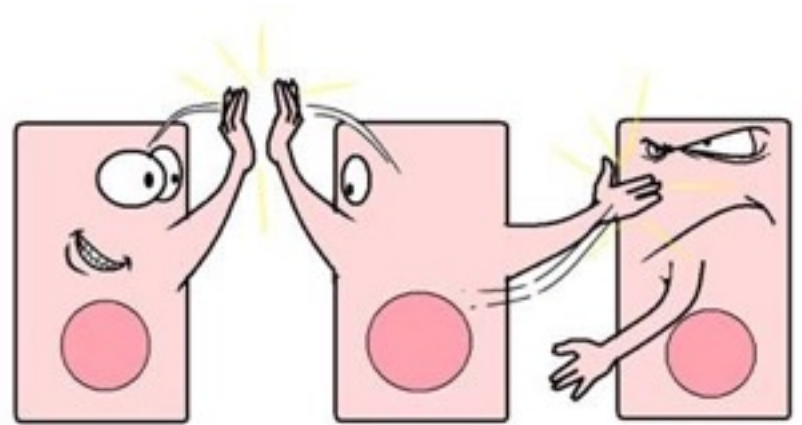
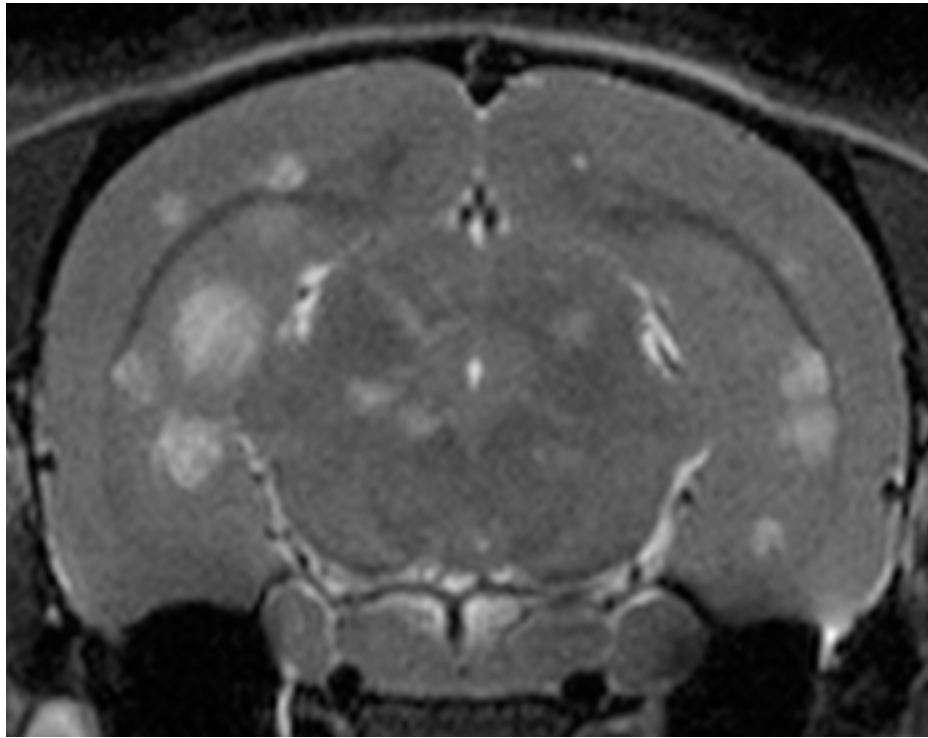
