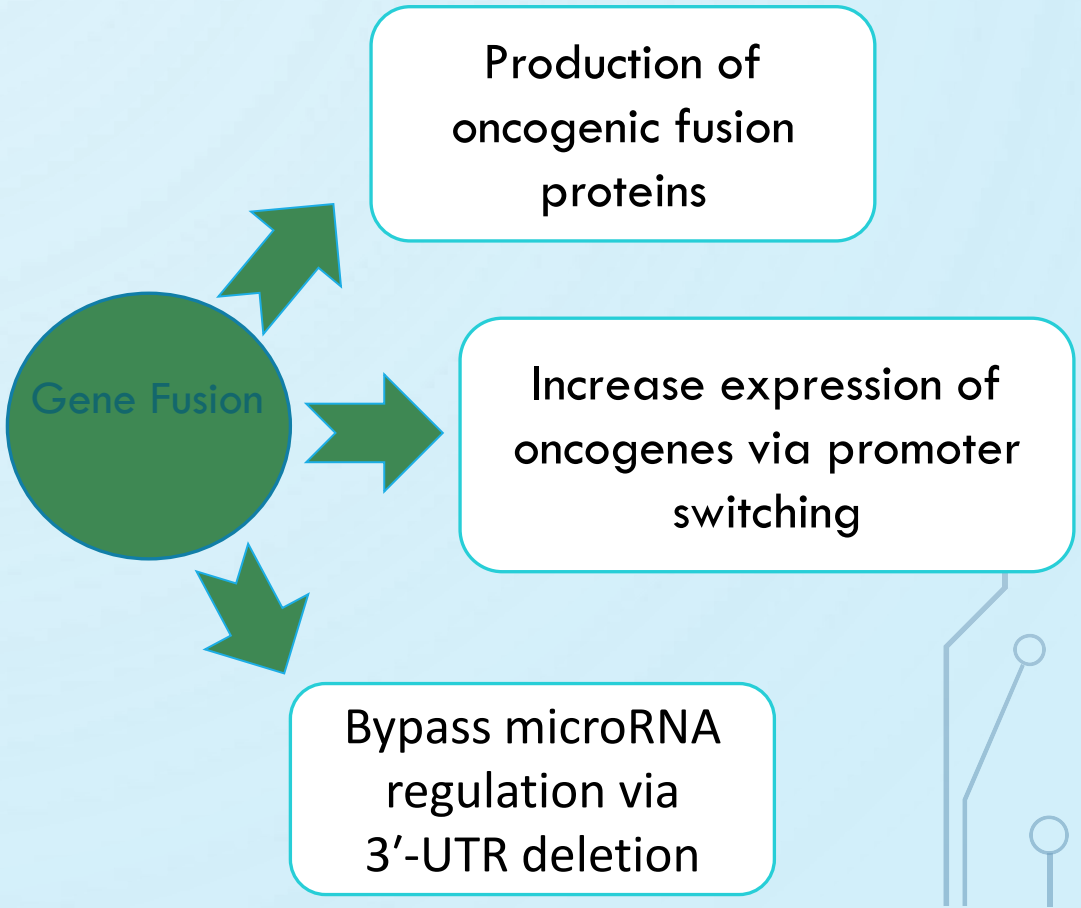
brain amyloid plaque formation (APP)

genome integrity (HFM1)

cell signaling (MAPK1)

not yet well known (CFLAR-TSR1)

… *Targeted Therapies*



CONCLUSIONS

mRNA expression profile can define a particular molecular hallmark able to influence patient survival and be used as a molecular diagnostic test

FUTURE PERSPECTIVES

More thorough analyses are needed, with larger cohorts of patients

A comprehensive better understanding of the molecular mechanisms underlying recurrence free survival would make a long step forward in the improvement of the clinical management of GBM patients

ACKNOLEDGMENTS

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