Imaging-genomic Analysis of TCGA/TCIA Diffuse Lower Grade Gliomas by Molecular Subtype

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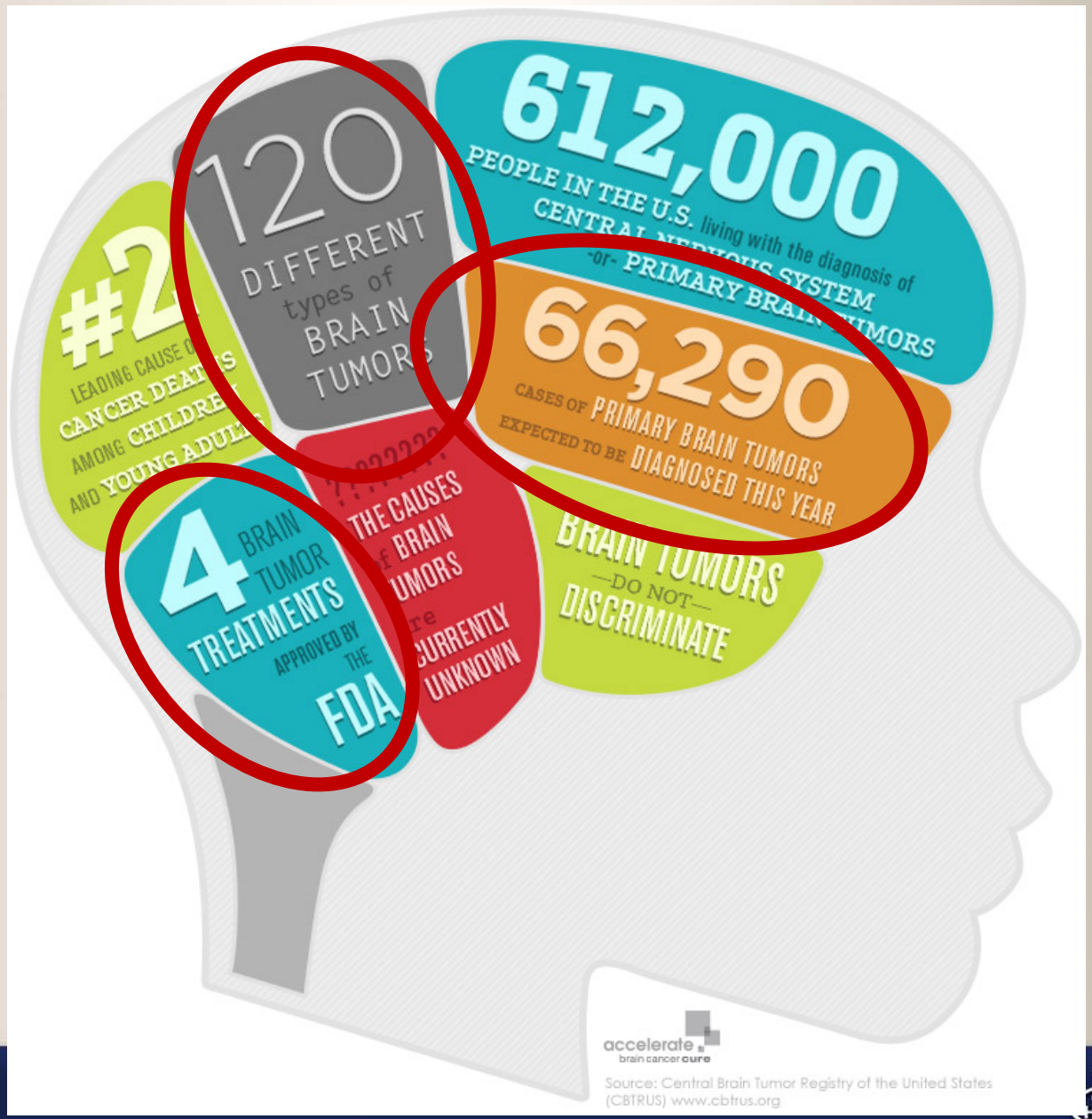
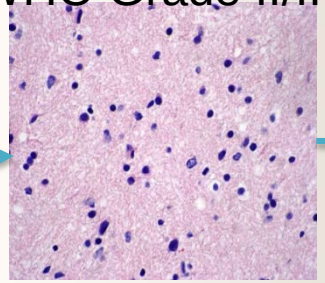
4th Annual TCGA Symposium (May 2015)

Cancer of the Brain and CNS

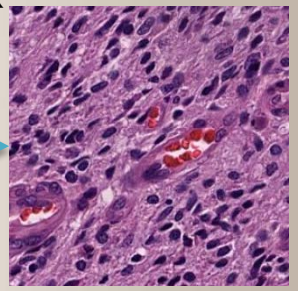


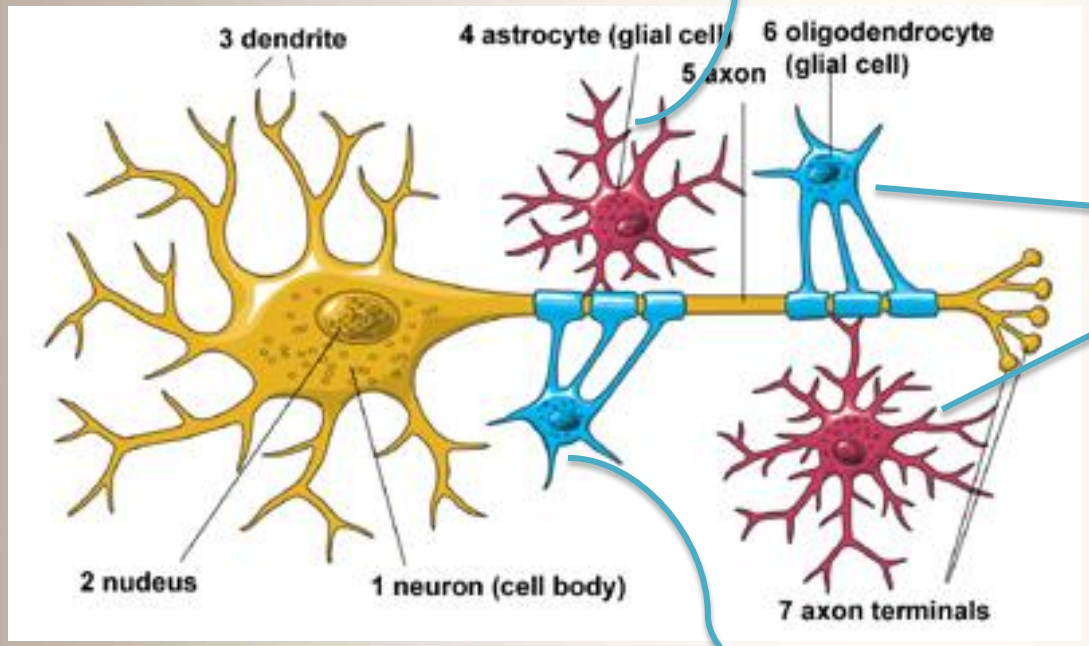
Glioma:
Cancer of glial cells

Astrocytoma
(WHO Grade II/III)