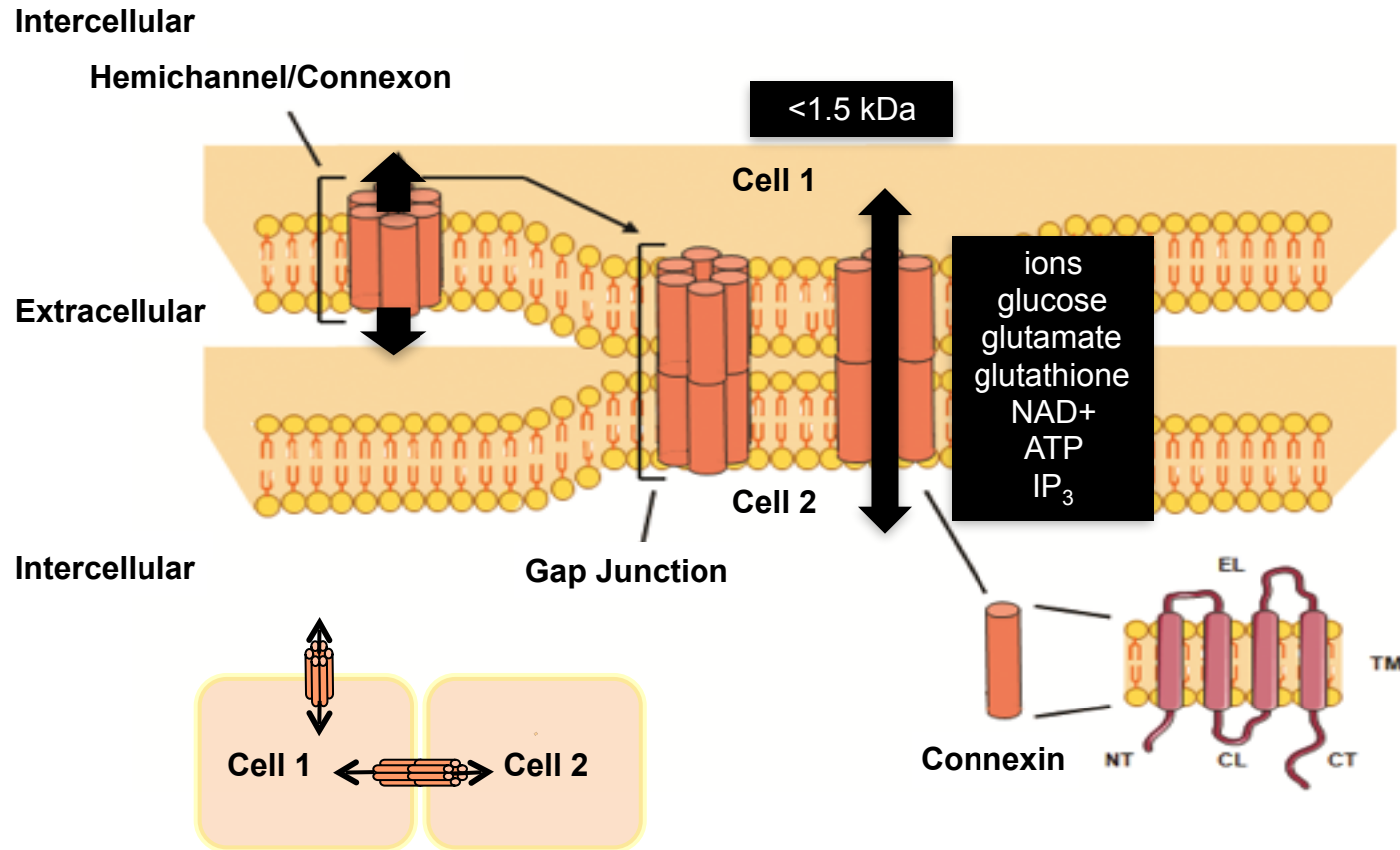


