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

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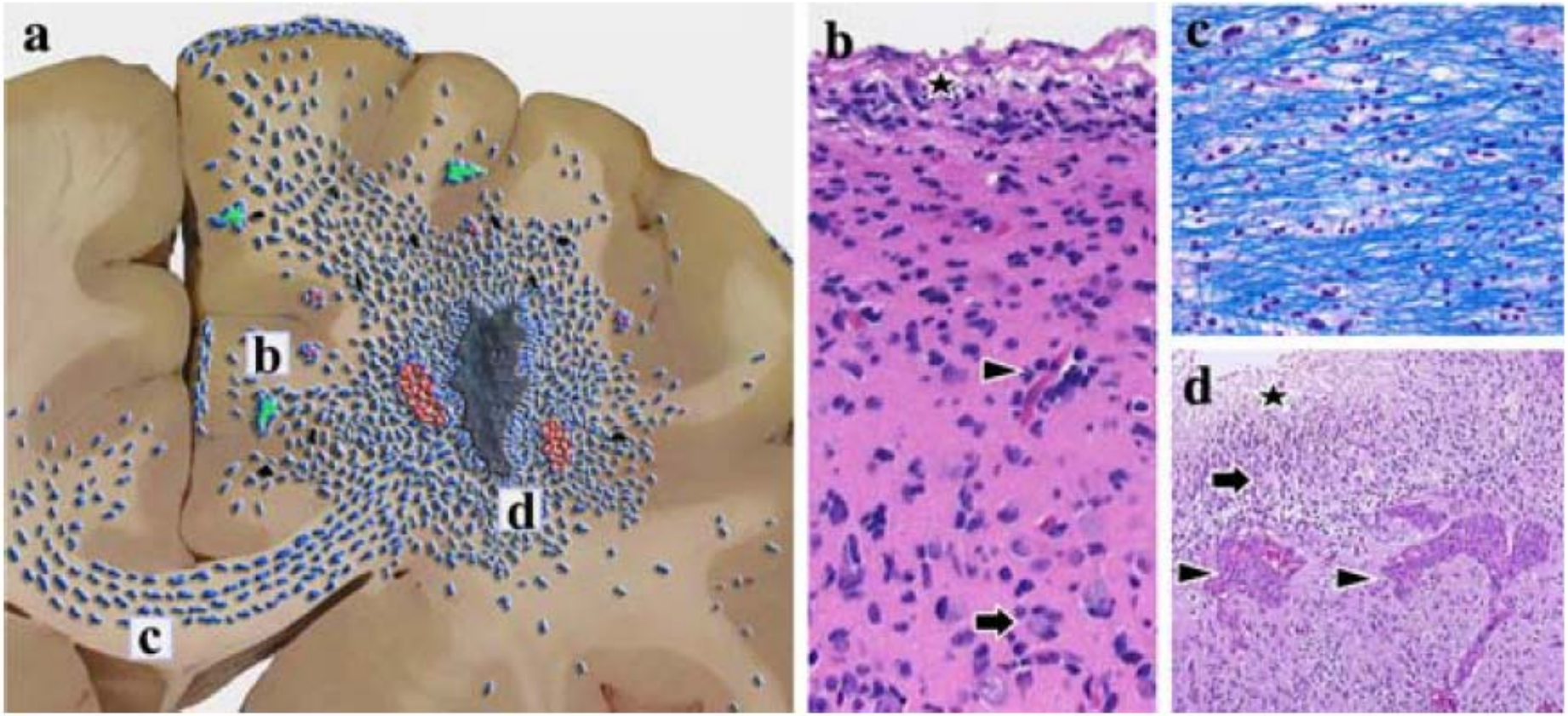
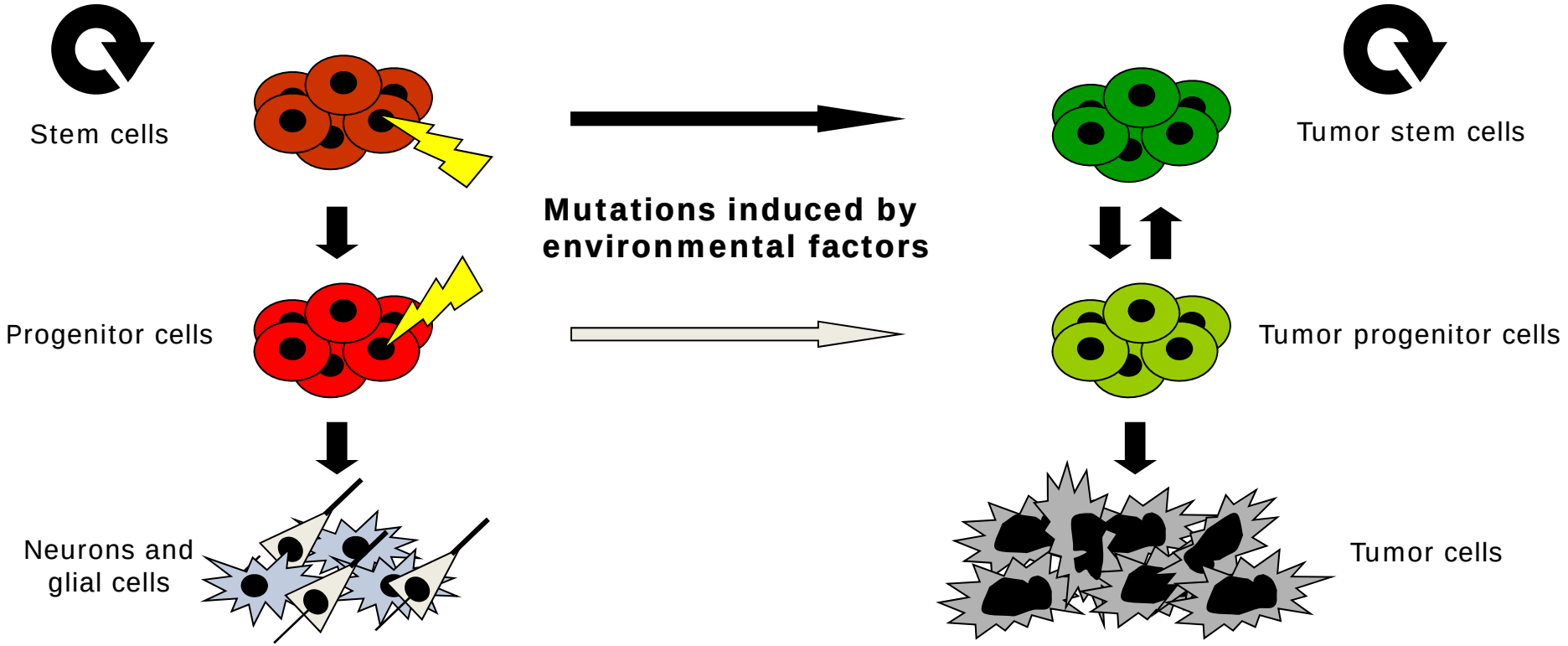
Survival rates of brain cancer patients