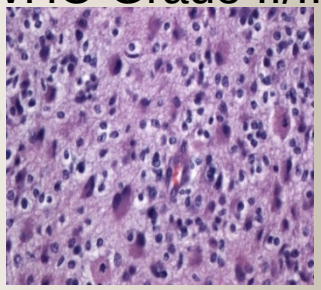


Glioblastoma
(WHO Grade IV)





Oligoastrocytoma
(WHO Grade II/III)



Oligodendroglioma
(WHO Grade II/III)

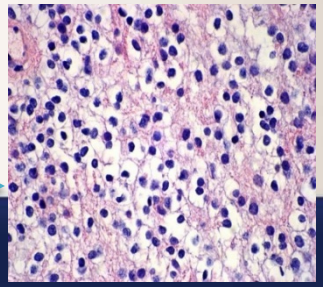
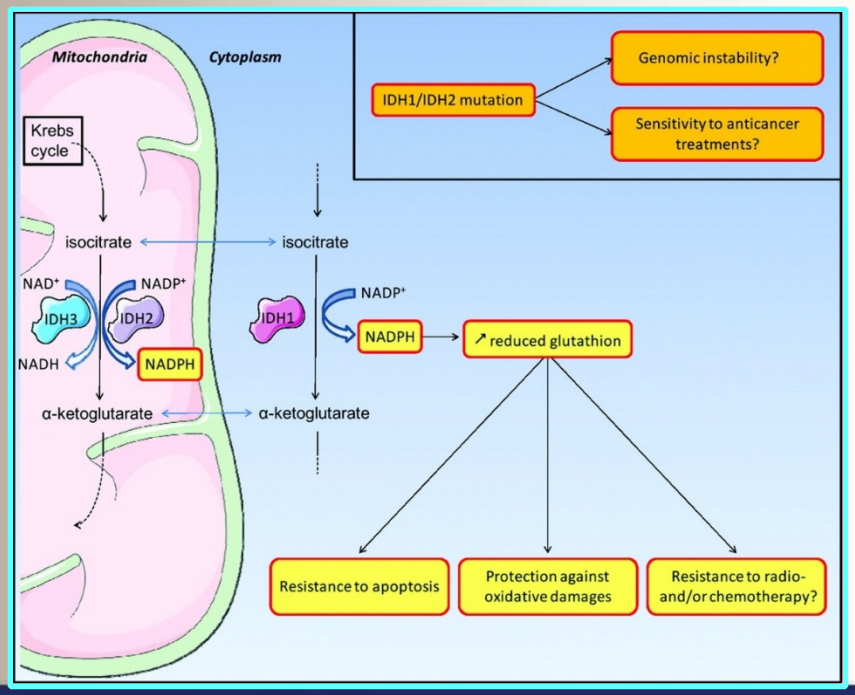


Image from: NIH/National Institute of Neurological Disorders and Stroke (NINDS)

Molecular markers in glioma

Mutation of Isocitrase Dehydrogenase (IDH1/2)



Role of IDH (Labussiere et al, 2010)

Co-deletion of Chr 1p and Chr 19q

Case TCGA-DU-6393,
visualized at www.cbioportal.org

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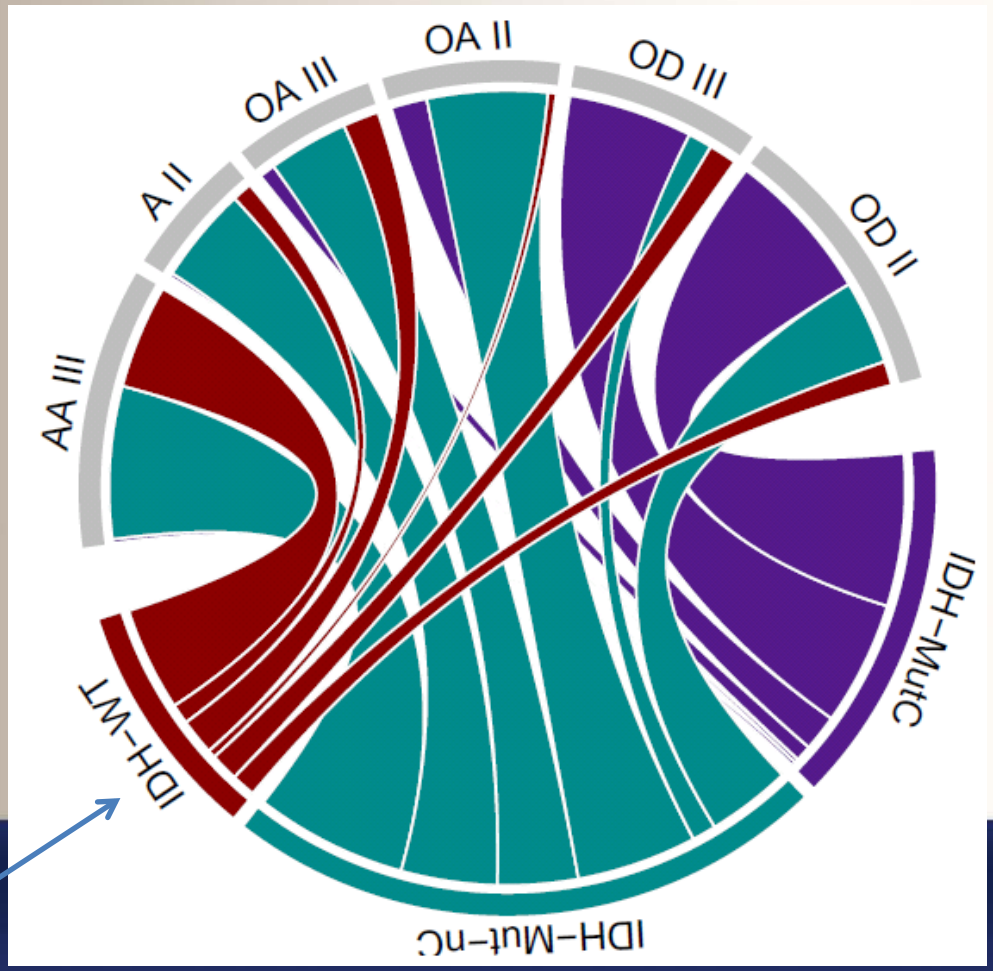
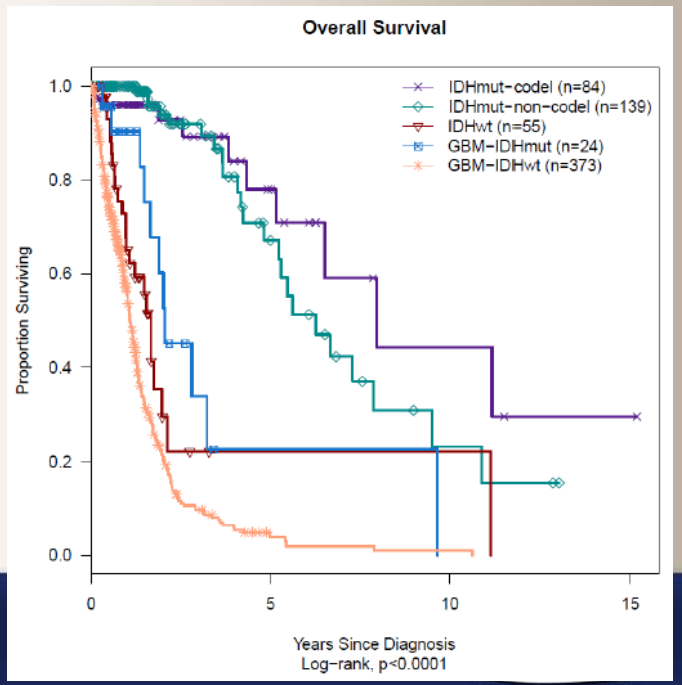
IDH/Codel vs Histology/Grade



