Mouse models of GBM: MRI characterization and caBIG[®] tools

Sanaz (Sunny) Jansen PhD Van Dyke Lab Mouse Cancer Genetics Program, National Cancer Institute CBIIT Seminar, February 29 2012



Outline

- The *Mouse GBM* project
- How do caBIG[®] tools support *Mouse GBM*?
 - Standardize MRI features (VASARI)
 - Archive and organize DICOM data (NBIA)
 - Integrate imaging and biology (caIntegrator)
- Summary and remaining challenges



Outline

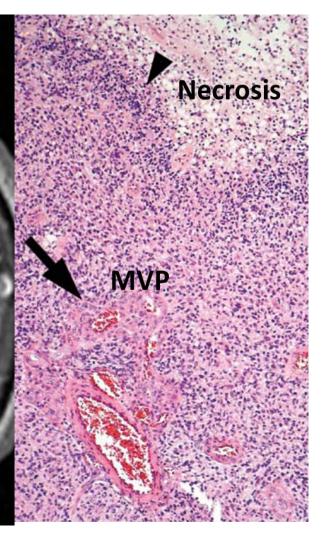
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High grade astrocytoma

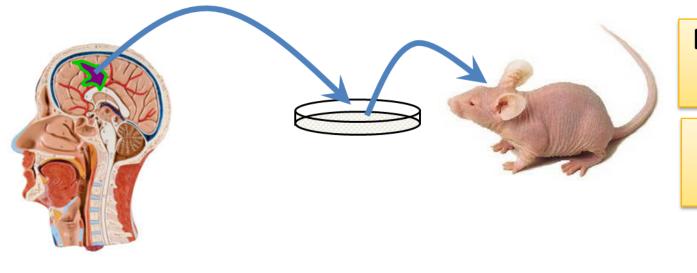
Grade III: anaplastic astrocytoma Grade IV: glioblastoma (GBM)

Most common brain tumor Poor prognosis No effective treatments



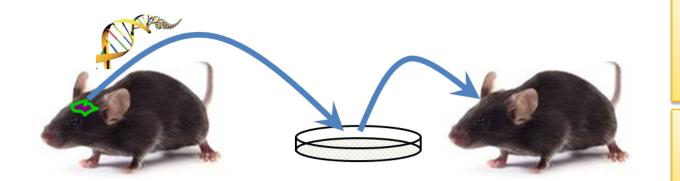


Mouse models of GBM



Established cell lines xenograft

Patient derived xenograft

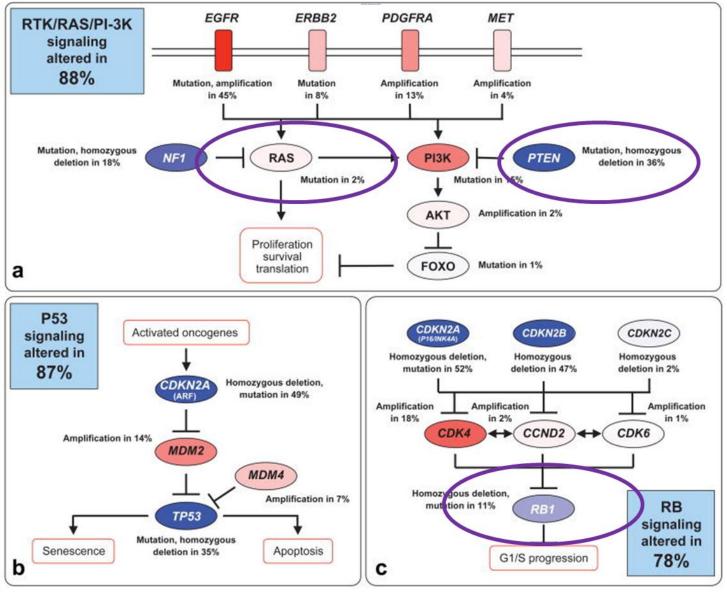


Genetically engineered mouse (GEM)

