



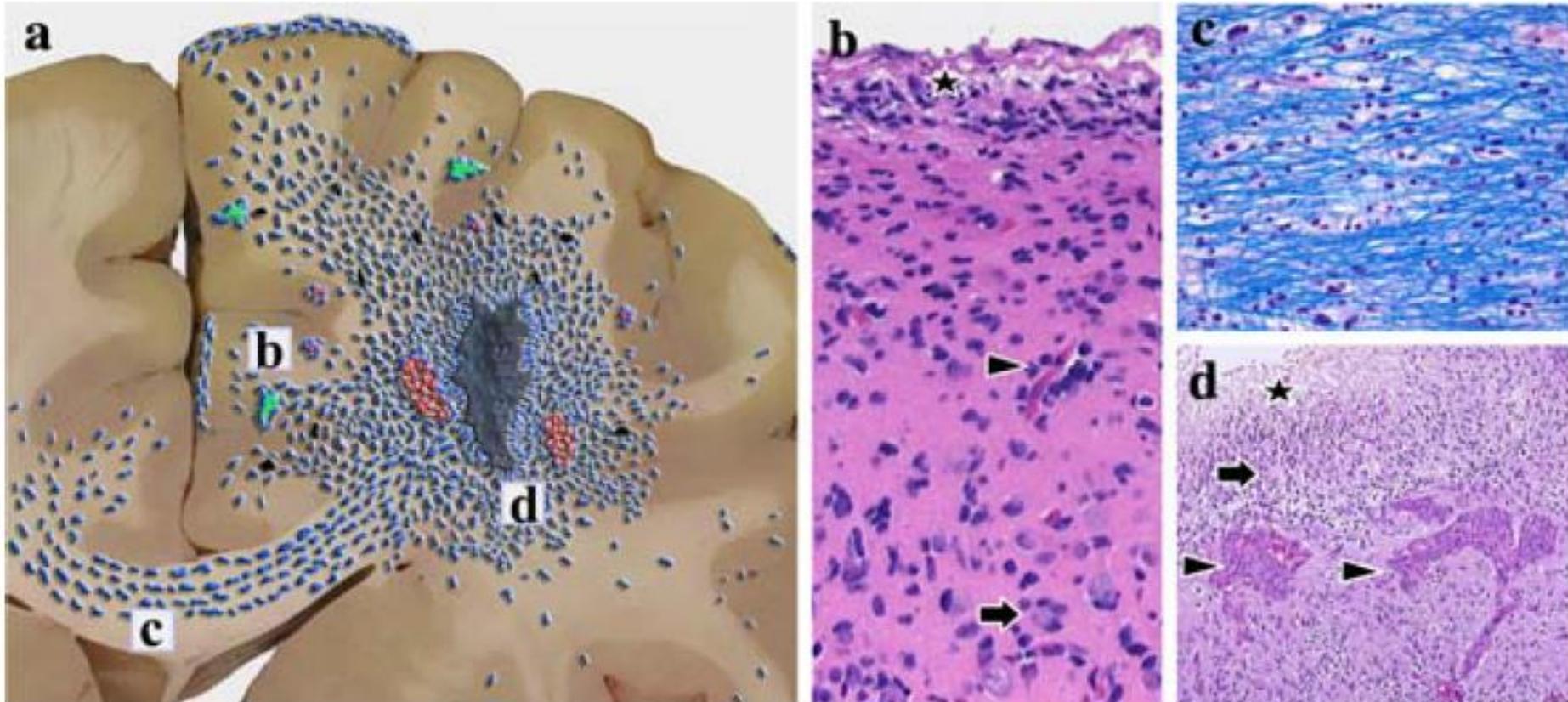
# Towards better brain cancer treatment with novel in vitro models and fewer animal experiments

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Department of Clinical Research, University of Southern Denmark

