

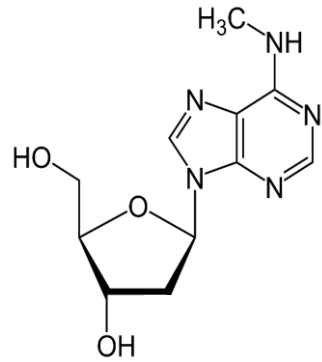
Developing a new generation of chemotherapy agents against cancer stem cells

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Discovery of N6-mA as a novel base in mammalian genomes



N6-methyl-adenine

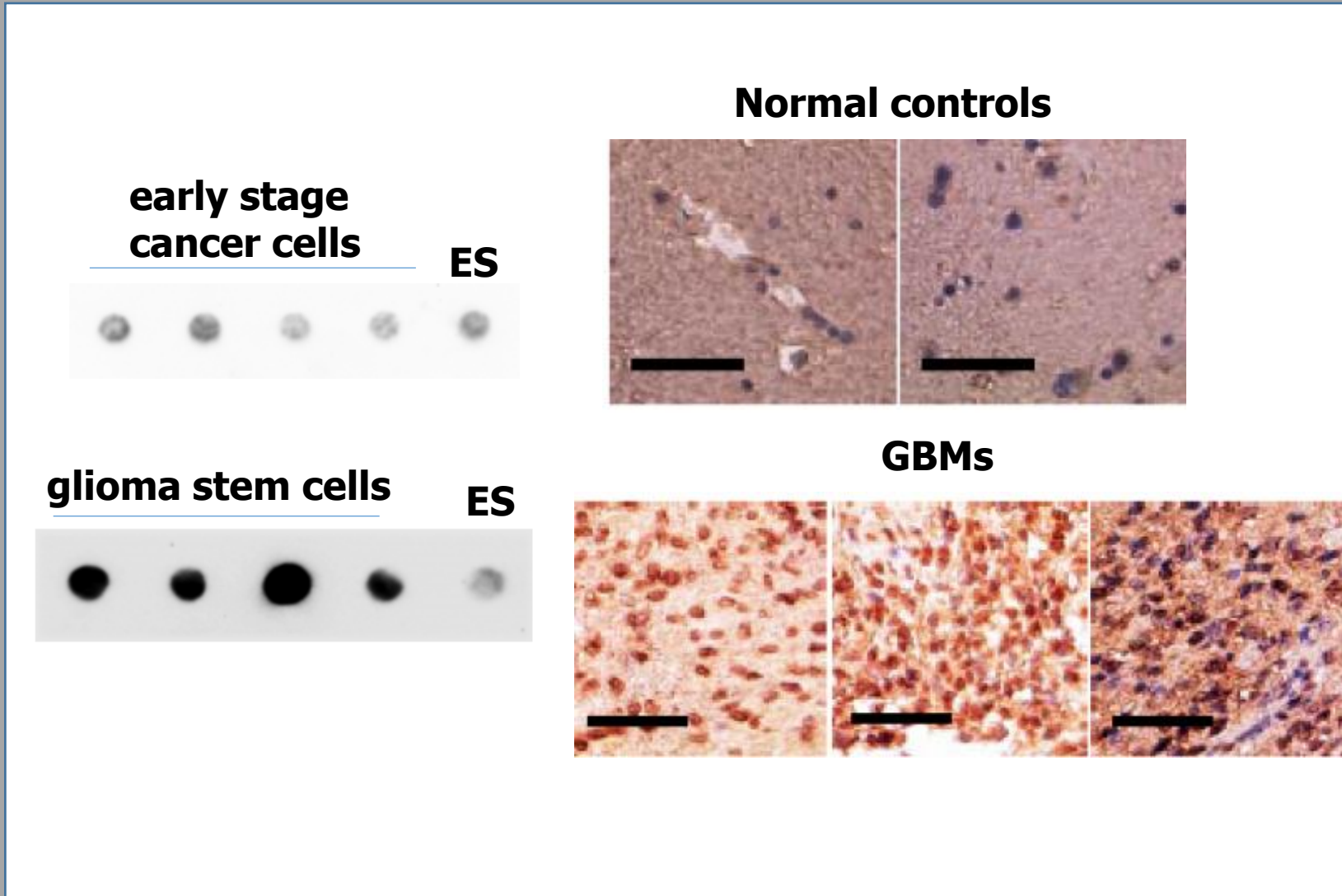
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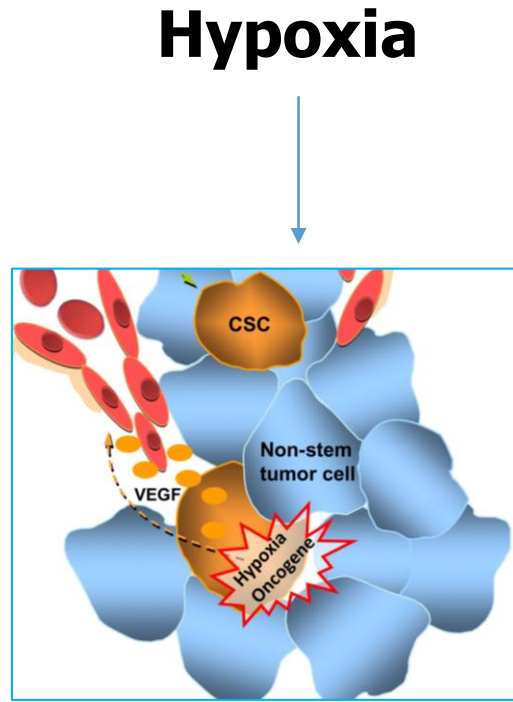
DNA methylation on N^6 -adenine in mammalian embryonic stem cells

