Anti-CD47 Peptide Combined with Oncolytic Vesiculovirus-Driven Intratumoral Immunotherapy for Colorectal Cancer

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PURPOSE

- In this study we engineered VMG genome to express a proteolytic enzyme (ENZ) that break down cellular debris in the tumor microenvironment to help immune cells reach and identify cancer cells.
- We combined GFM peptide with oncolytic virus VMG expressing ENZ and evaluated the synergistic effects.
- Our study suggests a new strategy for immune-virotherapy for colorectal cancer.

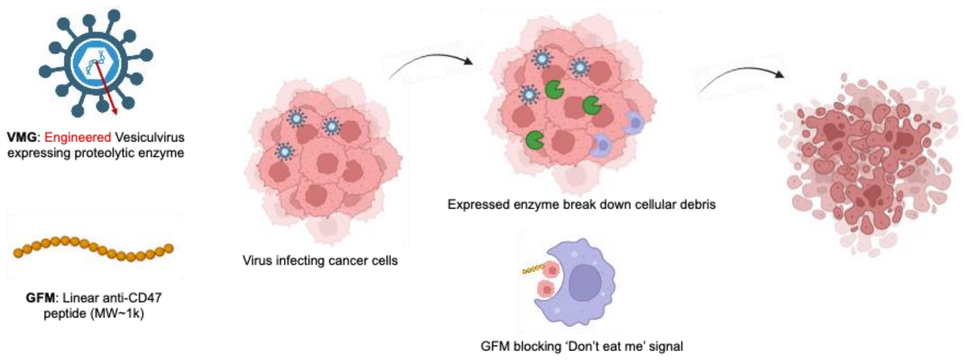


Figure 1: Combination of anti-CD47 peptide and oncolytic virotherapy

METHODS

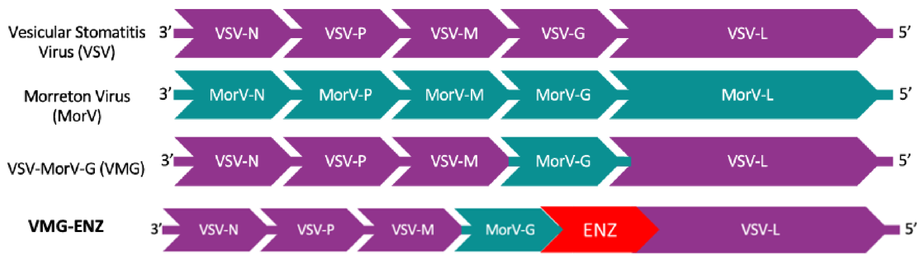


Figure 2: VMG-Hybrid Virus Construct

- The chimeric virus (VMG) was engineered by insertion of the MorV G gene and specific intergenic regions into the backbone of pVSV-XN2, replacing the VSV glycoprotein (G) gene.
- The resultant engineered virus VMG also included the proteolytic enzyme ENZ gene to express ENZ.

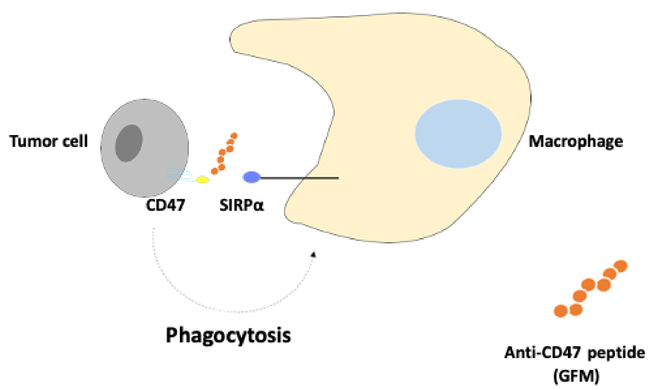
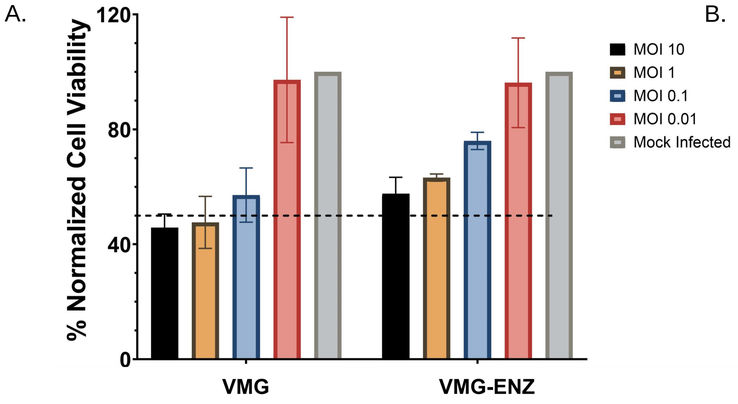


Figure 3: GFM peptide inhibiting 'don't eat me signal' of CD47

- CD47 is an integral membrane glycoprotein recognized as innate immune checkpoint overexpressed in several cancers including colorectal cancer.
- GFM is a 12-mer anti-CD47 peptide that we discovered by phage display biopanning. GFM showed to bind CD47 and blocking CD47/SIRPα interaction.