# Survival rates of brain cancer patients

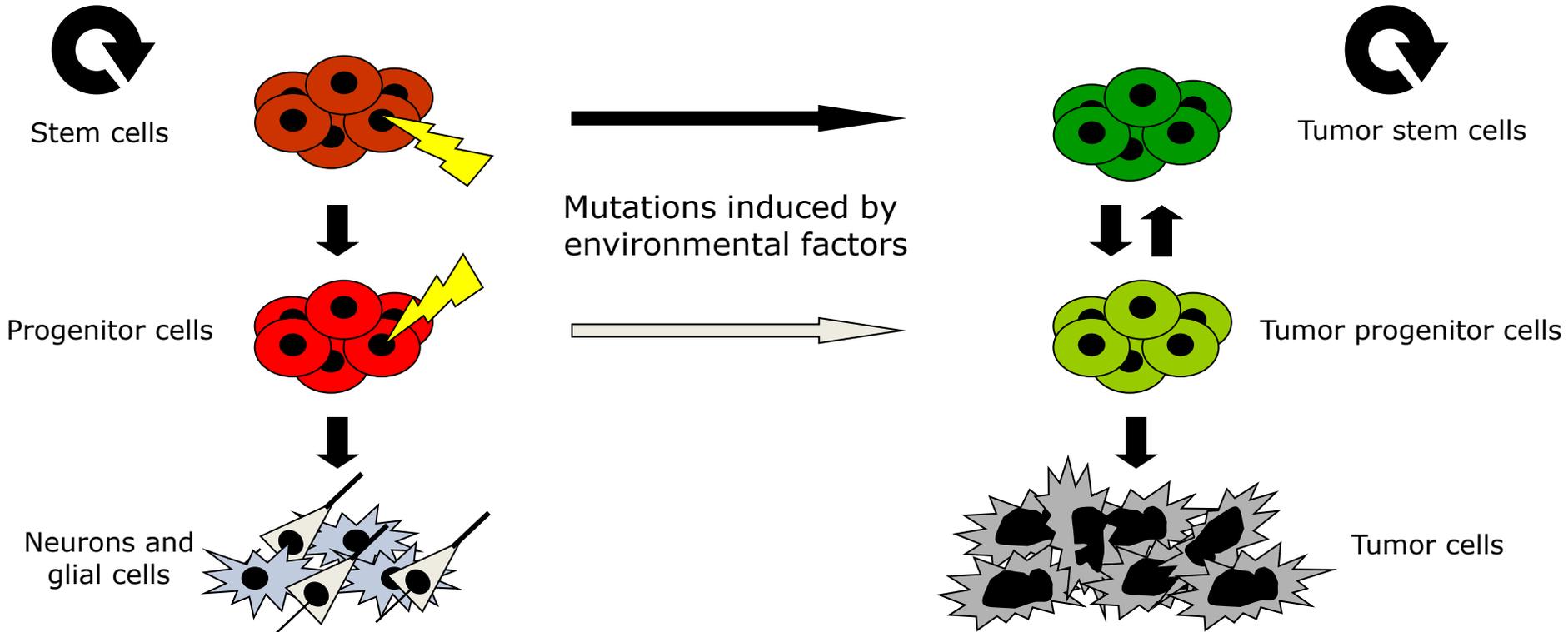


# Migrating tumor cells versus surgery



Claes A et al, Acta Neuropathol (2007)

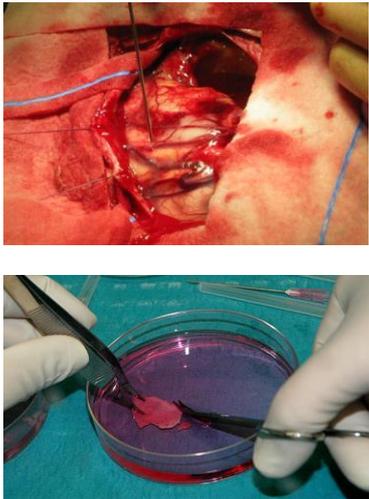
# Tumor stem cell paradigm



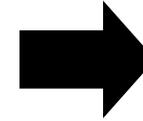
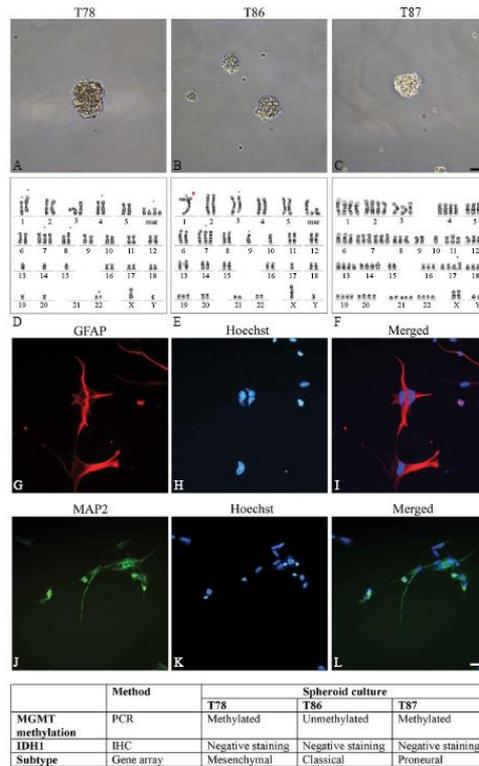
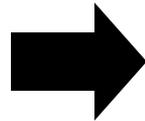
- Stem cells and tumor stem cells:
  - Self-renewal (asymmetric cell division)
  - Indefinite proliferation potential
  - Differentiation

# Experimental "patient-like" models

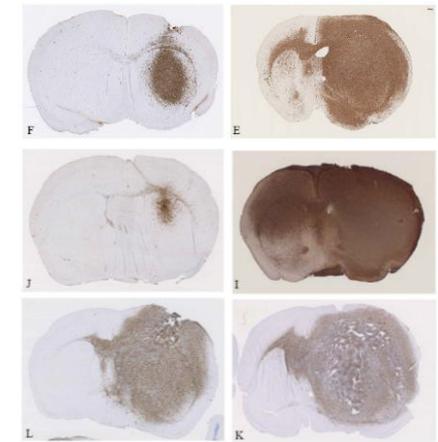
Biopsy



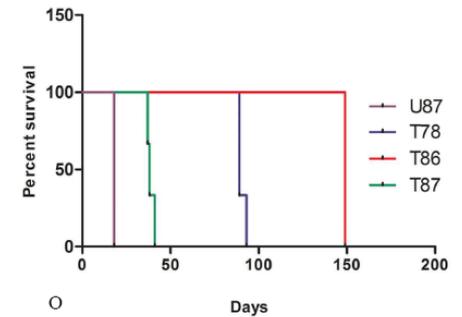
Cultures/Cell lines



In vivo model



Survival mice

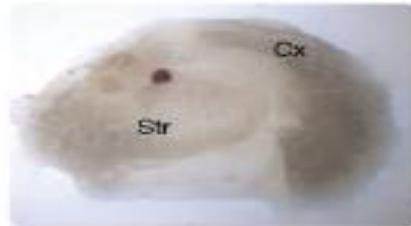
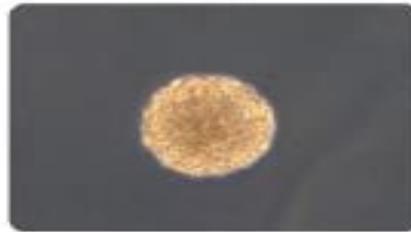


