

Mark cancer cells for CTL attack through coating with viral antigenic peptides

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Cancer Immunotherapies

Vaccination-

central tolerance

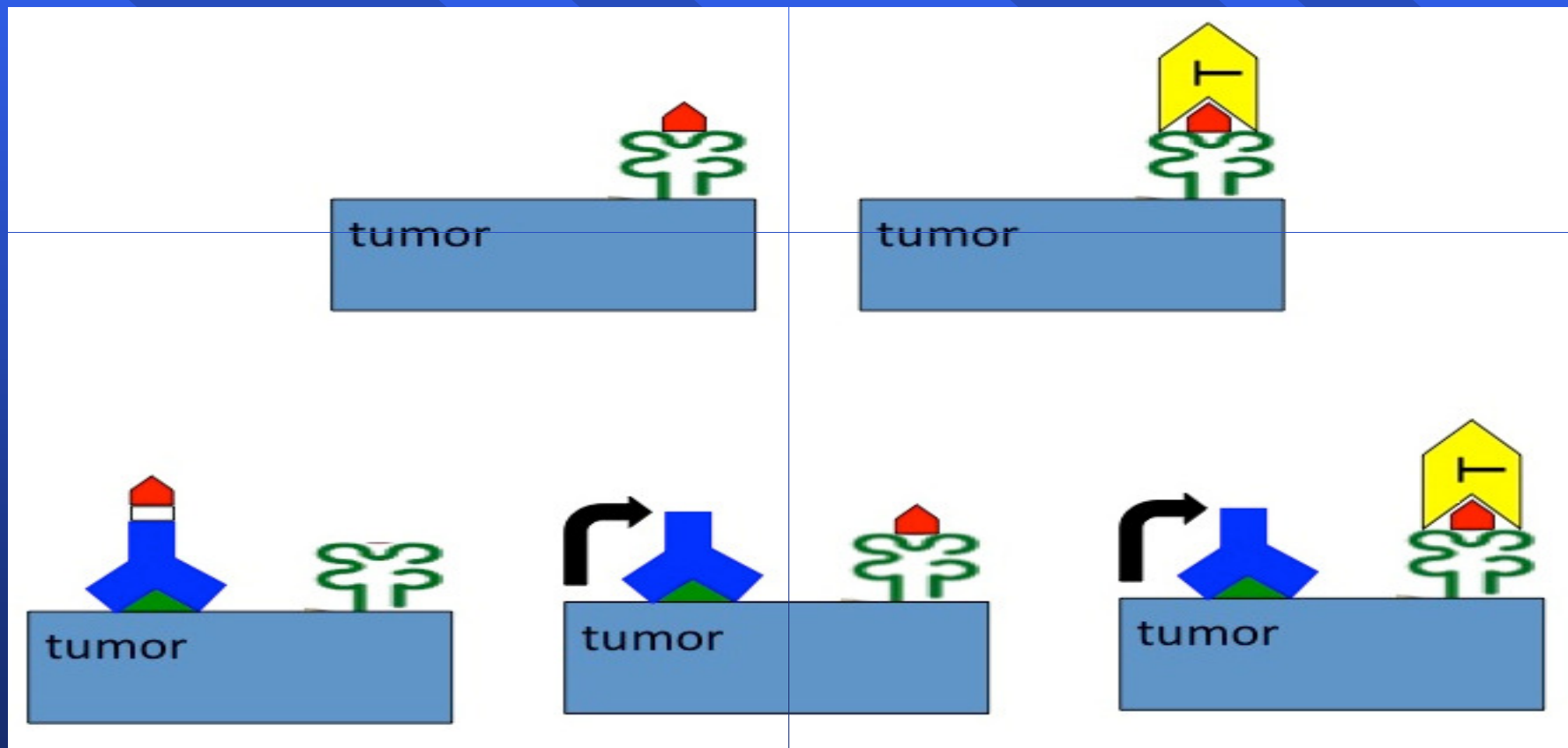
Adoptive transfer T cells-

