

# SVS UPDATE 2024

**Pim French**  
Dept Neurology, Erasmus MC



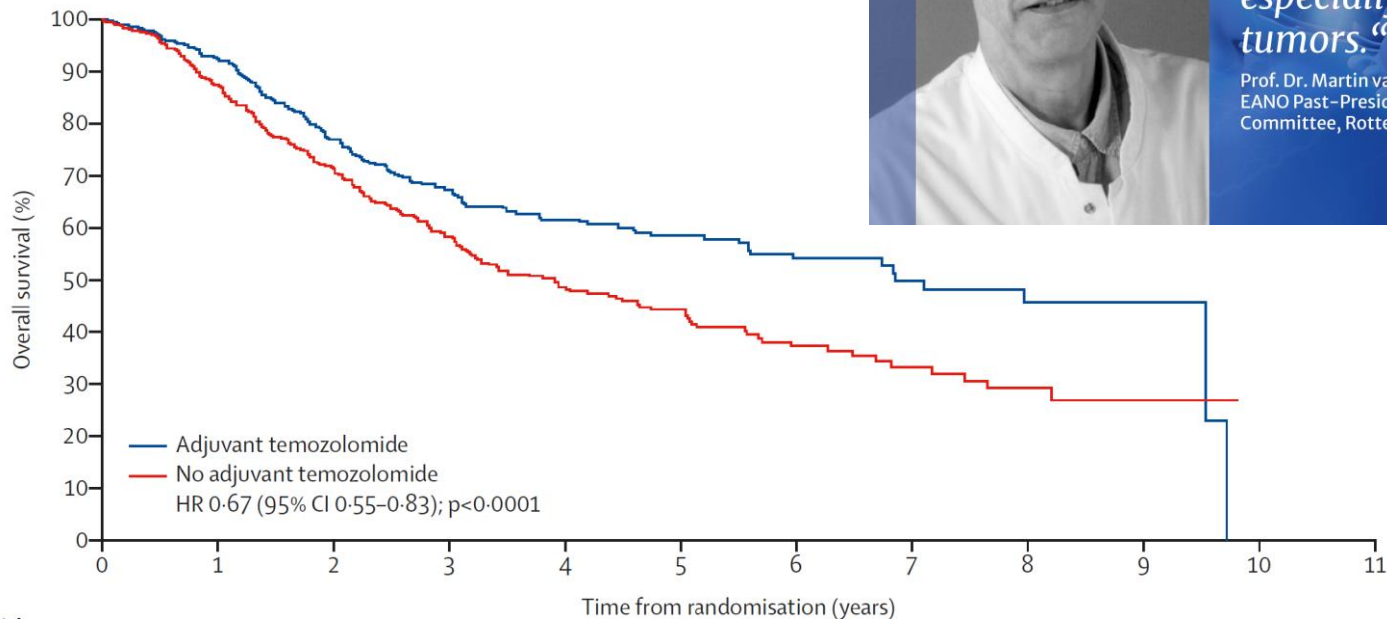
# Update SvS 2020 en 2021

## De CATNON trial

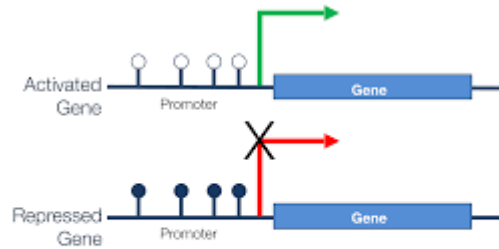
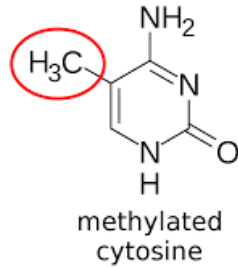
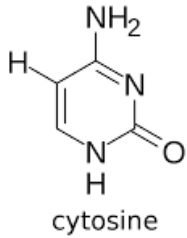


„This European led inter-continental study defines the standard of care of anaplastic astrocytoma, especially for the IDH with tumors.“

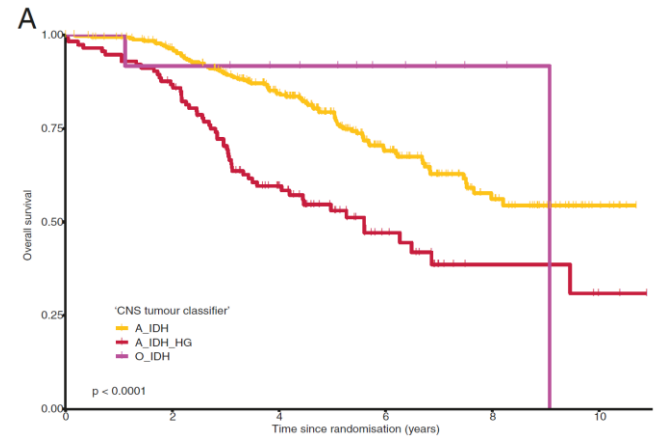
Prof. Dr. Martin van den Bent,  
EANO Past-President, Chair Guidelines  
Committee, Rotterdam, Netherlands



