MOLECULAR FEATURES OF THE INTEGRIN RECEPTOR AND ITS INTERACTION WITH THE FMDV, AN IN SILICO STUDY

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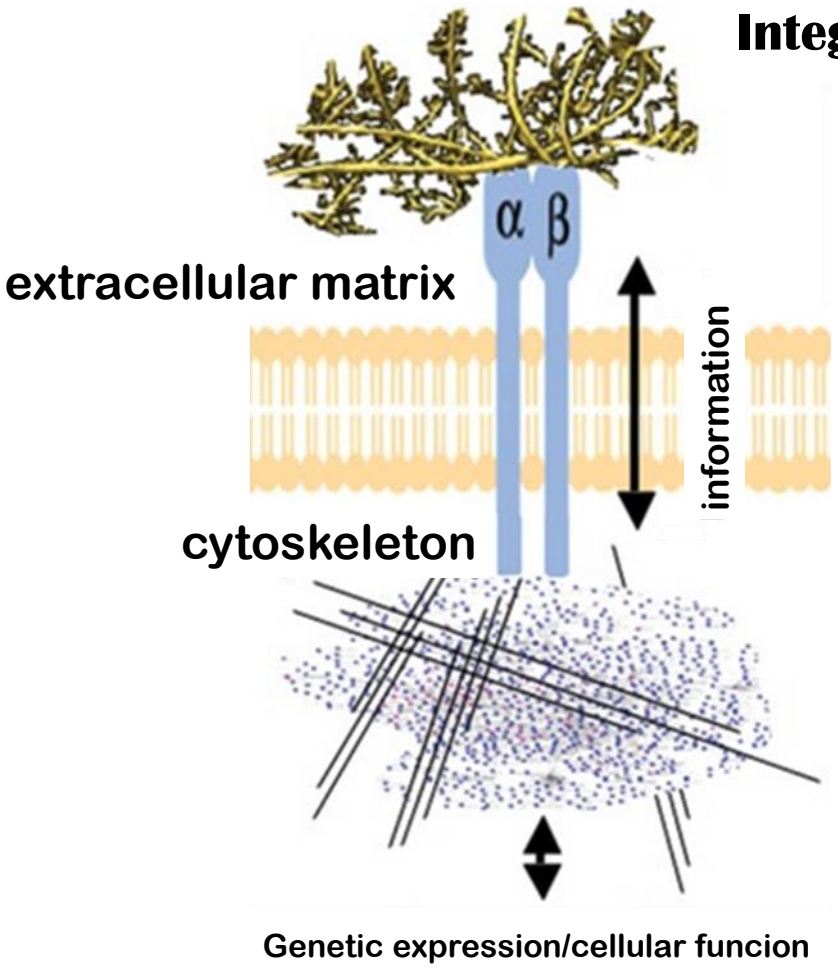
INTEGRIN RECEPTOR INTERACTION