# Effect of gap27 on breast cancer brain metastasis development: initial results



# Cx-mediated intercellular communication

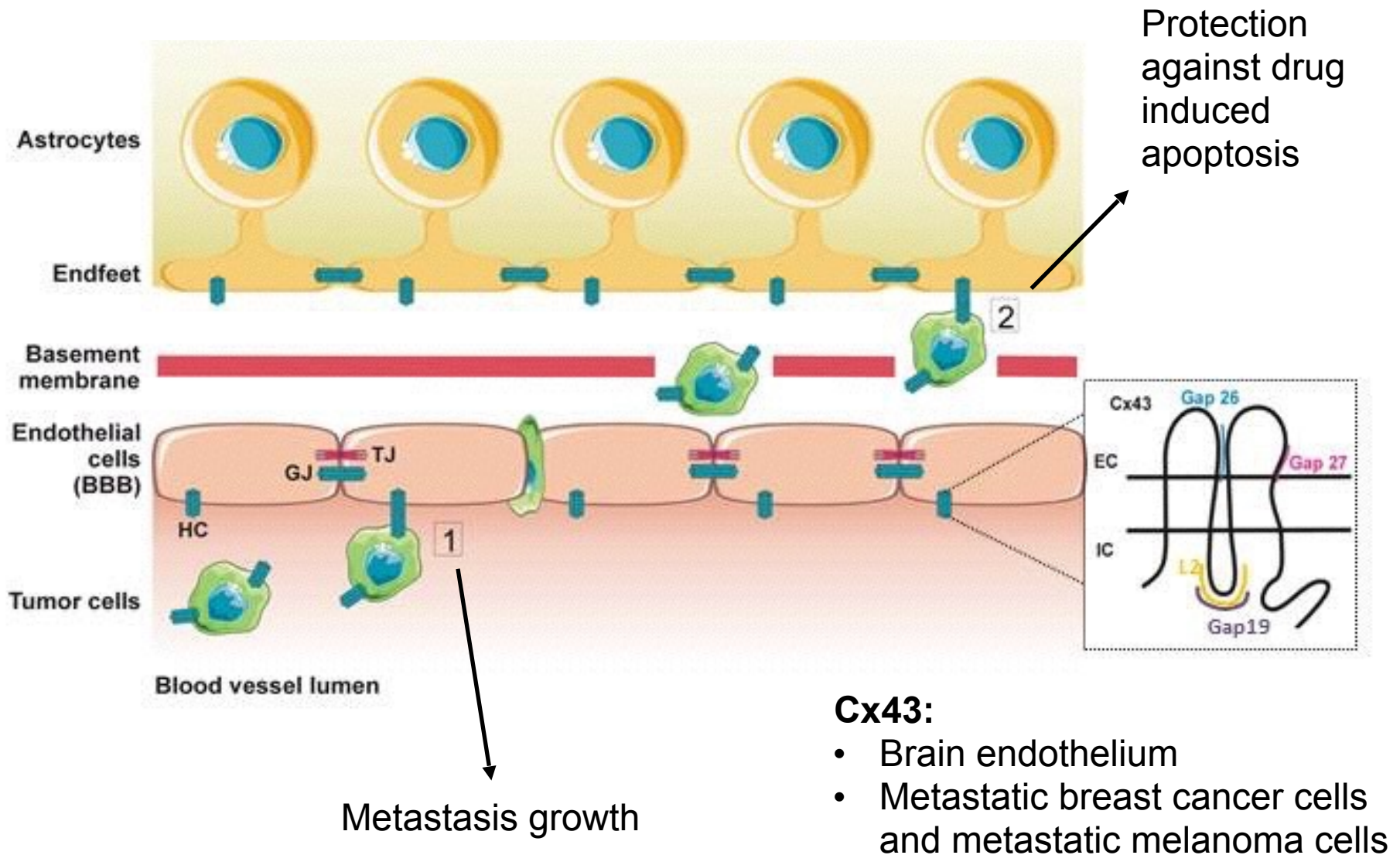


Saez et al., 2003/2010  
Evans et al., 2006  
Decrock et al., 2009

**Connexins play a crucial role in brain metastasis formation:**

- Tumor cell/host cell interaction
- Extravasation
- Survival of metastatic tumor cells

