

# ADV HSV-TK1 AGAINST IDH1(R132H) EXPRESSING CELLS IN GLIOBLASTOMA MULTIFORME

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Use of TK/GCV combination to induce apoptosis of  
tumor cells

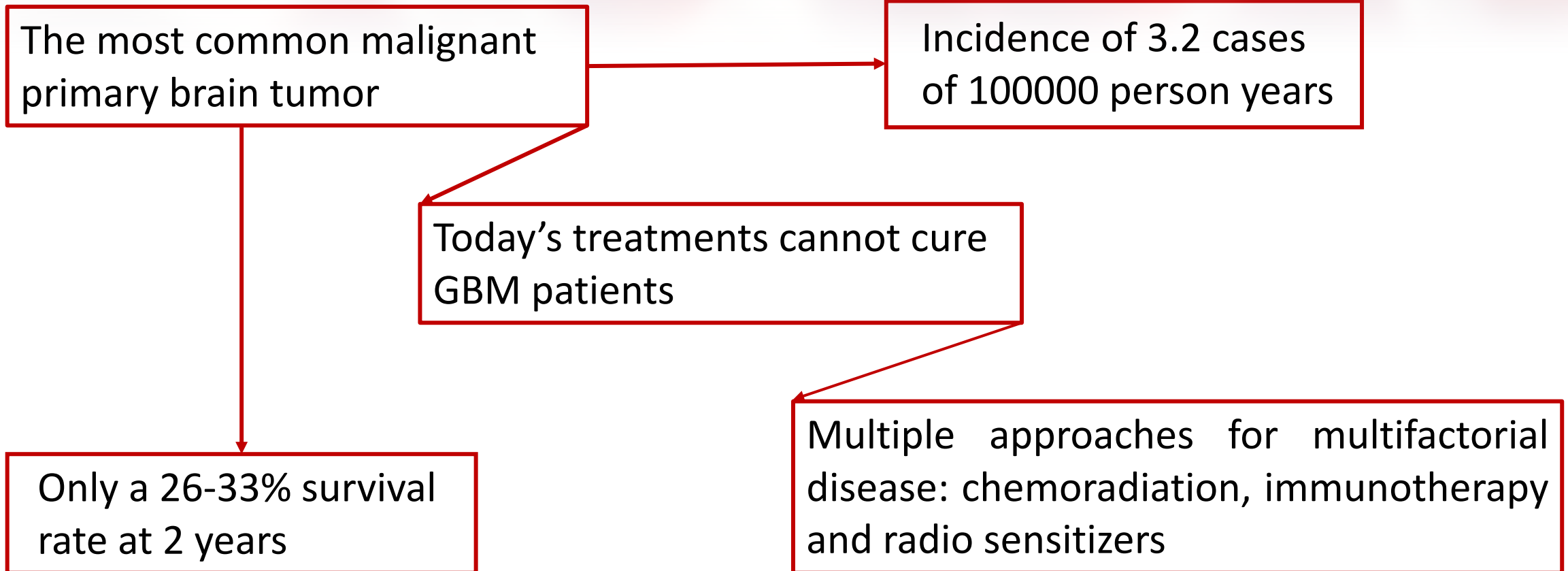
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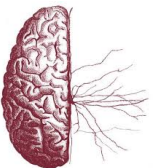