culture T cells and engineer T cells

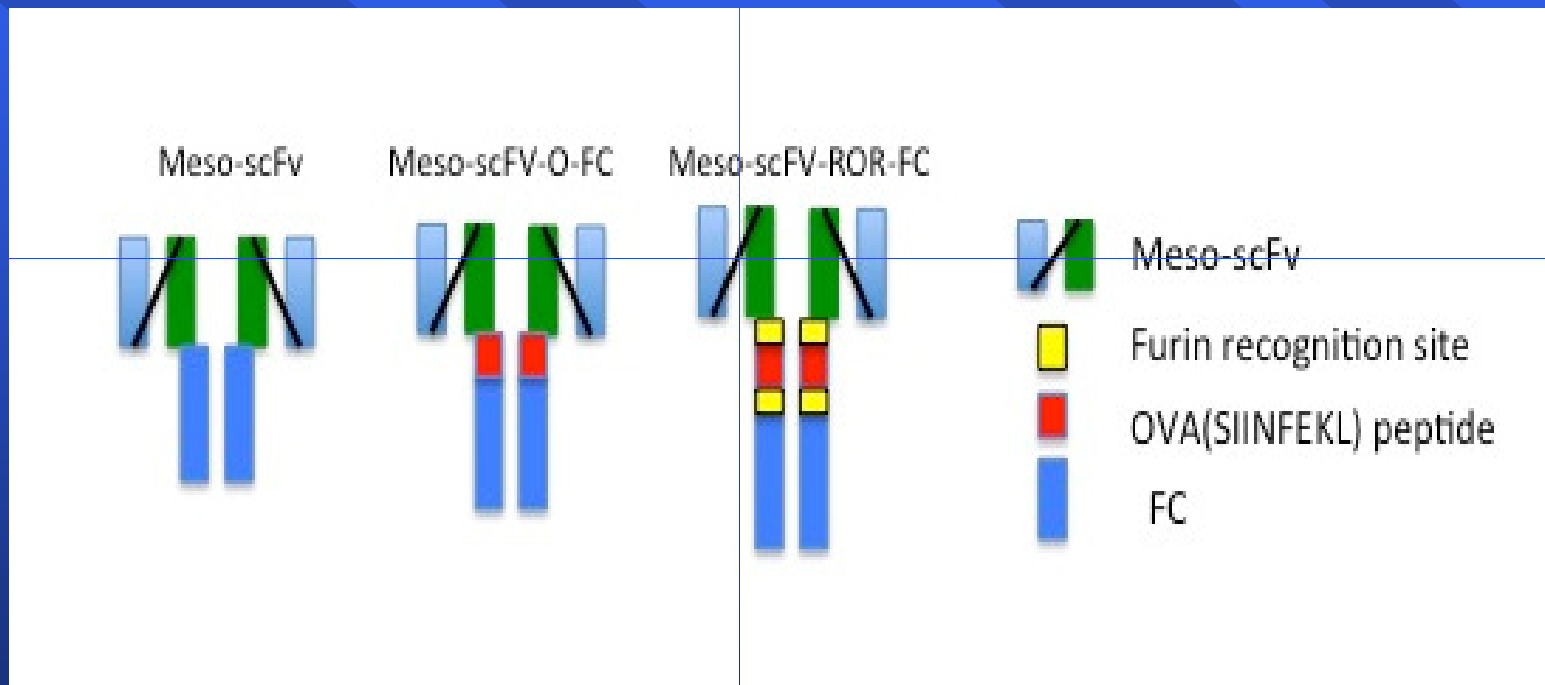
Targeted Coating With Antigenic Peptide

Renders Tumor Cells Susceptible to CD8+
T Cell-mediated Killing

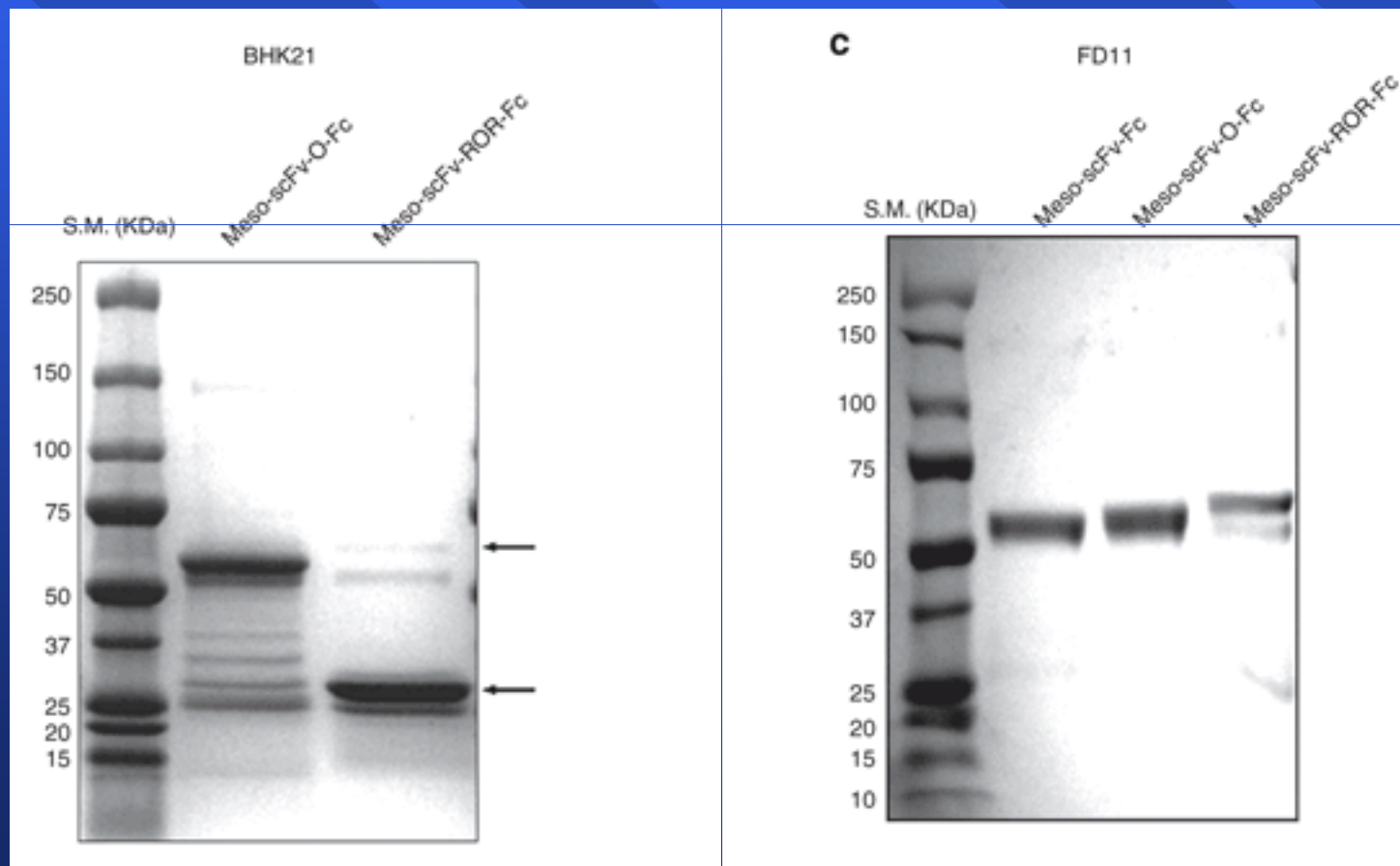
How to coat viral antigenic peptides on tumor cells