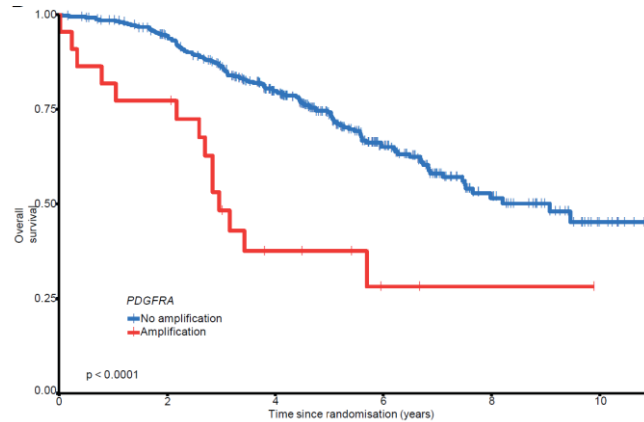
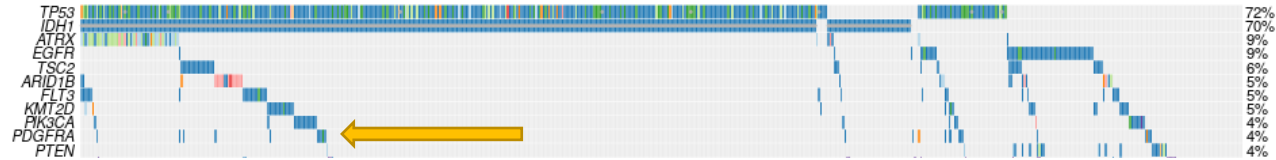
# SVS en de CATNON trial



● Methylated CpG ○ Unmethylated CpG

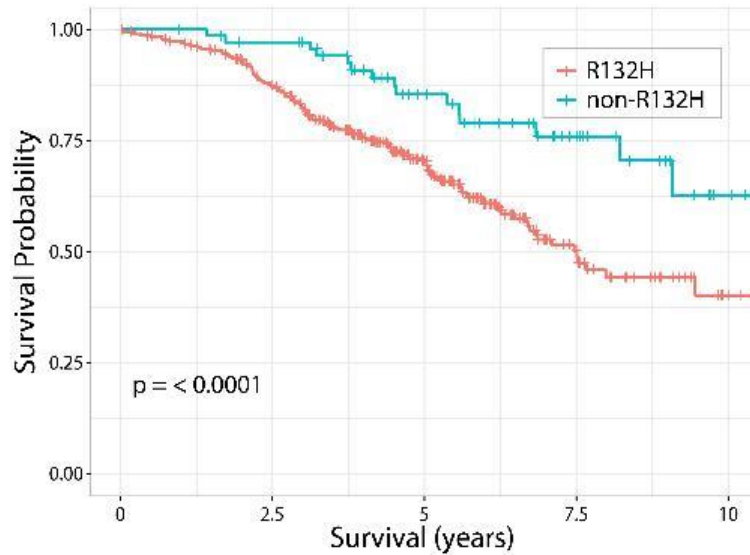


# de CATNON trial



# de CATNON trial

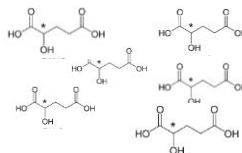
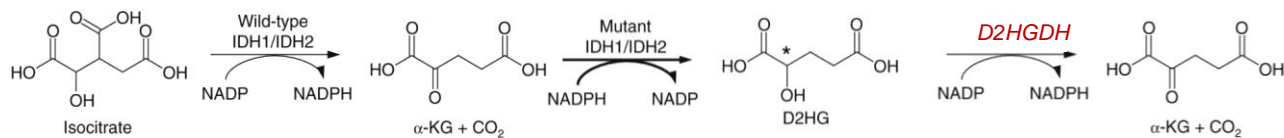
Niet elke IDH mutatie is gelijk



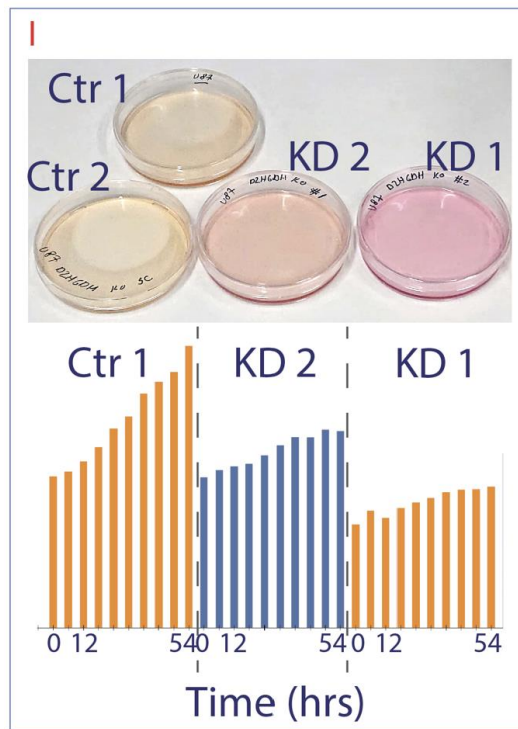
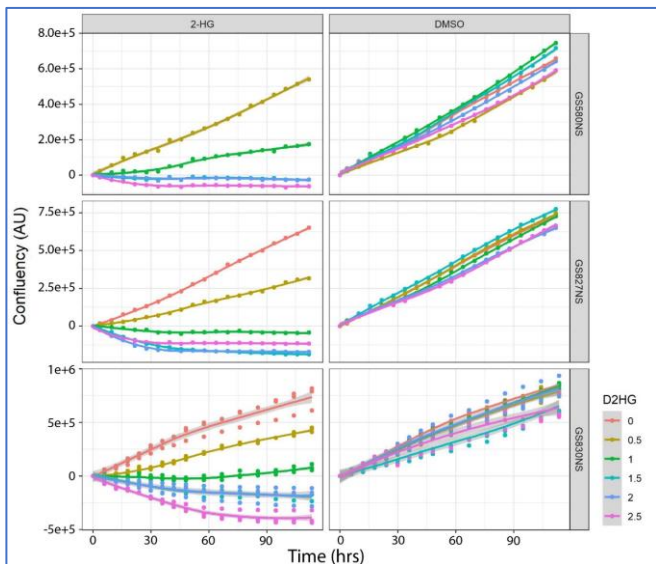
# Doel