RESULTS



B.

Cells	MOI	Virus	Cell Viability (%)
LoVo	0.1	VMG	56.60
		VMG-ENZ	78.08
	1	VMG	47.11
		VMG-ENZ	62.32
	10	VMG	45.56
		VMG-ENZ	53.52

Figure 4: A) *In-vitro* cytotoxicity activity of VMG-ENZ in LoVo cells. B) *In-vitro* cell viability assay results. Data were collected from three replicates. Bars indicate mean ± SEM.

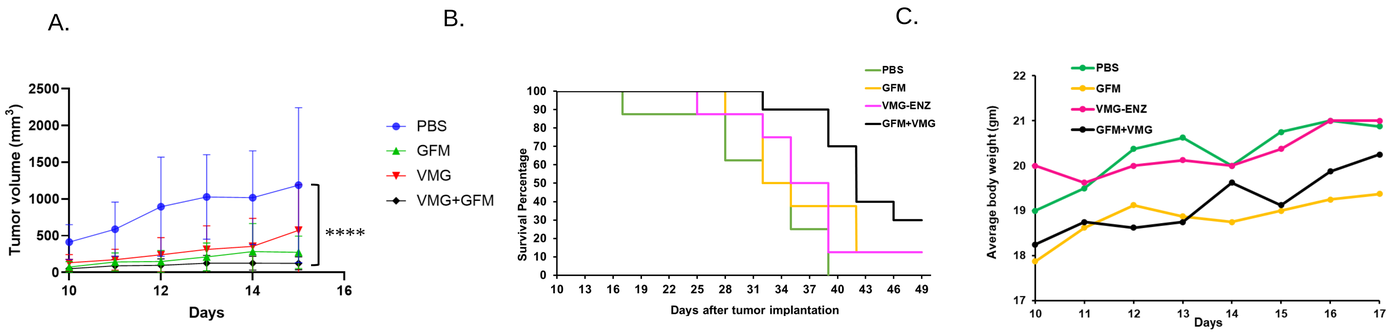


Figure 5: A) Antitumor activity of GFM and VMG-ENZ combination in CT26 colon cancer mouse model. B) Survival study of GFM peptide and VMG-ENZ combination in CT26 model. C) Body weight changes of CT26-tumor bearing BALB/c mice.

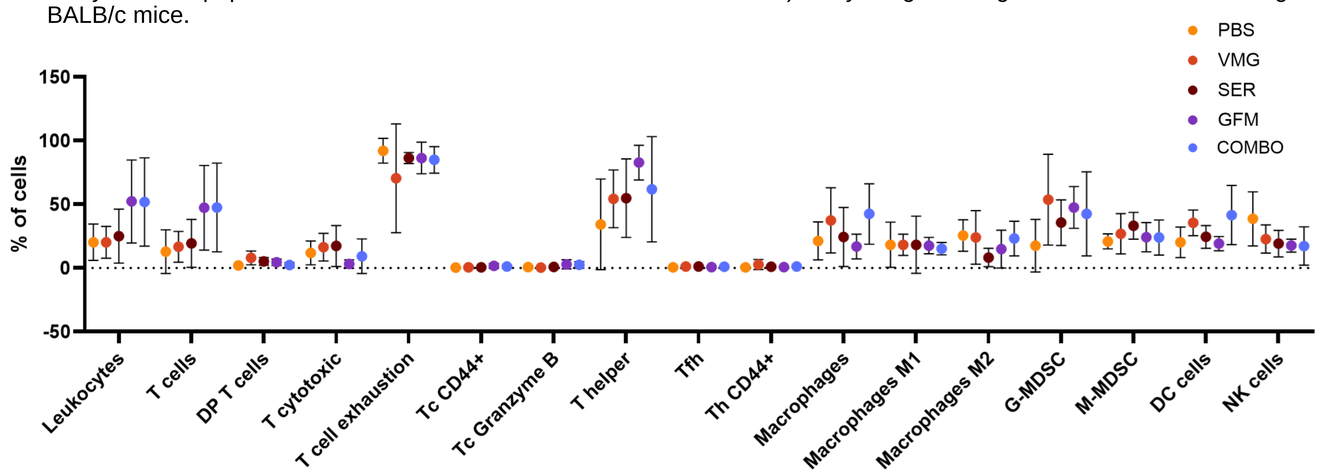


Figure 6: Flowcytometry analysis of tumor-infiltrating immune cells following treatments in MC38 mouse model.

CONCLUSIONS

- We observed a synergistic effect of oncolytic virus VMG-ENZ and anti-CD47 peptide.
- A new strategy between oncolytic virus expressing a proteolytic enzyme and immune checkpoint inhibitors can be considered for the treatment of colorectal cancer.

FUNDING

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