# 3R potential

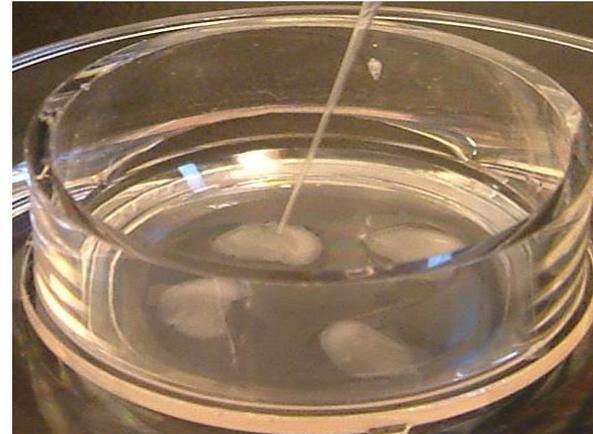
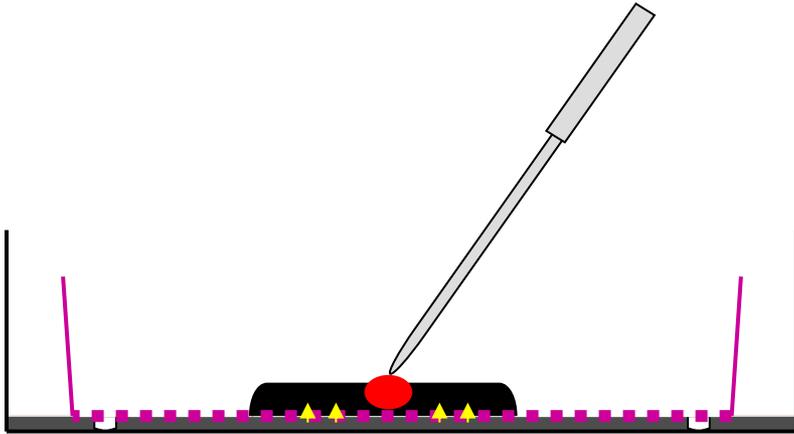
- A Pub Med search (“mice and glioma and year”) identified:
  - 263 brain cancer studies in 2004
  - 856 brain cancer studies in 2014
  - More than 3-fold increase over 10 years
- 50.000 mice are supposed to be used for brain cancer studies in 2015
- Orthotopic models are app. being used in 50% of these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