Migrating tumor cells versus surgery



Claes A et al, Acta Neuropathol (2007)

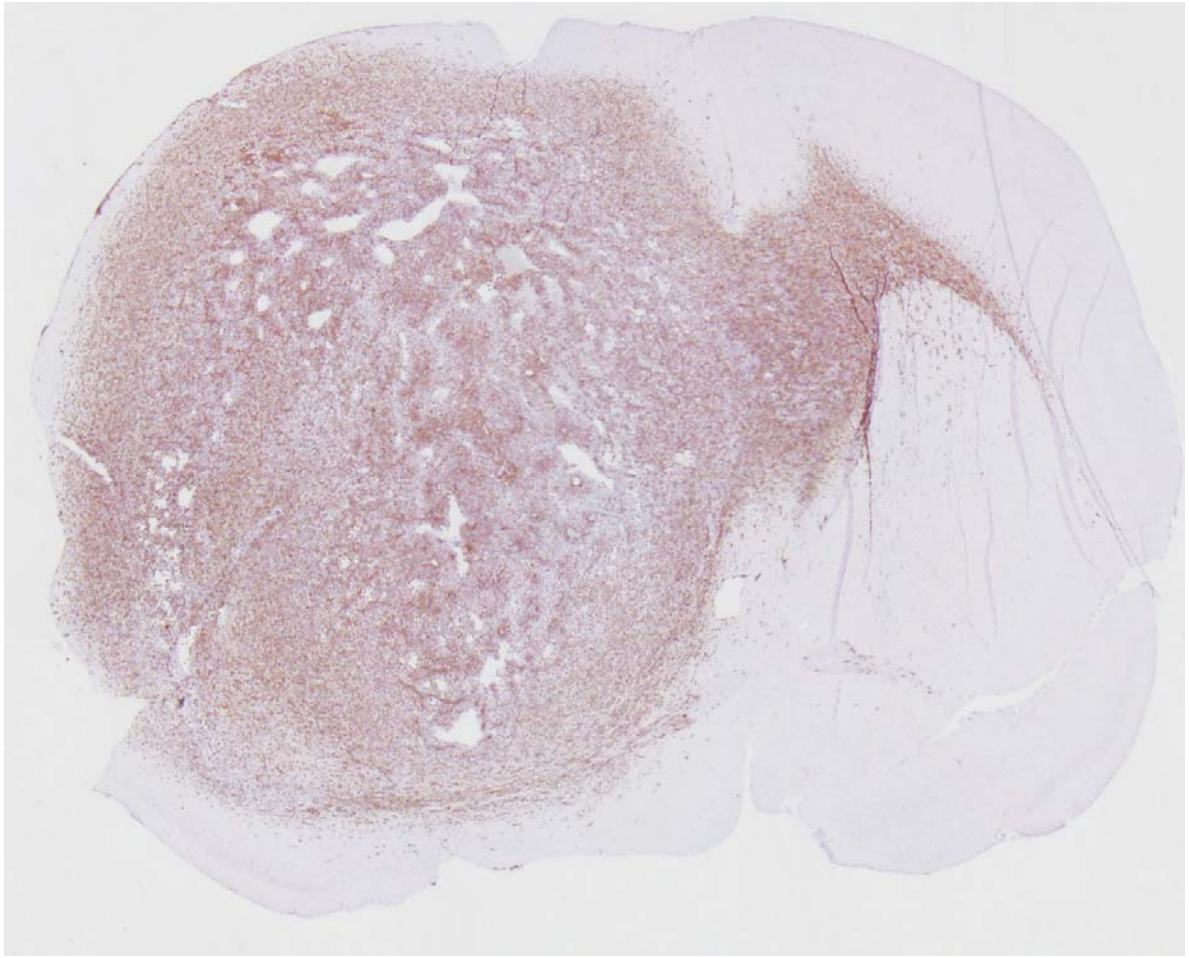
Tumor stem cell paradigm



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

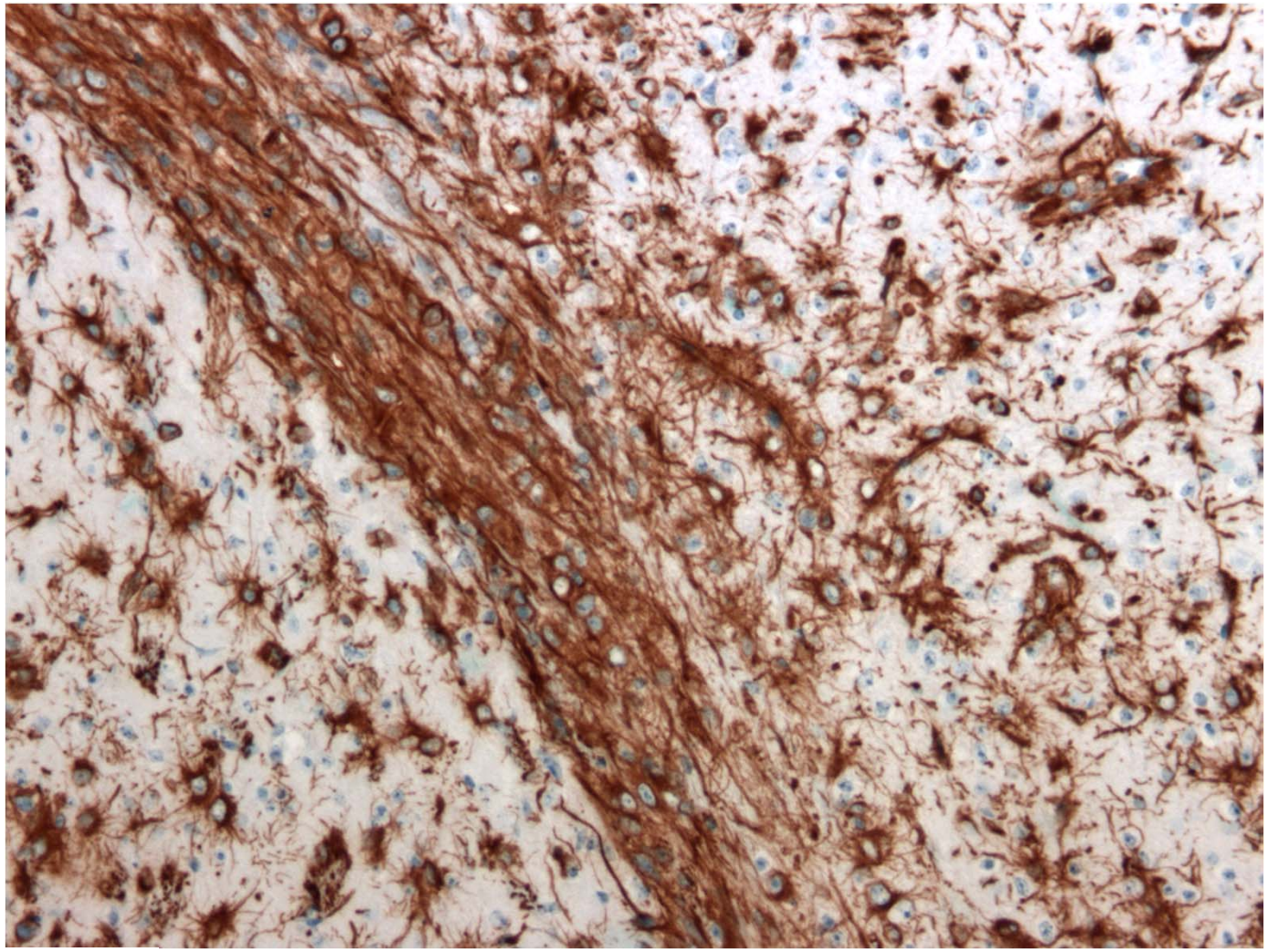
Tumor migration in mice – after 3 months

