Multi-modal analysis of distribution and efficacy of EGFR-targeted therapies in GBM

Jann N. Sarkaria
MIT/Mayo Physical Sciences Center for Drug Distribution and Efficacy in Brain Tumors
MIT/Mayo Physical Sciences Center for Drug Distribution and Efficacy in Brain Tumors

MR imaging

Drug distribution: LC/MS / MALDI-MSI

Tissue architecture/Signaling analyses
Is sub-therapeutic exposure bad?

Mayo PDXs – GBM6, 12, 39

EGFR inhibitors
MALDI-MSI/MRI description of erlotinib distribution:

GBM12

Randall et al., Nature Communications, 2018 in press
Physico-chemical parameters that influence drug distribution
MALDI-MSI and Stimulated Raman Scattering

Randall et al., Nature Communications, 2018 in press
Impact of drug exposure on signalling
RNAseq comparison of flank and intracranial tumors

Randall et al., Nature Communications, 2018 in press
Impact of sub-therapeutic drug exposure on signalling
Tyrosine phosphoproteomics

Randall et al., Nature Communications, 2018 in press
Impact of brain penetration on efficacy of ADC
Depatux-M (ABT-414)
Radiomic predictors of genomics and drug distribution

Erlotinib

Pre-treatment

1 mo

3 mo

EGFR amplified

Non amplified

Progressing

responding over time...

T1Gd

T2

Cells

Penetrant

Impenetrant

% of Tumor Cells

Min Drug Level Achieved

©2017 MFMER | 3674401-9
Acknowledgments

Mayo Rochester
Katie Bakken
Debra Brinkmann
Dani Burgenske
Terry Burns
Brett Carlson
David Daniels
Paul Decker
Jeanette Eckel-Passow
Caterina Giannini
Shiv Gupta
Lihong He
Lori Henrichs
Zeng Hu
Gaspar Kitange
Bianca Marin
Andrea McMahon
Cole McKean
Ann Mladek
Deanna Pafundi
Ian Parney
Mark Schroeder
Emily Smith
Rachael Vaubel

MIT
Allison Claas
Antje Dittmann
Brian Joughin
Ishwar Kohale
Doug Lauffenburger
Alison Tisdale
Forest White
Dane Wittrup

Harvard
Walid Abdelmoula
Nathalie Agar
David Calligaris
Amanda Clark
Begona Gimenez-Cassina Lopez
Frank Lu
Elizabeth Randall
Michael Reagan

Mayo Scottsdale
Kristin Swanson
Pamela Jackson
Andrea Hawkins-Daarud
Susan Massey
Kamala Clark-Swanson
Scott Whitmire
Nhan Tran
Mustafa Tuncali
Leland Hu
Gustavo deLeon

U of Minnesota
Bill Elmquist
Minjee Kim
Gautham Gampa
Jessica Griffith
Janice Laramy
Afroz Mohammad
Karen Parrish
Katelyn Swanson
Surabhi Talele

Funding: MIT/Mayo Physical Sciences of Oncology Center; U54 CA210180

©2017 MFMER | 3674401-10