



Towards better brain cancer treatment with novel in vitro models and fewer animal experiments

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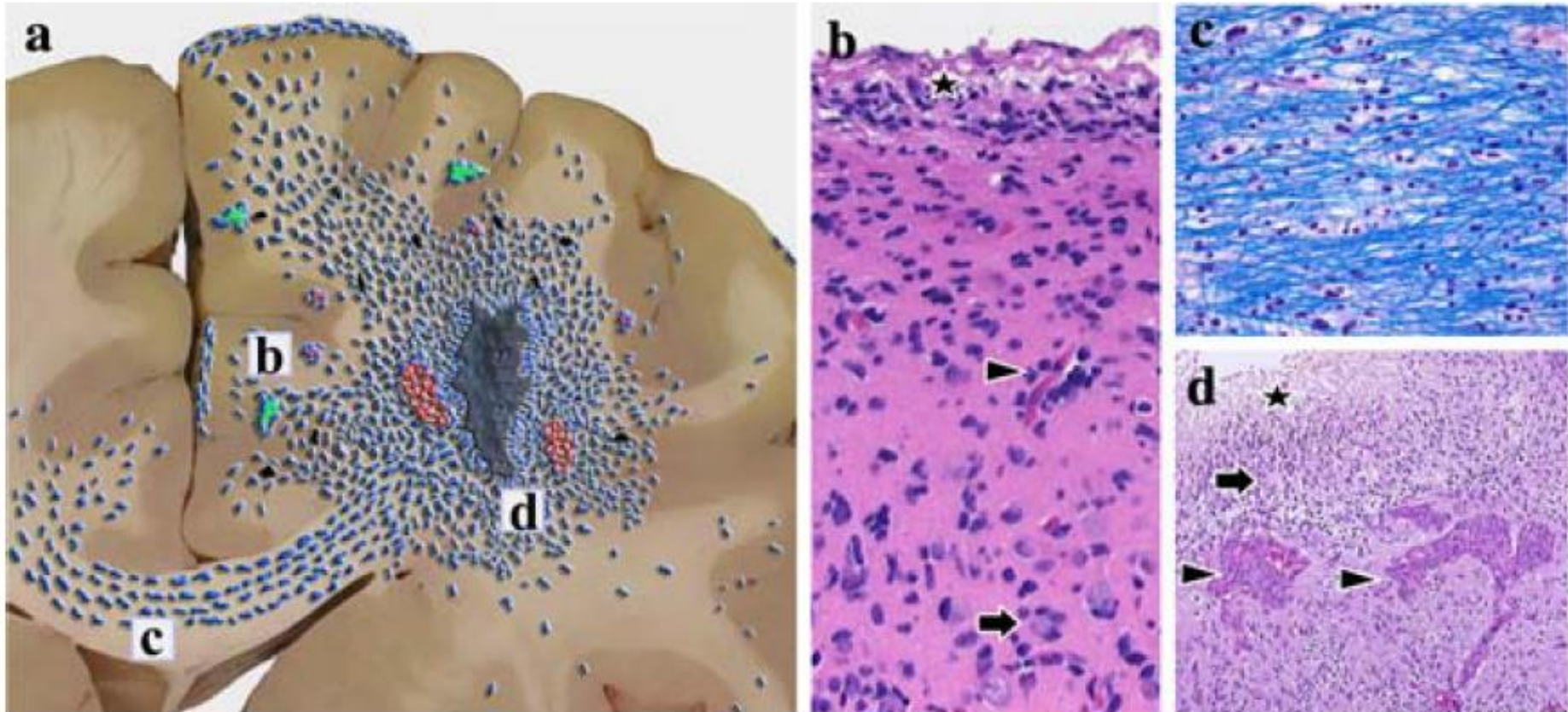
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Survival rates of brain cancer patients