anti-human vimentin IHC



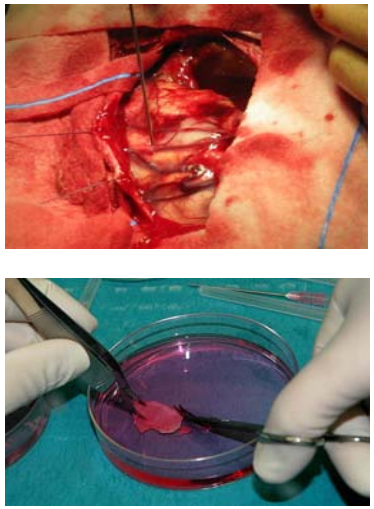
Tumor migration

anti-human vimentin IHC

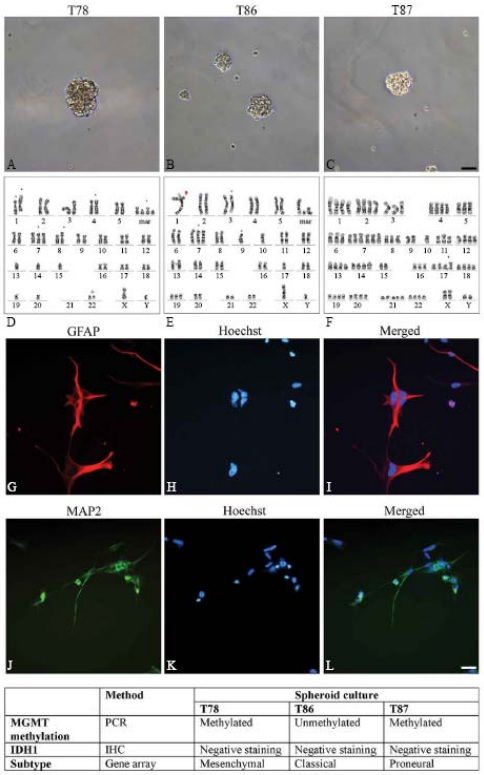


Experimental ”patient-like” models

Biopsy

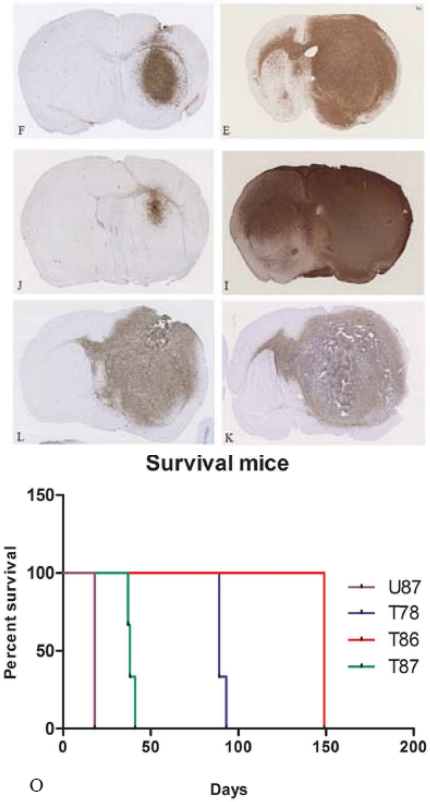


Cultures/Cell lines



	Method	Spheroid culture		
		T78	T86	T87
MGMT methylation	PCR	Methylated	Unmethylated	Methylated
IDH1	IHC	Negative staining	Negative staining	Negative staining
Subtype	Gene array	Mesenchymal	Classical	Proneural