IDH mut-codel

IDH mut-non-codel

IDH wt

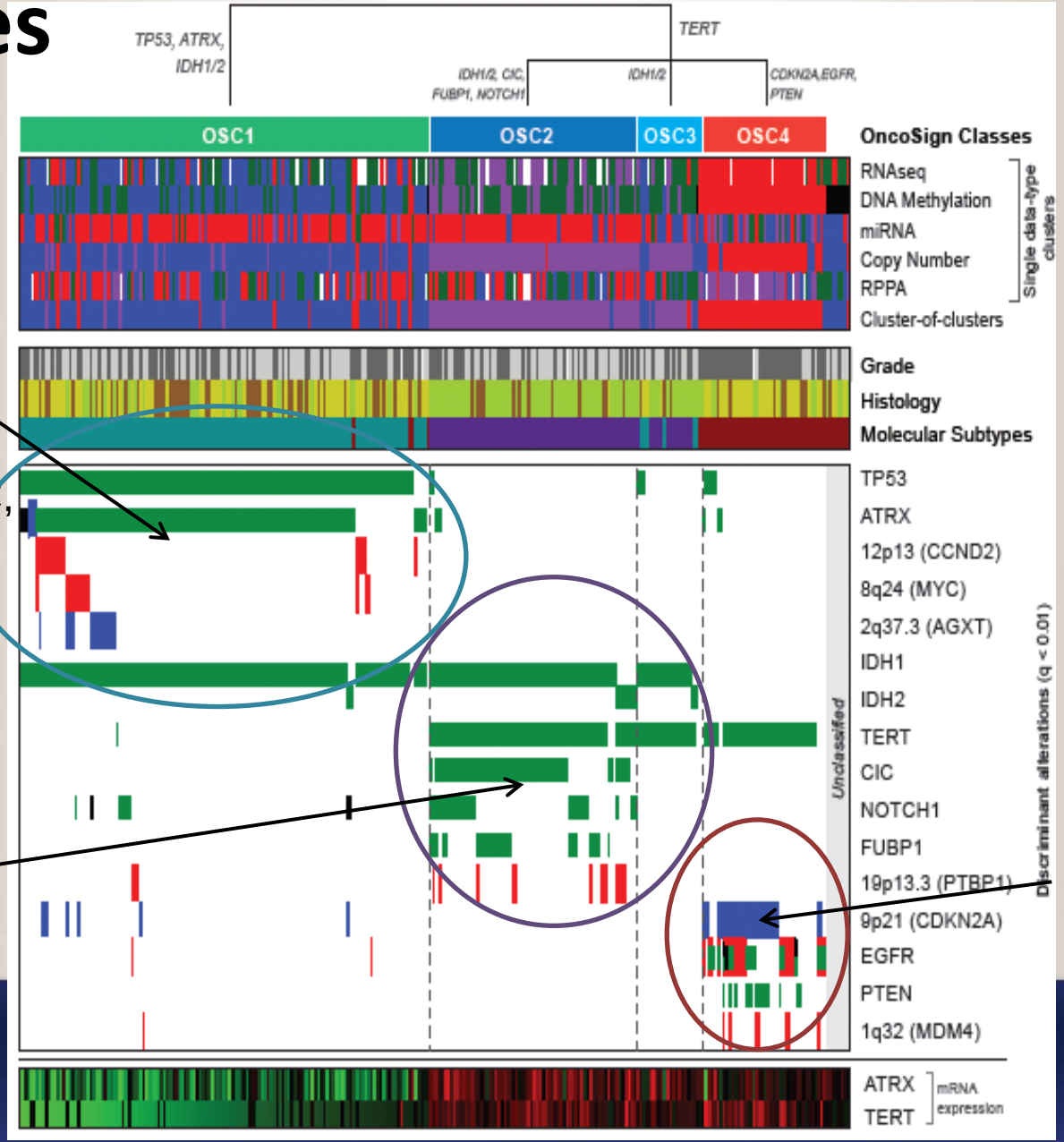


Brat et al (to appear)

Biology Follows IDH/Codel Molecular Subtypes

IDH Mut-Non-codel
TP53
ATRX
Gain of CCND2, MYC,
Loss of AGXT

IDH Mut-Codel
TERT
CIC
NOTCH1
FUBP1



Histology
- Astrocytoma
- Oligoastrocytoma
- Oligodendroglioma

Molecular subtype
- IDHwt
- IDHmut-non-codel
- IDHmut-codel

IDH WT
CDKN2A loss
EGFR gain/mut
PTEN mut
MDM4 gain

Brat et al (to appear)