> Syngeneic allograft



Core pathways altered in human GBMs

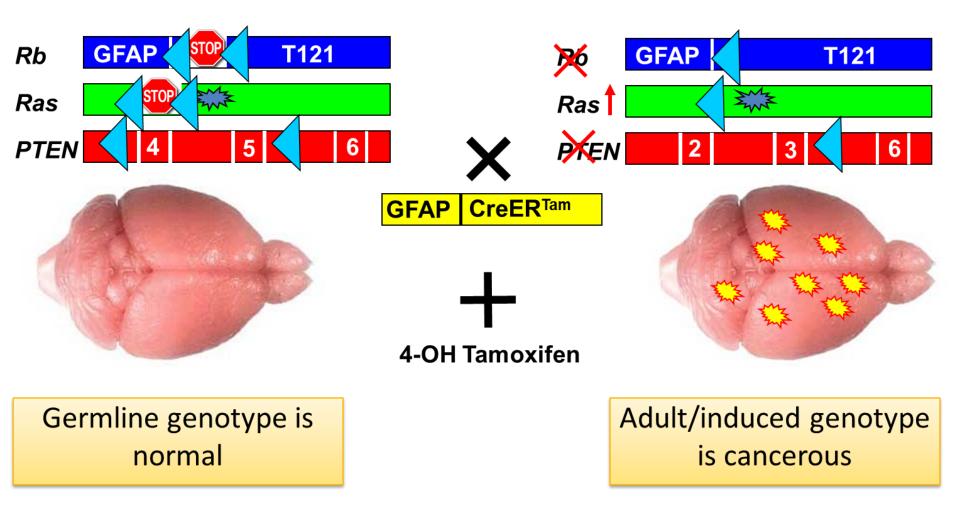


From Terry Van Dyke

The Cancer Genome Atlas (TCGA) 2008 Nature

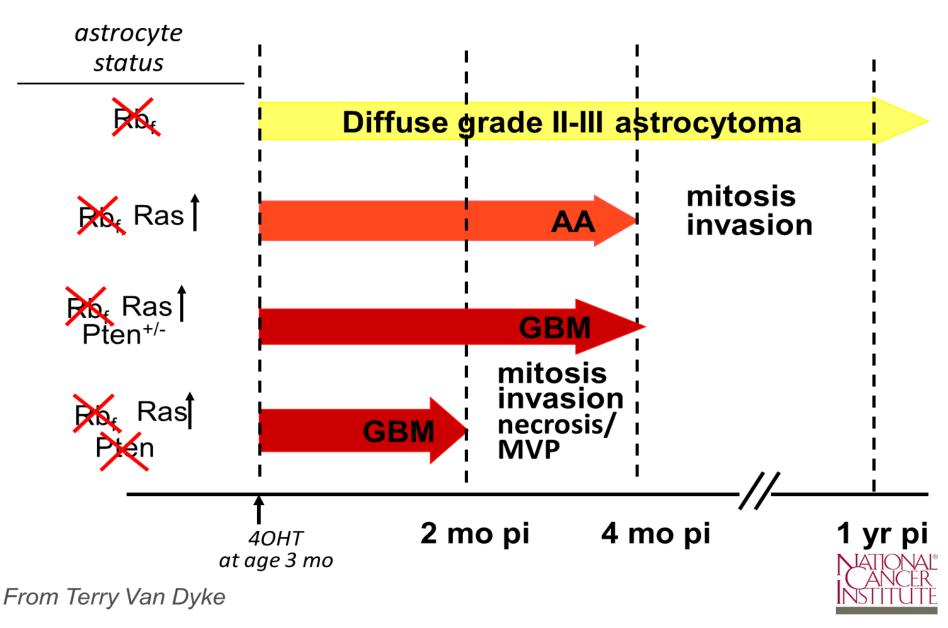


Genetically engineering astrocytoma

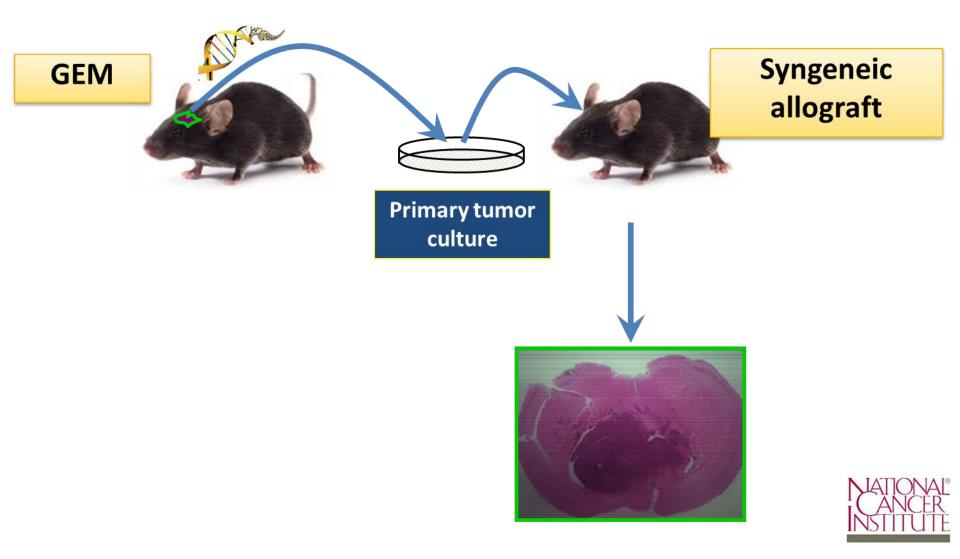




Inducible astrocytoma GEM models



Syngeneic orthotopic transplant

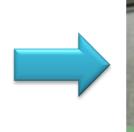


Mouse GBM Brain imaging workflow



Four mice imaged at once