In vivo model

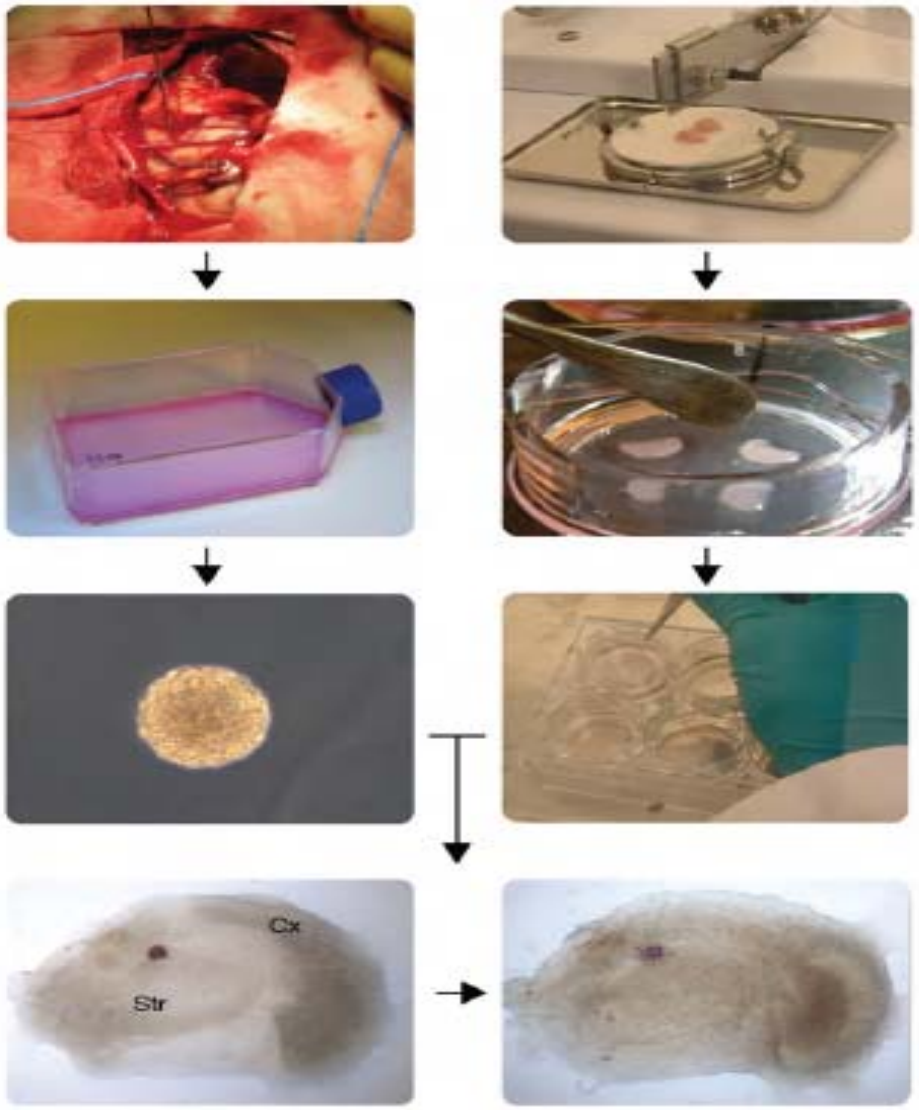


3R potential

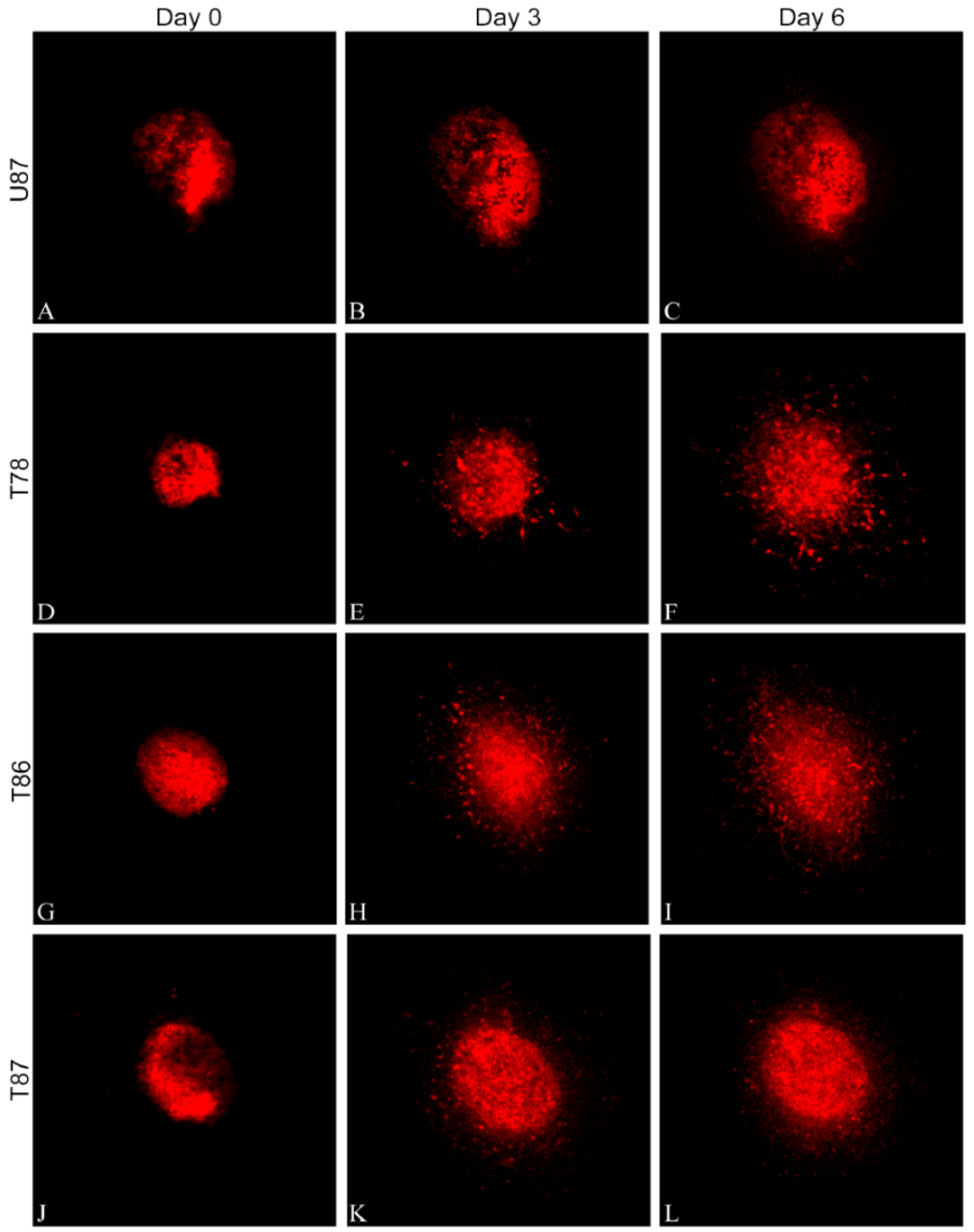
- A Pub Med search ("mice and glioma and year") identified:
  - 263 brain cancer studies in 2004
  - 856 brain cancer studies in 2014
  - More than 3-fold increase over10 years
- 50.000 mice are supposed to be used for brain cancer studies in 2015
- Orthotopic models are app. being used in 50% of these studies corresponding to 25.000 mice/year