Tao P. Wu¹, Tao Wang¹, Matthew G. Seetin², Yongquan Lai³, Shijia Zhu⁴, Kaixuan Lin¹, Yifei Liu¹, Stephanie D. Byrum⁵, Samuel G. Mackintosh⁵, Mei Zhong⁶, Alan Tackett⁵, Guilin Wang⁷, Lawrence S. Hon², Gang Fang⁴, James A. Swenberg³ & Andrew Z. Xiao¹

N6-mA levels during glioblastoma (GBM) development

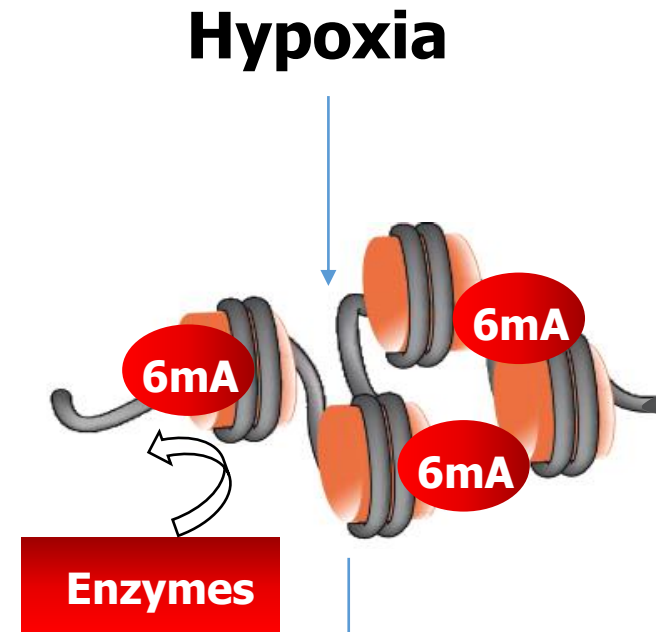


N6-mA is critical role for selecting cancer stem cells in GBM



Selection of CSCs

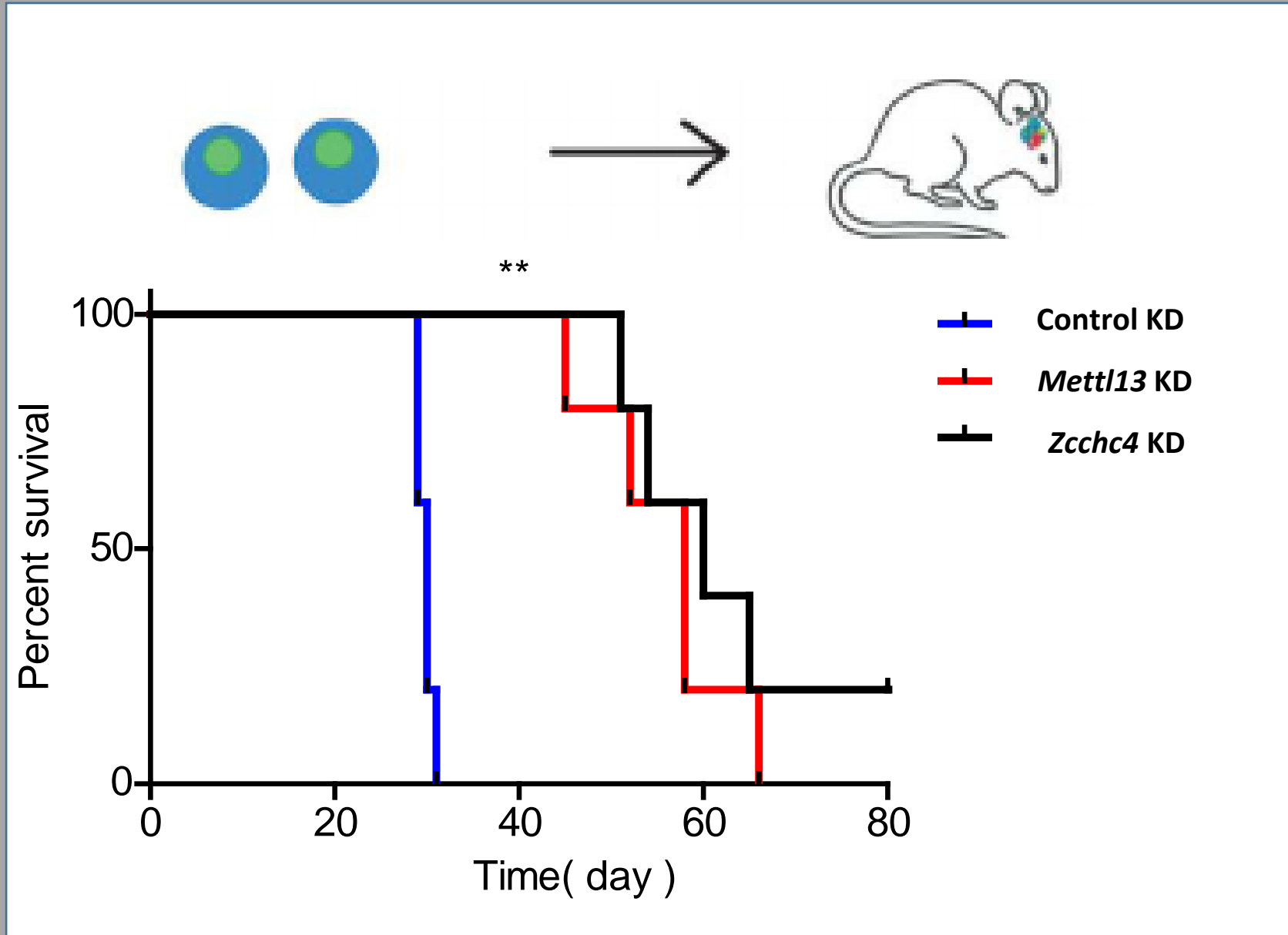
**chemoresistance, angiogenesis
& metastasis**