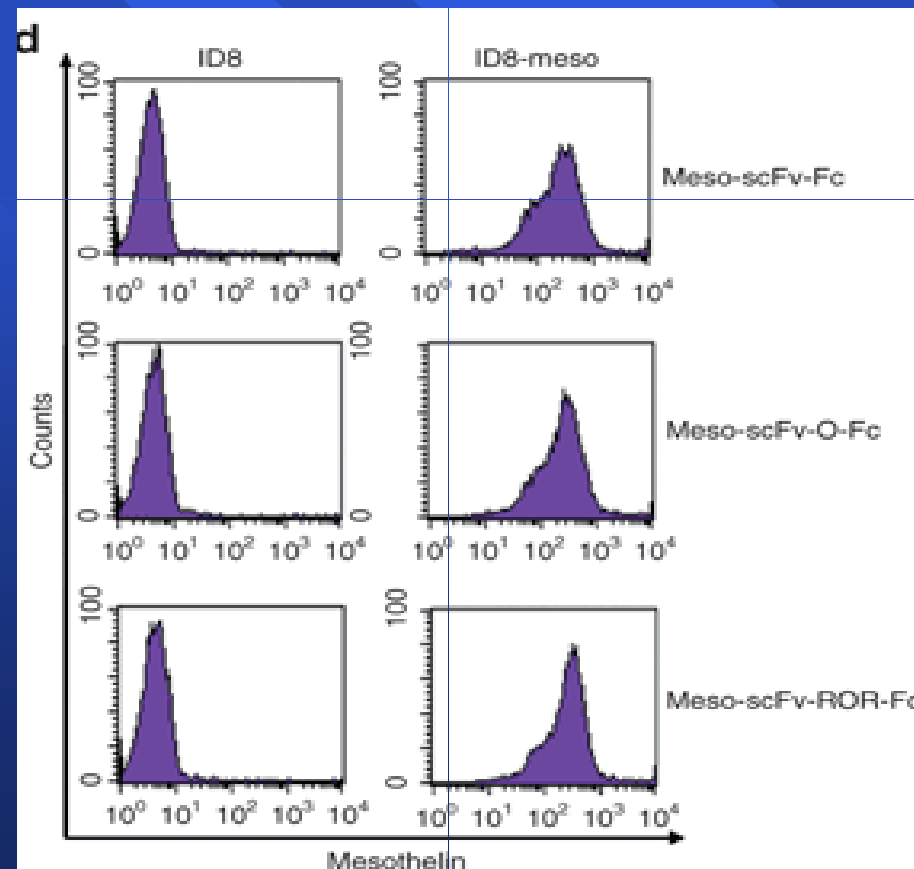
Generation of anti-human mesothelin single chain variable fragment (scFv) conjugated with Fc (IgG2a) protein containing OVA peptide alone or flanked by furin cleavage sites.



Characterization of anti-human mesothelin single chain variable fragment (scFv) conjugated with Fc (IgG2a) protein containing OVA peptide alone or flanked by furin cleavage sites.