# WHY GLIOBLASTOMA MULTIFORME?

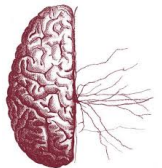
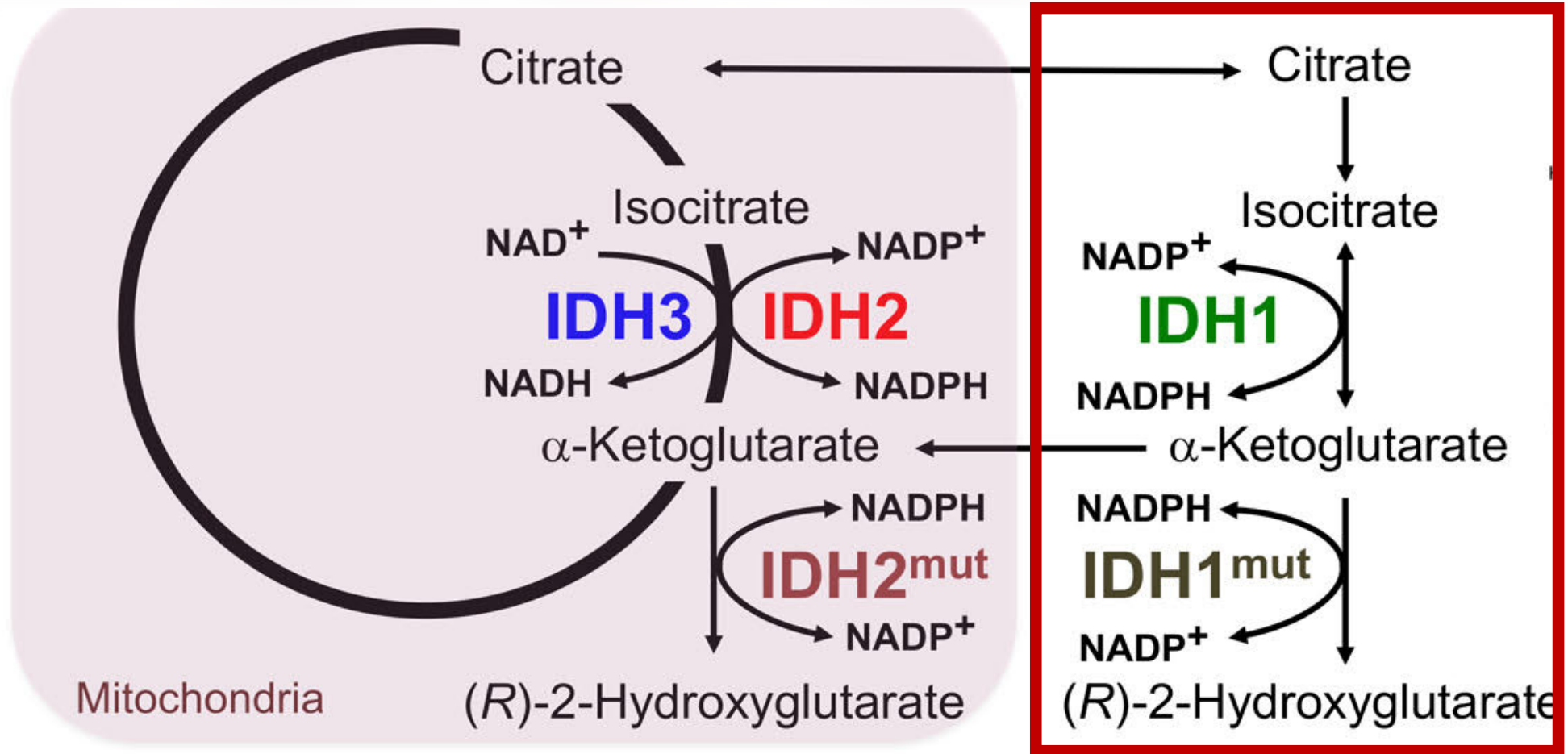


# MOLECULAR ALTERATIONS IN GBM

Gene	Alterations	Frequency (%)
EGFR	Amplification	40-60
TP53	Mutation	50-60
Pten	Mutation	60
MDM2	Polymorphism	40-60
CDK4	Mutation	20-30
IDH1	Mutation	40-50
P16ink4a	Elimination	31



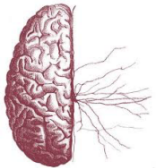
# IDH1 PHYSIOLOGICAL ROLE





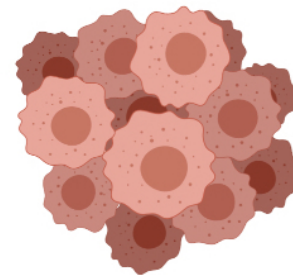
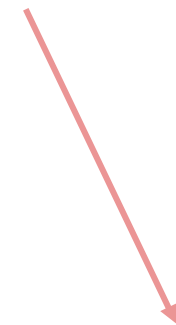
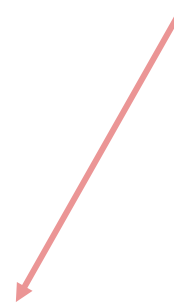
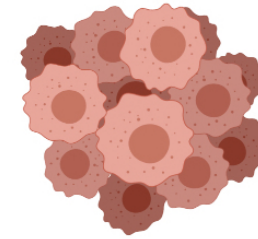
# GOALS

- INDUCE APOPTOSIS OF TUMOR CELLS EXPRESSING IDH1 (R132H);
- REDUCE THE TUMOR MASS;
- INCREASE PATIENT SURVIVAL.