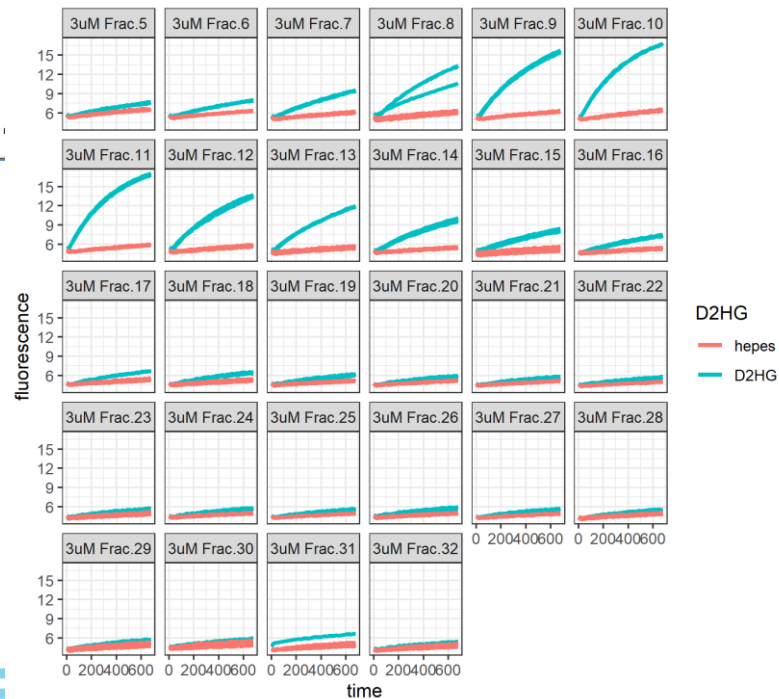
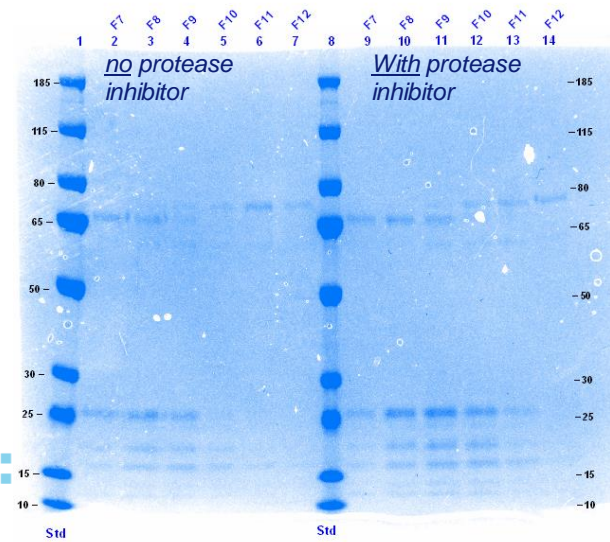
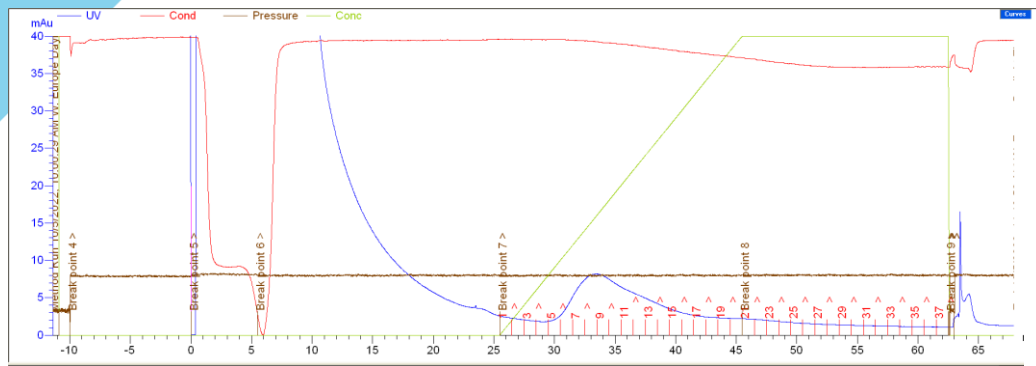
Verdere verhoging van D-2HG

## Indigo



# D-2HG is toxisch



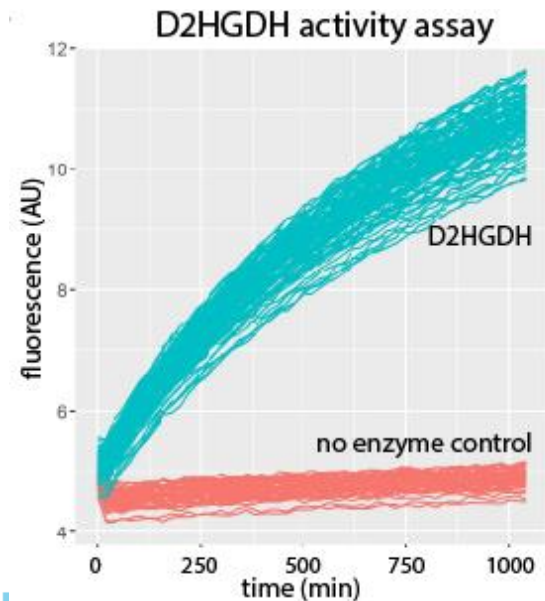
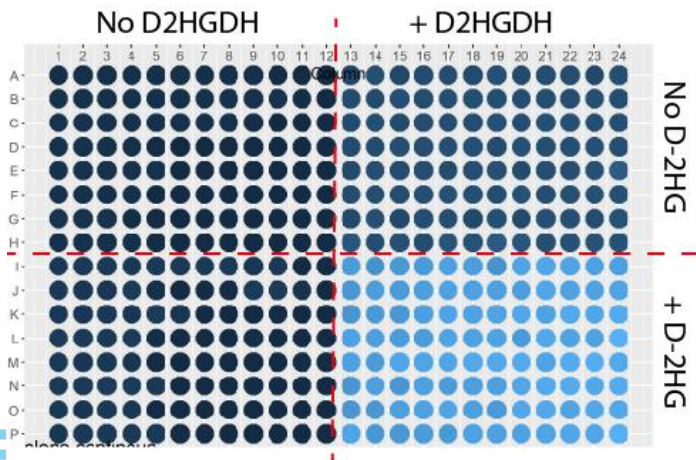