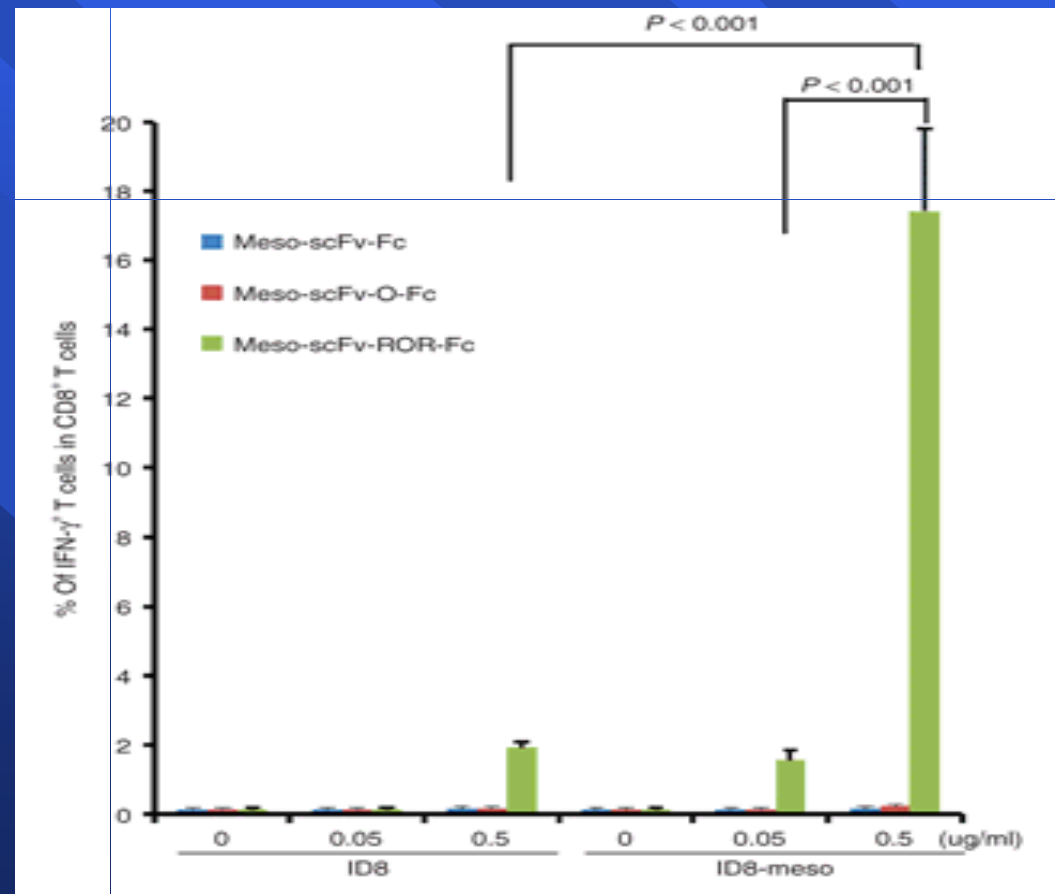
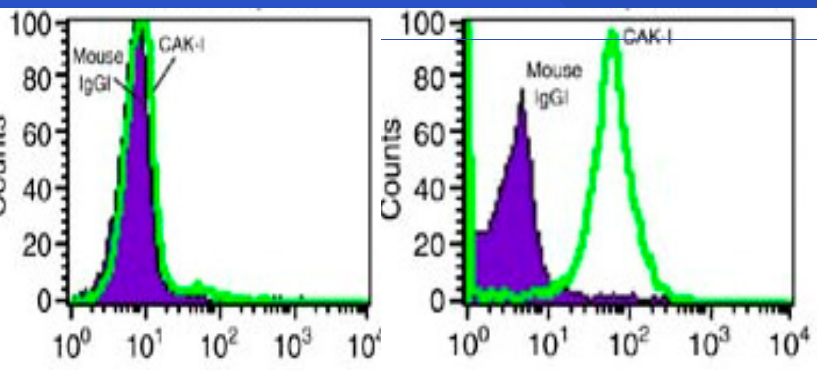
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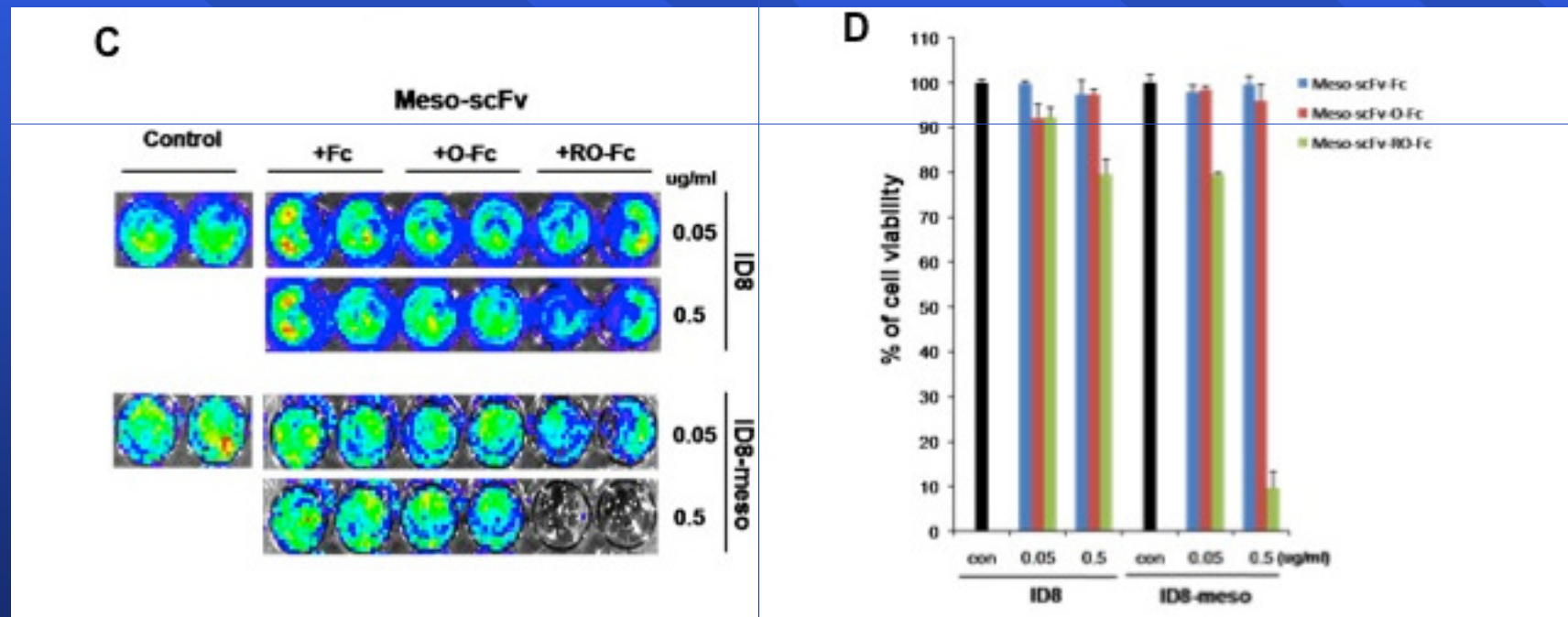
Characterization of the MHC class I presentation of OVA peptide to OVA-specific CD8⁺ T cells by ID8-meso tumor cells treated with Meso-scFv-ROR-Fc.

