GSK-3 inhibitor 9-ING-41 enhances genotoxic therapy of GBM leading to cure from intracranial brain tumor

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Disclosure of Conflict of Interest
Andrey Ugolkov is a founder of Actuate Therapeutics, Inc. which is developing 9-ING-41 and holds an equity interest in this company.
GSK-3β is required for NF-κB transcriptional activity in human cancer cells
Hypothesis: inhibition of GSK-3β overcomes NF-κB-mediated chemoresistance to conventional chemotherapeutic drugs in human cancer
GBM PDX (patient-derived xenograft) tumor model 373811

- Left hemisphere
- Right hemisphere
- GBM PDX tumor

H&E section of intracerebral GBM PDX tumor

- Formalin-fixed brain, coronal section
- Tumor

- Cachectic mouse (brain tumor)
- Normal mouse (no tumor)
GSK-3 inhibitor 9-ING-41 suppresses NF-κB transcriptional activity in orthotopic GBM PDX tumor (PCF 373811, NF-κB-luc-reporter)

- NF-κB is constitutively active in orthotopic GBM PDX tumor

- Intravenous injection of 25 mg/kg 9-ING-41
  - Image was taken before the injection
  - 4 hours after the injection: IVIS signal (p/s) 1.62x10^7
  - 24 hours after the injection: 1.47x10^6

NF-κB-luc-reporter expressing GBM PDX tumor
Treatment with CCNU+9ING41 arrests the growth of GBM6 PDX subQ tumors
Treatment with CCNU+9ING41 leads to a complete regression of intracranial CCNU-sensitive GBM6 tumors (1)
Treatment with CCNU+9ING41 leads to a complete regression of intracranial CCNU-sensitive GBM6 tumors (2)
Treatment with CCNU+9ING41 leads to a complete regression of intracranial CCNU-resistant GBM12 tumors.
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