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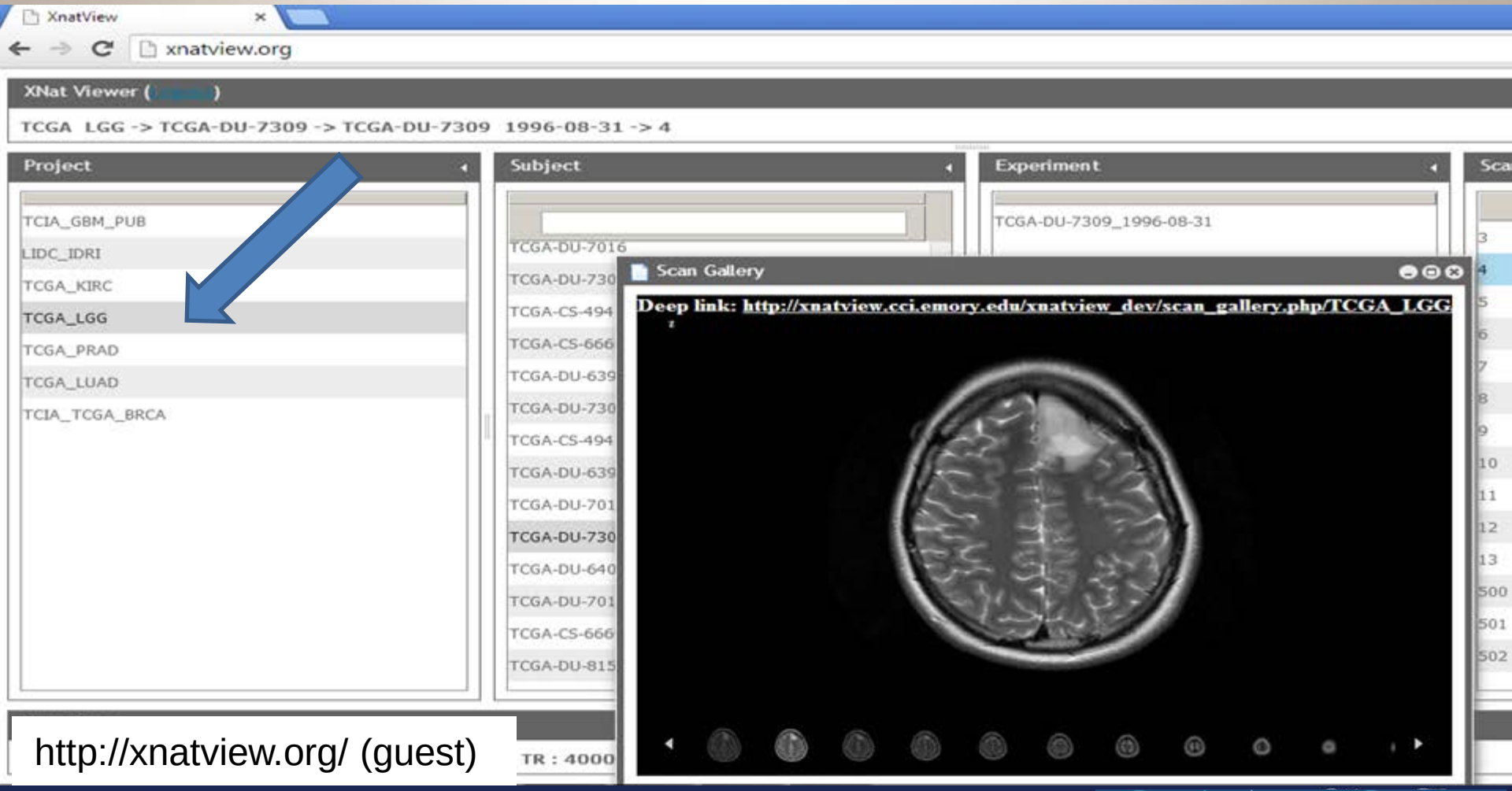
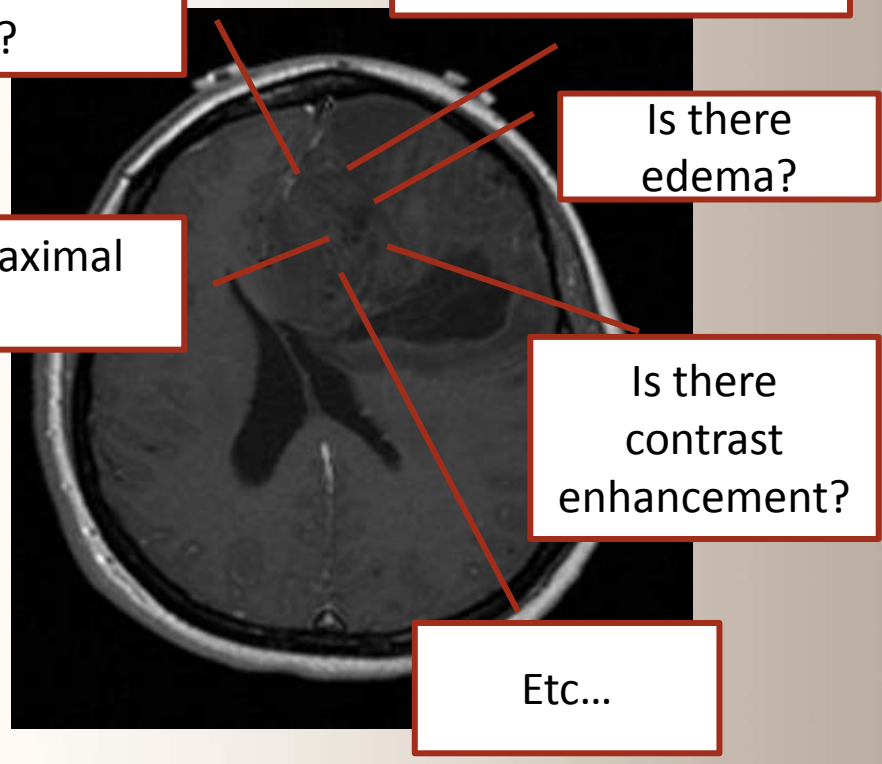
The Cancer Imaging Archive (TCIA)



http://xnatview.org/ (guest)

9 Neuroradiologists + 26 Features (LGG-VASARI set)

James Chen
(UC San Diego University)
Brent Griffith
(Henry Ford Hospital)
Chad Holder
(Emory University)
Scott Hwang
(St. Jude's Children's Research Hospital)
Michael Iv
(Stanford University)
Sugoto Mukherjee
(University of Virginia Health System)
Max Wintermark
(University of Virginia Health System)
Leo Wolansky
(Case Western Reserve University)
Kristen Yeom
(Stanford University)