3D
in vitro model

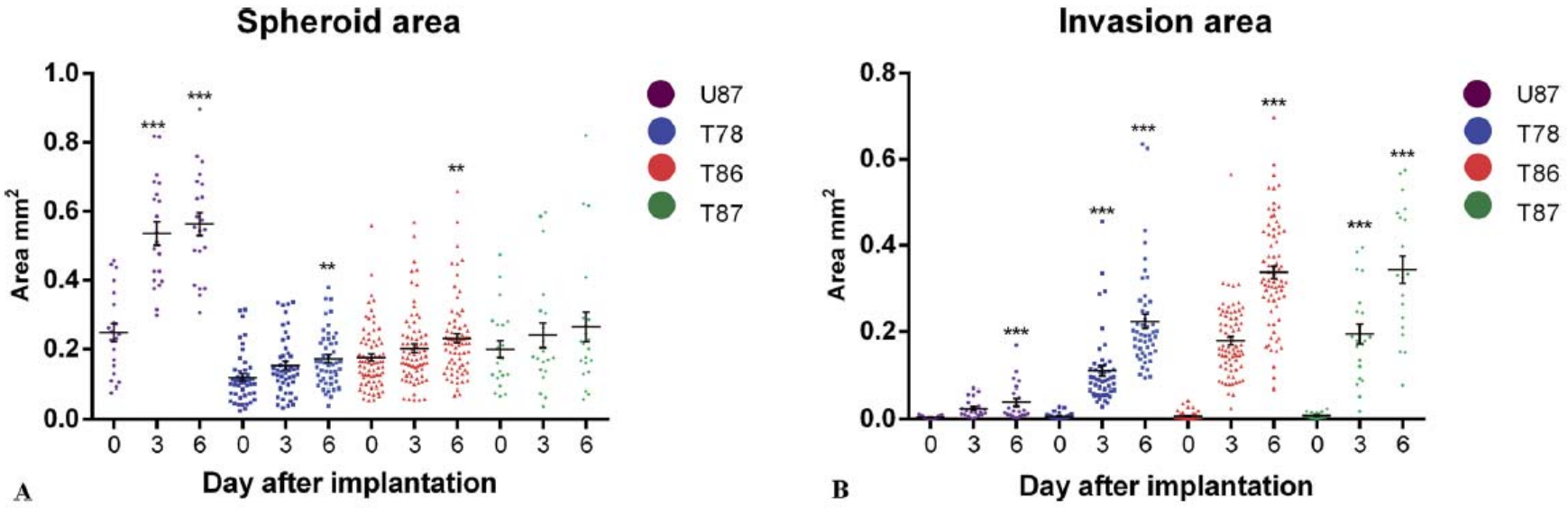
-In stem cell medium



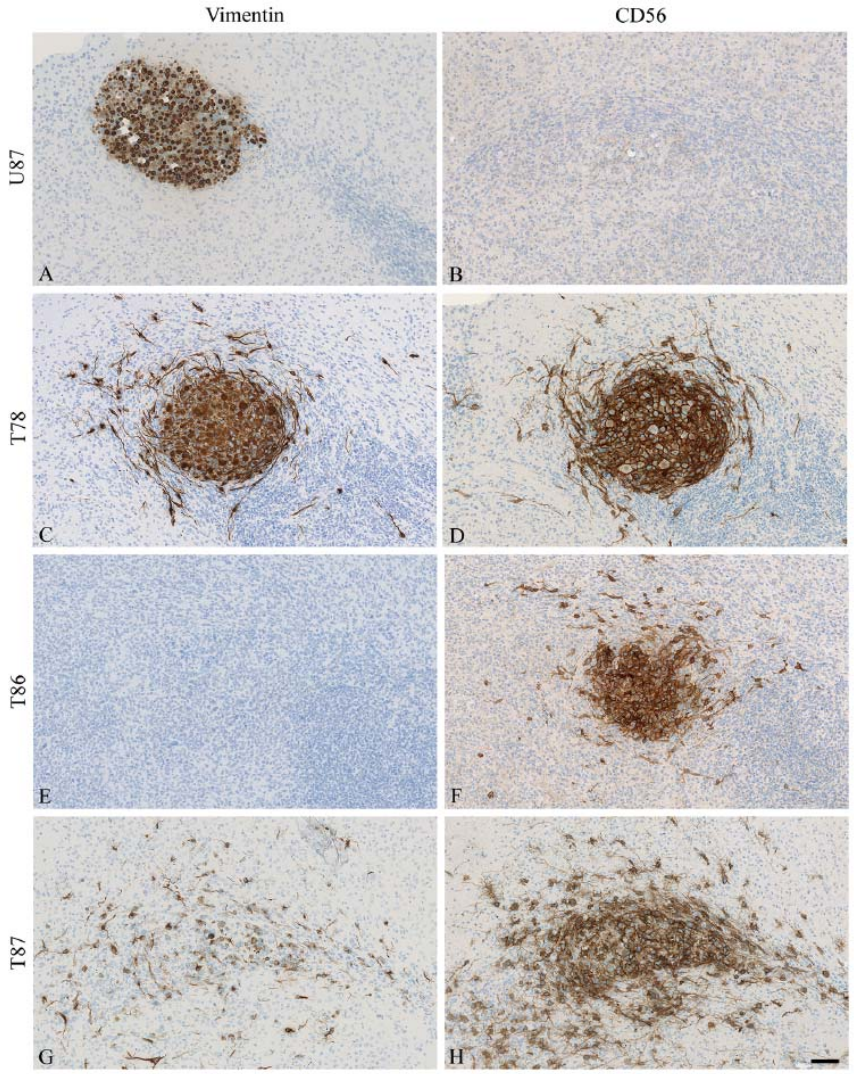
3D
in vitro model

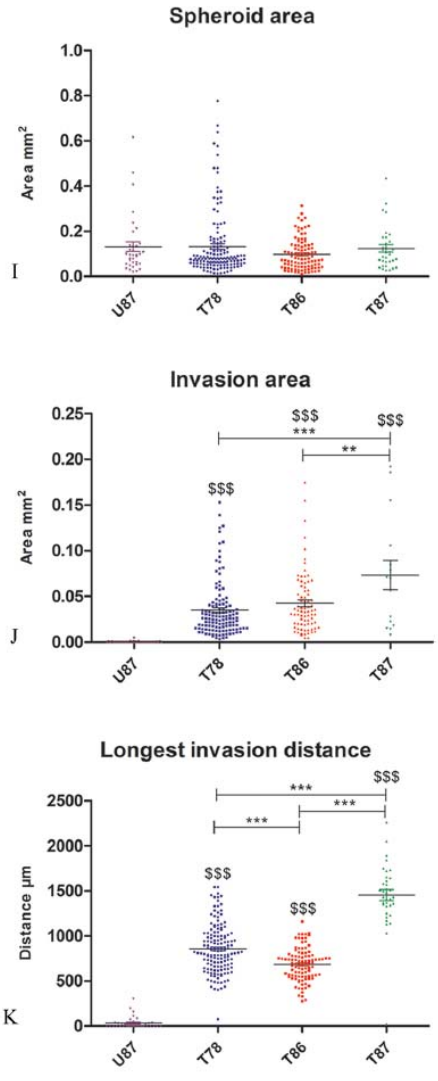


3D in vitro model

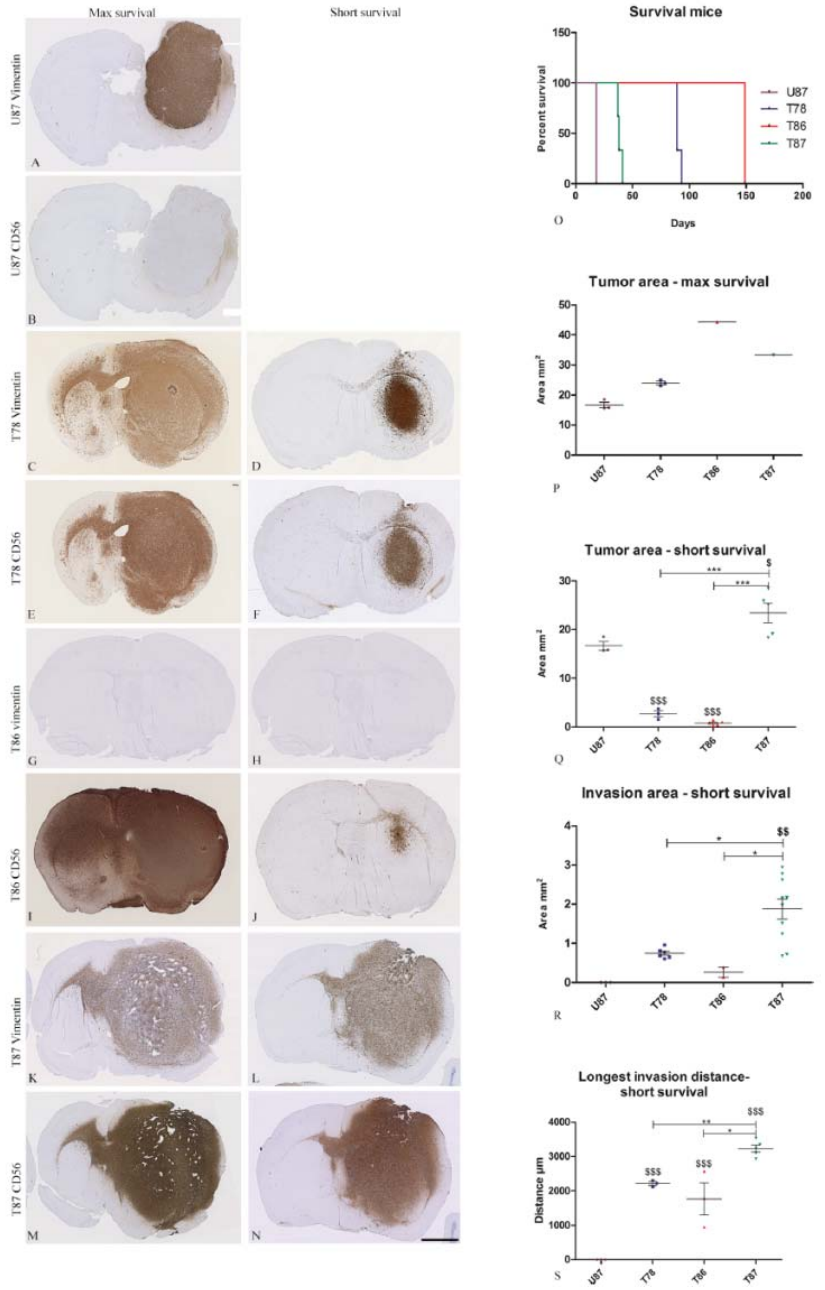


3D in vitro model