Philips Intera Achieva 3.0T MRI clinical scanner ~1hour imaging time

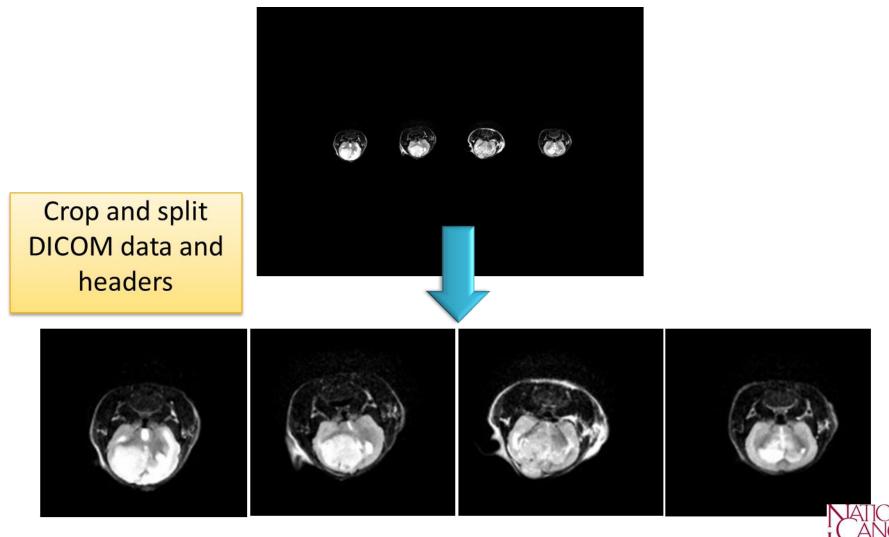
MRI acquisitions

- Pre-contrast T₁ FFE
- Pre-contrast T₂ TSE
- Dynamic contrast enhanced MRI (DCEMRI)
- Post-contrast T₁ FFE

Post imaging euthanize and histology



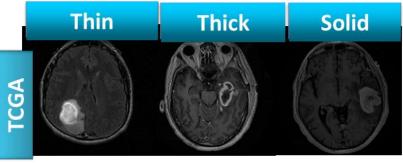
Challenge: cropping and splitting the data





MRI features: mVASARI

- VASARI lexicon used for analysis of human GBM in TCGA
 - e.g.. Thickness of Enhancing Margin (F11)