Integrate

Metalloprotein

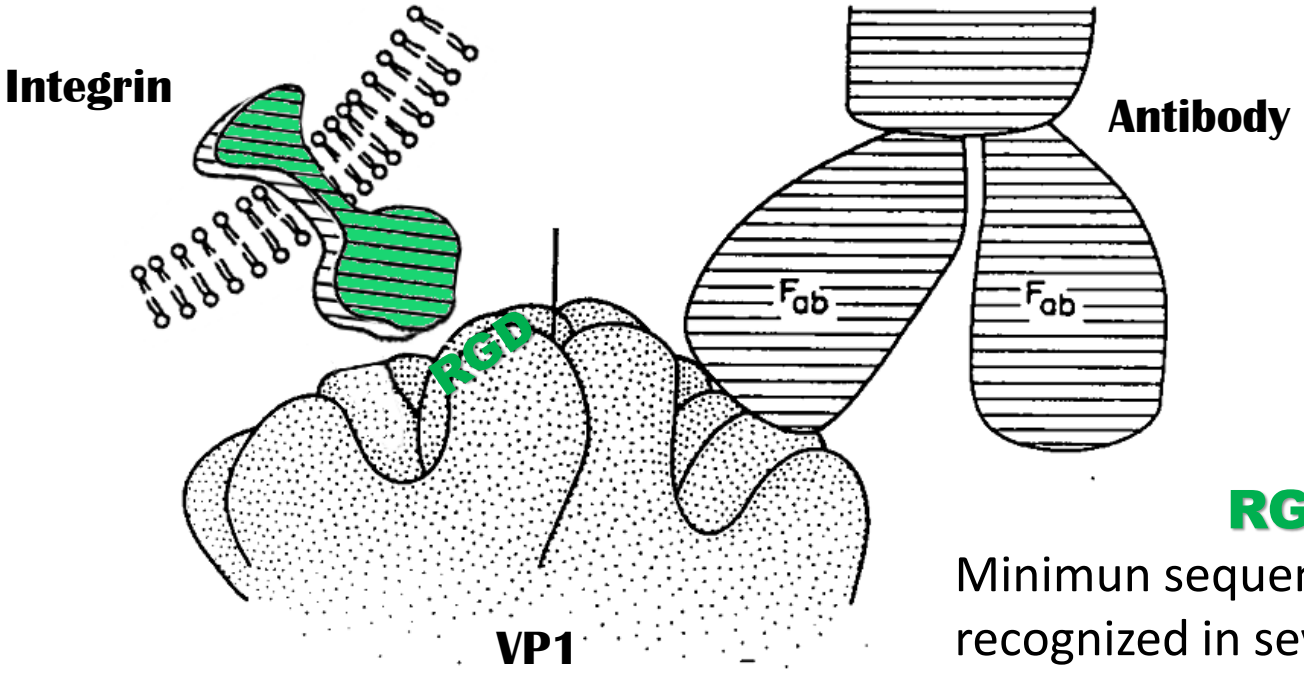
Two subunits

Three domains

Bovine β6 interacts better

INTEGRIN RECEPTOR INTERACTION

- **Goal**: exploring the full αVβ6 amino acidic sequence space at the interaction interface with the RGD motif region and compare with the other β subunits
- **Approach**: Molecular modeling by **FoldX** app.