TCGA-DU-6401
Axial T1 post-Gad contrast

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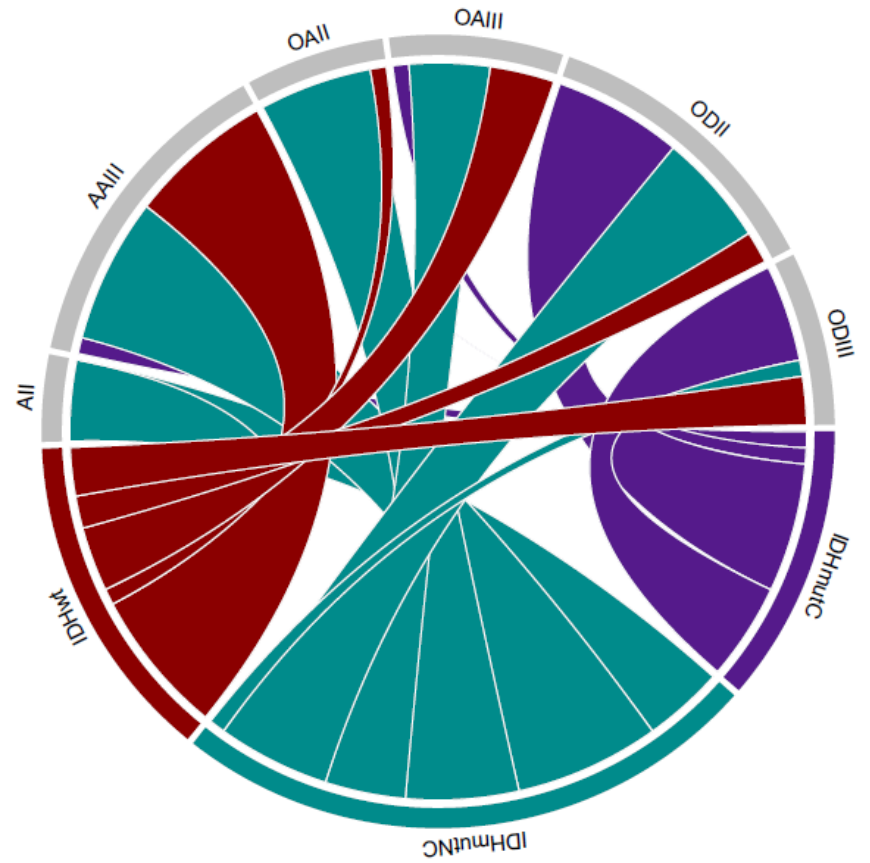
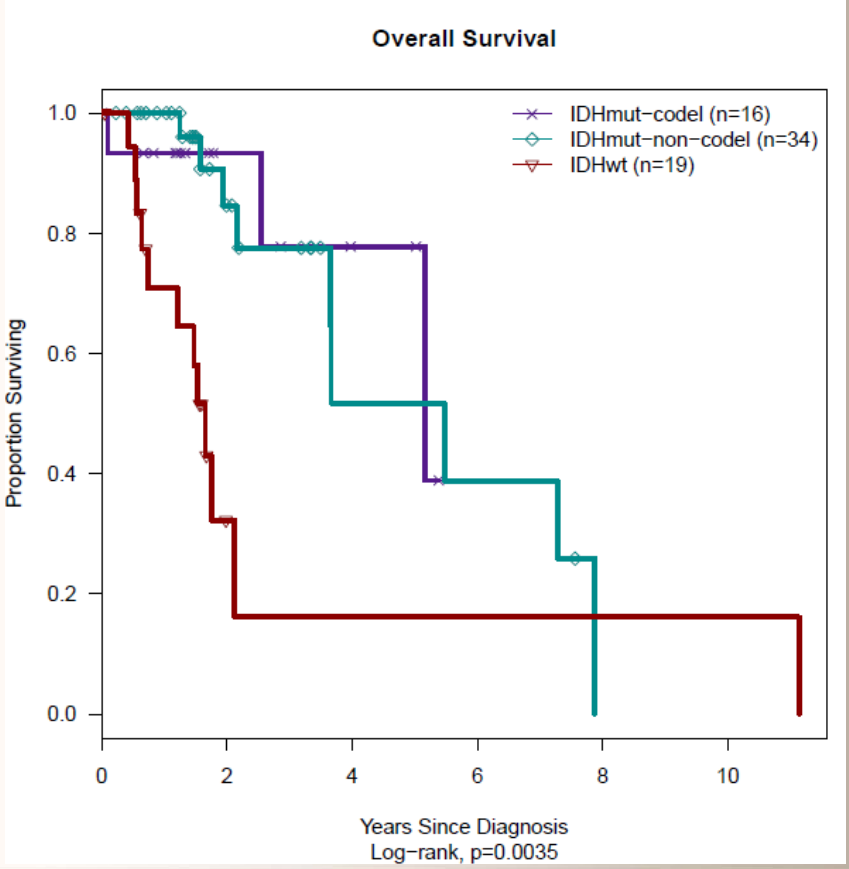
Are there neuro-imaging features associated with the IDH/Codel-defined molecular subtypes?

Radiogenomic Study Set (n=70)

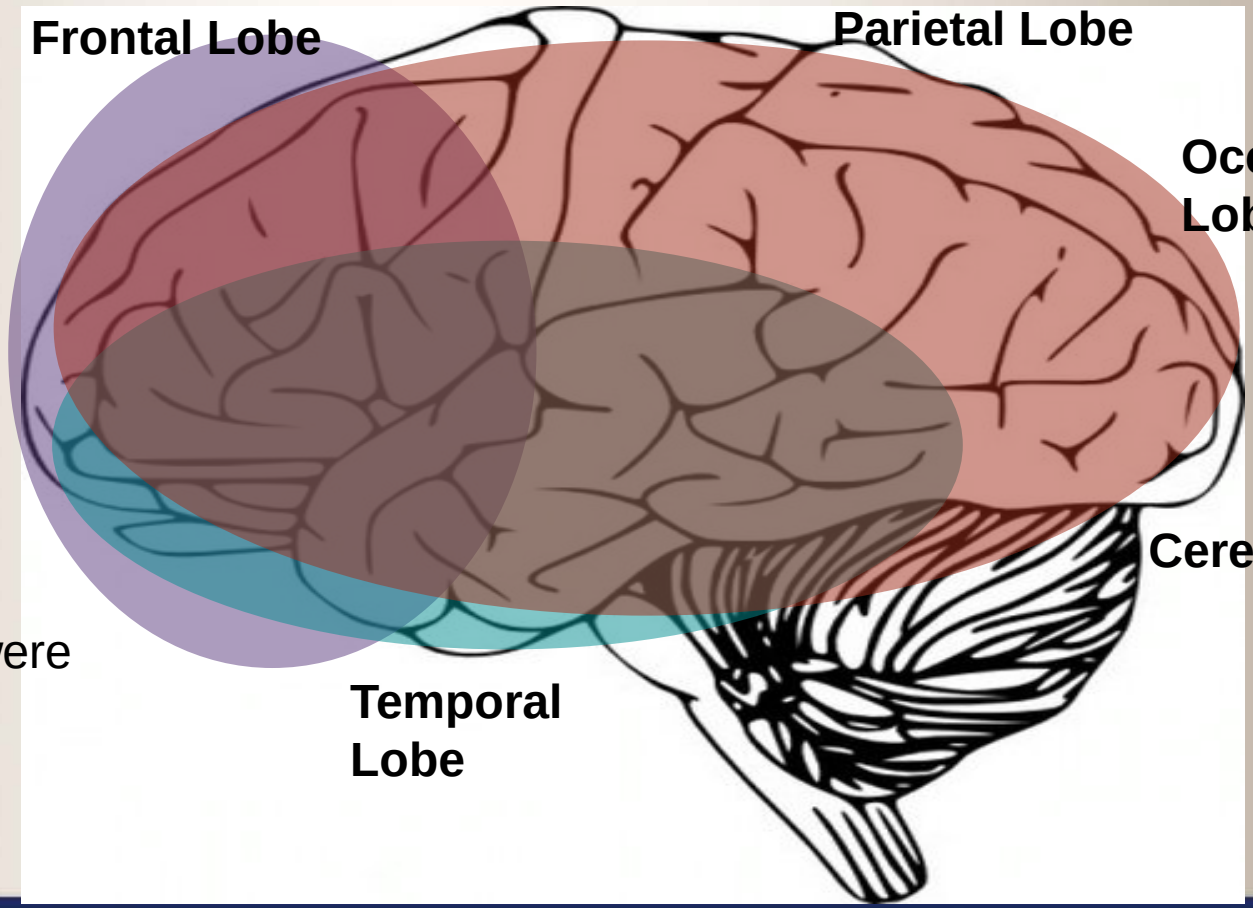




IDH-mut/codel tumors are likely to be centered in the frontal lobe

75% of IDH-mut/codel In frontal lobe vs other locations (FET p=0.026)