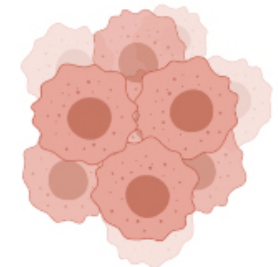


# STRATEGY

U138 GBM CELL LINE



Adv-HSVTK1



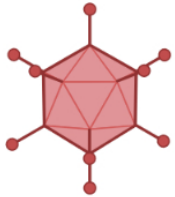
Adv-HSVTK1+GCV



# EXPERIMENTAL PLAN

## 1<sup>^</sup> STEP

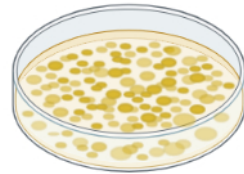
Create Viral Vector



- AdvHSV-TK1

## 2<sup>^</sup> STEP

Model *Vitro*



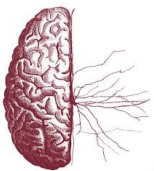
- IN VITRO EXPANSION OF HSV-TK1+,
- INOCULATION GCV.

## 3<sup>^</sup> STEP

Model *Vivo*



- TRANSPLANT USING XENOGRAFT STEREOTASSIC SURGERY,
- AdvHSV-TK1 INJECTION (14 DAYS LATER),
- GCV INJECTION (2-3 DAYS LATER).



