

# Combined Drug Efficacy using EGFR and ASCT2 Inhibitors in Preclinical Models of Colorectal Cancer

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## Introduction

### Colorectal Cancer (CRC)

- 3rd most commonly diagnosed cancer & 2nd leading cause of cancer death in men and women combined in the U.S.
- Each year, about **150,000 Americans** are diagnosed with this disease and **more than 50,000 die**.
- Symptoms** include a change in bowel habits, diarrhea, constipation, discomfort in the abdomen
- Treatments** include Surgery, Radiation Therapy, Chemotherapy, Targeted Therapy

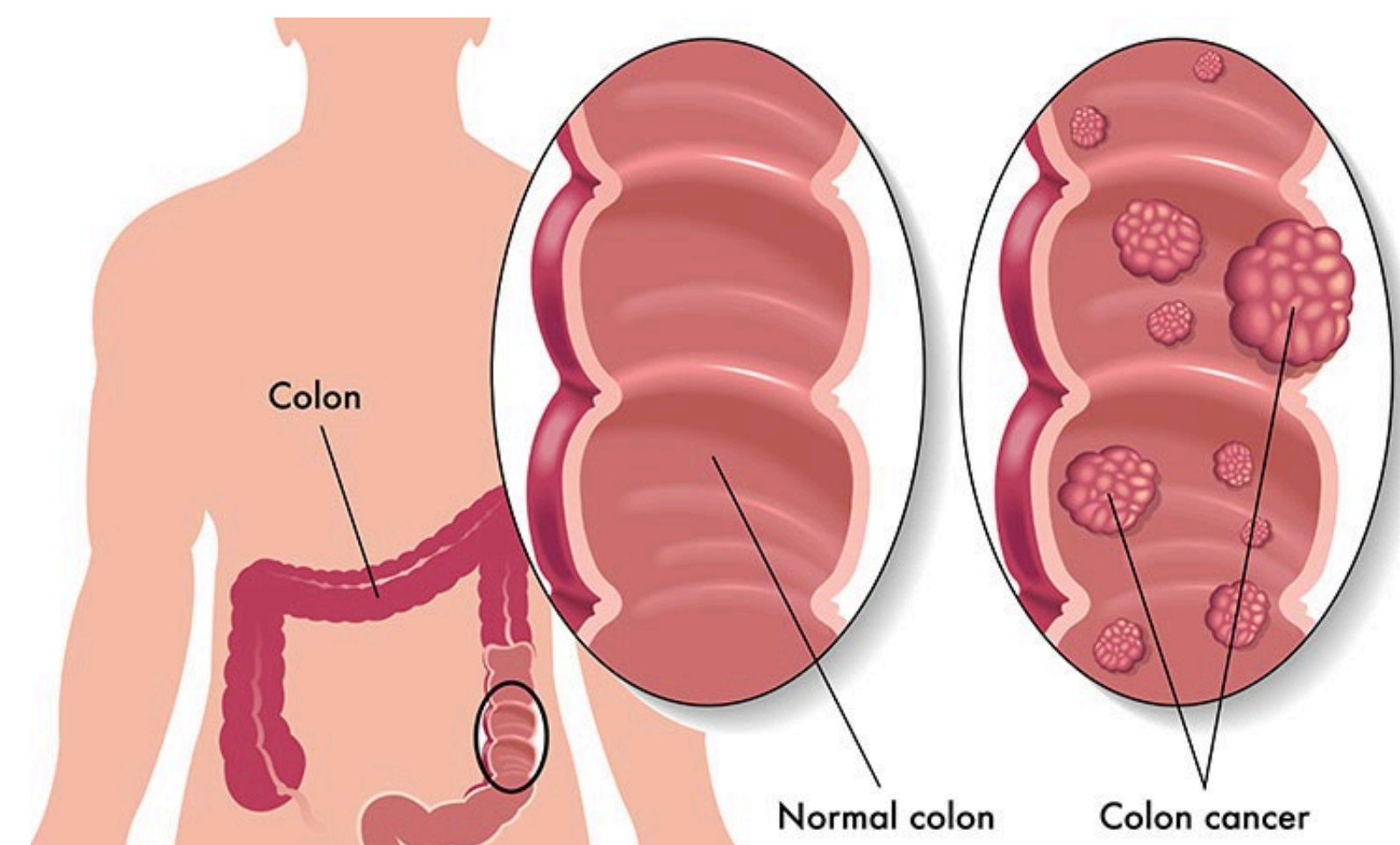