# 3D in vitro model

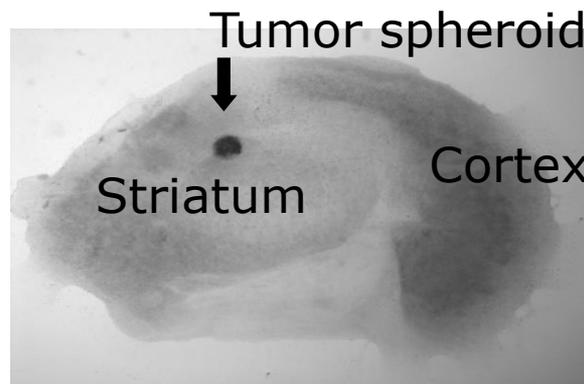
-In stem cell medium



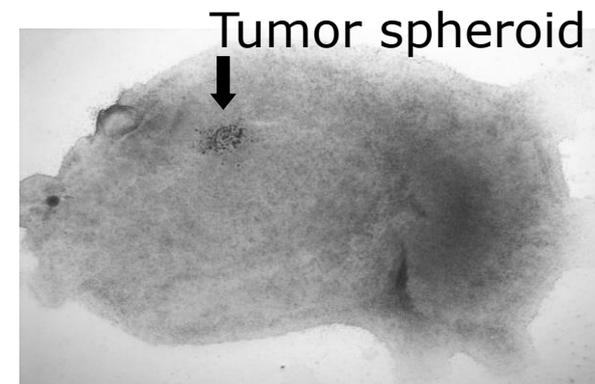
# Implantation of tumor cells



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

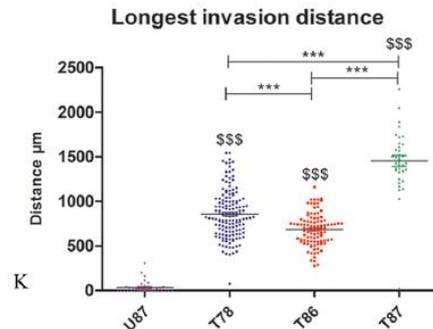
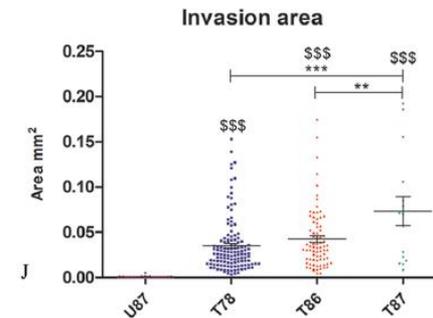
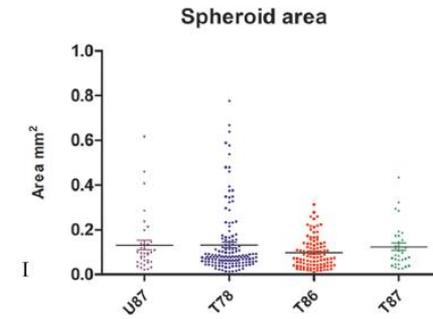
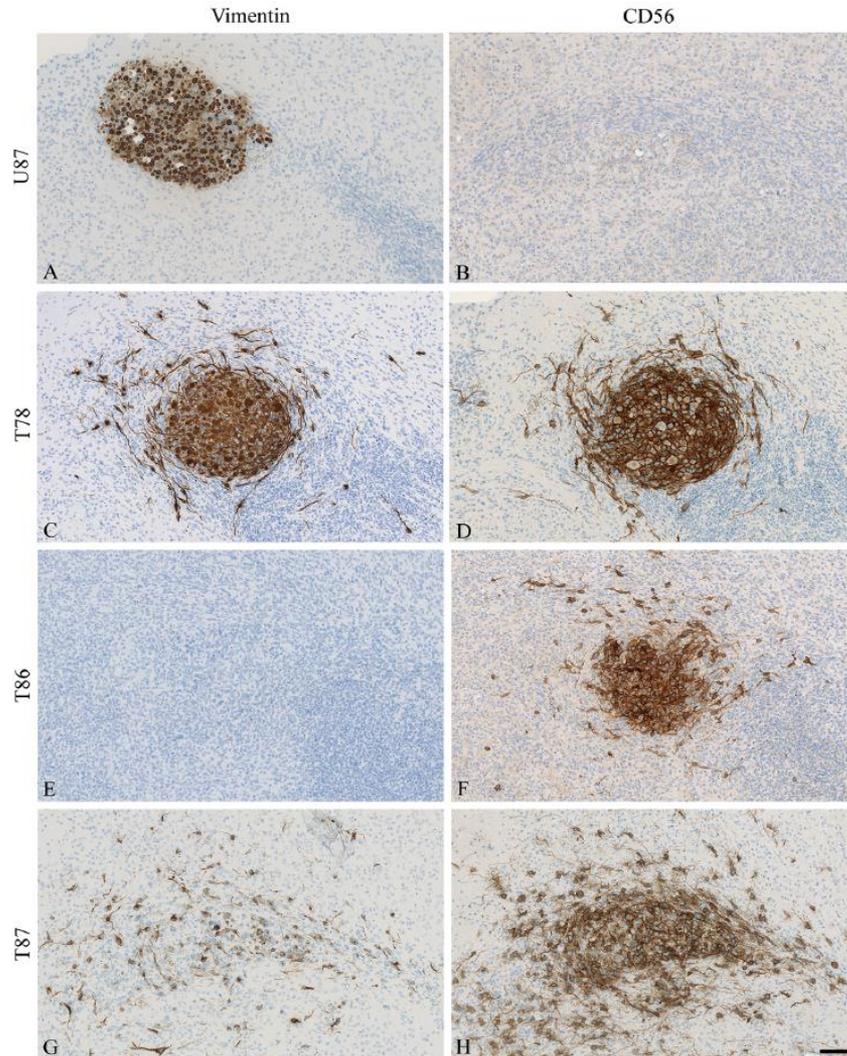