# PRODUCTION OF THE VIRAL VECTOR AdvHSV-TK1

CELL LINE

HEK-293  
E1+

ADENO GENOME



VIRAL VECTOR



PROMOTER

SUICIDE GENE

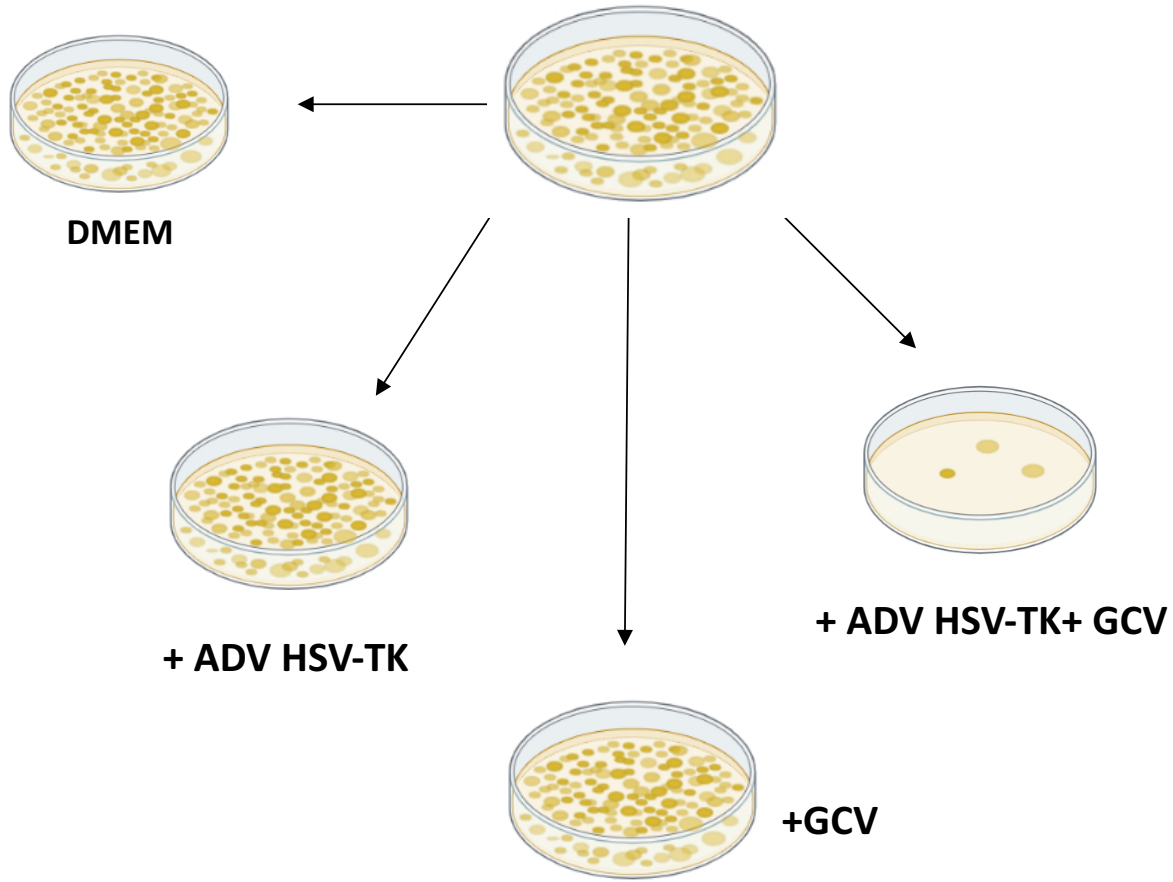
REPORTER



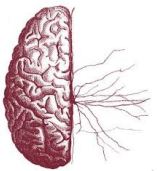
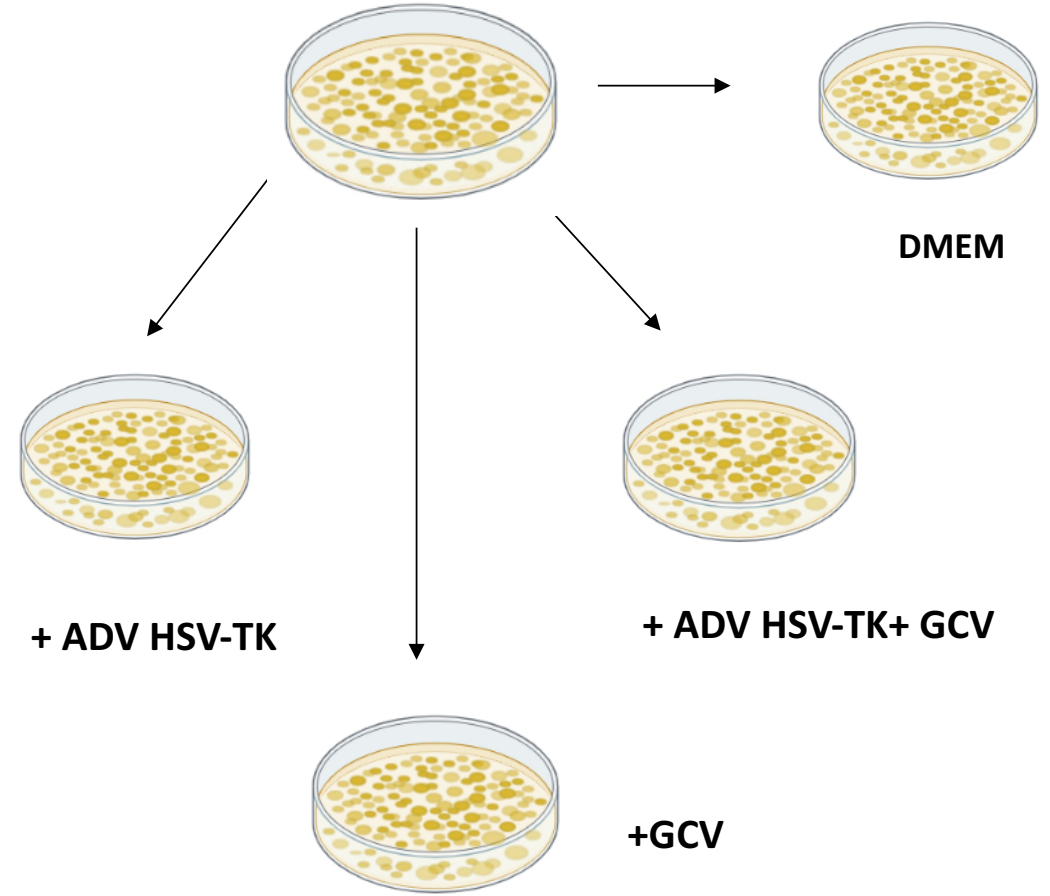