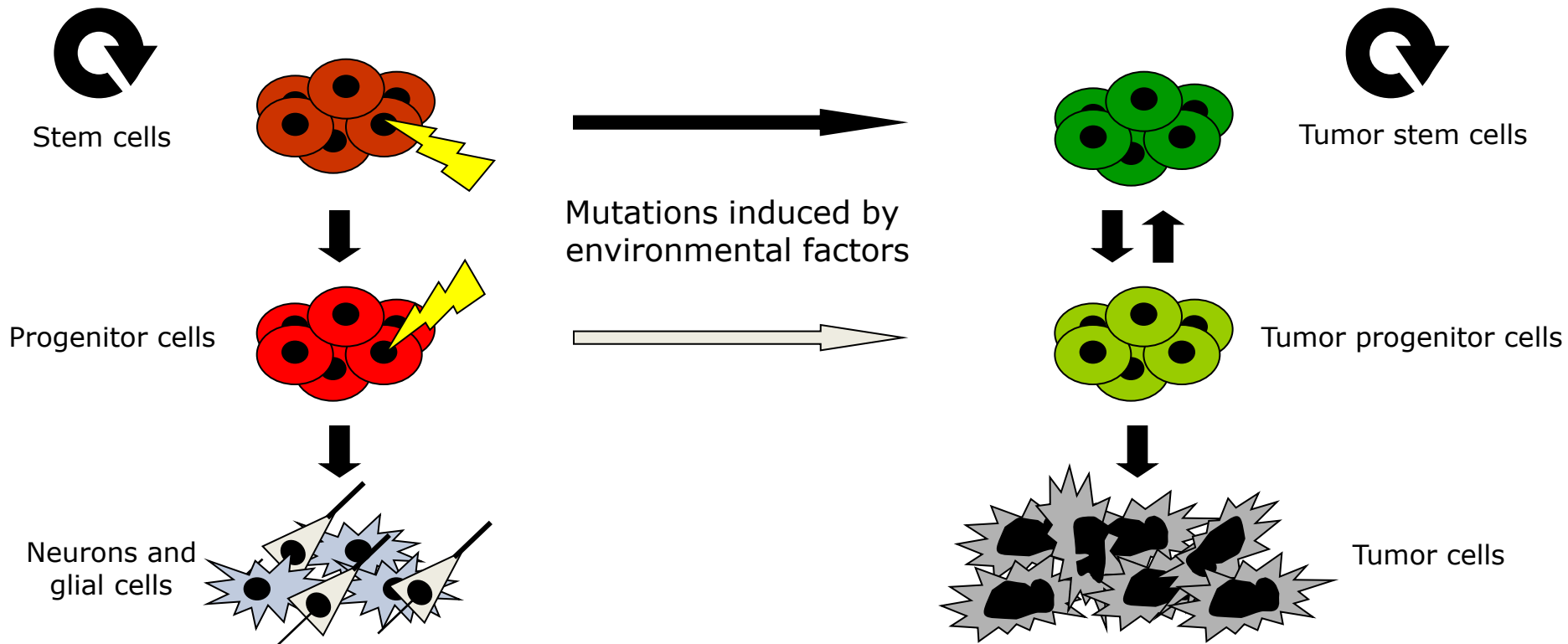


Migrating tumor cells versus surgery



Claes A et al, Acta Neuropathol (2007)

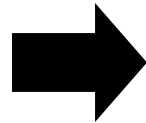
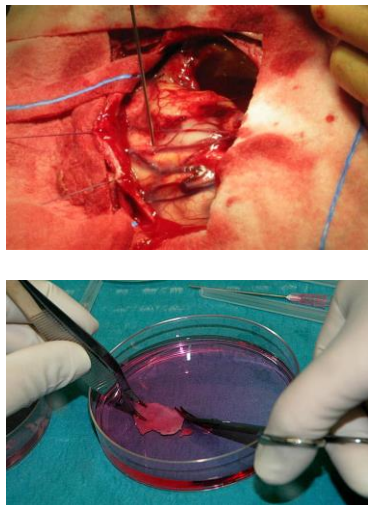
Tumor stem cell paradigm



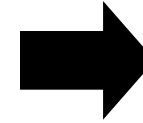
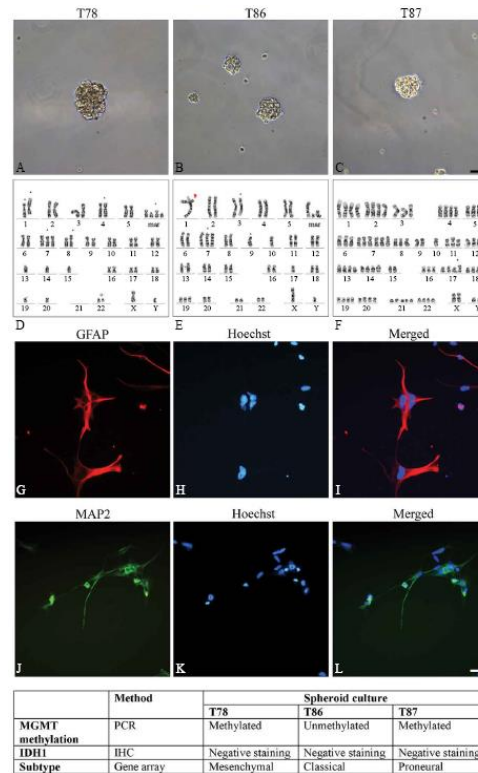
- Stem cells and tumor stem cells:
 - Self-renewal (asymmetric cell division)
 - Indefinite proliferation potential
 - Differentiation