Day 0



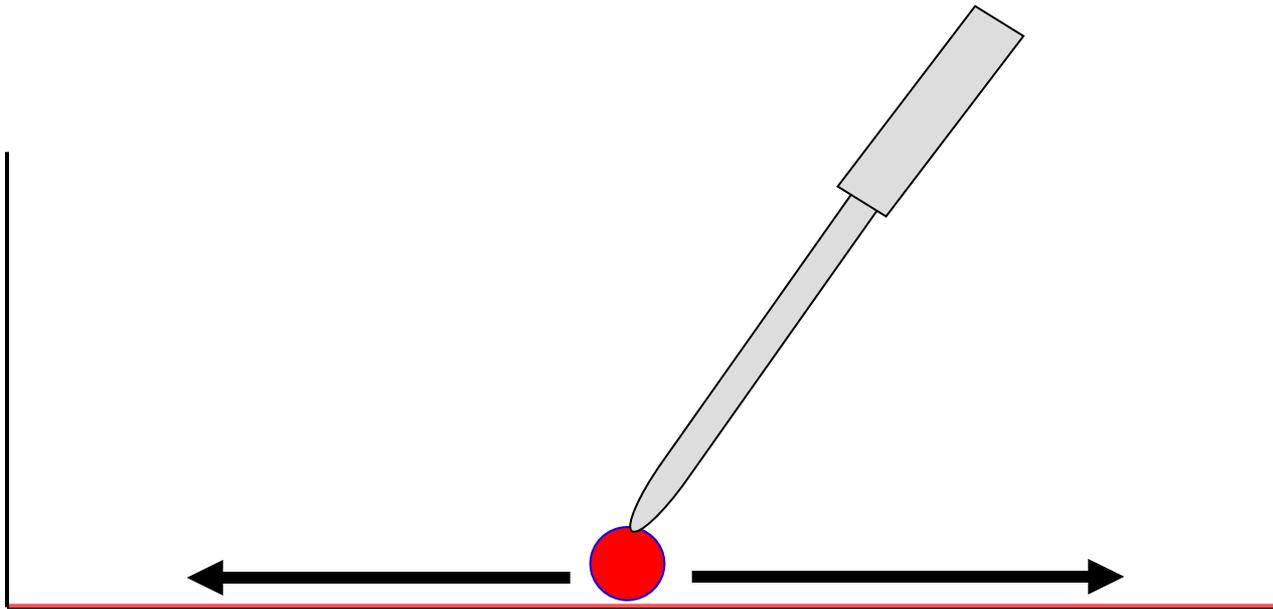
Day 14

# 3D in vitro model

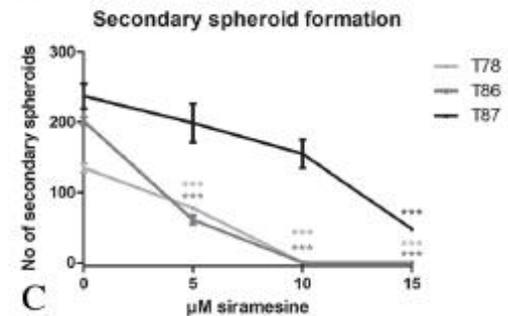
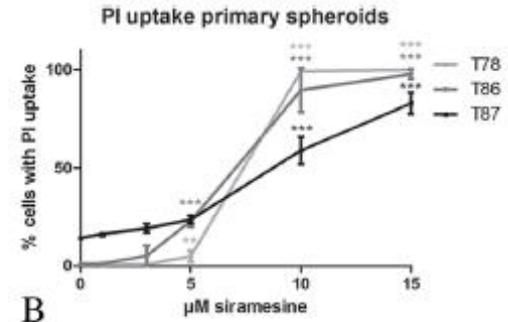
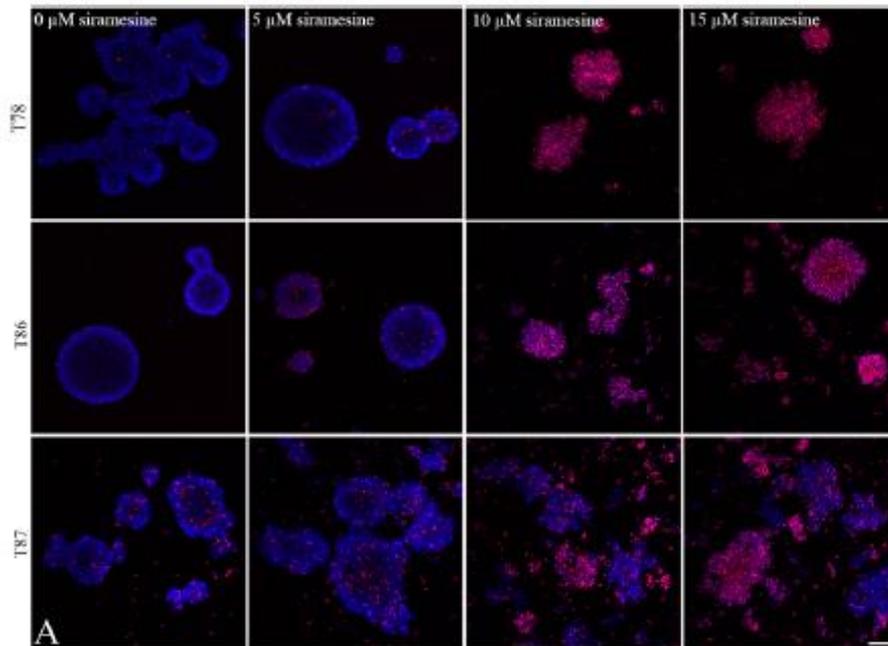