# Reaction+test performance

Reproduceerbaar

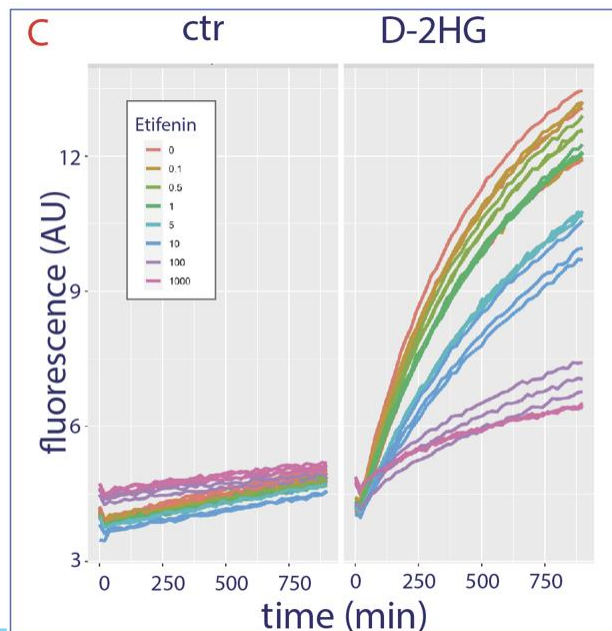
Test performance in 384 well plaat



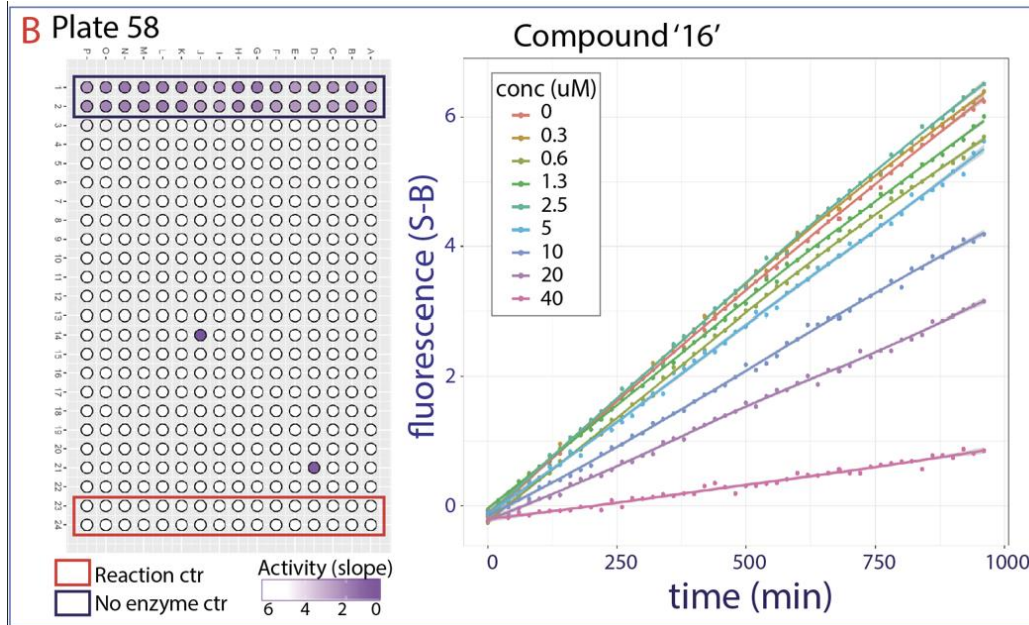
C

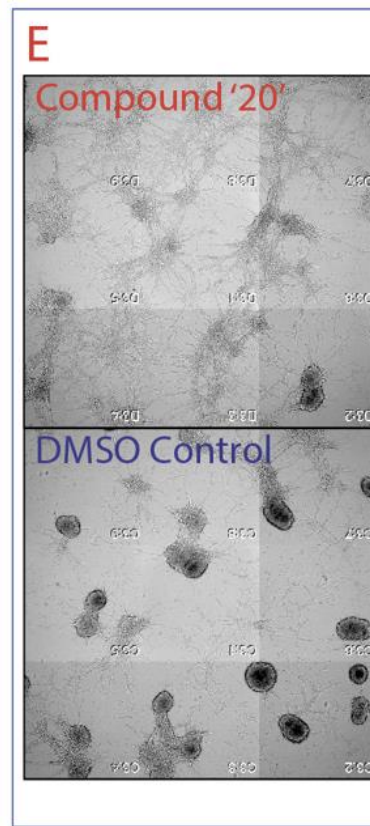
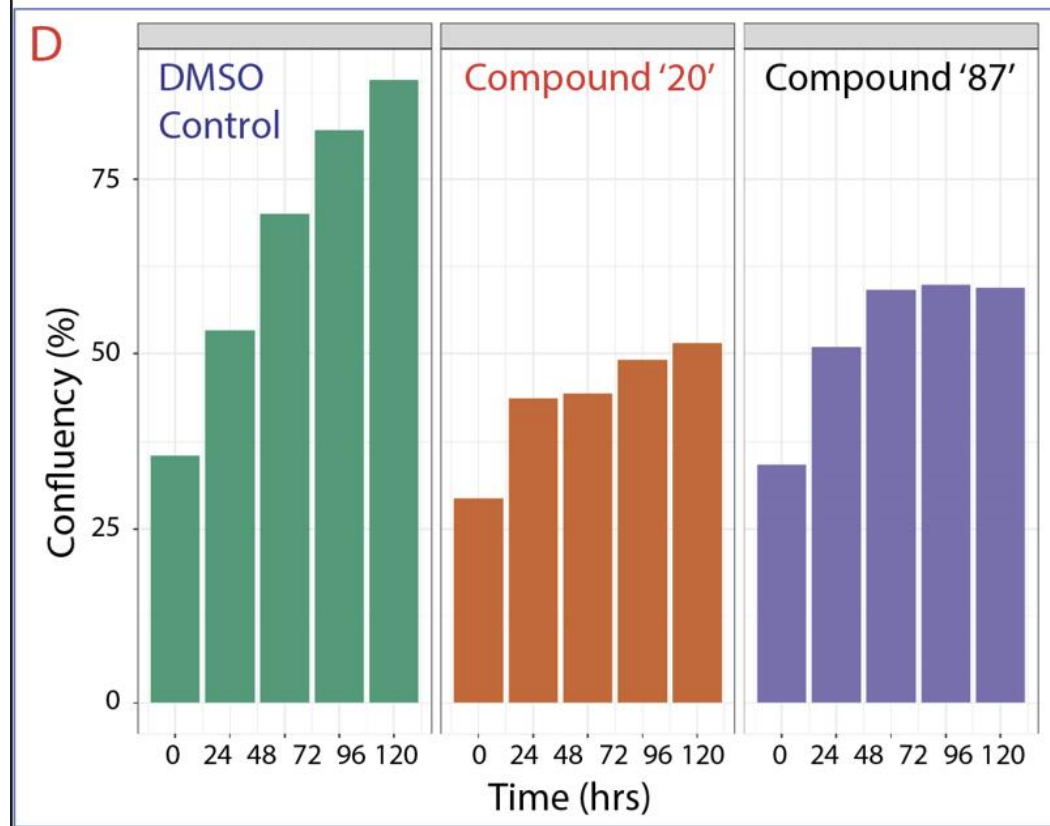
# 1 positieve hit: Etifenin

Test screen: Prestwick library 1270 FDA approved compounds



# 40.000 stoffen getest



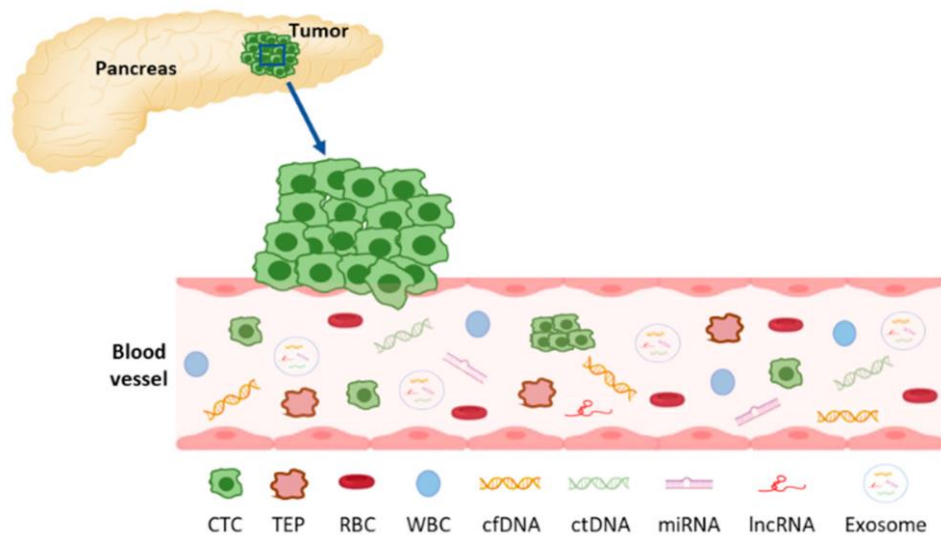


# Vervolg

1. Vervolg onderzoek alle “hits”
  1. *Dose response*
  2. *Counterscreen*
  3. *Effect op celgroei*
  4. *D-2HG verhoging in cellen*
  
2. Verdere zuivering van het D2HGDH eiwit
  1. *Opslag*
  2. *Binding aan “hits”*
  3. *Hit-optimalisatie*



# Update SVS 2022



**Kunnen we sporen van de tumor in bloed vinden?**

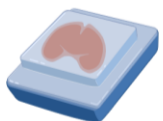
En wat is de beste manier om dit te doen

DNA methylering?