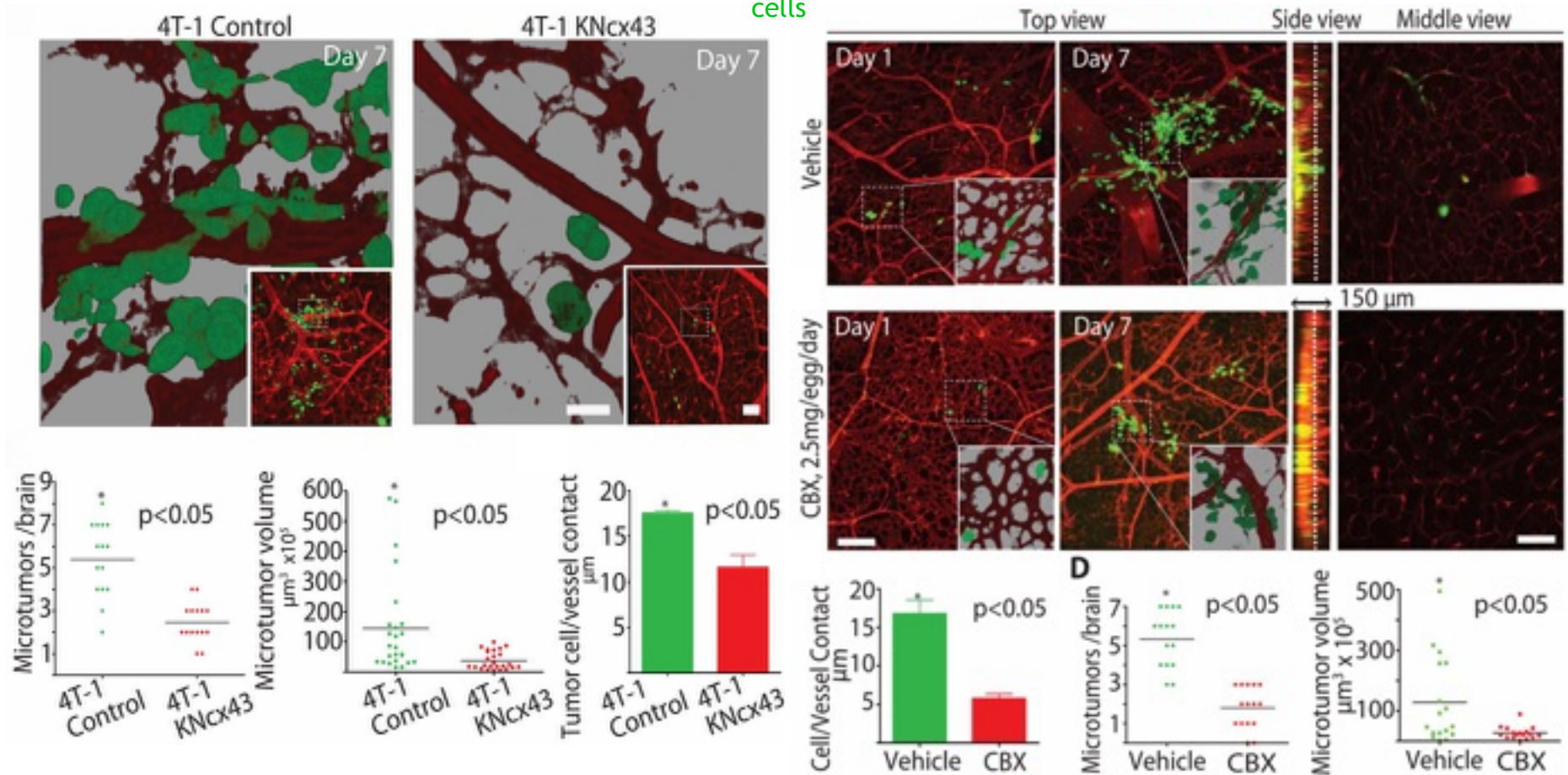
# Role of transmembrane connexin proteins in brain metastasis