ID8

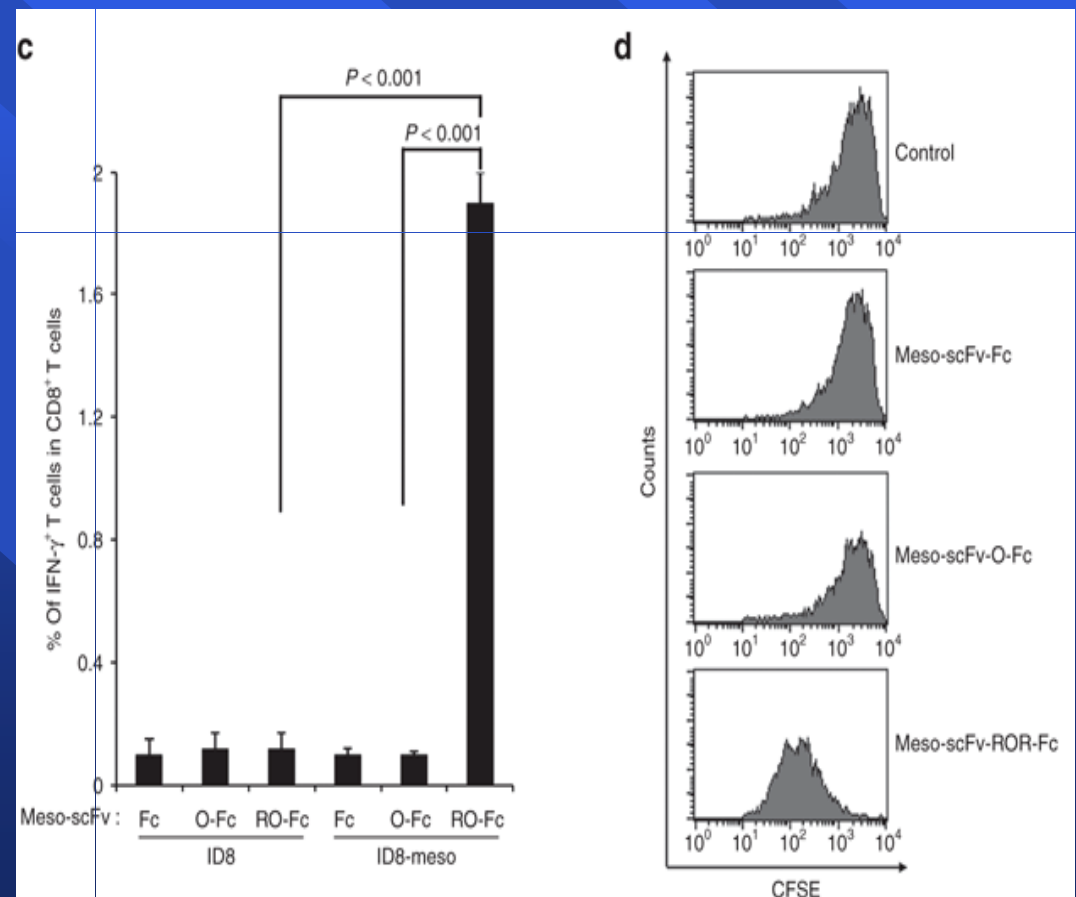
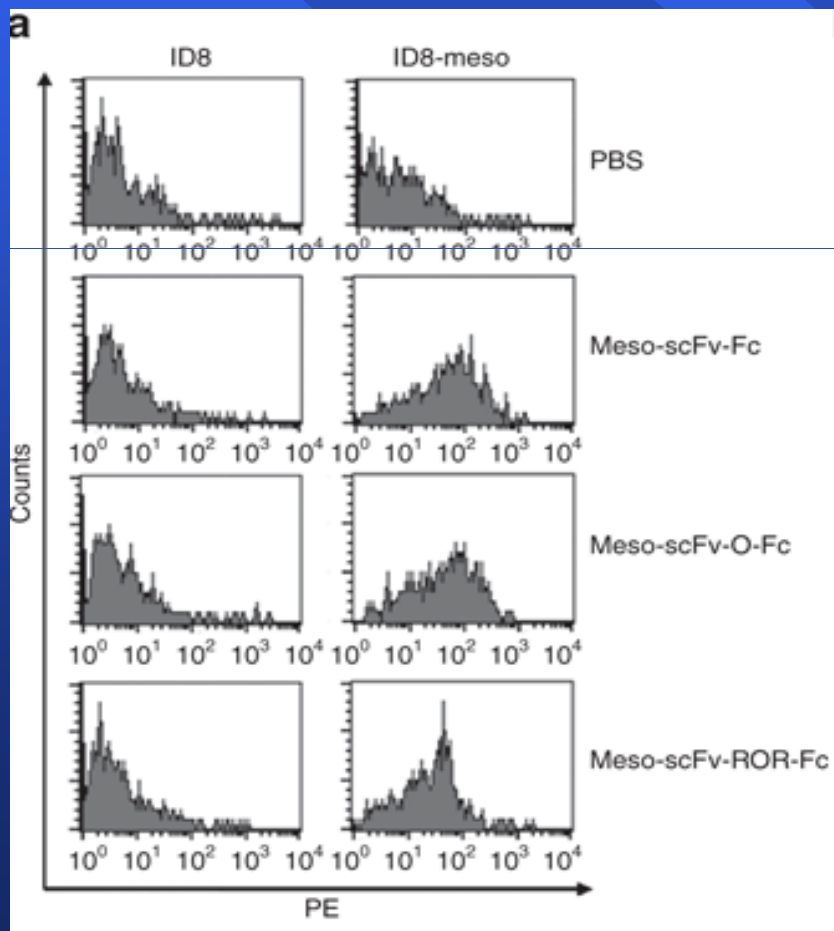
ID8-meso