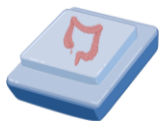
# 1e test

Amount (ng)

FFPE tissue



100	30	10	3	1	30	10	3	1	0
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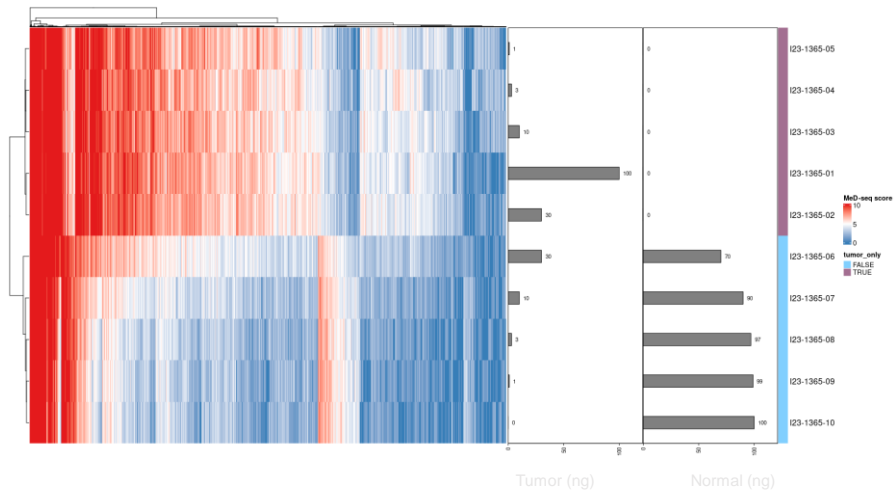
0	0	0	0	0	70	90	97	99	100
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Different input tumor DNA  
(100ng, 30ng, 10ng, 3ng, 1ng)

Different tumor fractions  
(30%, 10%, 3%, 1%, 0%)

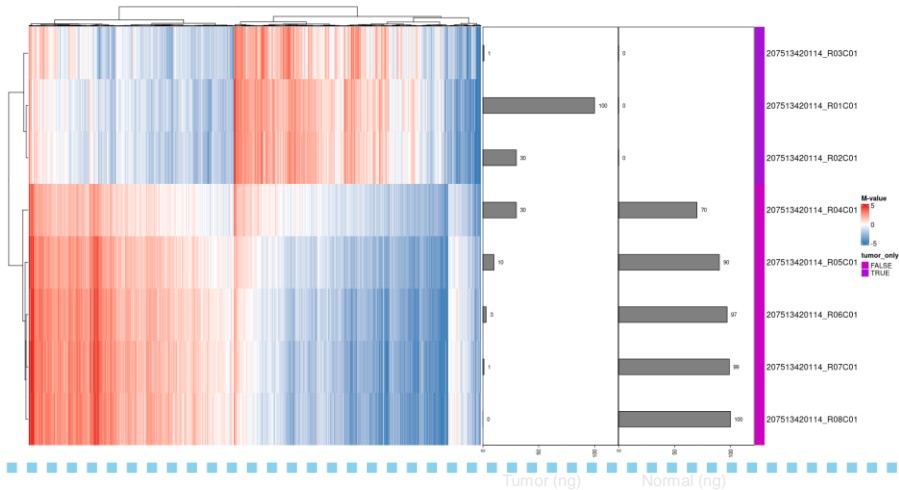


Samples (n=10)



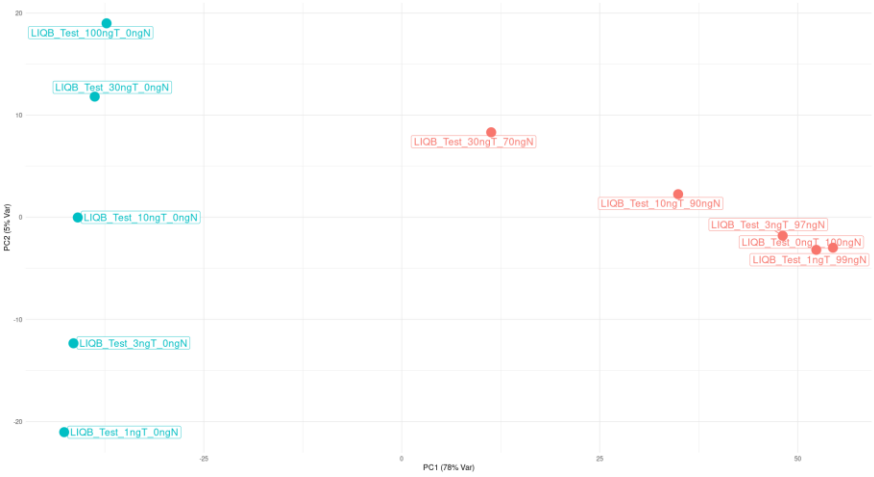
MeD-seq

Samples (n=8)