# IN VITRO MODEL

U138MG (GBM)



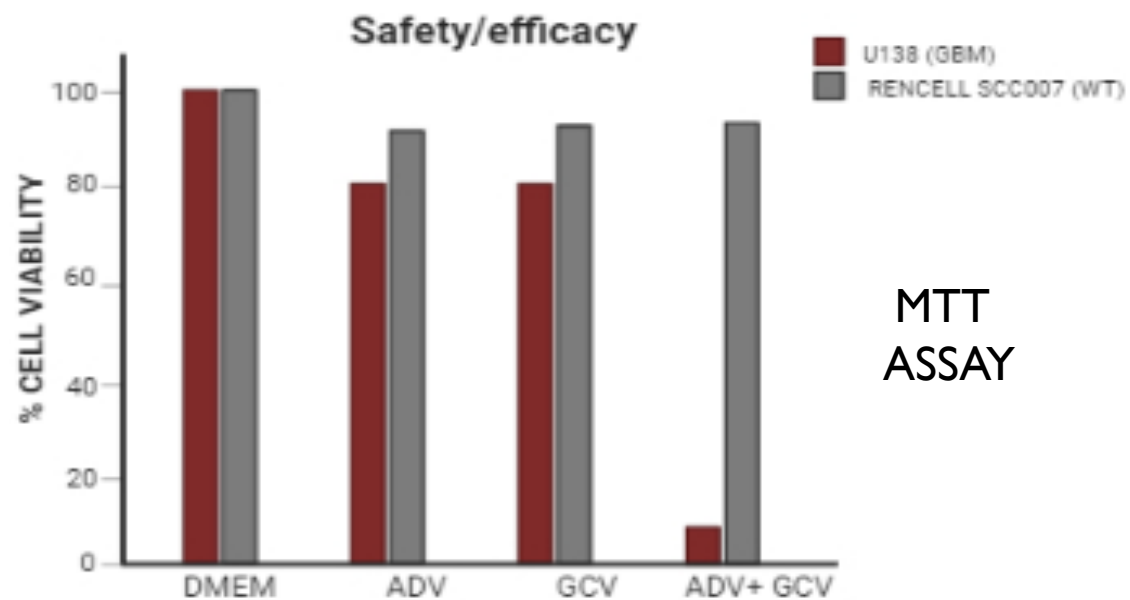