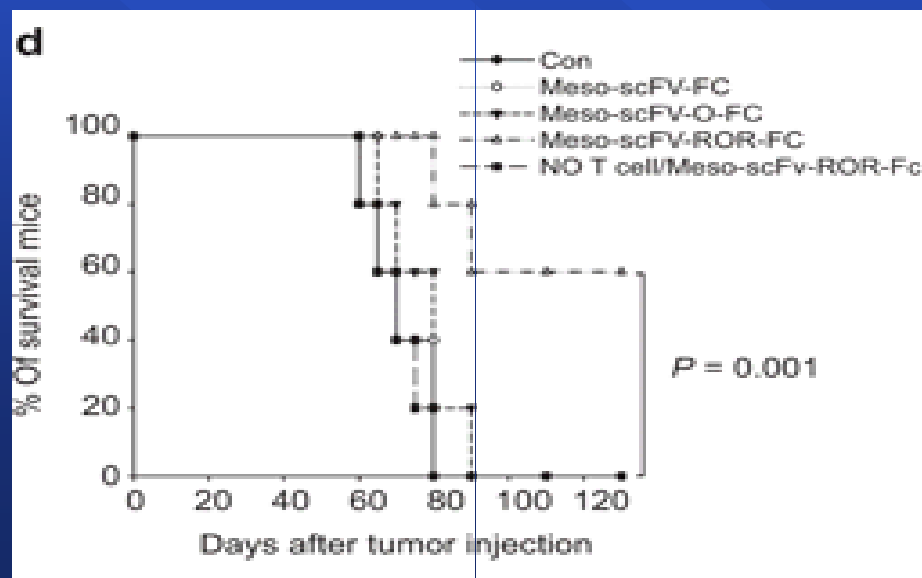
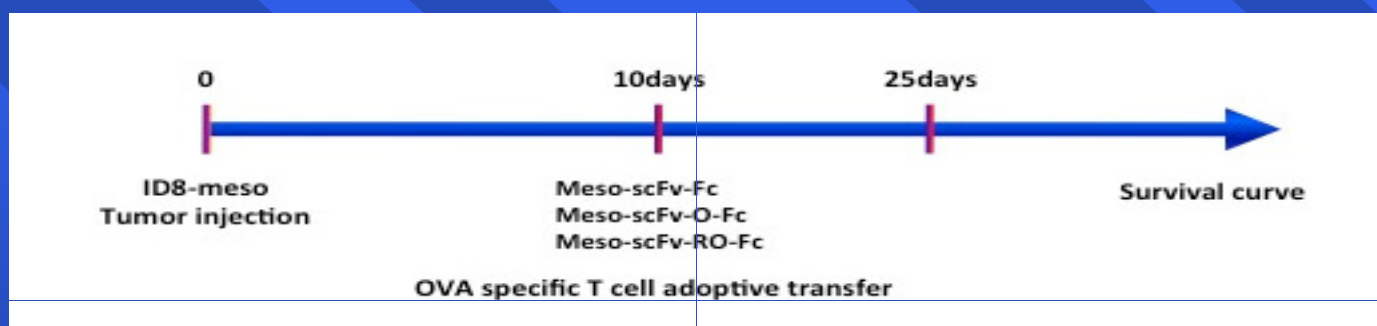
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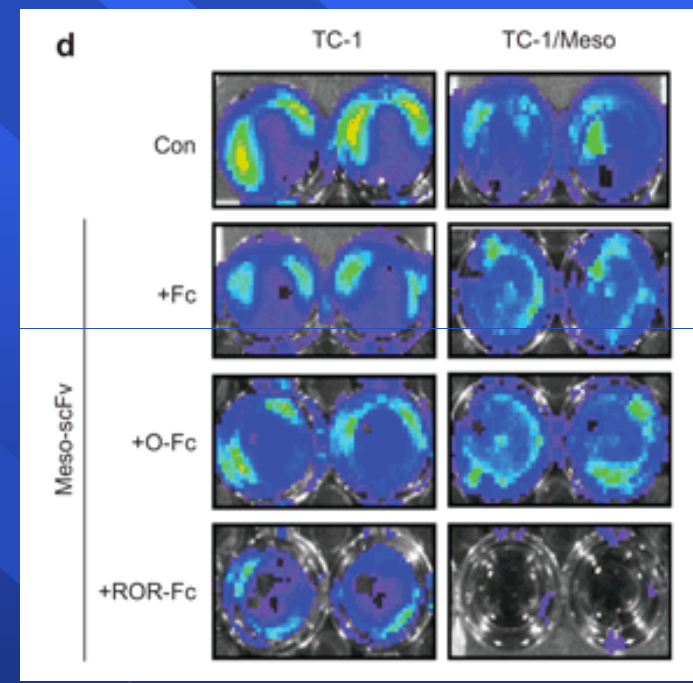
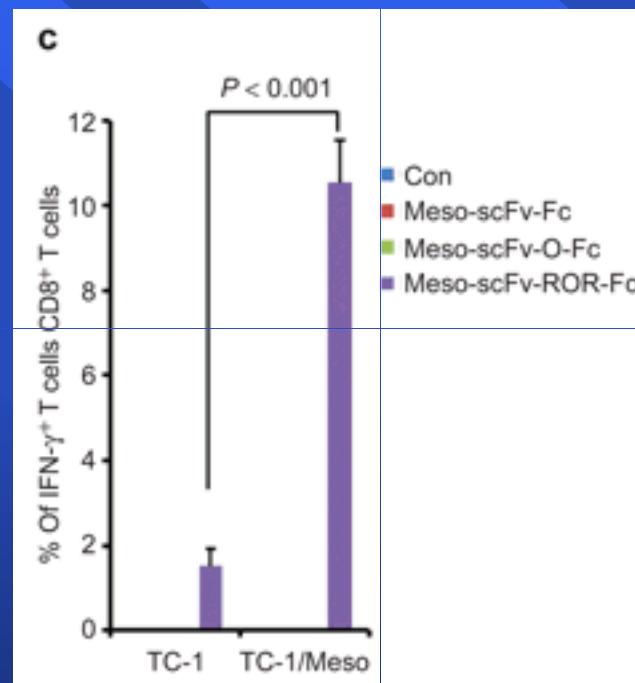
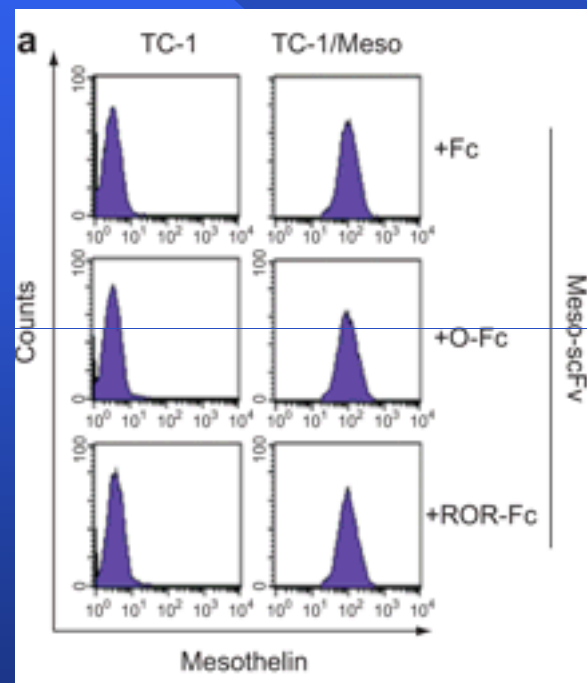
Characterization of the MHC class I presentation of OVA peptide to OVA-specific CD8⁺ T cells by Meso-scFv-ROR-Fc-treated ID8-meso tumor cells derived from the peritoneal cavity *in vivo*.