Experimental "patient-like" models

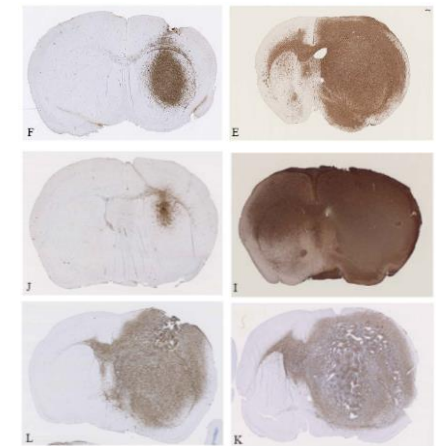
Biopsy



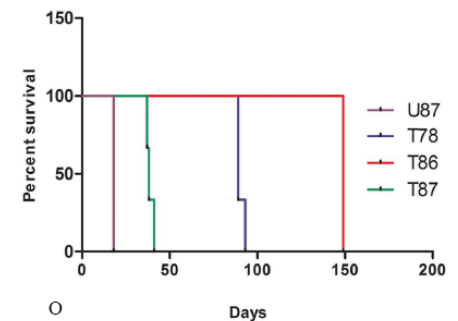
Cultures/Cell lines



In vivo model



Survival mice

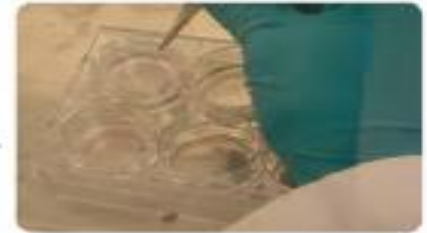
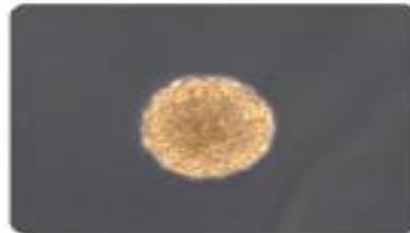
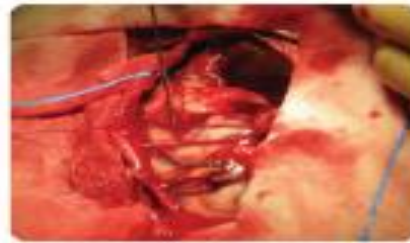


3R potential

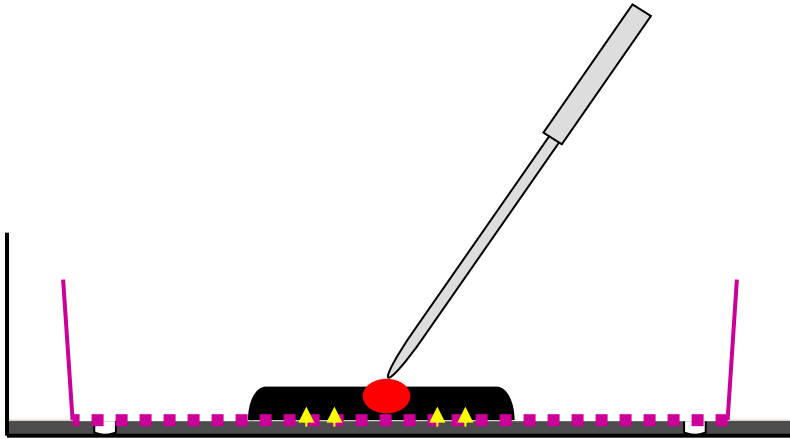
- A Pub Med search (“mice and glioma and year”) identified:
 - 263 brain cancer studies in 2004
 - 856 brain cancer studies in 2014
 - More than 3-fold increase over 10 years
- 50.000 mice are supposed to be used for brain cancer studies in 2015
- Orthotopic models are app. being used in 50% of these studies corresponding to 25.000 mice/year

3D in vitro model

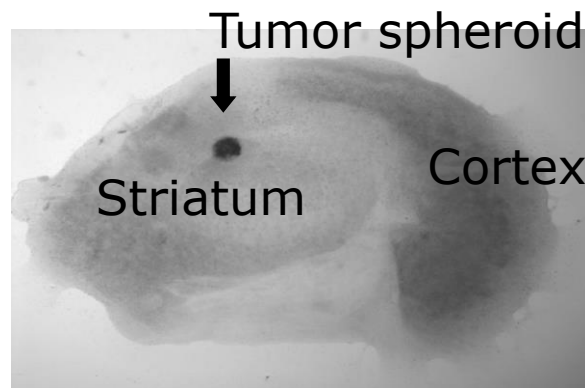
-In stem cell medium



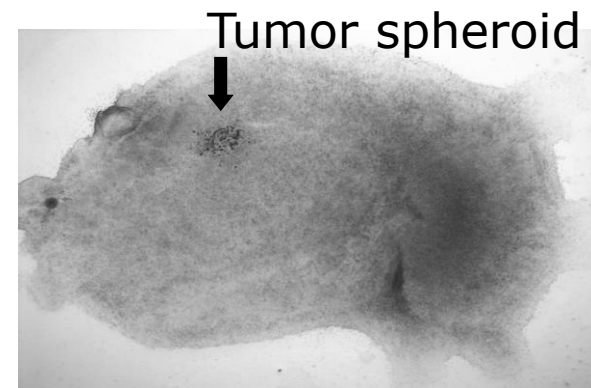
Implantation of tumor cells



- Culture medium
- Brain slice
- Tumor spheroid
- Millicell insert with semi-permeable membrane