# 2D model

## Tumor cell migration on a flat surface -in stem cell medium

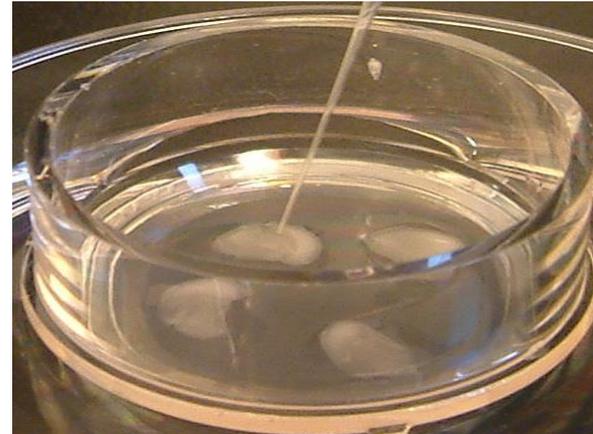
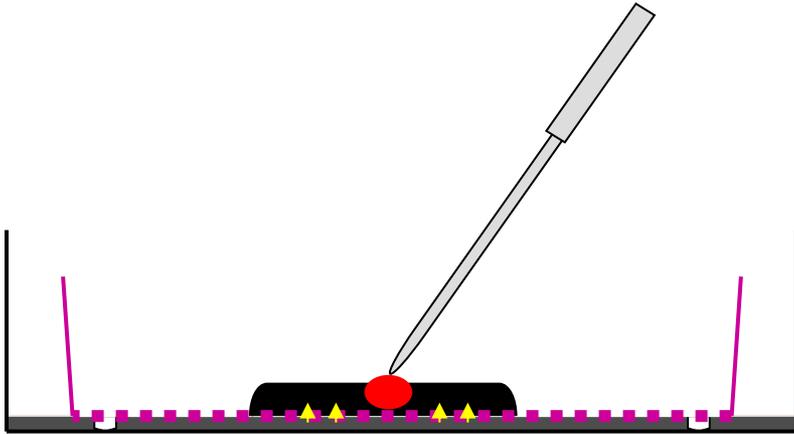


# Effect on patient-derived spheroids

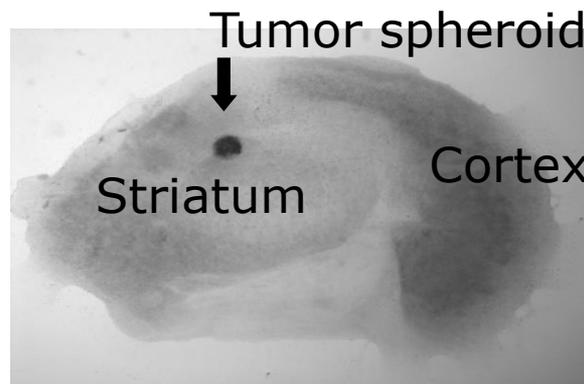


**No effect in vivo**

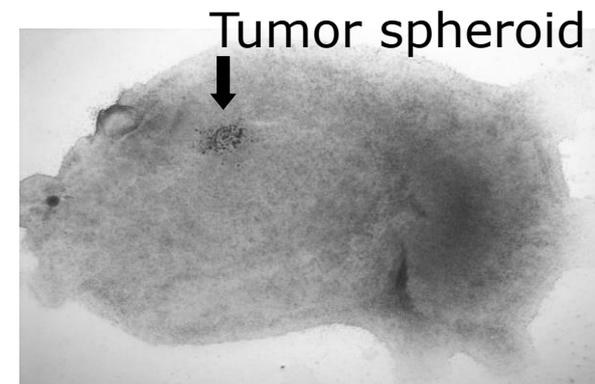
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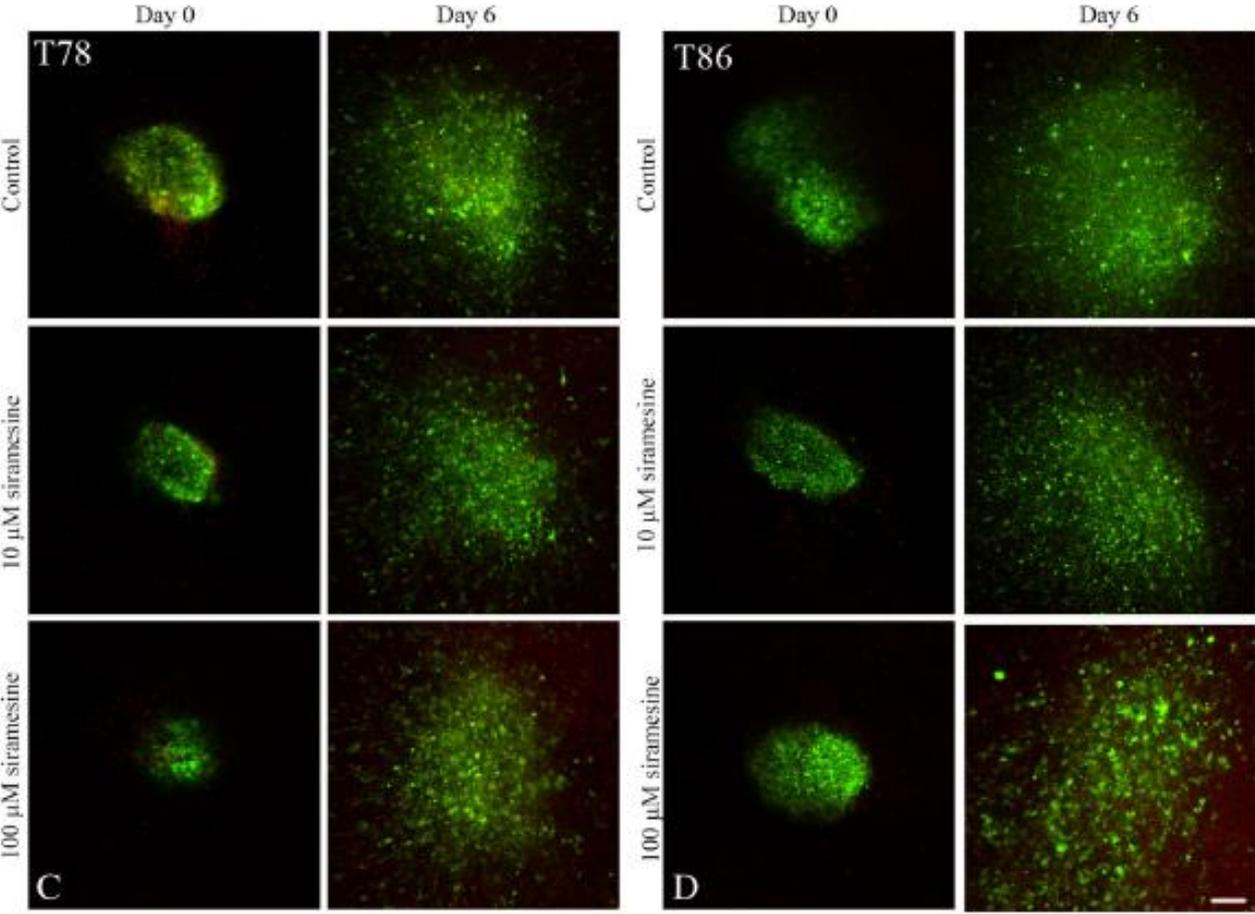