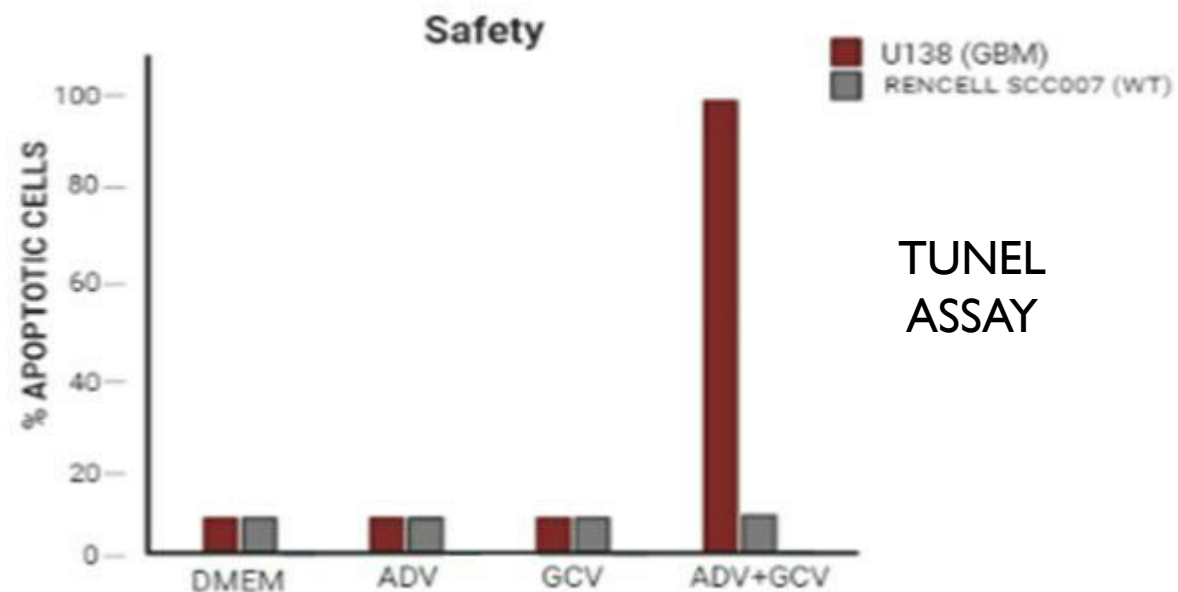
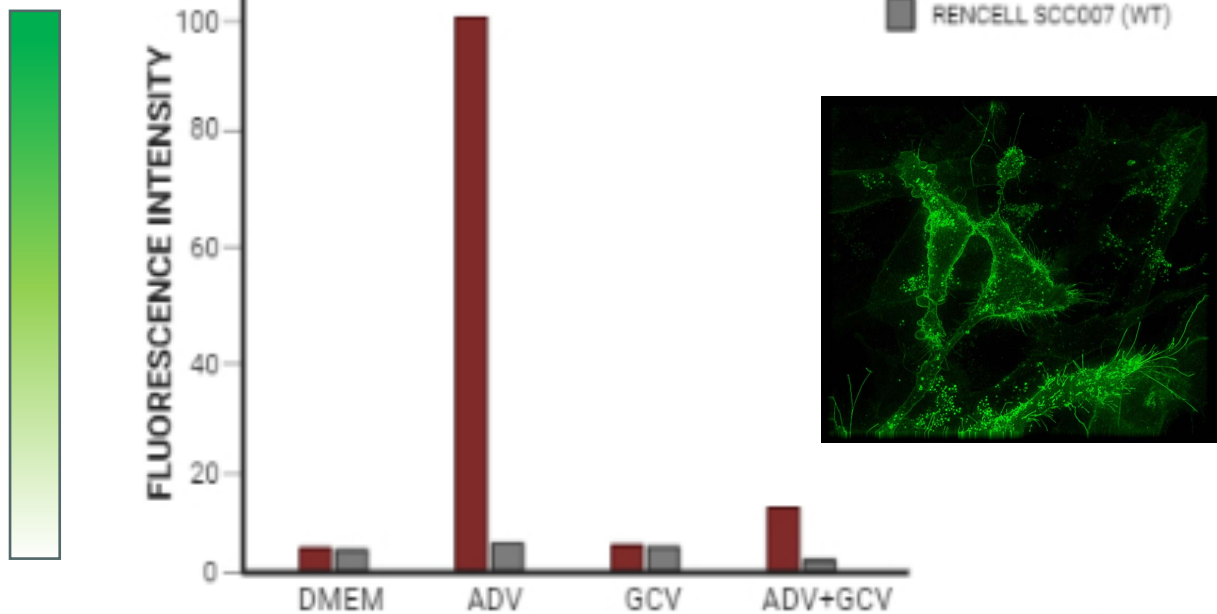
RENCELL SCC007 (WT)