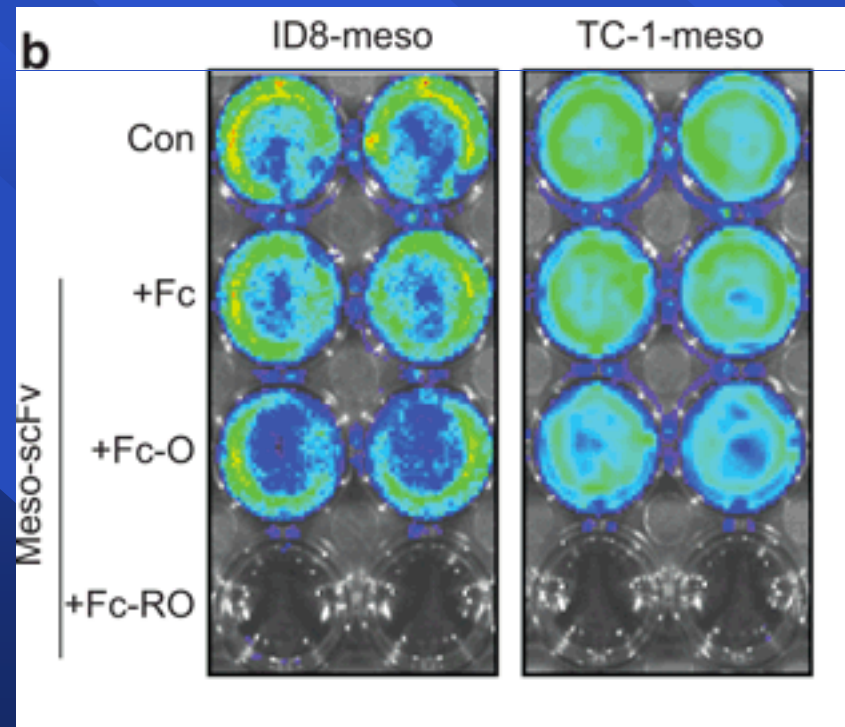
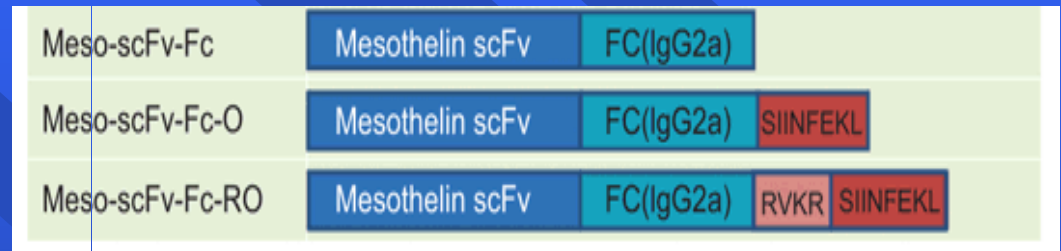
Characterization of *in vivo* therapeutic antitumor effects by various Meso-scFv-Fc chimeric proteins in conjunction with adoptive transfer of OVA-specific CD8⁺ T cells.



Meso-scFv-ROR-Fc facilitated activation of OVA-specific CD8⁺ T cells is not specific to ID8-meso cells

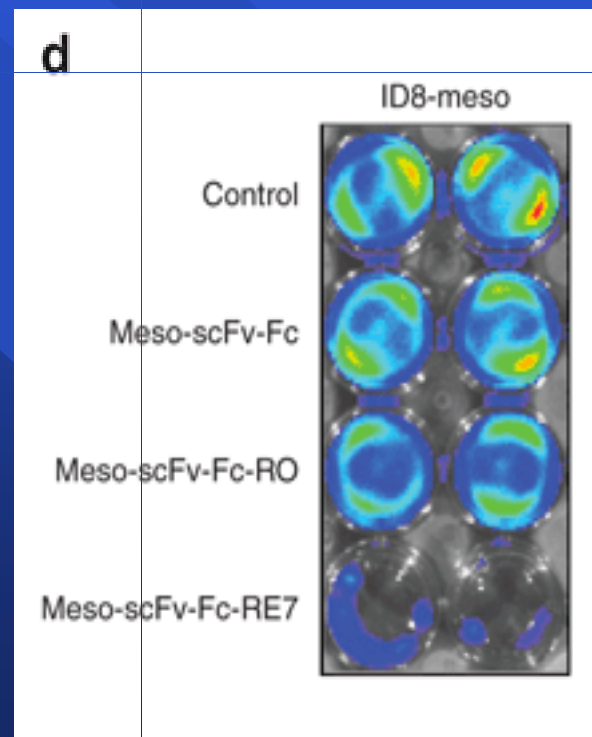
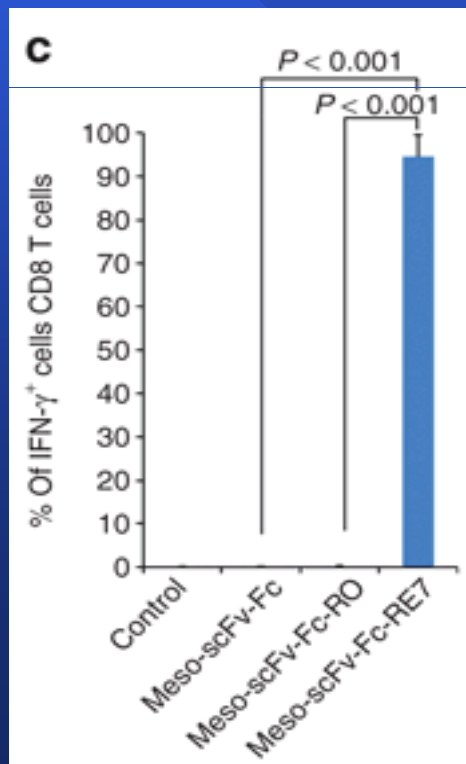


OVA peptide located at the carboxyl end of Meso-scFv-Fc chimeric protein can lead to MHC class I presentation of OVA peptide in different human mesothelin-expressing tumor cells, ID8-meso and TC-1/Meso