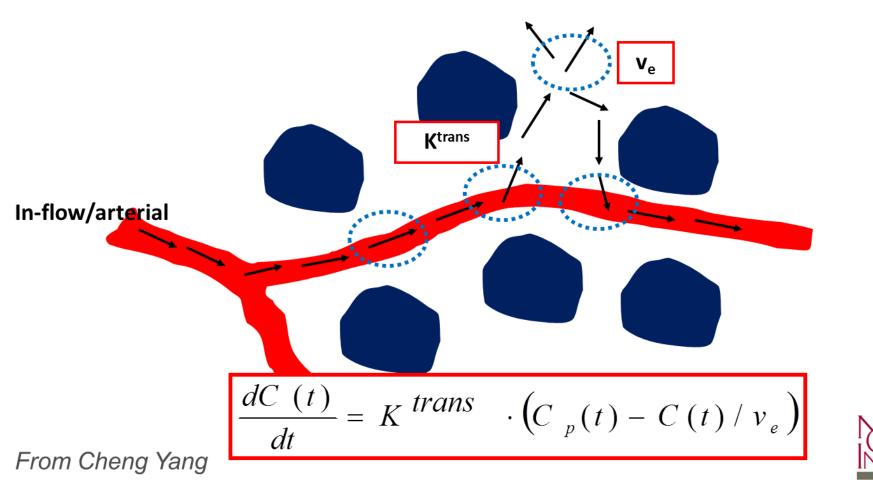


- Mouse VASARI=mVASARI
- Publically available VASARI features for human GBM from calntegrator

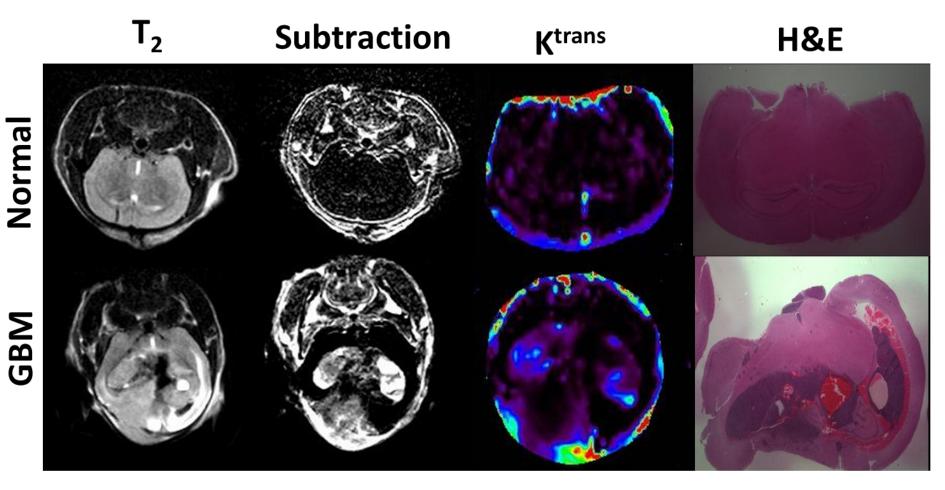


Mouse GBM MRI features: BBB permeability

• Quantifiable information on the blood brain barrier permeability is extracted from the pattern of contrast agent uptake



MRI reveals disease pathology noninvasively





MRI reveals disease pathology noninvasively

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	Yes, not pseudopalisading		20									
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Proliferation	Yes		2]	0		_					
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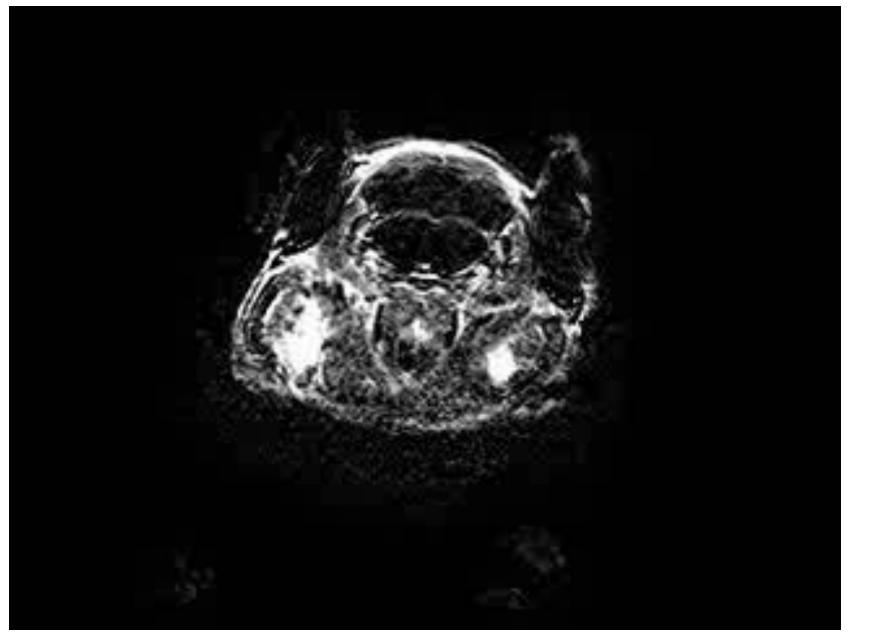