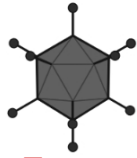
# ADV-TK1 + GCV TREATMENT REDUCES SPECIFICALLY CELLS VIABILITY





# IN VIVO MODEL

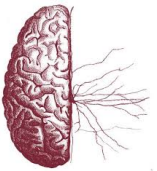
ADVHSV-TK1 INJECTION  
(14 DAYS LATER)



TRANSPLANT OF U138 CELLS USING  
XENOGRAFT STEREOTASSIC SURGERY

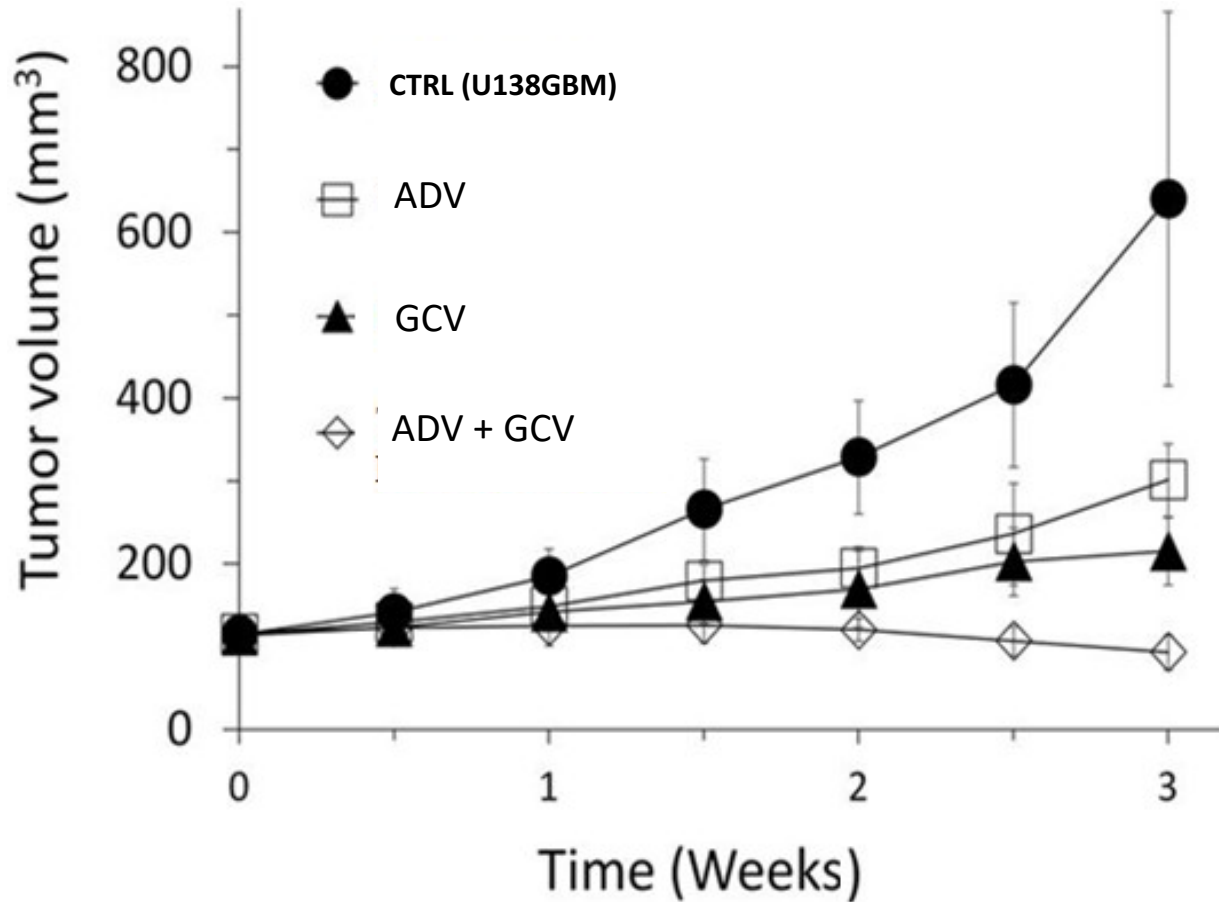


GANCICLOVIR INJECTION  
(2-3 DAYS LATER)