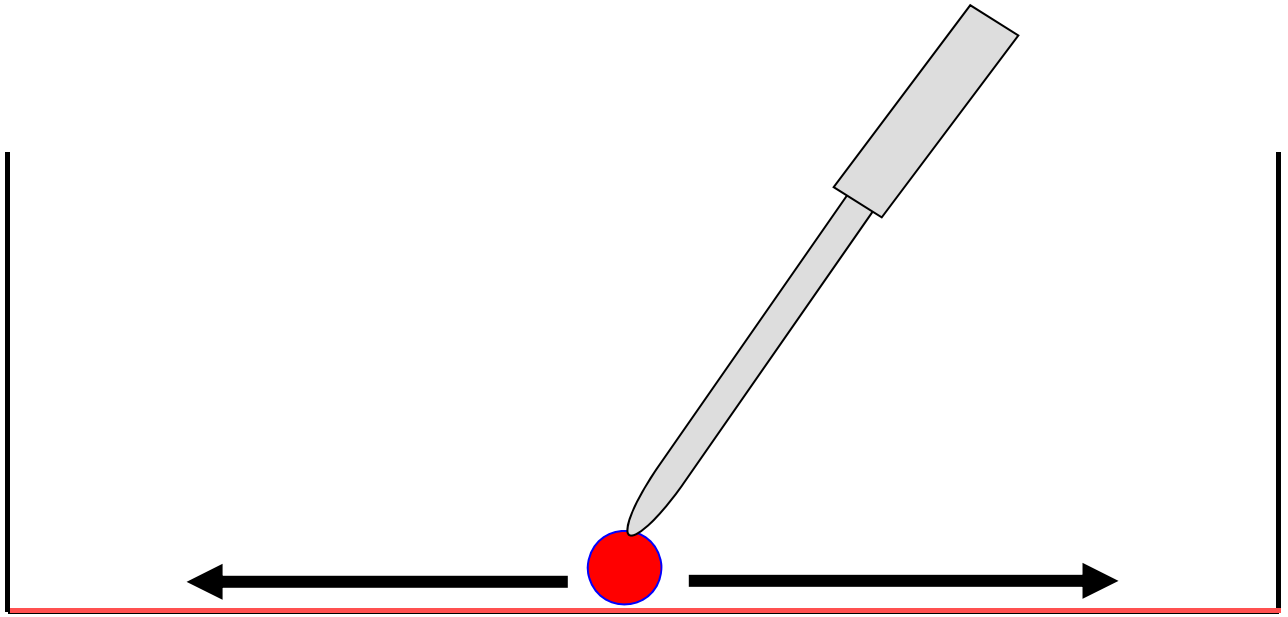


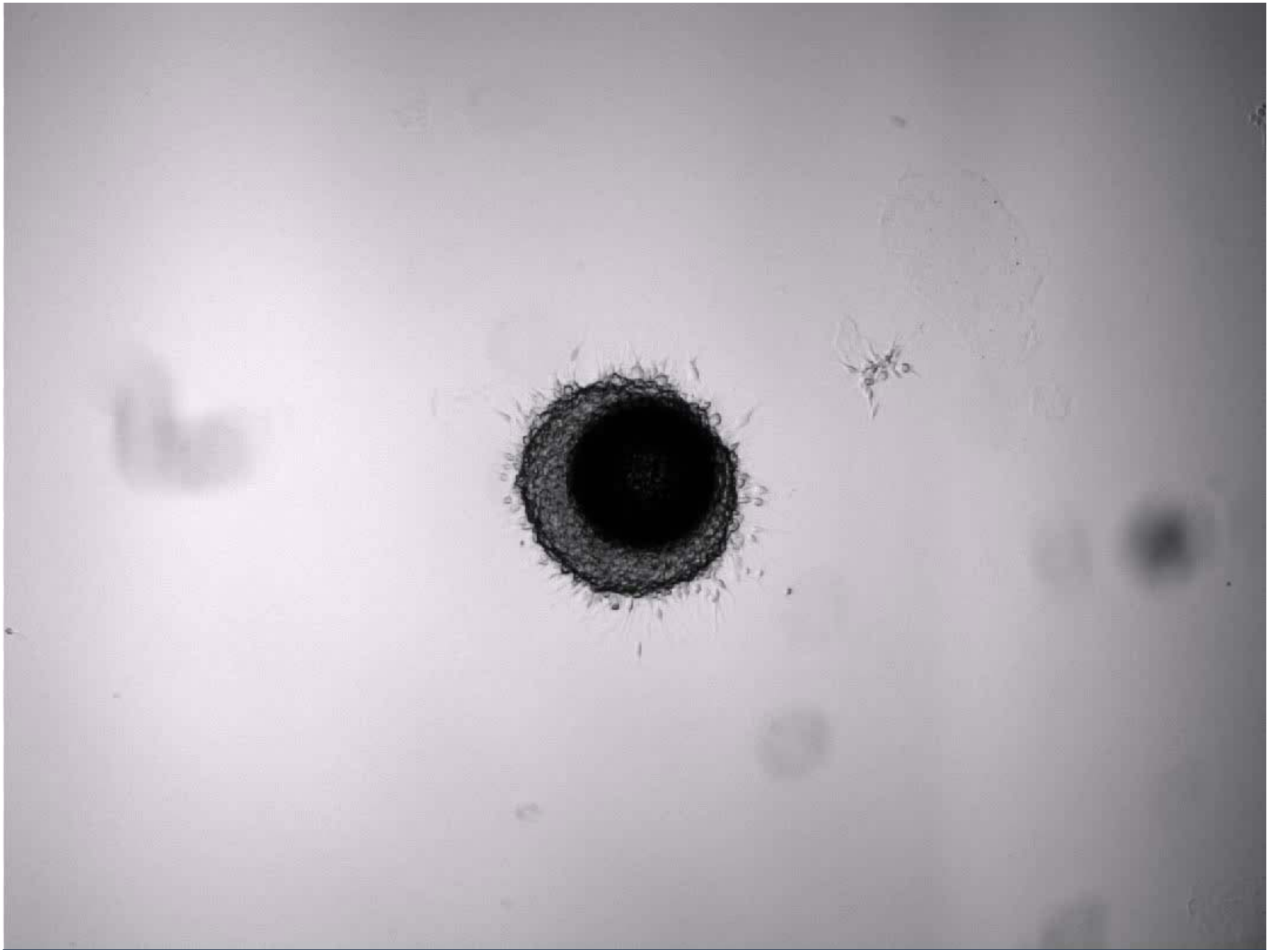


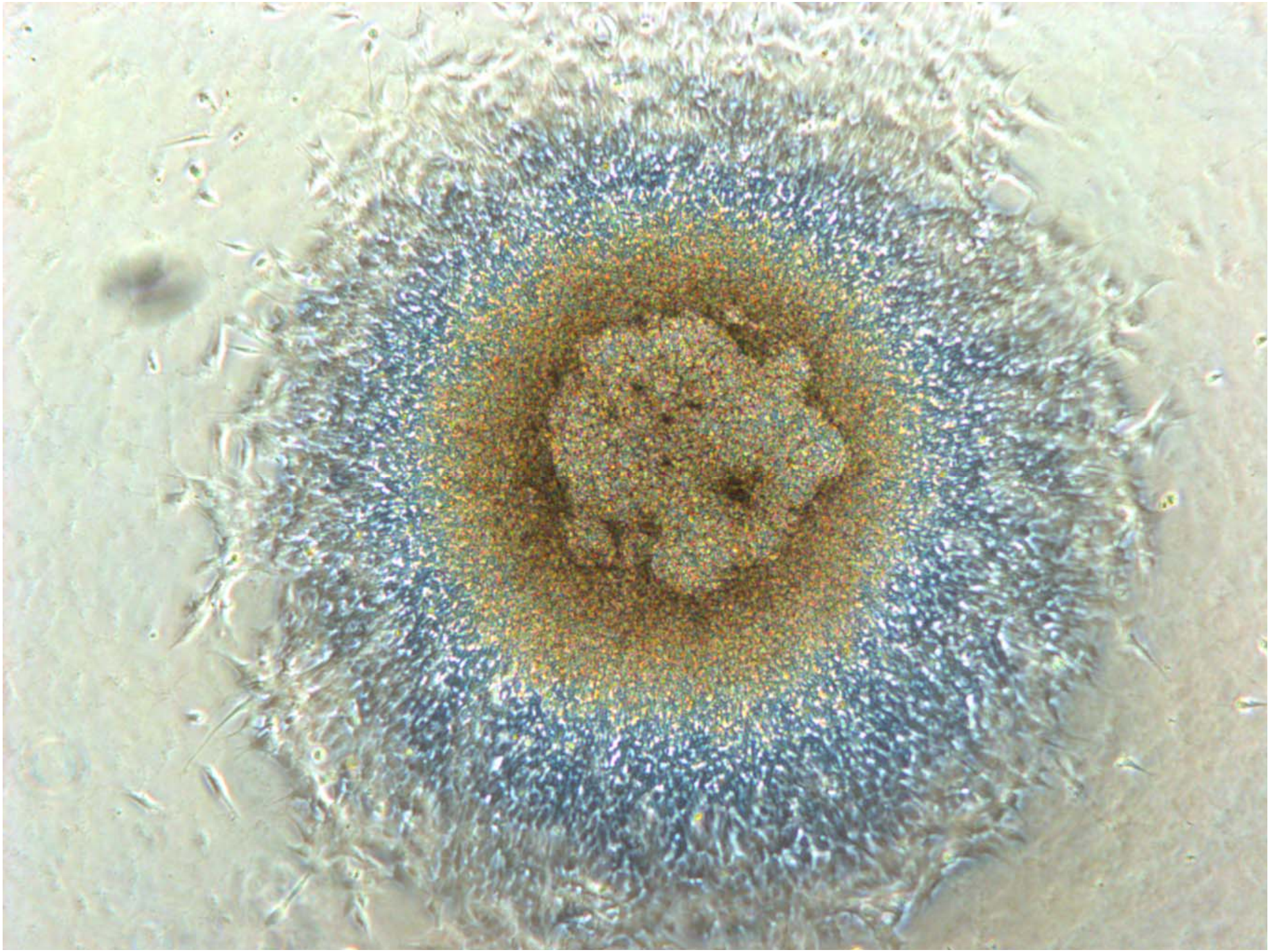
In vivo model



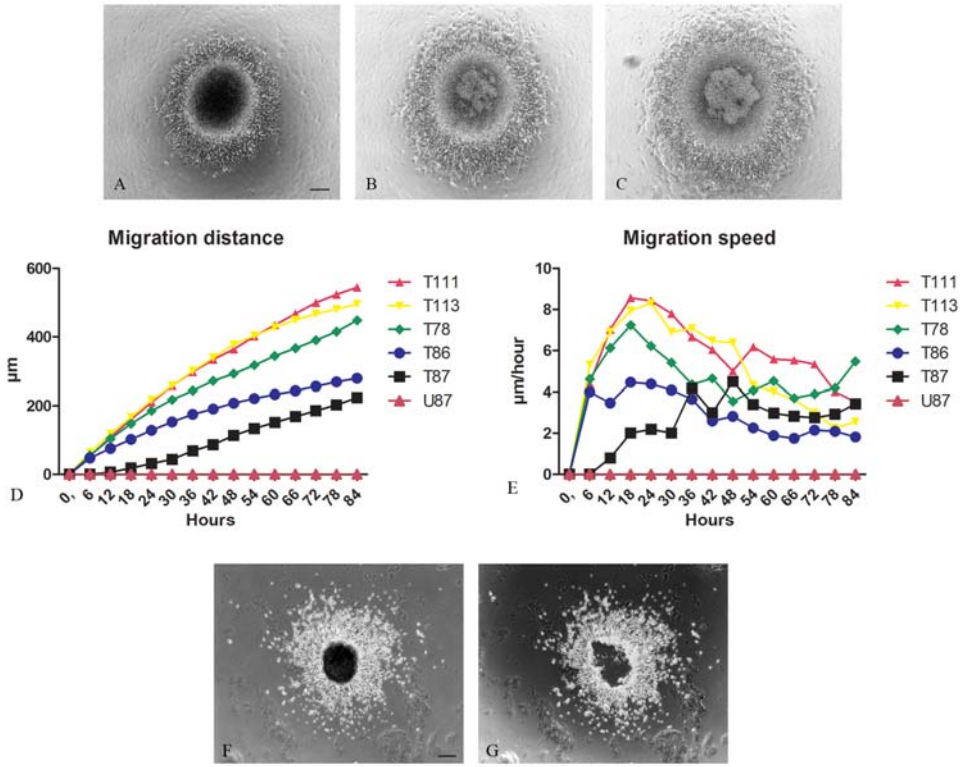
2D model
Tumor cell migration on a flat surface
-in stem cell medium