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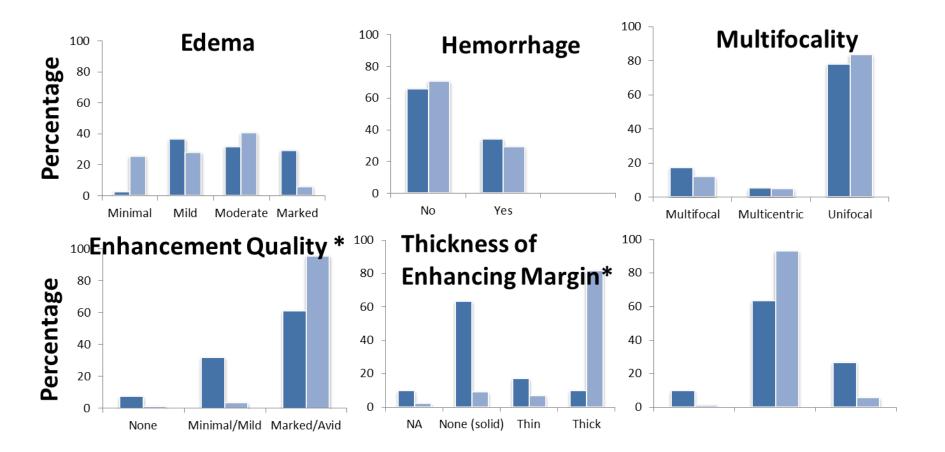
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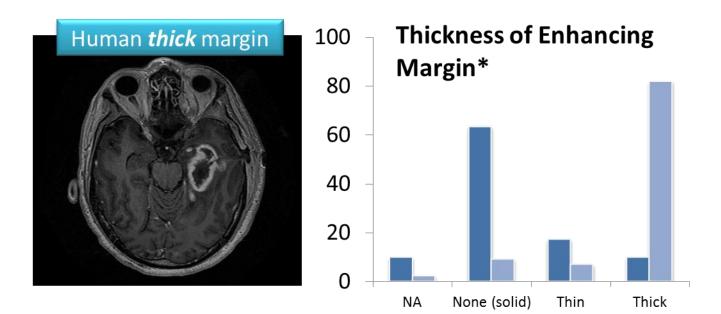




Mouse models can capture many features of human GBM...



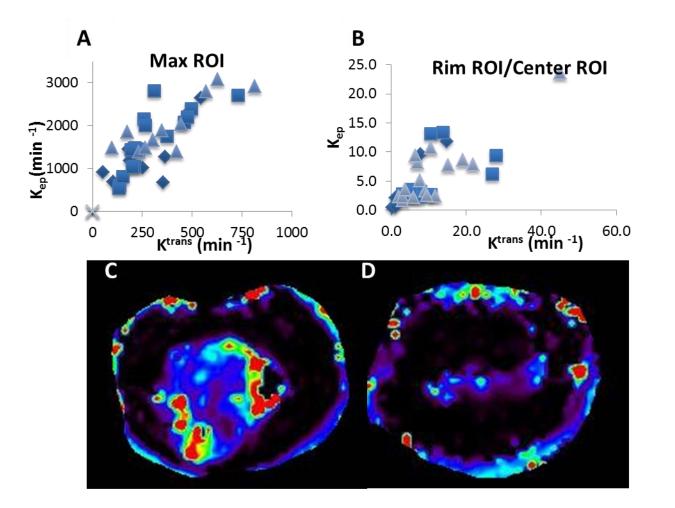
... but not the necrosis?