Day 0

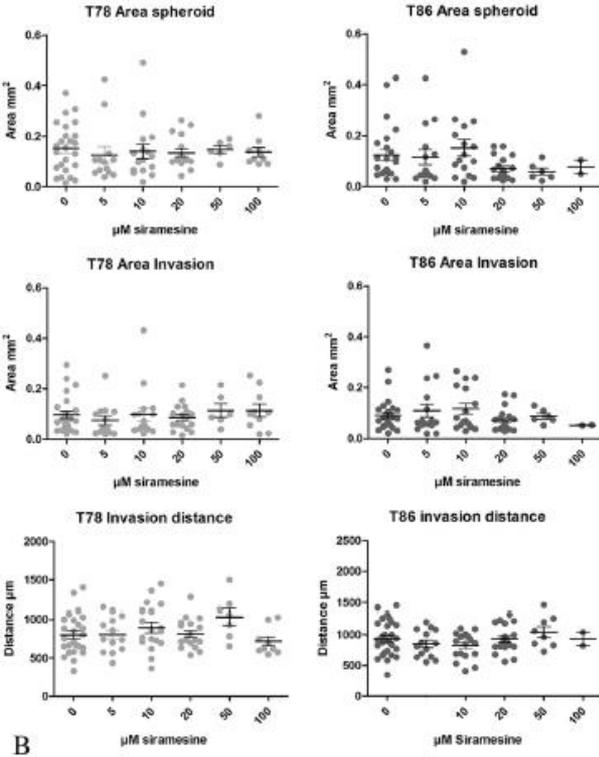
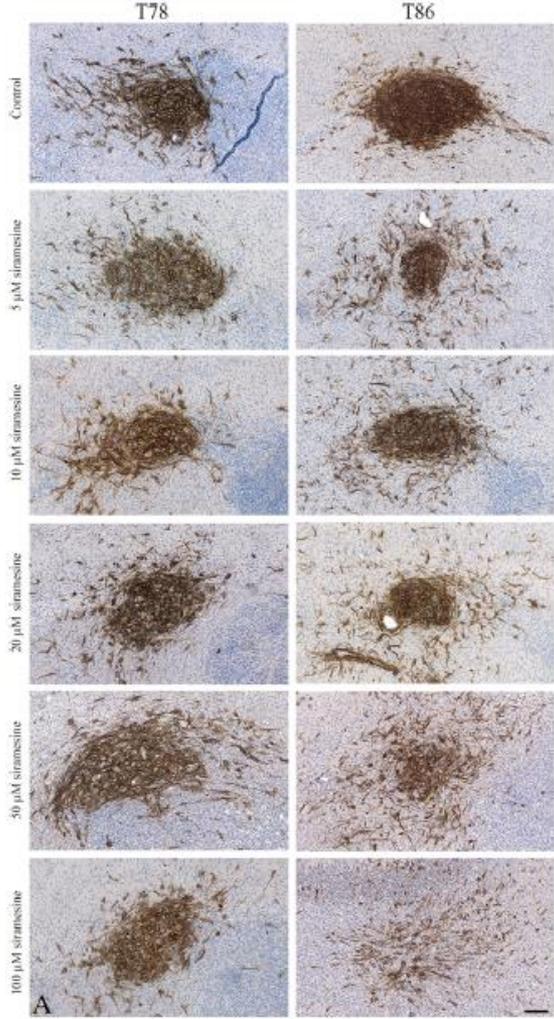