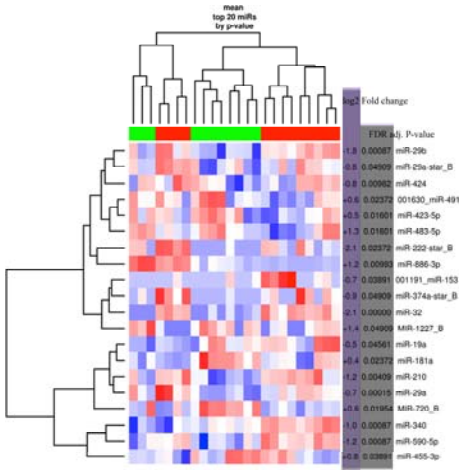


Migration speed

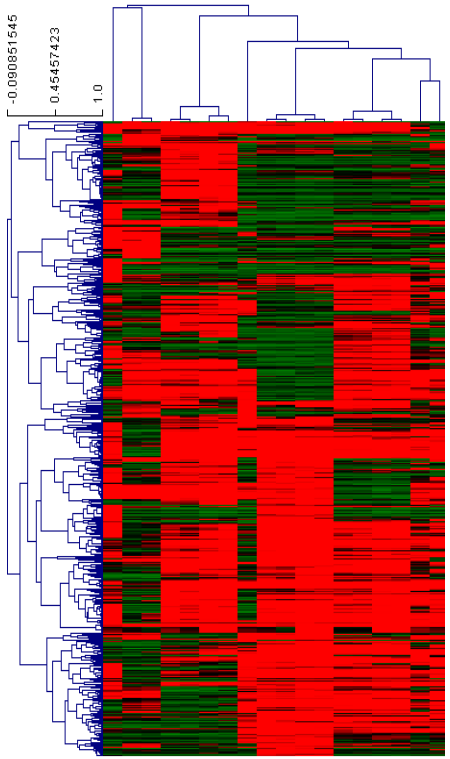


Molecular characterization

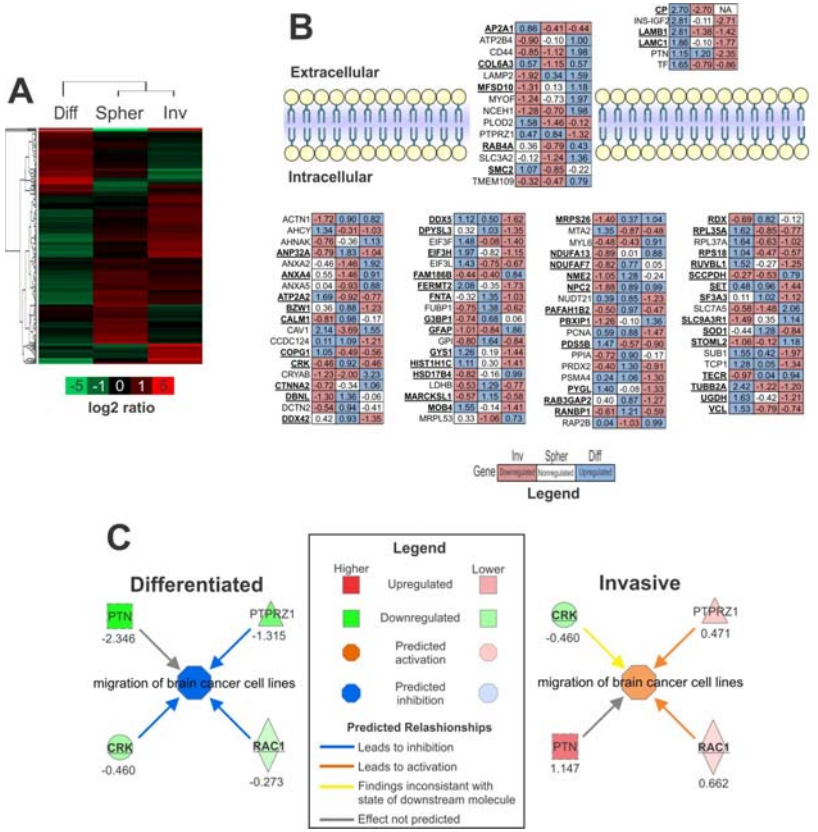
microRNA



mRNA



Protein



Conclusions – to be continued…

- Pronounced migration in 3D model
  - Stem cell medium
  - Fluorescence
  - Validated with stainings
  - Potential reduction of animal experiments
- Pronounced migration in 2D model
  - Stem cell medium
  - Potential reduction of animal experiments

Funding

Denmarks 3R-Center

OUH
Odense
Universitetshospital