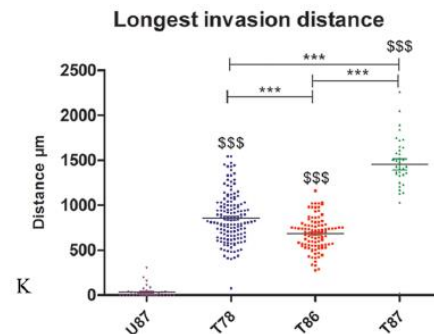
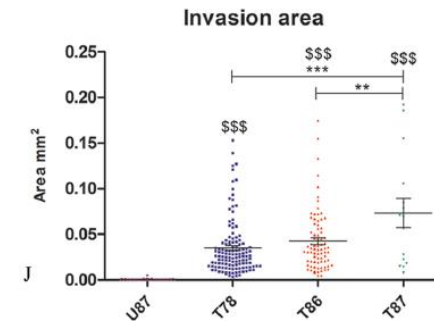
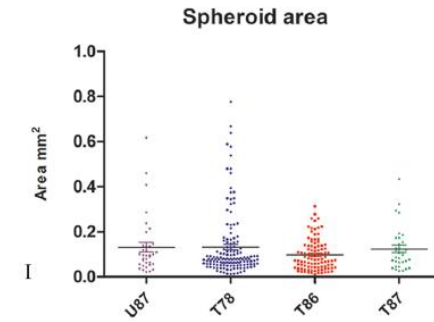
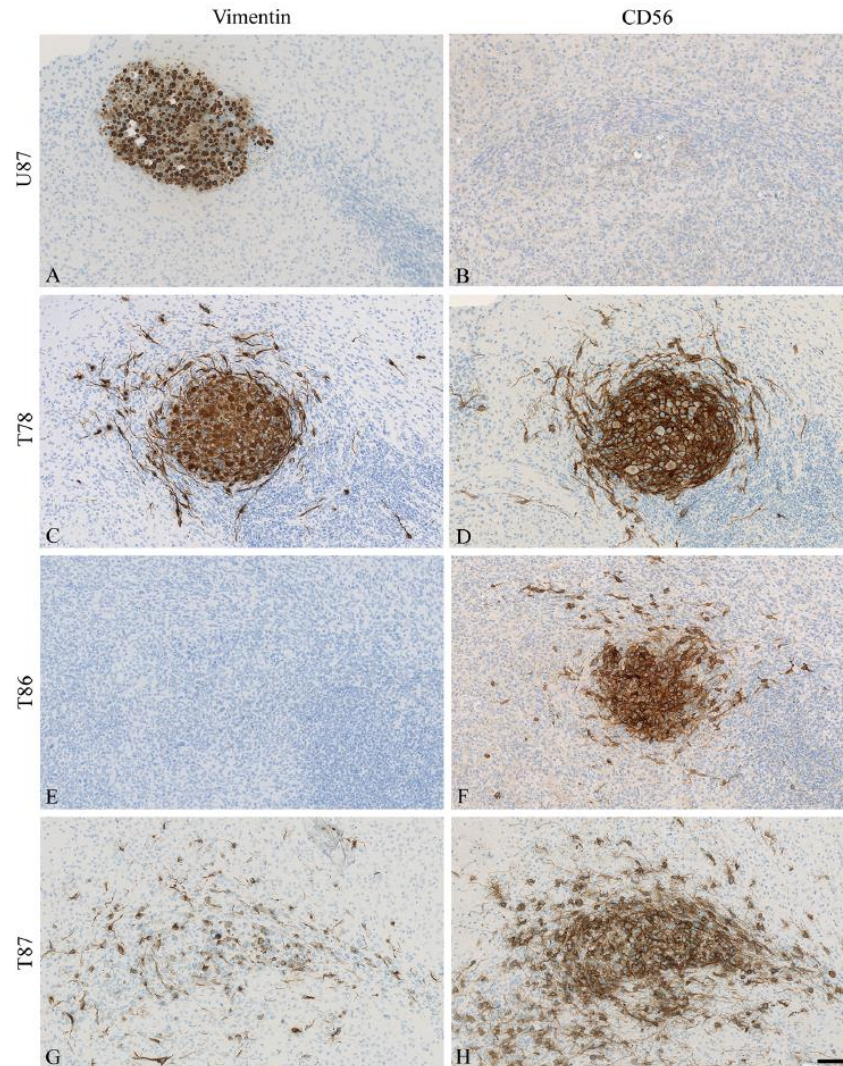