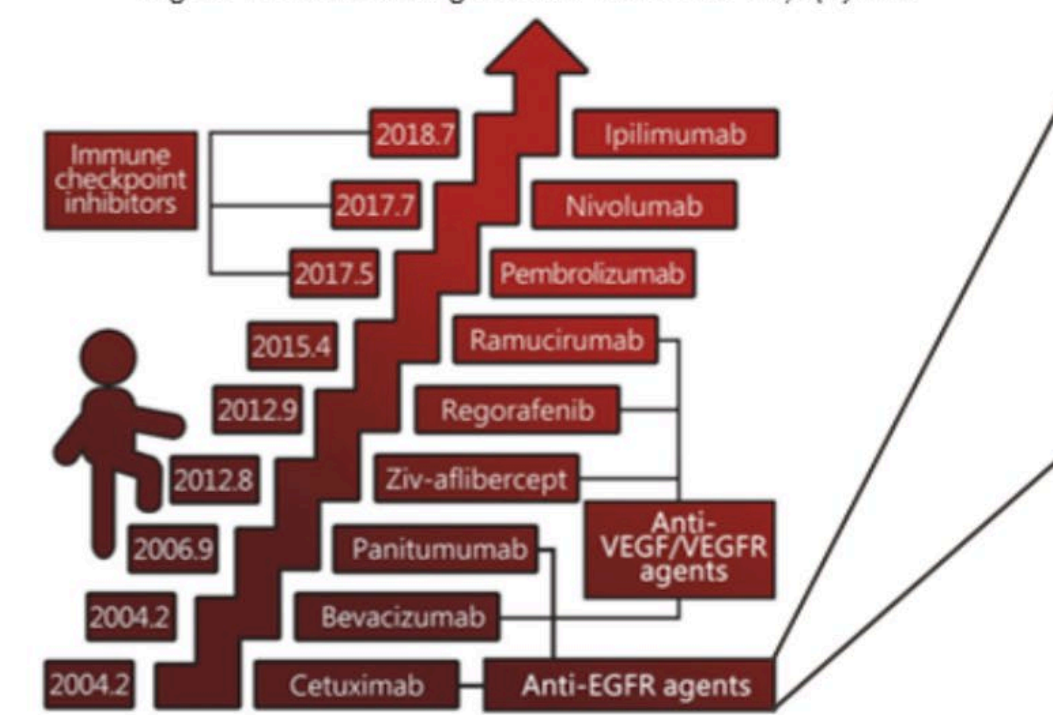
Illustration of cancer in body.

## Hypothesis

Combination drug treatment using EGFR and ASCT2 inhibitors will lead to greater response in colorectal cancer compared to single-drug therapy.

### Failure of EGFR-targeted therapies in colorectal cancer

Signal Transduct Target Ther. 2020 Mar 20;5(1):22.



• **Response to Cetuximab<sup>1</sup>:**  
17% of KRAS WT CRC patients,  
0% of KRAS mut CRC patients

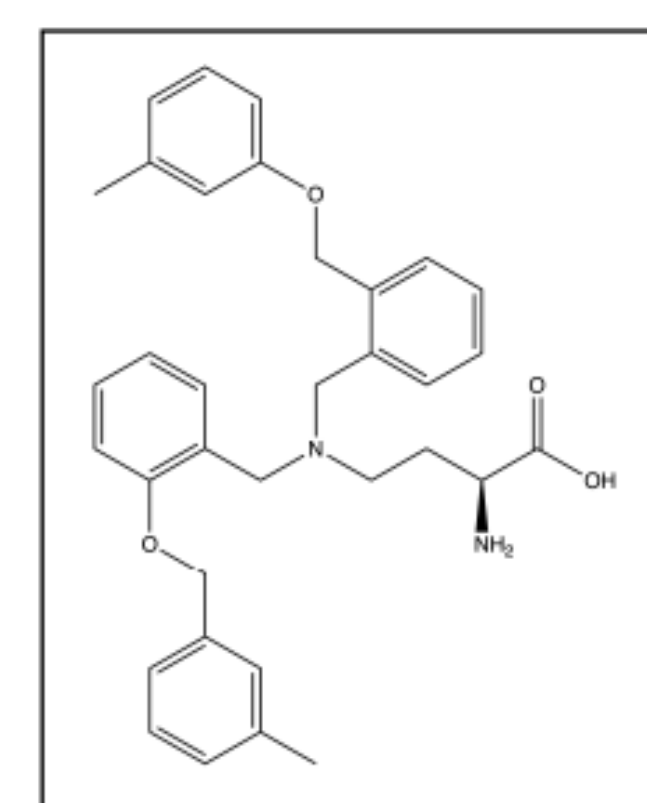
• **Response to Panitumumab<sup>2</sup>:**  
10.8% of mCRC patients

Reference  
1. N Engl J Med. 2004 Jul 22;351(4):337-45.  
2. J Clin Oncol. 2009 Apr 1;26(10):1628-34.