# RESULTS: tumor mass reduction




THE GRAPH INDIRECTLY REFLECTS THE INCREASE IN LIFE EXPECTANCY

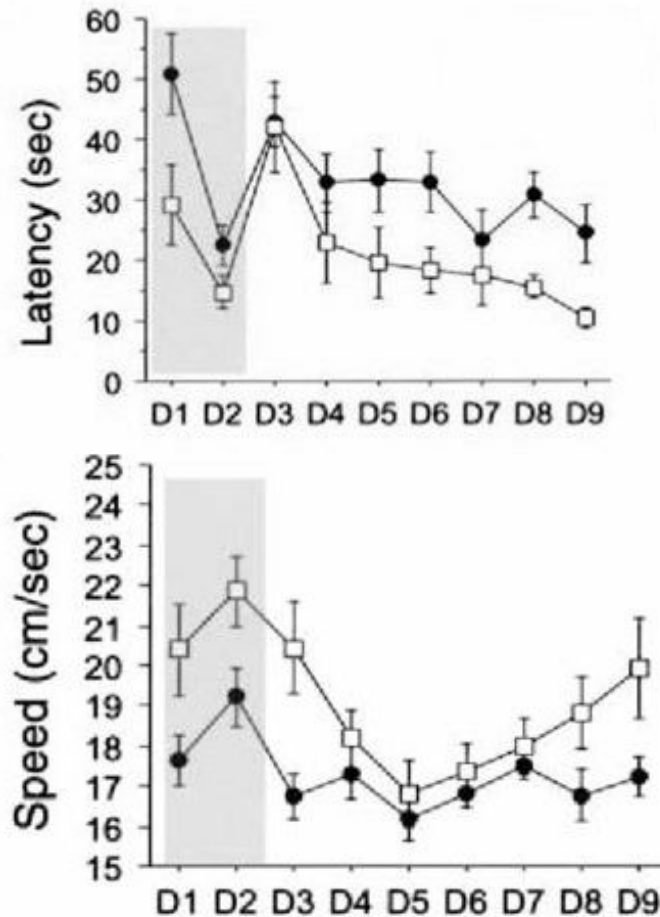


# EVALUATION OF DIFFERENT BEHAVIORAL PHENOTYPES ASSOCIATED WITH GBM

## Morris Water Maze Test

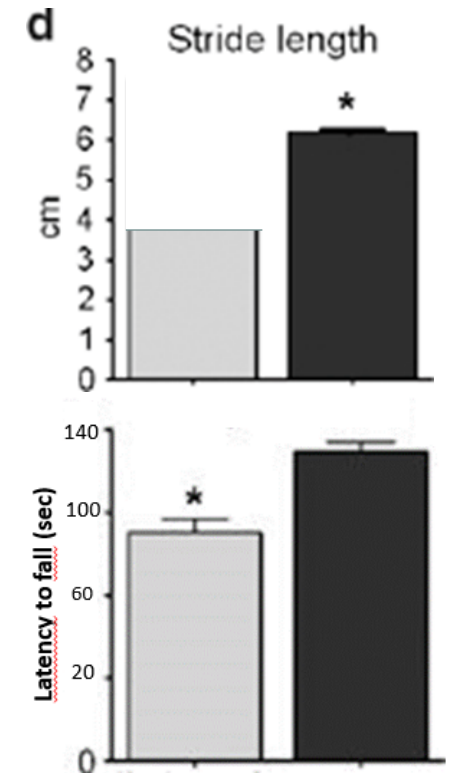


-  U138 GBM
-  U138+ ADVHSV-TK+GCV



Adapted from Dumas, Sandin, Chen Kobayashi et al.; 2008

## Foot Print Test



-  U138 GBM
-  U138+ ADVHSV-TK+GCV

Adapted from Carter et al. 1999





# HURDLES...

- ❖ CURRENTLY THERE IS NOT HUMAN EXPERIMENTATION YET
- ❖ XENOTRANSPLANTATION DOES NOT ALWAYS MIMIC WHAT REAL HAPPENS
- ❖ THERAPY MAY NOT WORK ALONE
- ❖ WIDE ADENOVIRUS TROPISM

## ...AND SOLUTION




- ❖ USE OF ORGANOIDS AS A NEW FRONTIER
- ❖ MINIMISING THE DISTRESS RESULTING FROM XENOTRANSPLANTATION
- ❖ SUPPORT THERAPY BY OTHER METHODS
- ❖ SPECIFY THE TARGET AREA OF ADENOVIRUS

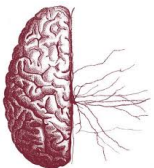




# MATERIALS & COSTS

- U138MG **€595** «ATCC»
- RENCELL SCC 007 **€3110** «SIGMA ALDRICH»
- HEK-293 **€595** «ATCC»
- GANCICLOVIR **€319** «ADOOQ»
- HOMOZYGOUS FOR Prdk Scid **€123,16 x 4** «THE JACKSON LABORATORY» 
- STABULATION **€ 18000**
- MTT KIT **€375** «THERMOFISHER»
- HSV **€1400**
- TUNEL ASSAY KIT **€822**
- KIT MORRIS WATER MAZE TASK **€2000**
- KIT FOOT PRINT TASK **€ 500**

**TOT: €28.208,64**



(WITHOUT LABORATORY MATERIALS AND RESEARCHERS SALARIES)