IDH-mut/non-codel were split 41% frontal and 41% temporal lobes



IDH-mutant/Codel
IDH-mutant/non-Codel
IDH-wt

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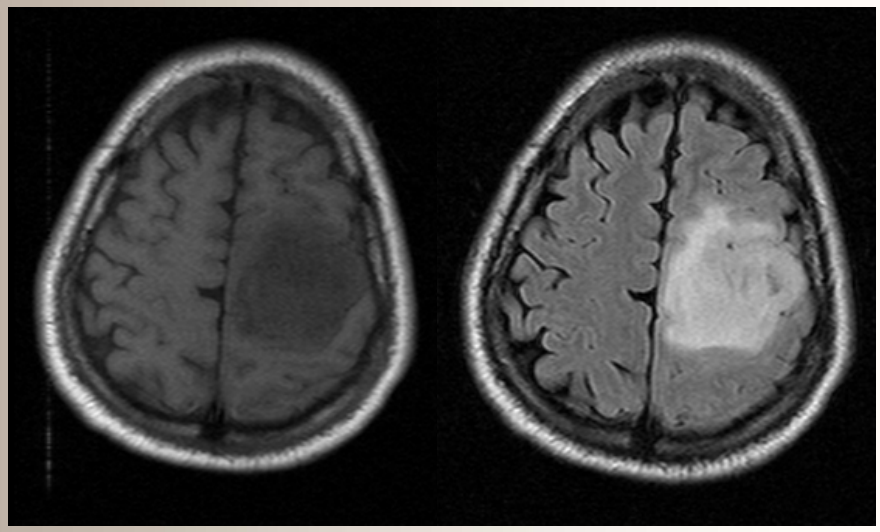
Other IDHmut Associated Features

- IDHmut-codel tumors were more likely to have:
  - T1/FLAIR signal cross the midline (FET p=0.007)
  - Have presence of hemorrhage (FET p=0.009)
  - Have presence of cysts (FET p=0.066)
- IDHmut-non-codel tumors were least likely to have presence of satellites (FET p=0.030)

IDHwt tumors tend to be more infiltrative

IDH-mut-codel

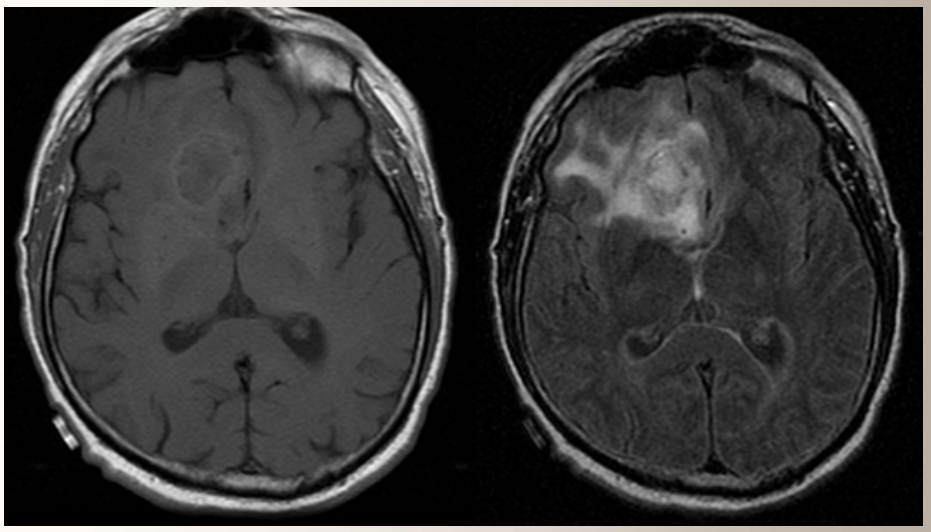
TCGA-CS-4943 (T1 ~ FLAIR)



T1W T2 FLAIR

IDH-wt

TCGA-CS-4941 (T1<<FLAIR)



T1W T2 FLAIR

FLAIR region likely to be larger than T1 (FET, p=0.003)

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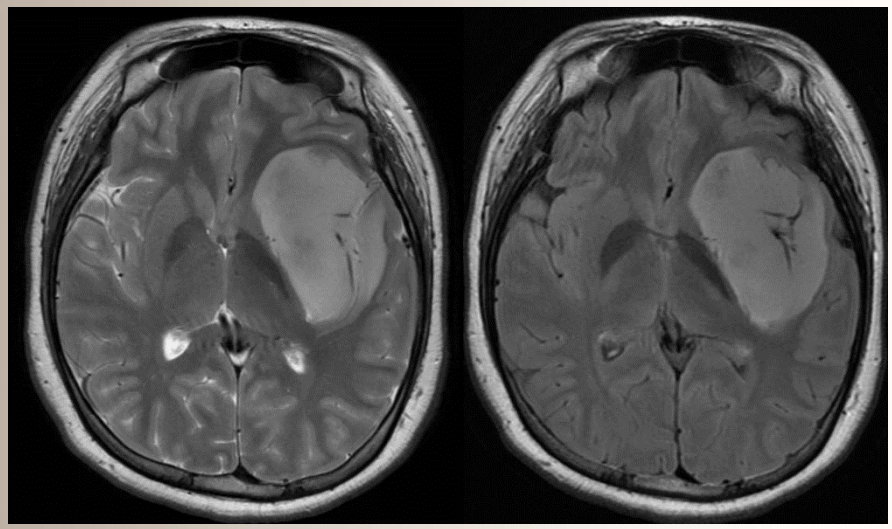
IDH-wt tumors are less likely to have well defined non-enhancing regions

IDH-mut-non-codel

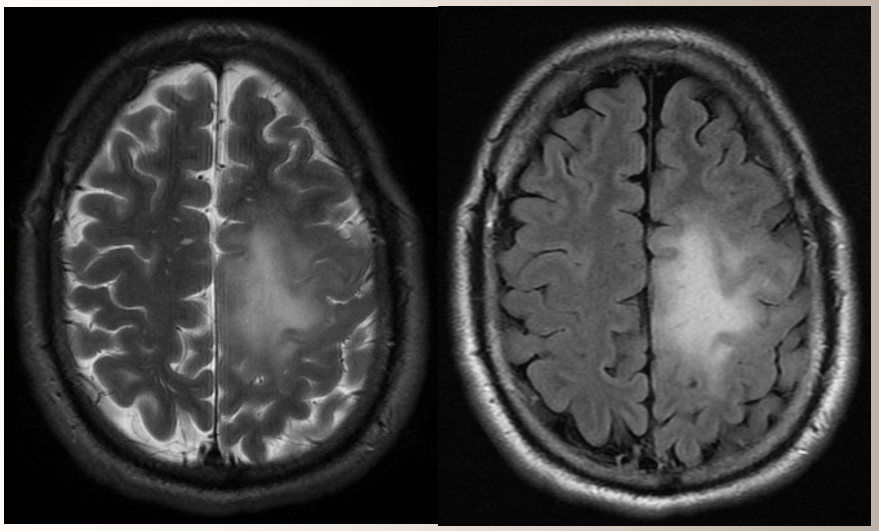
Well-defined NER



T2W T2 FLAIR

IDH-wt

Poorly-defined NER



T2W T2 FLAIR

56% IDH-mut/Codel and 76% IDH-mut/Non-codel vs. 32% for IDH-wt (FET, p=0.027)