## Targeted Therapy

### EGFR

- Found at high levels in cancer cells which causes proliferation
- Panitumumab is an EGFR inhibitor and is for treating metastatic colorectal cancer



V-9302

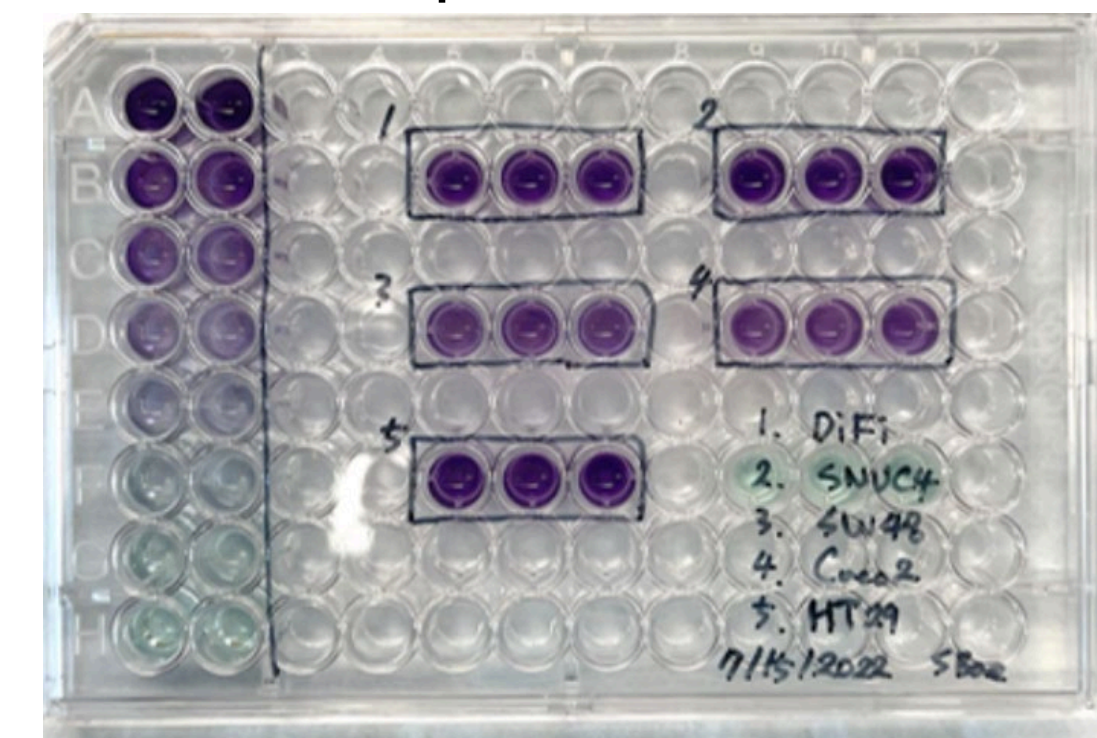
### ASCT2

- Found at high levels in cancer cells which causes proliferation
- Inhibitor of glutamine metabolism V-9302 and CDP selectively target the amino acid transporter ASCT2