• Thick enhancing margin rarely seen in mice



Heterogeneous patterns of BBB permeability





Mouse GBM Summary

Mouse GBM captures heterogeneity on MRI But where is the enhancing rim? Why such diverse patterns of BBB leakiness?



Outline

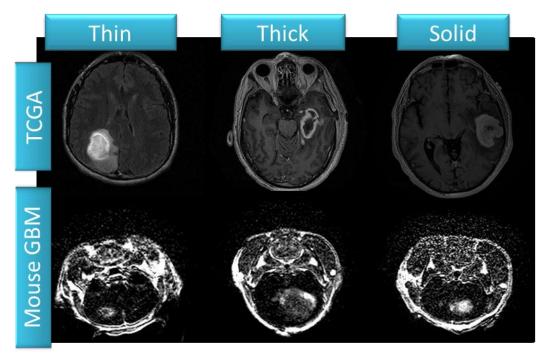
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caBIG[®] tools support *Mouse GBM* Standardized lexicon: mVASARI features

Thickness of the Enhancing Margin (VASARI feature 11)

VASARI features essential for comparing *Mouse GBM* to human GBM





caBIG[®] tools support *Mouse GBM*

NBIA: Demo

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Images from *Mouse GBM* stored in NBIA



caBIG[®] tools support *Mouse GBM*

NBIA: Demo

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Images from Mouse GBM stored in NBIA



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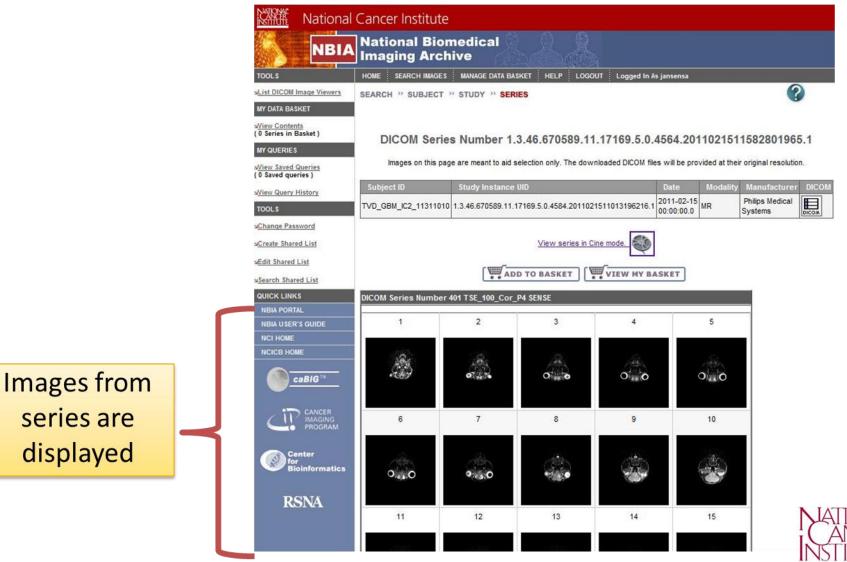
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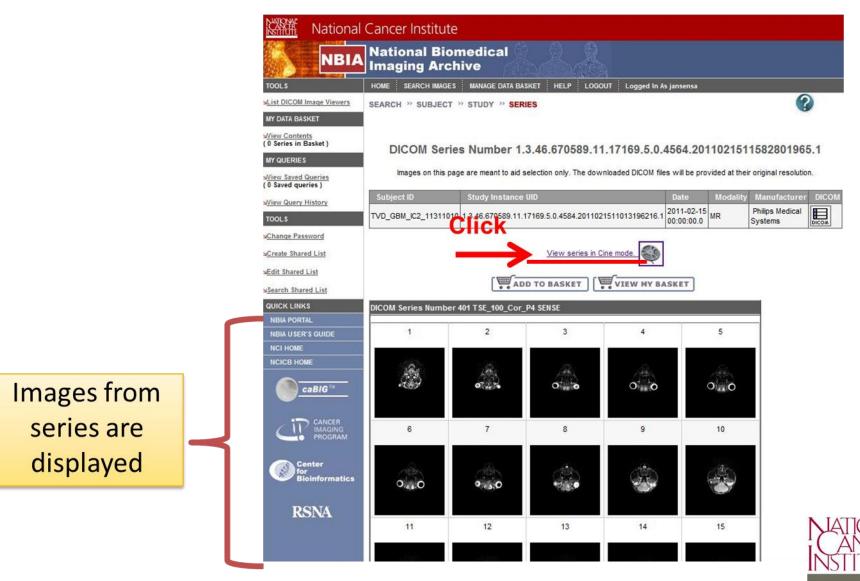
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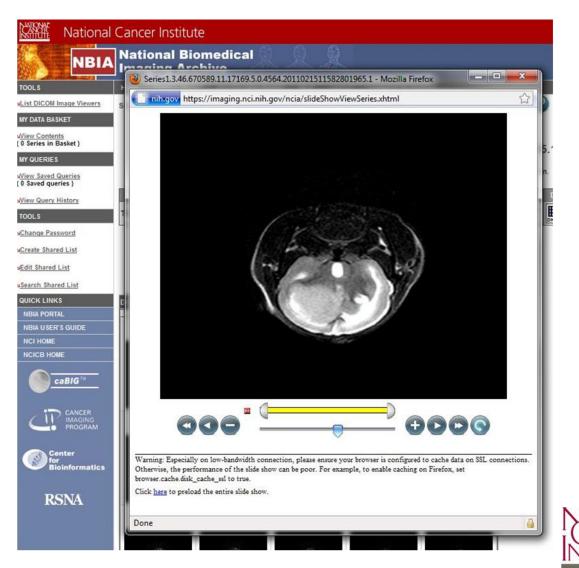
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caBIG[®] tools support *Mouse GBM*