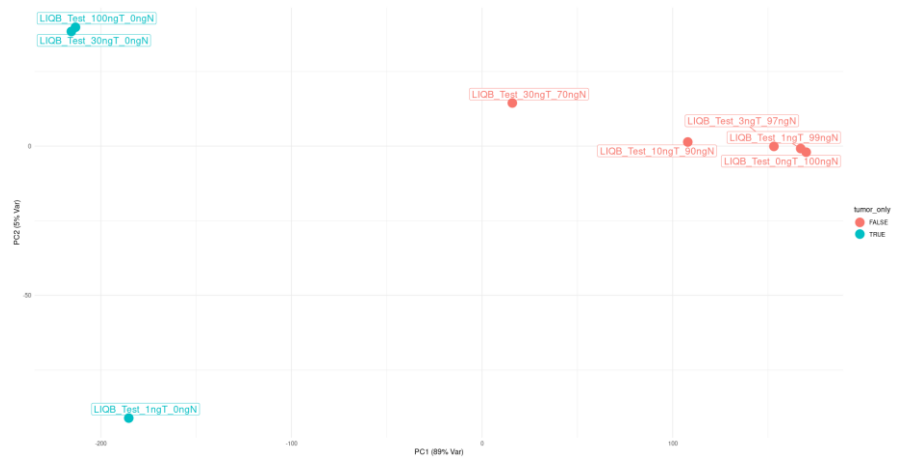


EPIC array

# Unsupervised PCA (5% most variable regions)



MeD-seq



EPIC array

# Conclusies en vervolg

## Conclusies

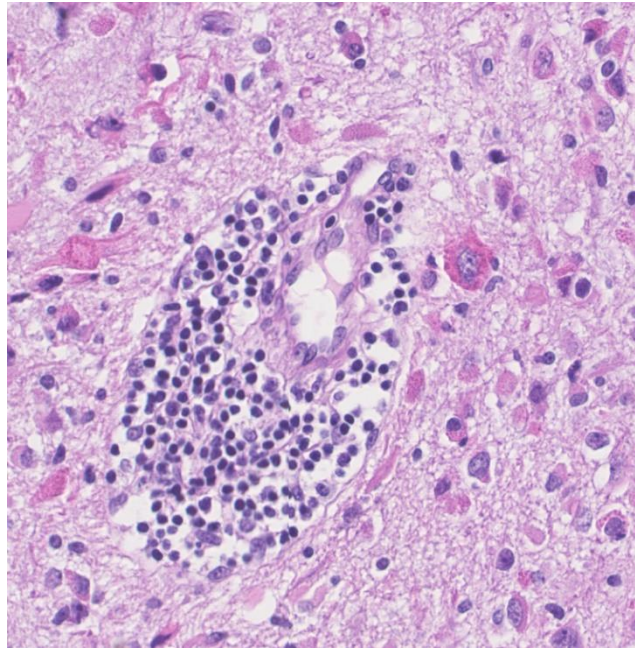
1. MedSeq en Epic arrays zijn ongeveer even gevoelig qua input DNA
2. MedSeq en Epic arrays zijn ongeveer even gevoelig in detecteren van tumor DNA in normaal DNA

## Vervolg

1. Herhaling van deze test met andere samples en met één andere techniek (Twist)
2. Doorgaan met verzamelen bloed van patienten
3. Verzamelen bloed van Sanquin (toestemming aangevraagd 17 juli 2023)
4. Uitvoeren van ctDNA op meest gevoelige techniek.

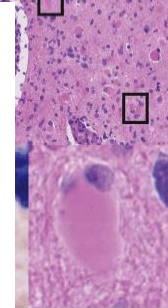
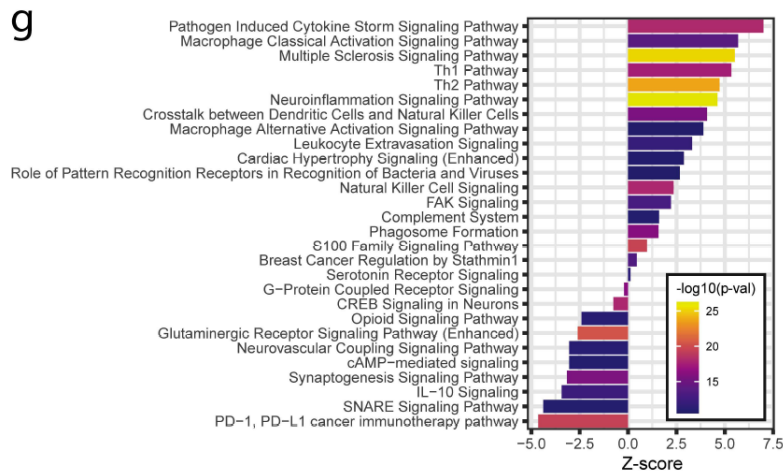
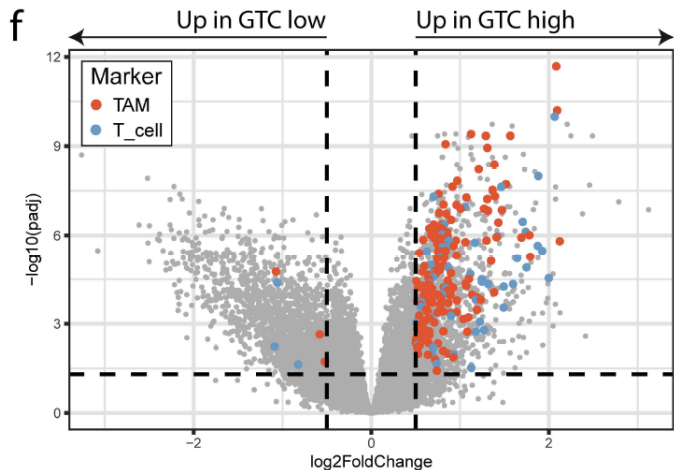
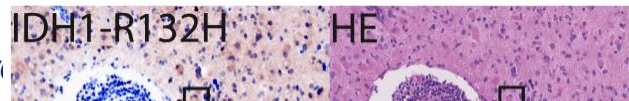


# SVS 2023: Let me in



# Voortgang 2023

1. Analyse van immuuncelinfiltratie in glioblastomen (ongoing)
2. Analyse van het micromilieu rond de T-cel 'cuffs':
  1. *Specifiek type tumorcel aanwezig (gemistocyten) waarvan het lijkt dat deze de immuuncellen buiten de tumor houden.*
  2. *Specifiek type microglia aanwezig die stimulerend w*