## Materials & Methods

### BCA Protein Assay

- Quantitate protein concentration of each sample



### Monotherapy & Combined Drug Therapy (Cell Viability Assay)

#### ○ Panitumumab Treatment

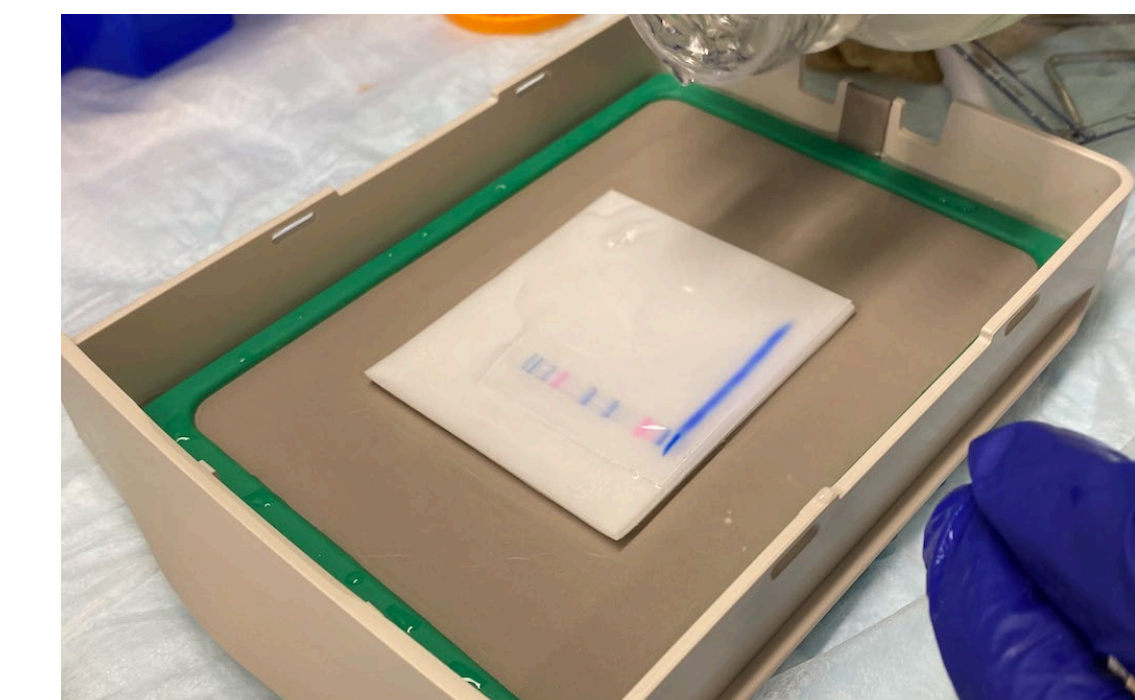
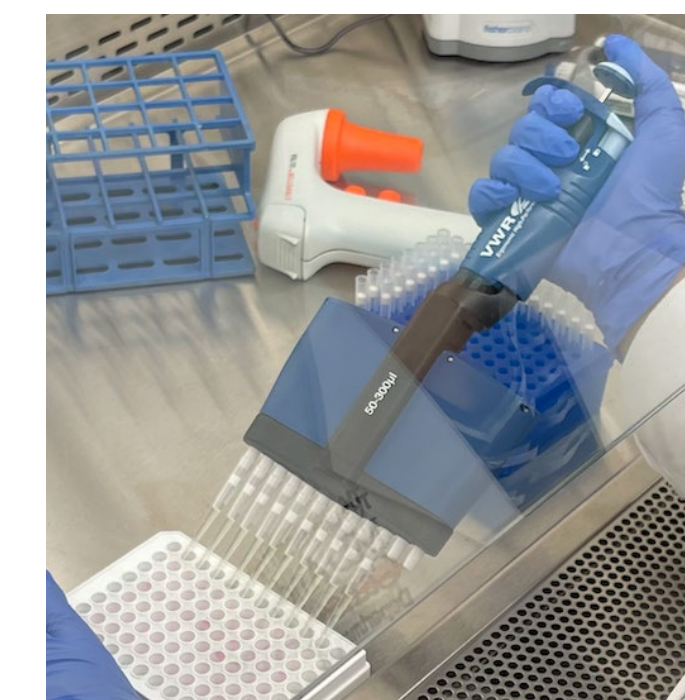
Cell Number: 5000 cells/well  
Dose (ug/mL): 0.01, 0.1, 1, 10, 25, 50, 100, 500, 1000  
Incubation time: 48 hrs

#### ○ V-9302 Treatment

Cell Number: 5000 cells/well  
Dose (uM): 0.001, 0.01, 0.1, 1, 5, 10, 25, 50, 100  
Incubation time: 48 hrs