## Metastatic breast cancer cell extravasation and brain colonization require Cx43 expression

## The GJ inhibitor CBX inhibits breast cancer brain colonization

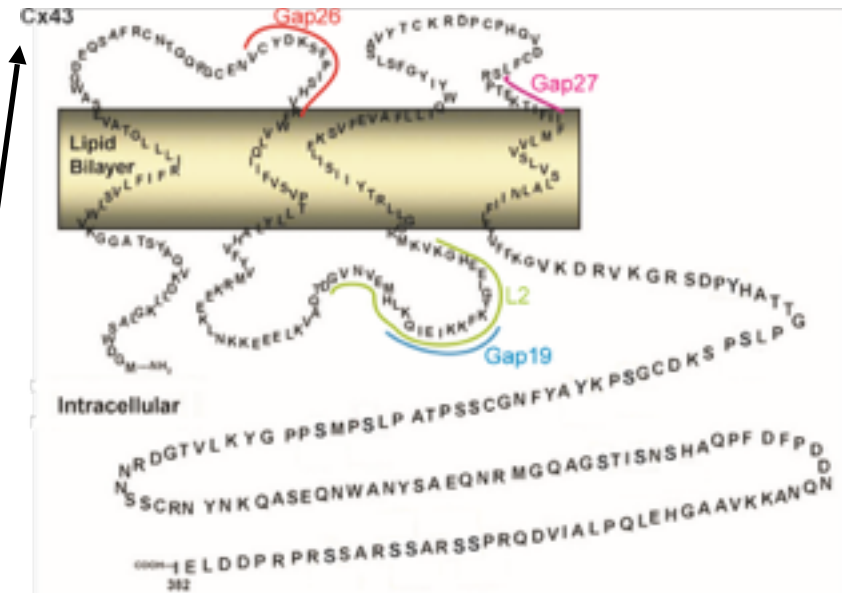
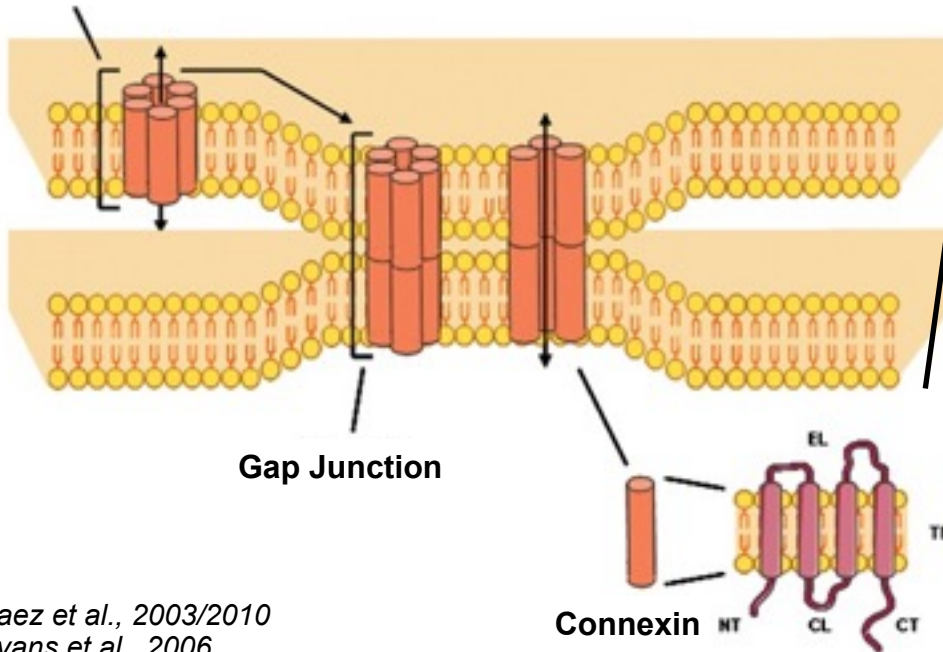
Chicken brain vasculature - 4T1 cells