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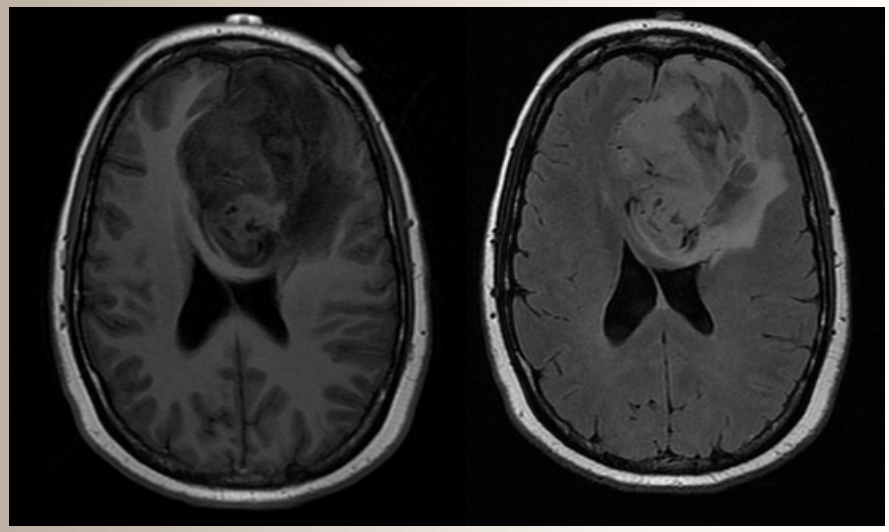
IDHwt tumors tend to be smaller

IDH-mut-codel

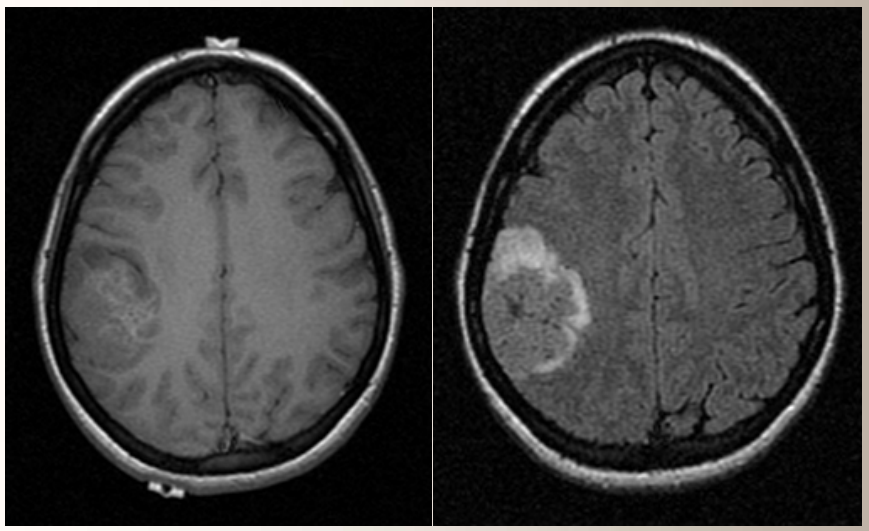
TCGA-DU-5871 (57.6 cm^2)



T1W T2 FLAIR

IDH-wt

TCGA-DU-6404 (21.5 cm^2)

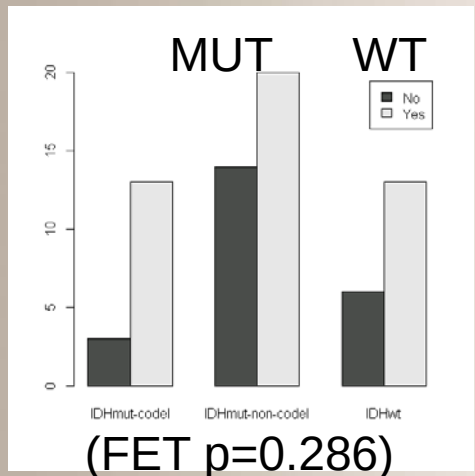


T1W T2 FLAIR

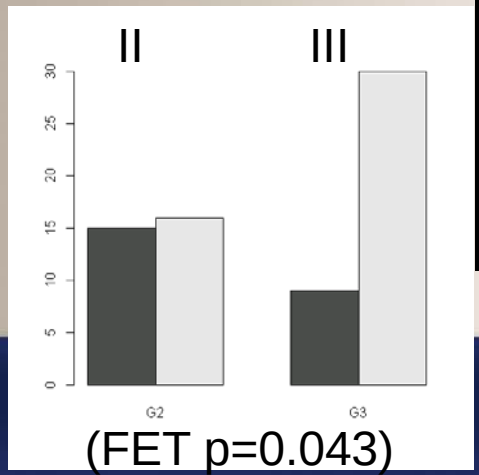
Mean: 23.0 cm^2 vs 39.7cm^2 maximal area (t-test $p<0.001$)

Features of GBM were not more common in IDH-wt tumors

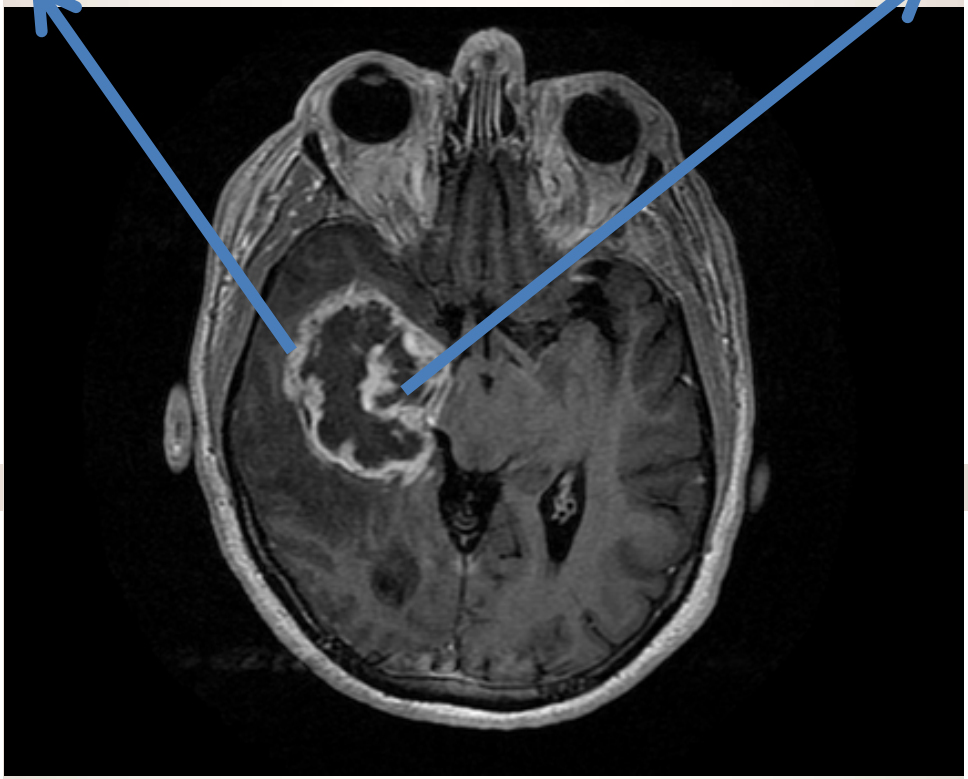
Enhancing Component



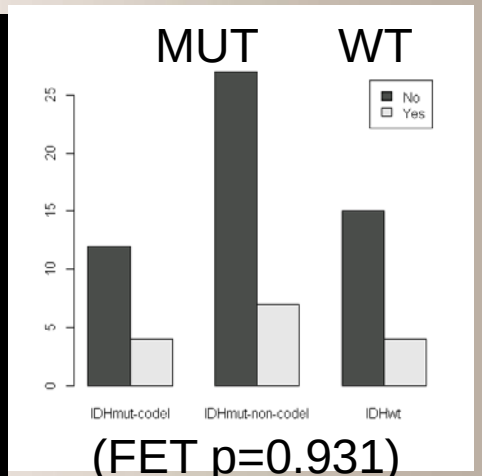
(FET p=0.286)