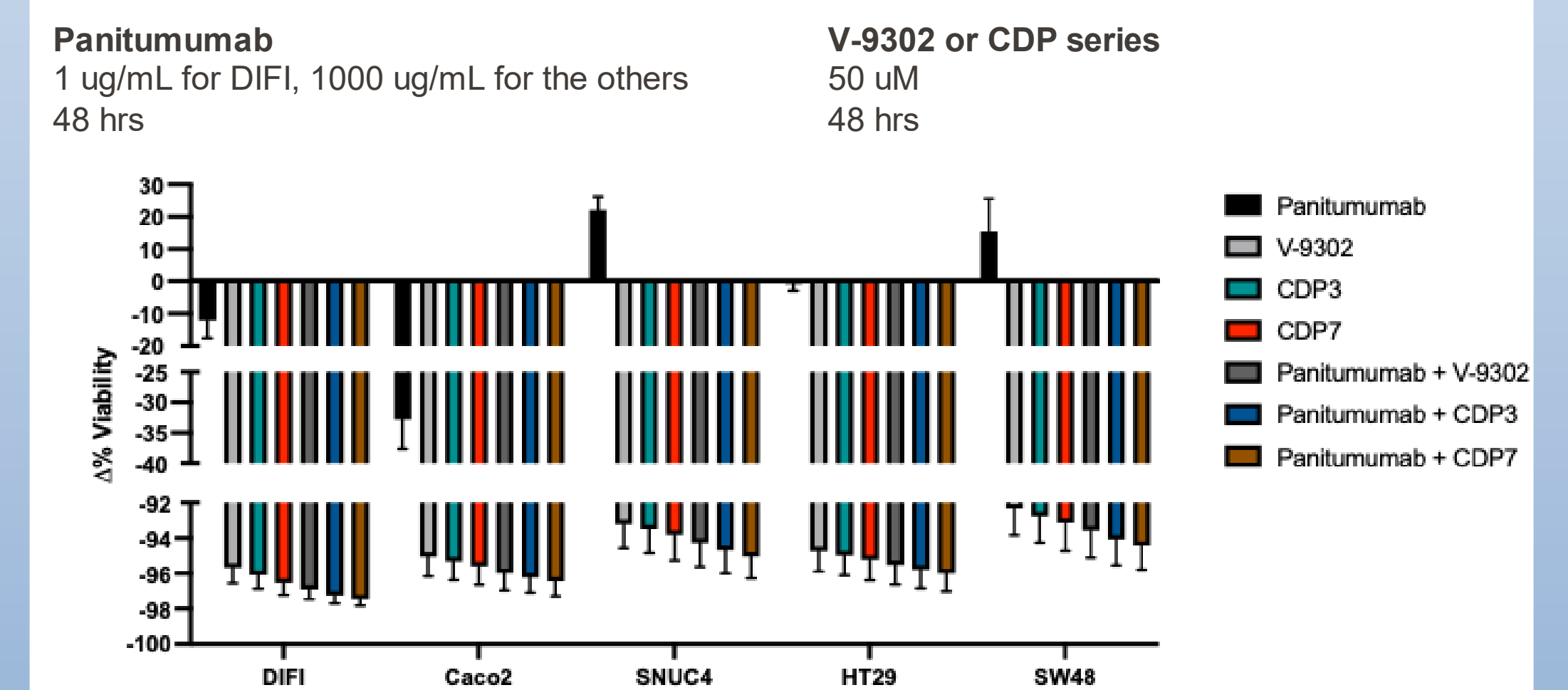
### Western Blot

- Running & Transfer Condition
  - Run 70V for 20 minutes until sample has run through the stacking gel. At that point run 150V for 30 minutes
  - The membranes were transferred (1.3A, 25V, 10 minutes)
- Antibody: Phospho-EGF Receptor, EGF Receptor, ASCT2, Anti-GAPDH antibody, Anti-rabbit IgG HRP-linked Antibody