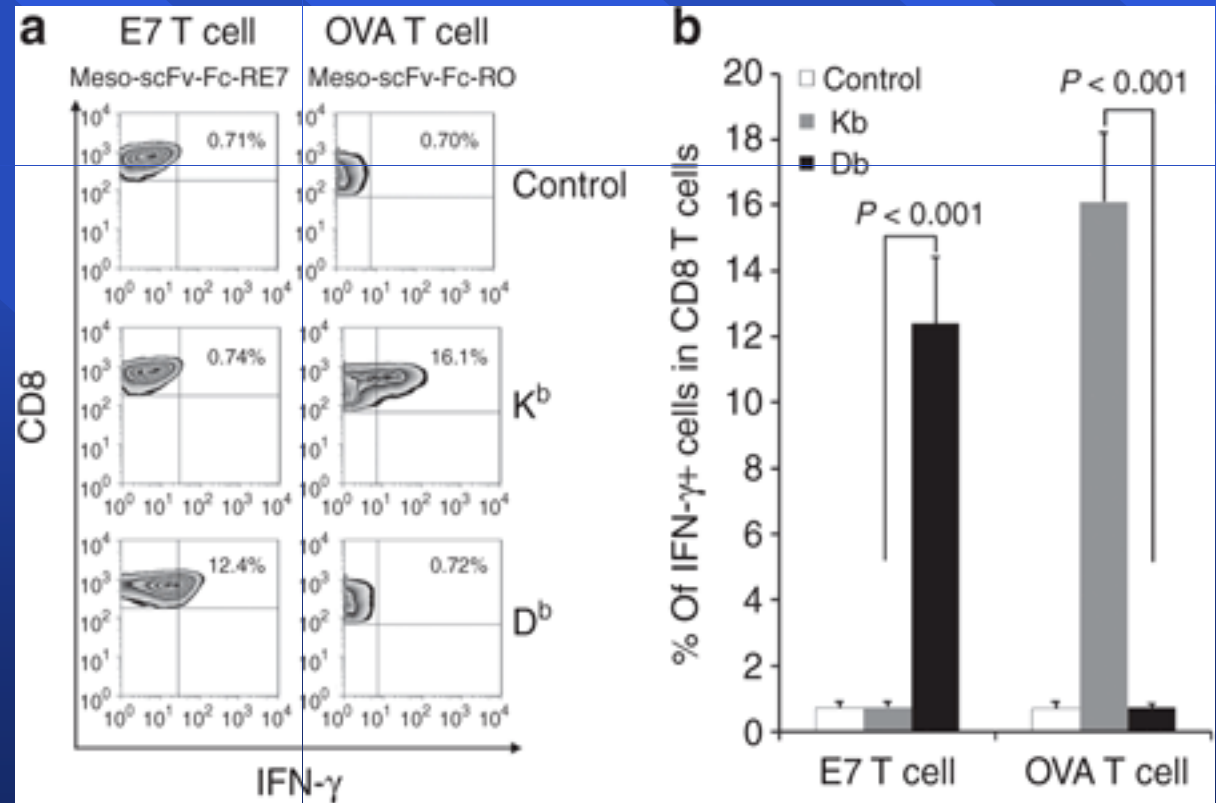
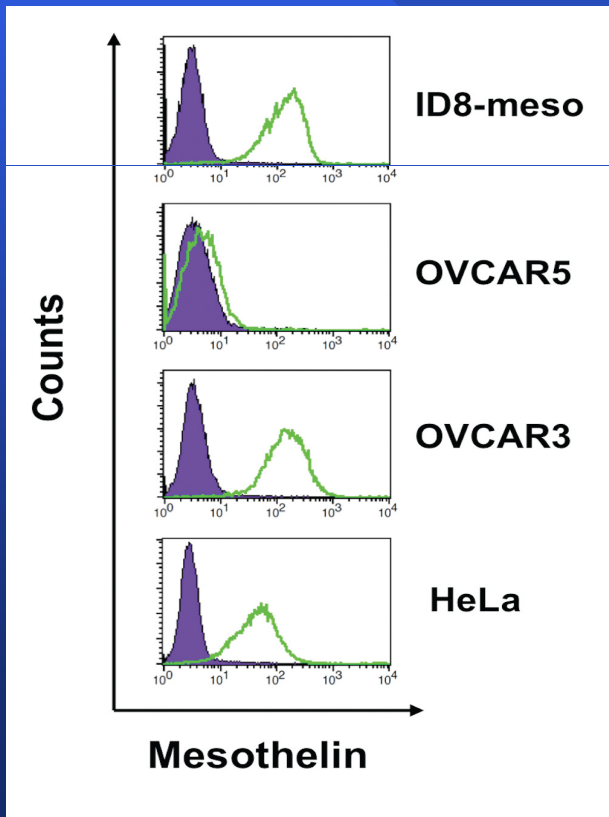


The Meso-scFv-Fc chimeric protein can be extended to HPV-16 E7 CTL epitope to induce loading of E7 peptide on MHC class I molecules of mesothelin-expressing tumors

Meso-scFV-Fc-RE7 Mesothelin scFv Fc(IgG2a) RVKR RAHYNIVTE E7 49-57



Human tumors expressing human mesothelin can also be targeted by the chimeric protein resulting in loading of CTL epitopes on MHC class I molecules



Summary

- **Meso-scFv-ROR-Fc binds mesothelin-expressing tumor cells and leads to MHC class I presentation of OVA peptide to OVA-specific CD8+ T cells.**
- **Meso-scFv-ROR-Fc combined with adoptive transfer of OVA-specific CD8+ T cells produces a potent antitumor effect**
- **OVA peptide located at the carboxyl end of Meso-scFv-Fc chimeric protein (Meso-scFv-Fc-RO) can lead to MHC class I presentation of OVA peptide in different human mesothelin-expressing tumor cells.**
- **The Meso-scFv-Fc chimeric protein can be extended to HPV-16 E7 CTL epitope to induce loading of E7 peptide on MHC class I molecules of mesothelin-expressing tumors**

Future experiments

Name	Structure
Meso-scFv-Fc	Meso-scFv Fc(IgG2a)
Meso-scFv-Fc-RM	Meso-scFv Fc(IgG2a) RVKR GILGFVFTL
Meso-scFv-Fc-multi	Meso-scFv Fc(IgG2a) GILGFVFTL FMYSDFHFI GLCTLVAML NLVPMVAYV
Meso-scFv-Fc-R-multi	Meso-scFv Fc(IgG2a) RVKR GILGFVFTL RVKR FMYSDFHFI RVKR GLCTLVAML RVKR NLVPMVAYV

2 influenza A peptides (GILGFVFTL and FMYSDFHFI)

1 EBV peptide (GLCTLVAML)

1 HCMV peptide (NLVPMVATV)

Acknowledgements

Tae Heung Kang

T.-C. Wu