# GAP27: inhibition of Cx-based intercellular communication

Hemichannel/Connexon



Saez et al., 2003/2010

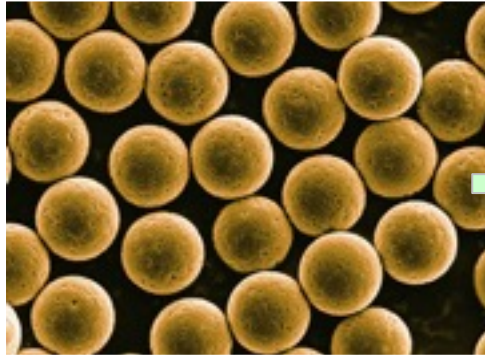
Evans et al., 2006

Decrock et al., 2009

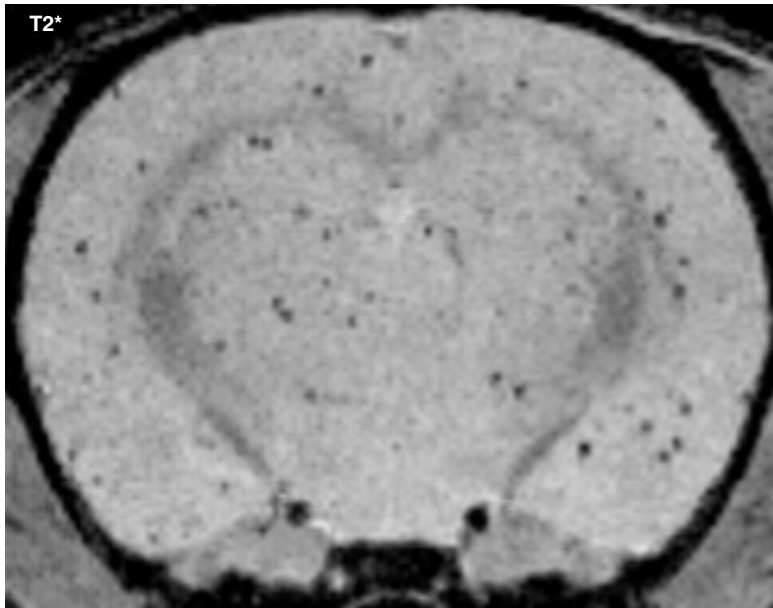
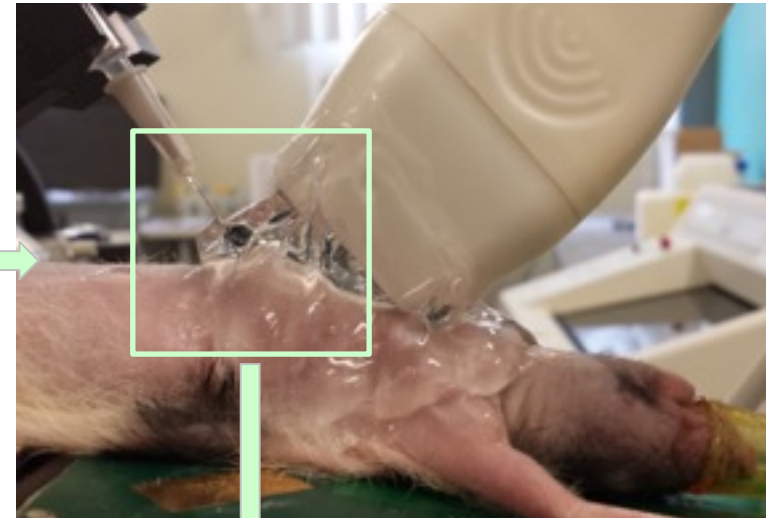
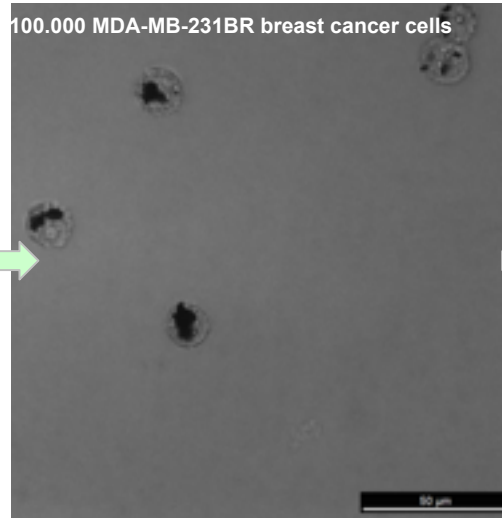
## GAP27

- Connexin mimetic peptides
- Mimicking sequences on the second extracellular loop regions of Cx43
- Working mechanism so far unknown

# In vivo brain metastatic cell tracking using MPIO labeled MDA-MB-231BR cells



In vitro cell labeling using MPIO



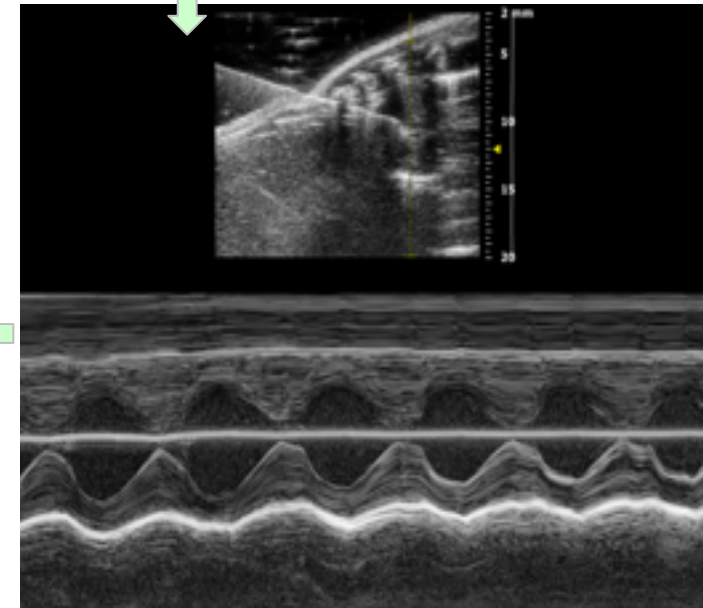
In vivo brain imaging using high resolution MRI

Treatment group (n=4):