Day 0



Day 14

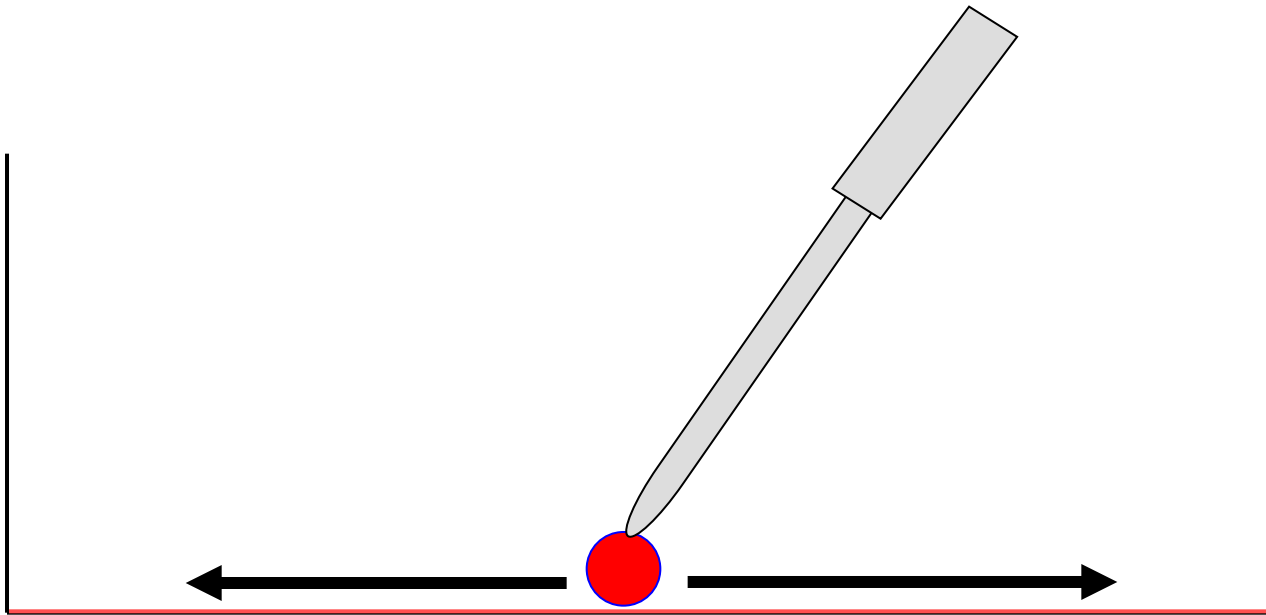
3D in vitro model



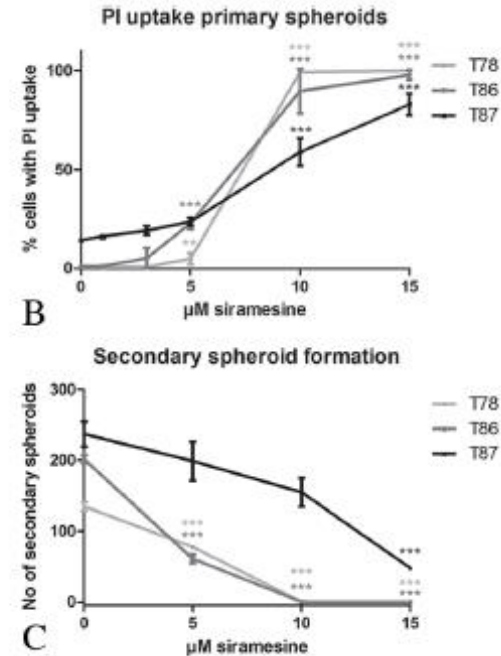
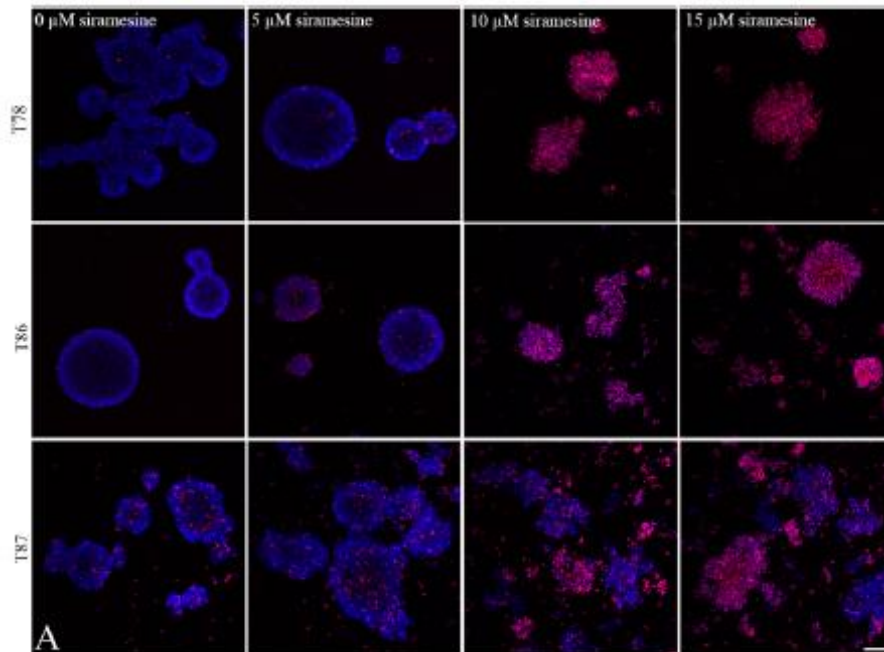
2D model

Tumor cell migration on a flat surface

-in stem cell medium

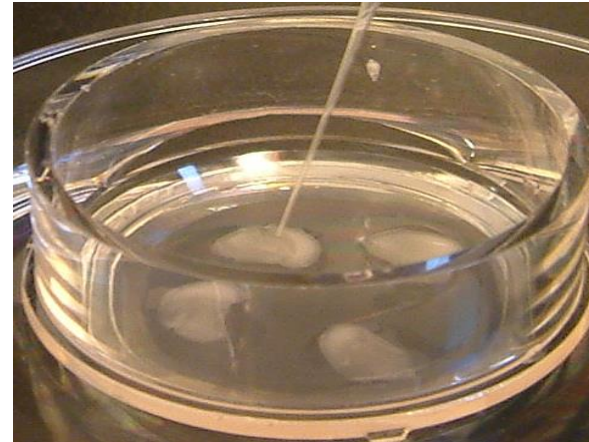
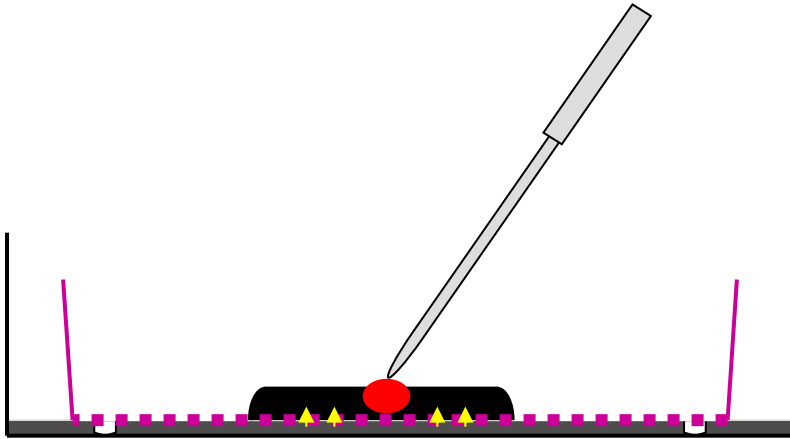