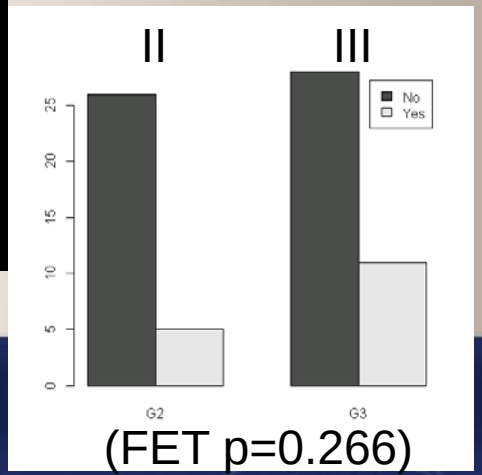
(FET p=0.043)



Necrotic Component



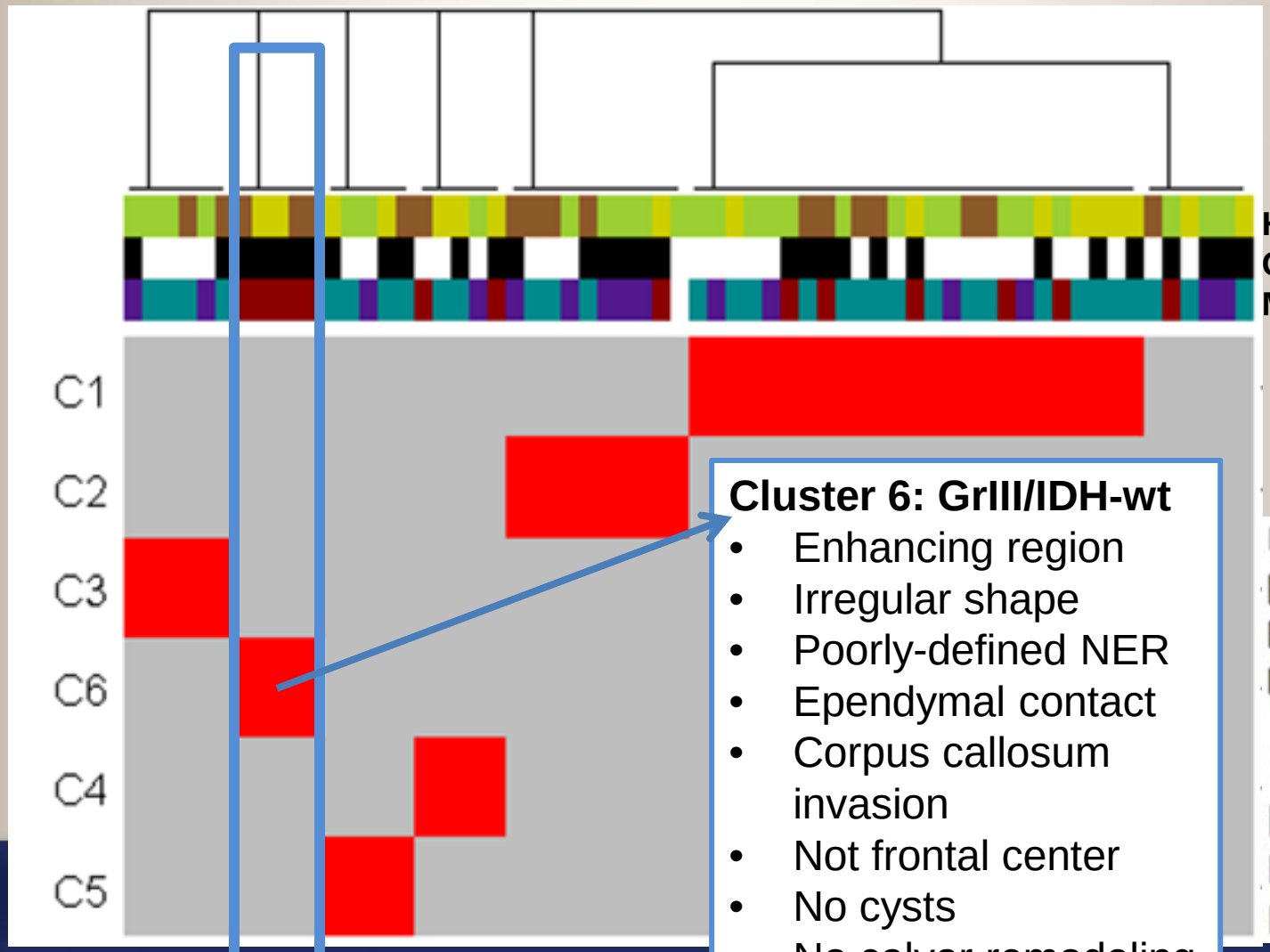
(FET p=0.931)



(FET p=0.266)

TCGA-06-0189 (GBM)
T1 Post-gad

Bi-clustering finds sets of samples with consistent imaging characteristics



Conclusions

- Several MR imaging features are associated with LGG molecular classes
- IDH-wt LGG does show association with aggressive features
- IDH-wt LGG is not likely under-diagnosed GBM
- Imaging patterns are present
- Further work needs to be done to determine if the associations in MR Imaging have clinical implications or other genomic associations

Acknowledgements

The Cancer Imaging Archive –
TCGA Glioma Phenotype Research Group

- James Chen (UC San Diego University)
- Brenda Fevrier-Sullivan (Frederick Nat. Lab. for Cancer Research)
- Adam Flanders (Thomas Jefferson University)
- John Freyman (Frederick Nat. Lab. for Cancer Research)
- Brent Griffith (Henry Ford Hospital)
- David Gutman (Emory University)
- Chad Holder (Emory University)
- Erich Huang (NIH)
- Scott Hwang (St. Jude's Children's Research Hospital)
- Michael Iv (Stanford University)
- Carl Jaffe (Boston University Medical Center)
- Rajan Jain (New York University Medical Center)
- Justin Kirby (Frederick Nat. Lab. for Cancer Research)
- Sugoto Mukherjee (University of Virginia Health System)
- Arvind Rao (MD Anderson Cancer Center)
- Max Wintermark (University of Virginia Health System)
- Leo Wolansky (Case Western Reserve University)
- Kristen Yeom (Stanford University)

Henry Ford Health System –
Hermelin Brain Tumor Center
Josephine Ford Cancer Institute

- Tom Mikkelsen
- Lisa Scarpace

National Cancer Institute National Human Genome Research Institute

The Cancer Genome Atlas *Understanding genomics to improve cancer care*

TCGA LGG Analysis Working Group

- Dan Brat (Emory University)
- Lee Cooper (Emory University)

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Poster #98