- Co-injection GAP27
- IV injections GAP27

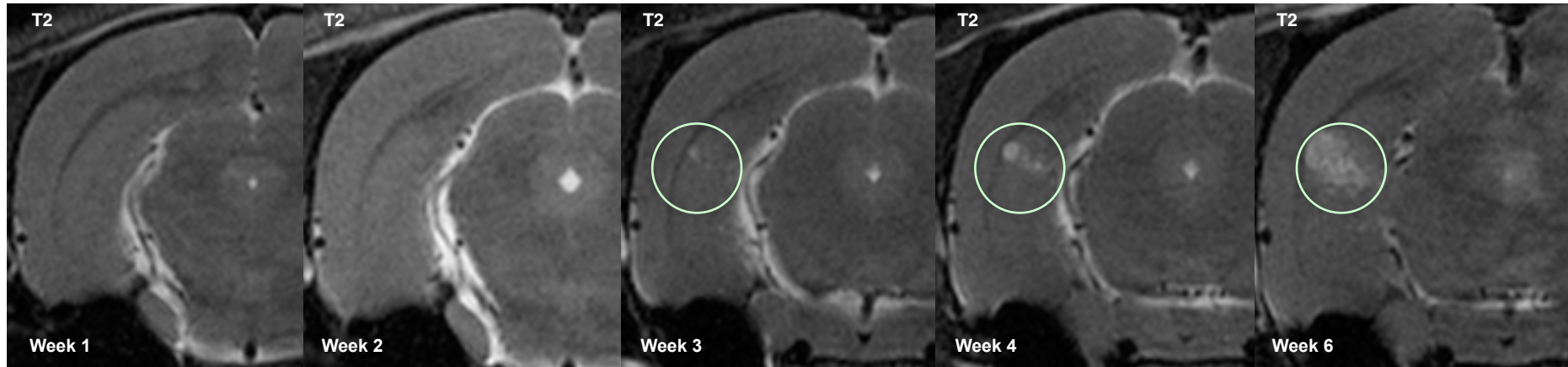
Control group (n=4):