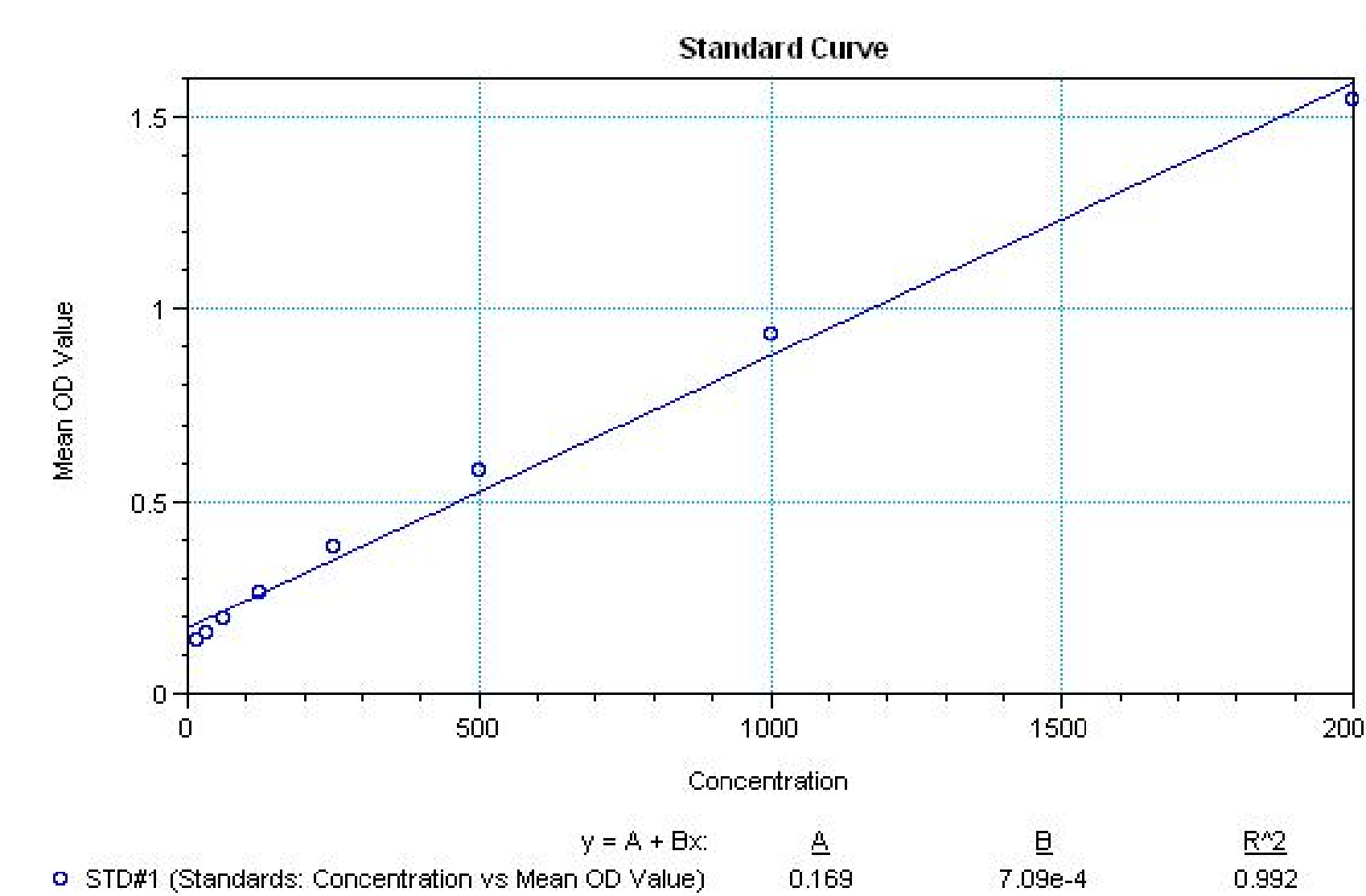
## Combined Drug Therapy Results

### Combination treatment using Panitumumab and V-9302 as well as CDP

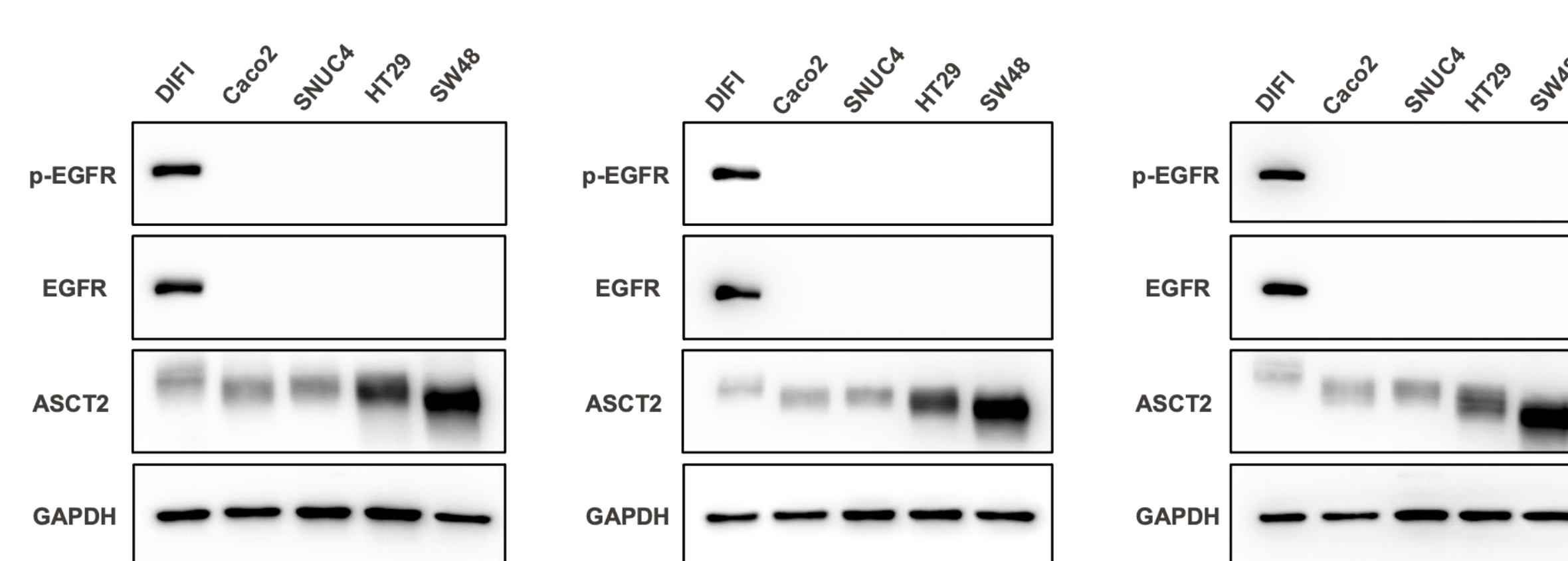


## Results

### BCA Protein Assay

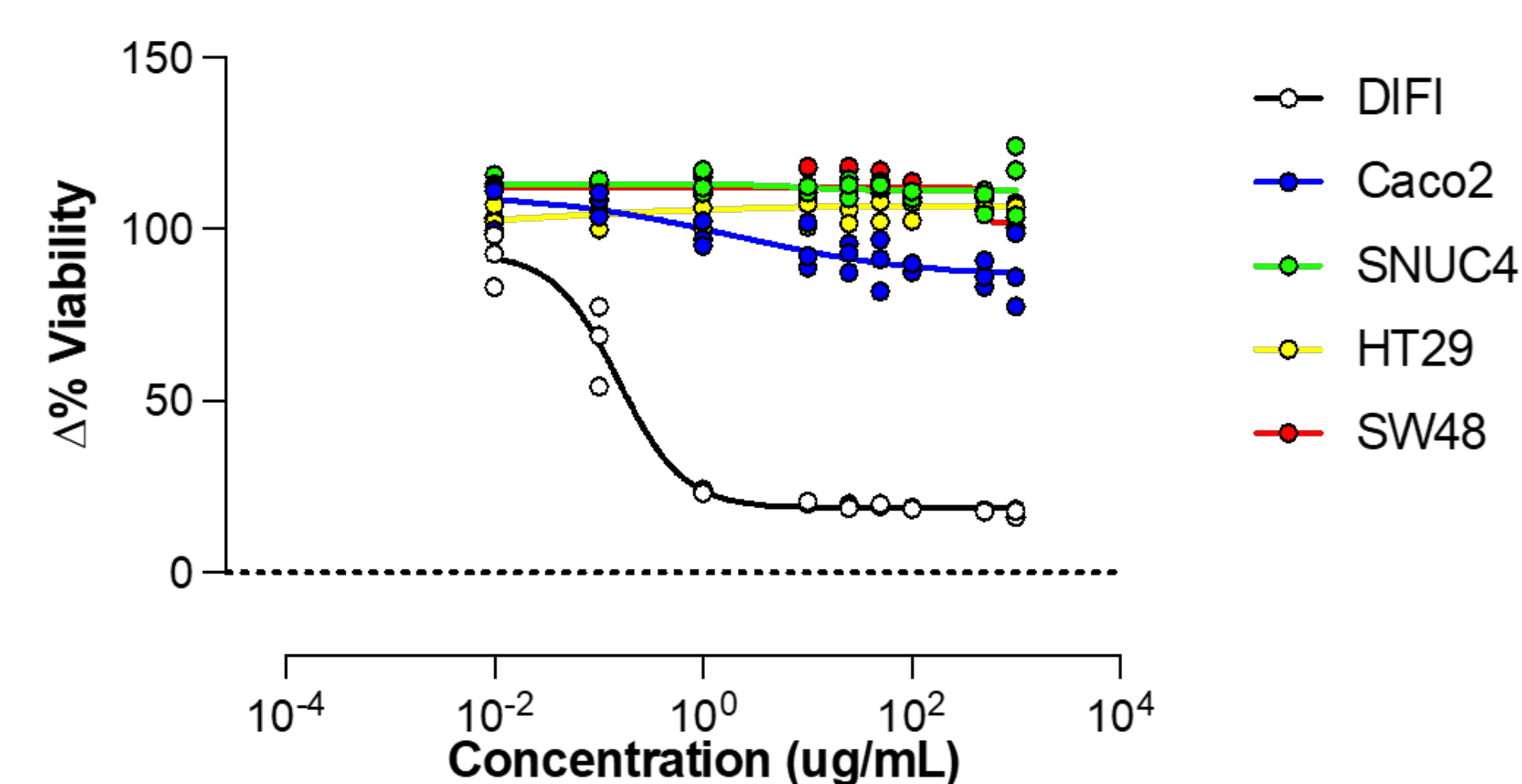