**represses cell death-
related genes**

growth advantages

N6-mA is a promising drug target for GBM

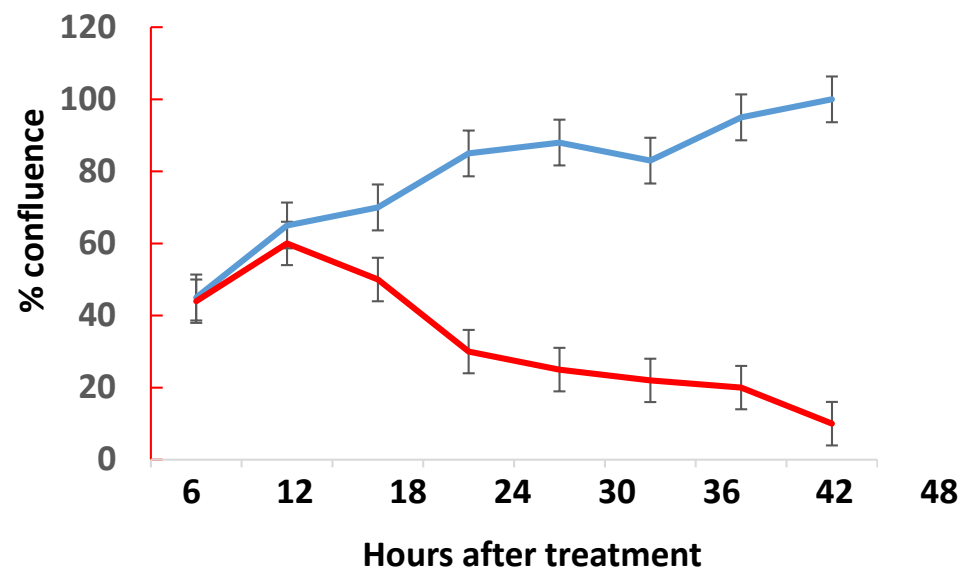
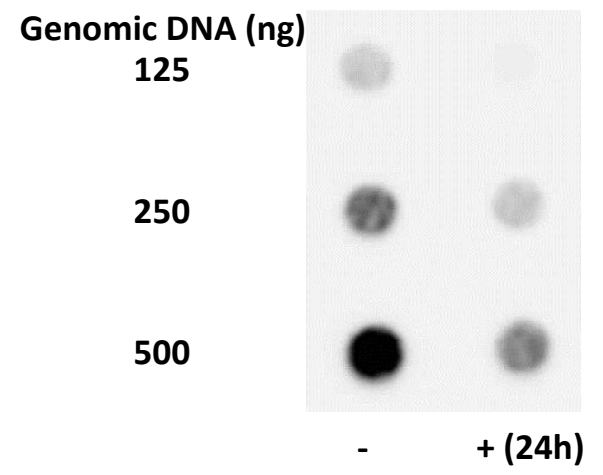


An *in vitro* system to screen N6-mA inhibitors

small chemical library \longrightarrow *In vitro* methyltransferase assay

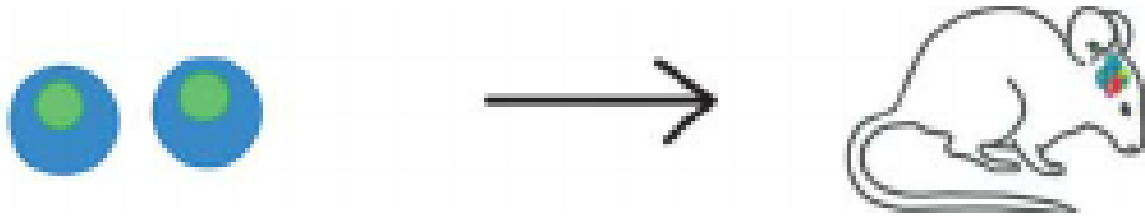


N6-mA inhibitor-1



Future directions and Milestones

- **Screening for additional specific N6-mA inhibitors (nM range and specific for each N6-mA MT)**
- **Evaluate *in vivo* efficacy of the inhibitors by PDX models**



Rarebase Therapeutics:

- *developing inhibitors against methyltransferases and reader molecules of N6-mA*
- *Target cancers and other diseases, such as Autism and congenital heart disease (VSD)*
- *Aiming to launch Phase I trial in GBM in 3-5 years*
- *Potential investors: Elm Street Venture*