- Co-injection PBS
- IV injections PBS

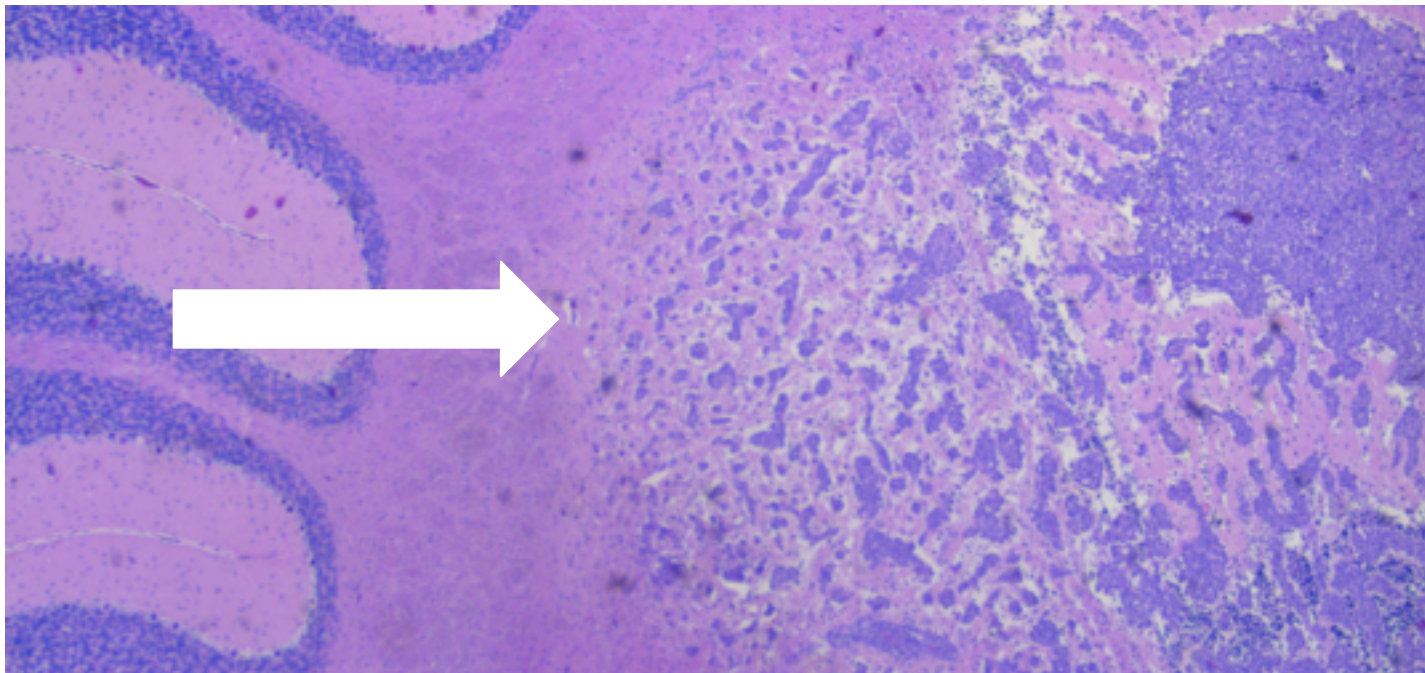


Intracardial US guided injection of labeled cells

## Results

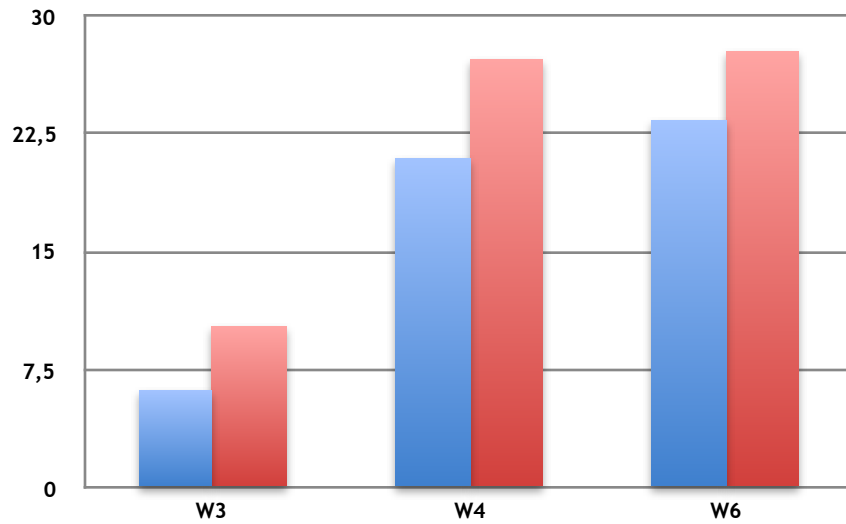


**H&E staining of the established metastasis in the cerebellum**



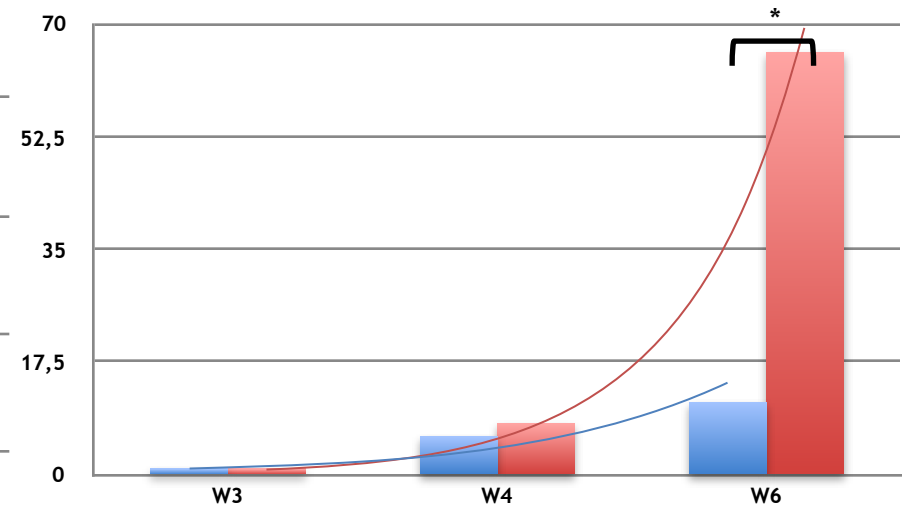
# Results

## Number of Metastases



Gap27 (n=4) - Control (n=4)

## Volume of Metastases (mm<sup>3</sup>)



Gap27 (n=4) - Control (n=4)



## Conclusions

Early administration of gap27:

- No significant impact on metastatic seeding in the brain
- Reduction of metastatic colonization of the brain

## Future Experiments

Gap27:

- Continuous administration of Gap27
- Treatment of established metastases

Cx43EL2-antibody:

- Early administration of Cx43EL2-antibody

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