### Western Blot

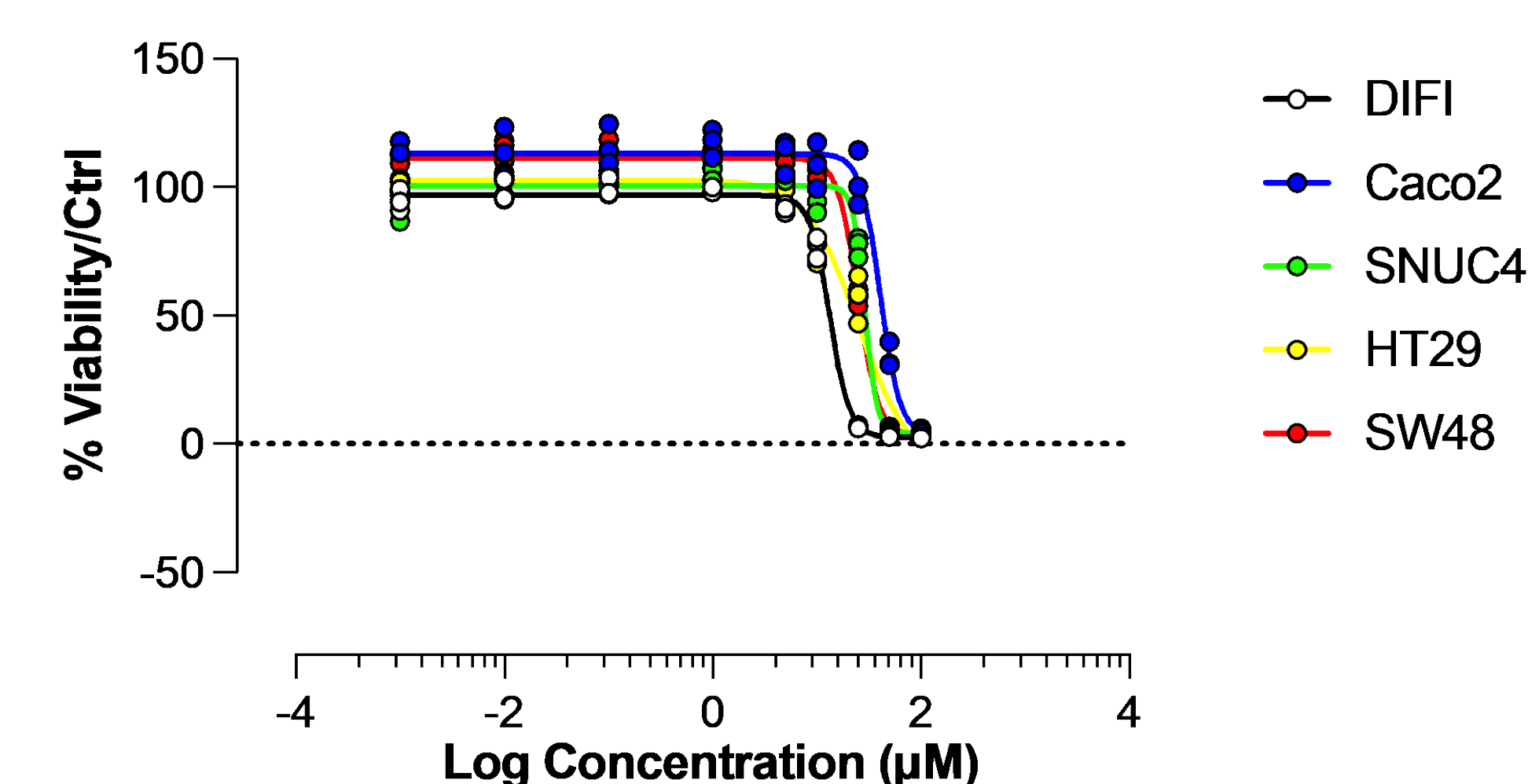


## Single Drug Therapy

### Panitumumab



### V-9302



## References

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- Cohen, A. S., Geng, L., Zhao, P., Fu, A., Schulte, M. L., Graves-Deal, R., Washington, M. K., Berlin, J., Coffey, R. J., & Manning, H. C. (2020). Combined blockade of EGFR and glutamine metabolism in preclinical models of colorectal cancer. *Translational oncology*, 13(10), 100828.
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