Effect on patient-derived spheroids

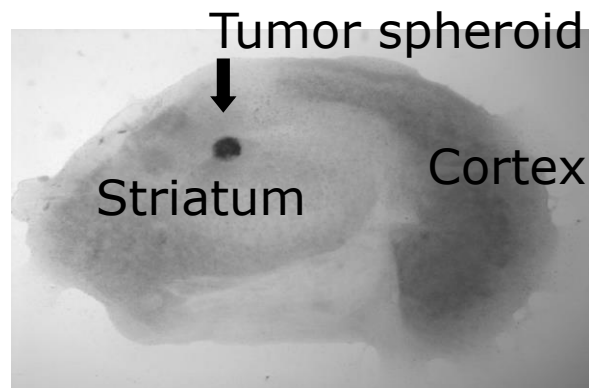


No effect in vivo

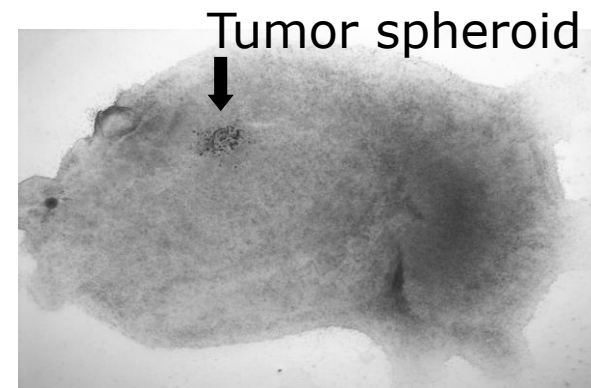
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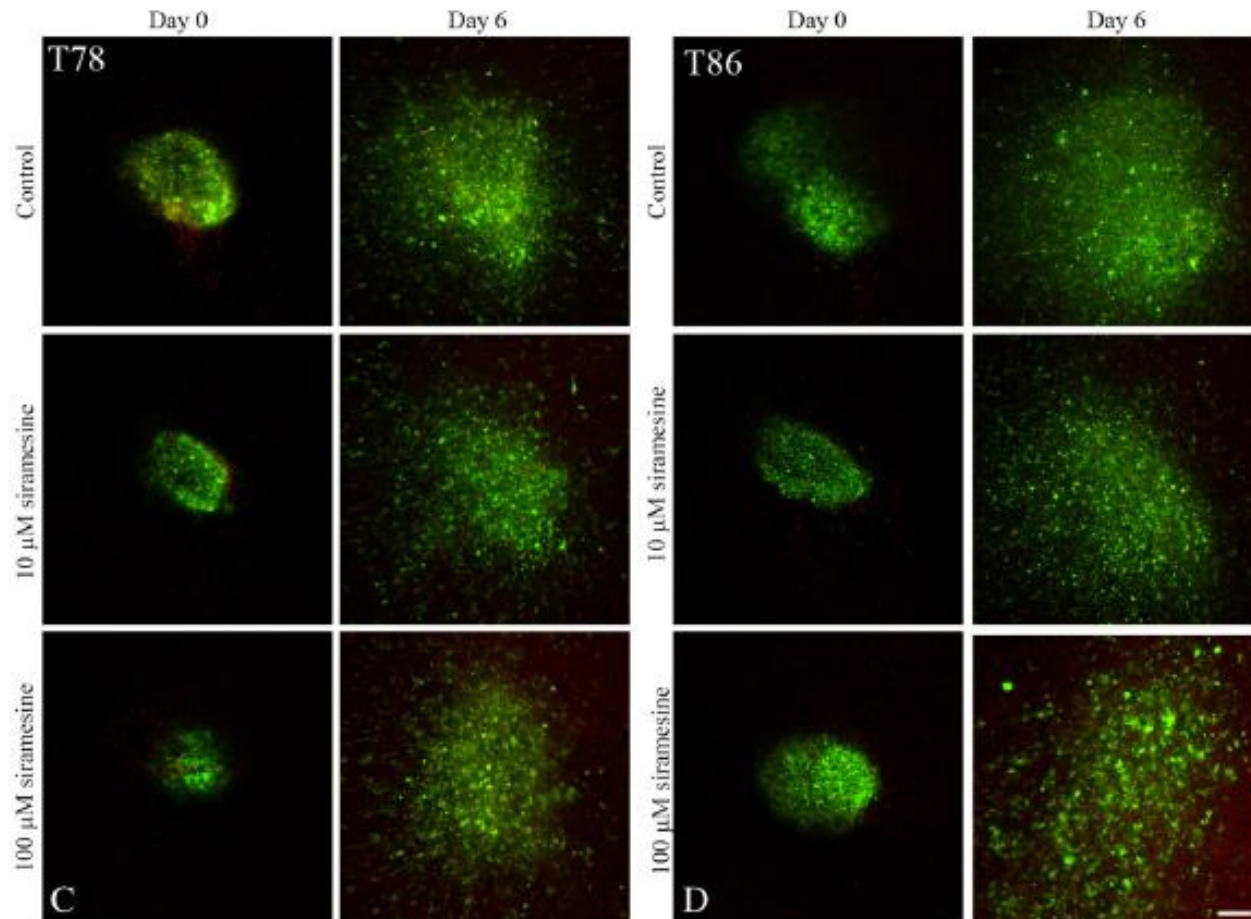