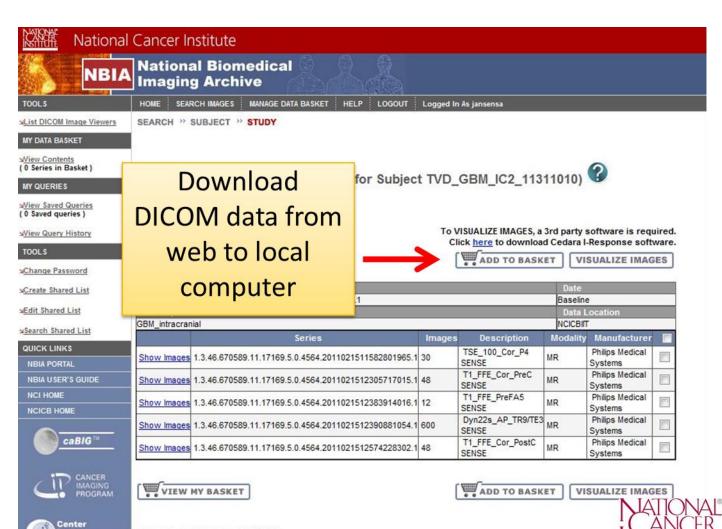
NBIA: Demo



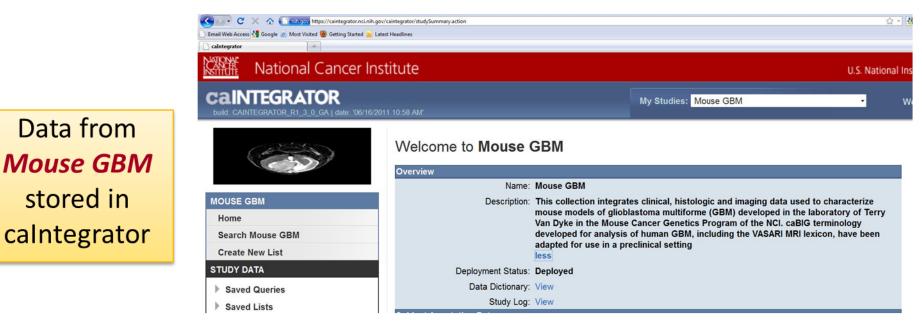




Images can be viewed in Cine mode



caBIG[®] tools support *Mouse GBM* calntegrator: Demo





caBIG[®] tools support *Mouse GBM* calntegrator: Demo

National Cancer I	nstitute	U.S. National Institutes of Health www.cancer.gov
CAINTEGRATOR	2011 10:58 AM [*]	▼ Welcome, jansensa <u>Logout</u>
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or clinical features		Run Query
Integrative Genomics Viewer		