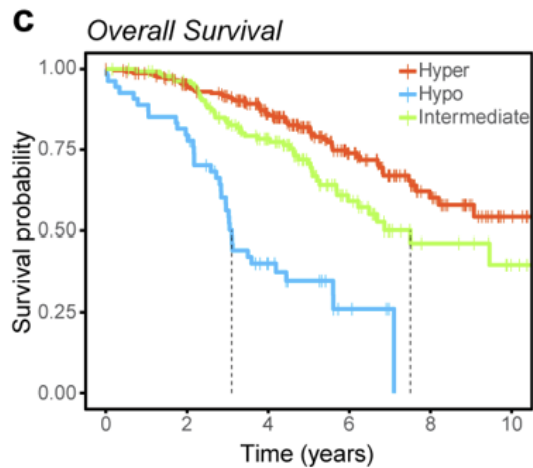
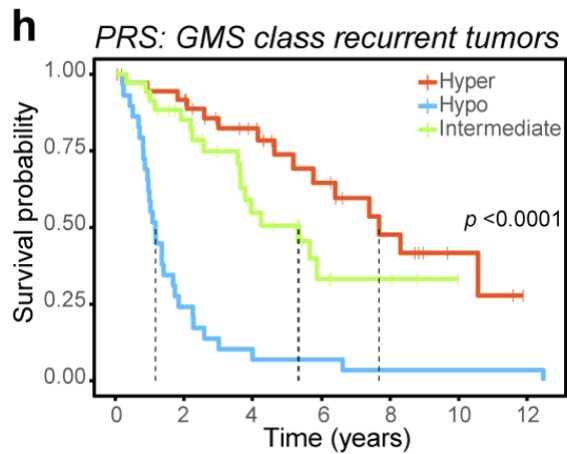
# Projectvoorstel 2024

## what's in a grade

1. Het graderen van hersentumoren is voorspellend voor de prognose van de patiënt.
2. Graderen belangrijk omdat het mede bepaalt welk behandeltraject gevolgd wordt

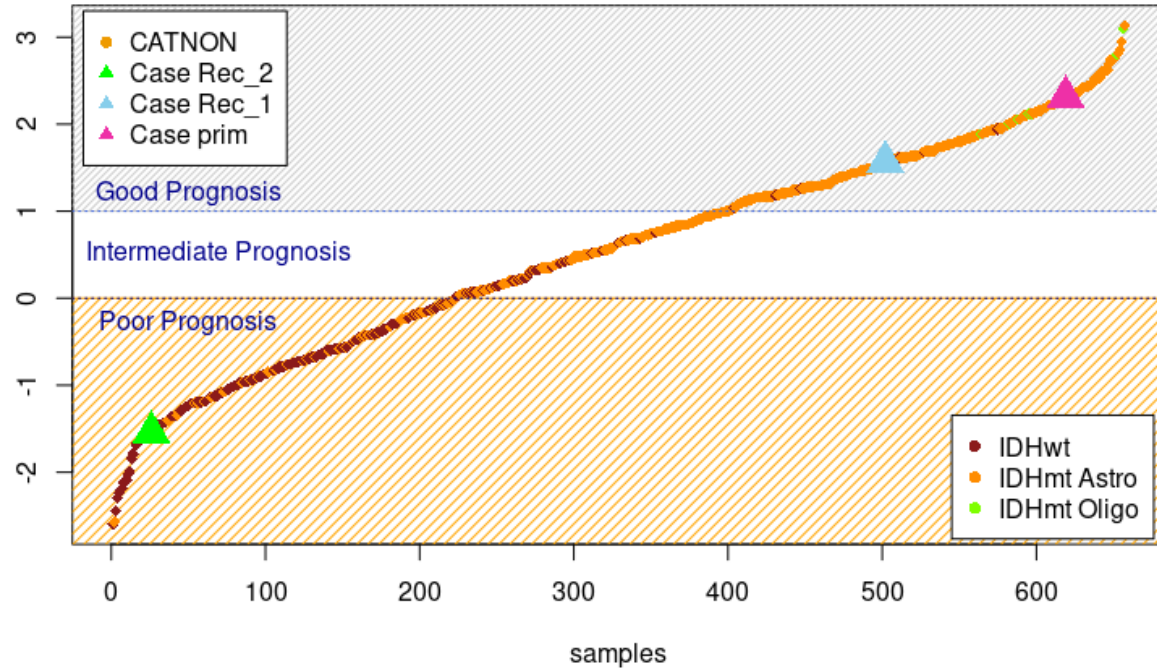
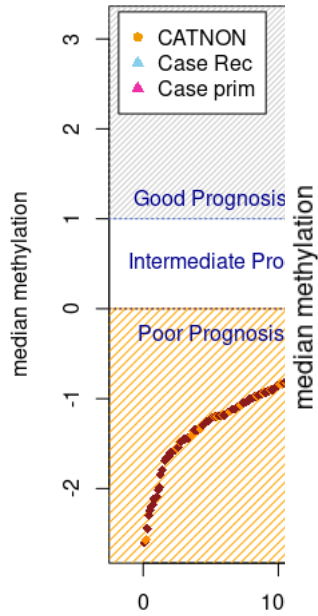
Gradering obv histologie is lastig

Vooronderzoek: Profiel obv methylering is voorspellend voor prognose





# Voorbeelden



# Voorstel

Doel: De graderingsmarkers naar de kliniek te brengen om te helpen bij de diagnostiek

Onderzoek:

1. werkt de gradering ook bij oligodendrogliomen
  1. *Te weinig oligodendrogliomen tot nu toe onderzocht,*
  2. *deze hebben wel vergelijkbare mechanismen van maligniteit*
  
2. Inclusie van andere prognostische markers
  1. *Om de waarde in te schatten moet je alle variabelen die van belang zijn voor de overleving van de patient gezamenlijk bekijken*
  2. *Met name 'residual tumour volume' niet goed onderzocht*

# Methode

1. ~150-200 methylerings arrays van oligodendrogliomen en astrocytomen en bepaling van het maligniteitsprofiel
2. Bepaling van het residuele tumor volume en verzamelen andere (prognostische) klinische data
3. Analyse van de prognostische waarde van ons profiel.

# Heel veel dank namens het hele Erasmus Team en tot volgend jaar!!