Day 0

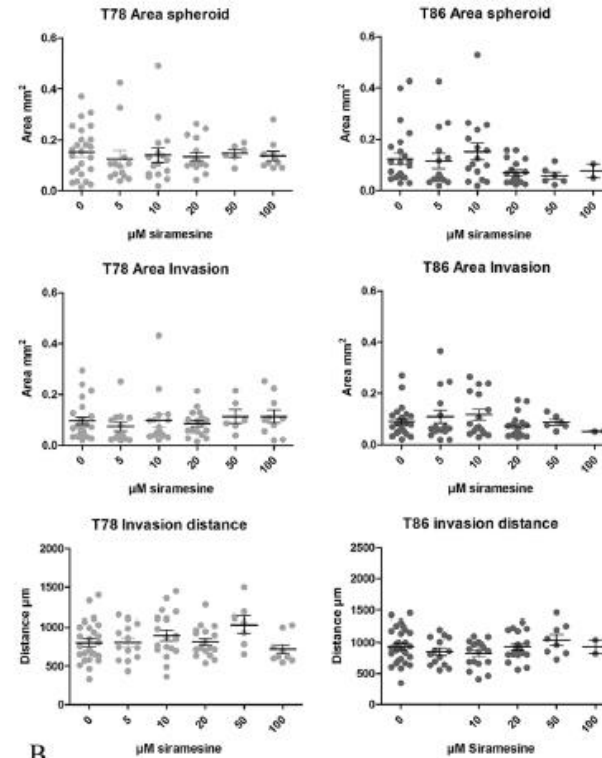
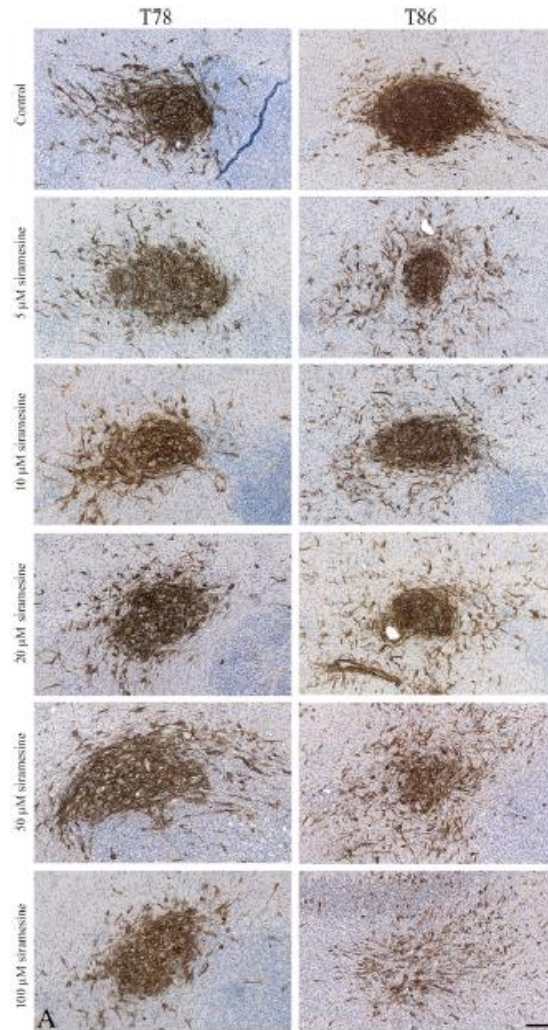