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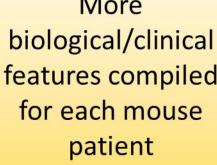
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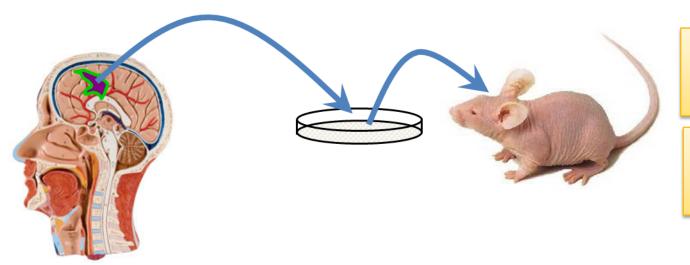


Outline

- The *Mouse GBM* project
- How do caBIG[®] tools support *Mouse GBM*?
 - Standardize MRI features (VASARI)
 - Archive and organize DICOM data (NBIA)
 - Integrate imaging and biology (caIntegrator)
- Summary and remaining challenges

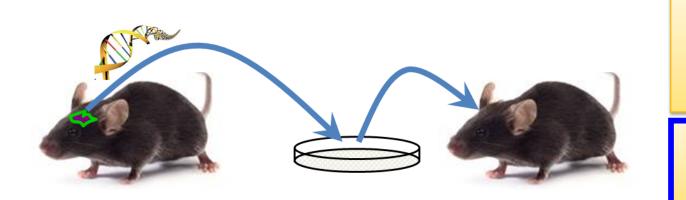


Mouse models of GBM



Established cell lines xenograft

Patient derived xenograft

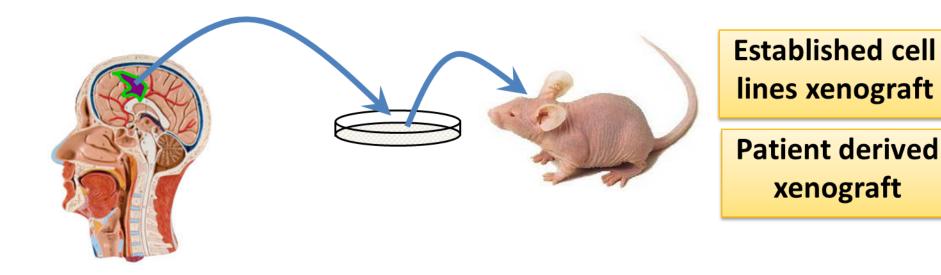


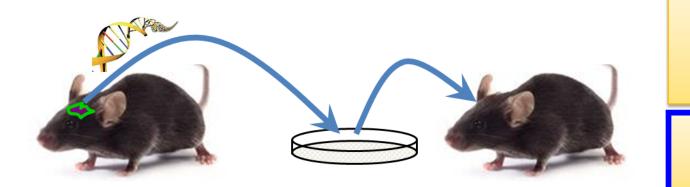
Genetically engineered mouse (GEM)

> Syngeneic allograft



Mouse models of GBM





Genetically engineered mouse (GEM)

Syngeneic allograft



caBIG[®] tools for preclinical research Remaining challenges

- Standardized features for mouse vs. human comparison
- NBIA: Non-DICOM images
- calntegrator: Archiving vs. integrating



Preclinical research for caBIG[®] tools

- Data stream is similar to humans!
 - Multimodality imaging
 - Chemotherapy (novel), radiation therapy
 - Histology, molecular and genetic analysis
- Large numbers with standardized data
- Full access to tissue
- Tumors at different stages



Acknowledgements

<u>TVD Lab</u>

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<u>CAPR</u>

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LASP Dan Logsdon