Day 14

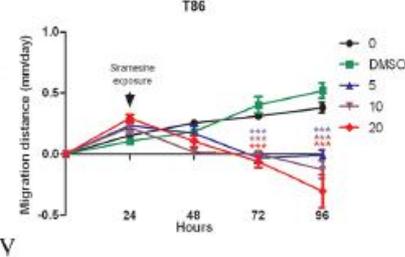
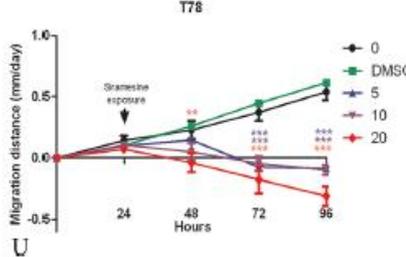
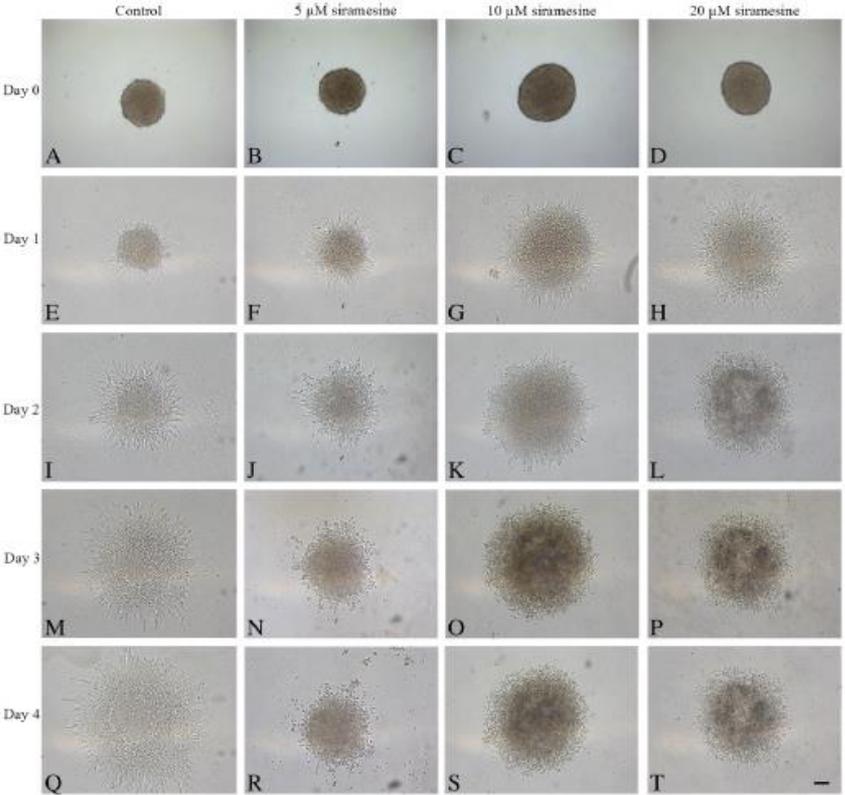
# No effect on migrating tumor cells



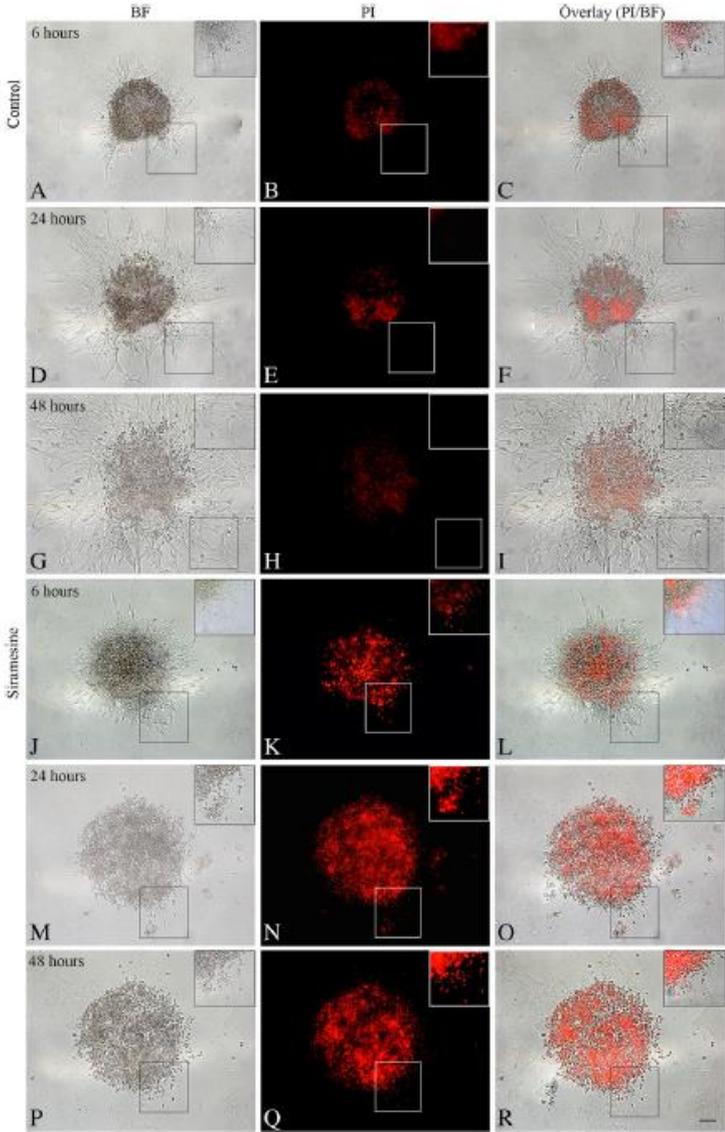
# No effect on migrating tumor cells



# 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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  - 263 brain cancer studies in 2004
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- 50.000 mice are supposed to be used for brain cancer studies in 2015
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# Funding



Denmarks 3R-Center

OUH  
Odense  
Universitetshospital