Day 14

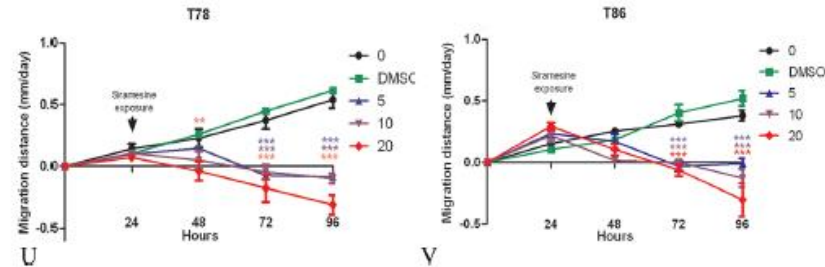
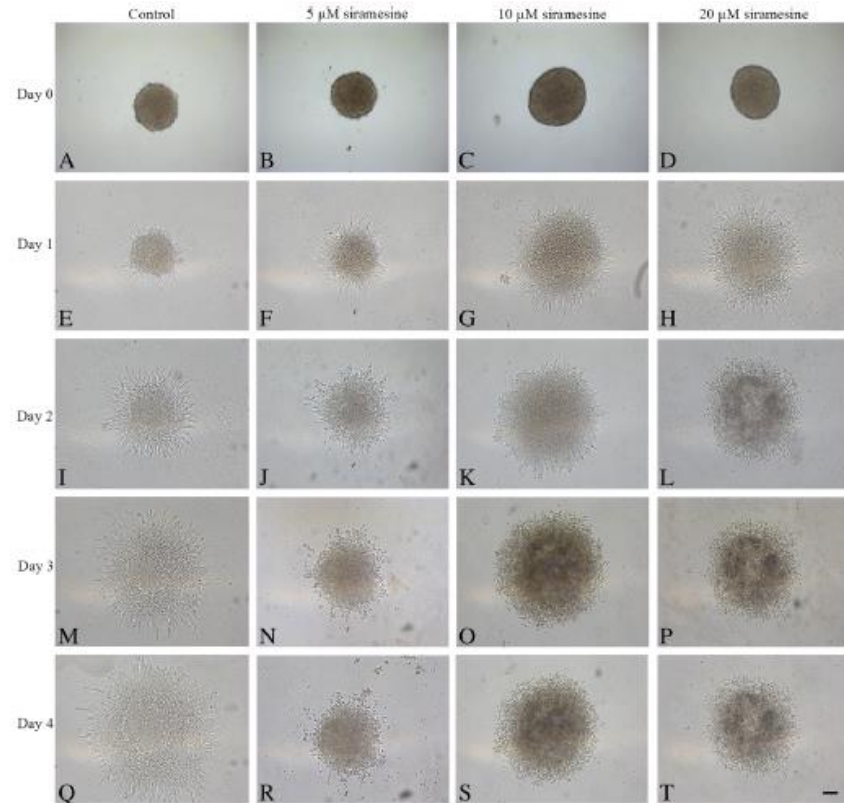
No effect on migrating tumor cells



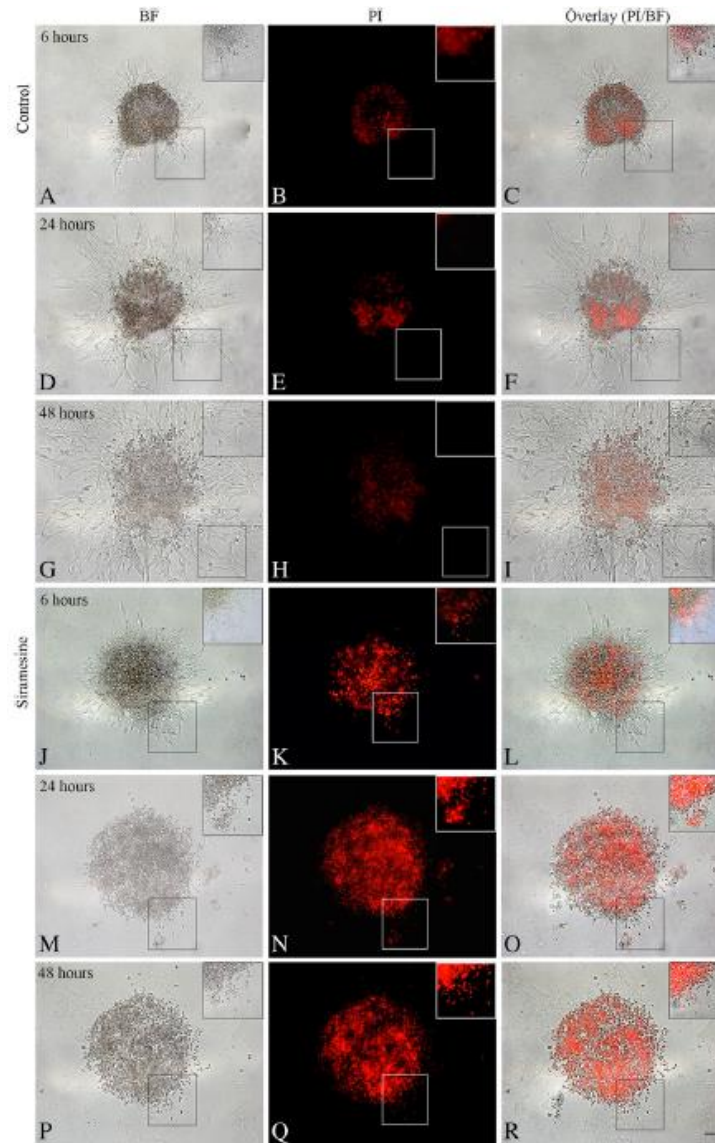
No effect on migrating tumor cells



Effect on migrating tumor cells



Effect on migrating tumor cells



Conclusions

- 3D model
 - Migration and stem cell features
 - *Prediction of drug effect in vivo*
- 2D model
 - Migration and stem cell features
- 3R potential
 - Replacement of animal experiments
 - Reduction of animal experiments

3R potential

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Funding



Denmarks 3R-Center

OUH
Odense
Universitetshospital