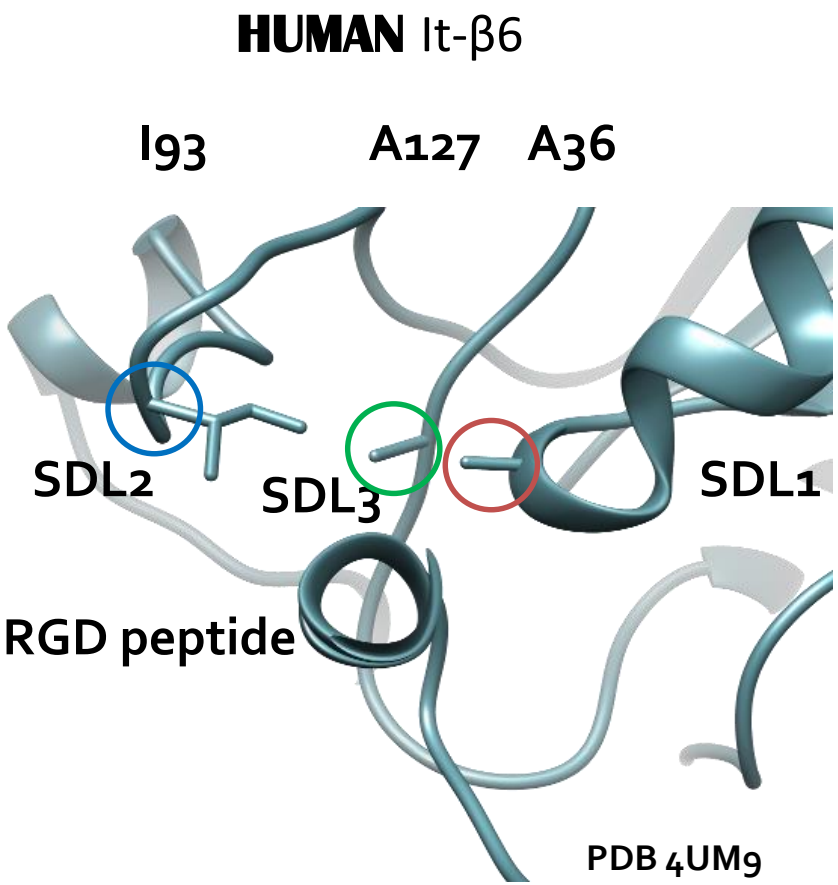
RGD

Minimun sequence recognized in several ligands

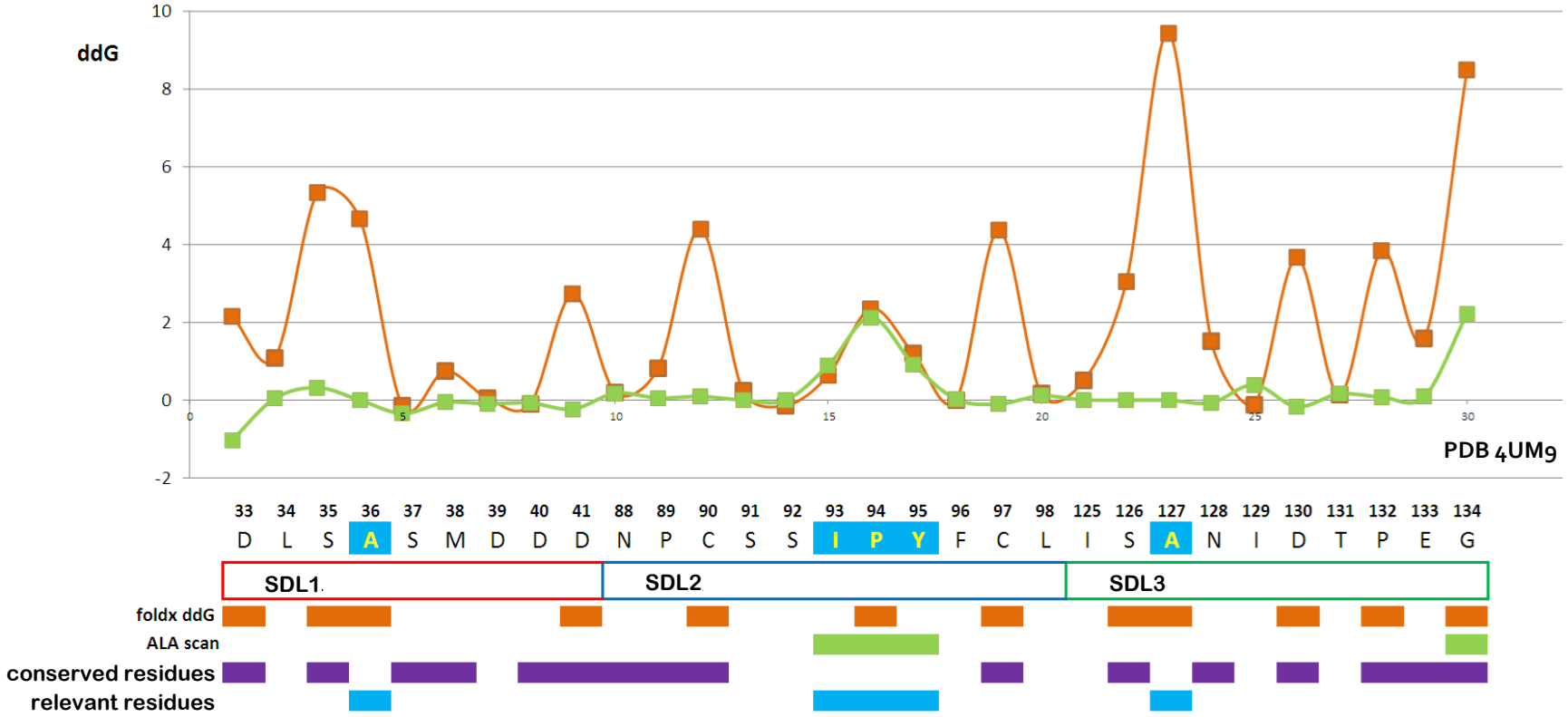
INTEGRIN RECEPTOR INTERACTION

Reference:

Representation of the quasi-atomic structure of the human αVβ6 integrin, in complex with an RGD peptide. Key residues are circled for each of the **3 specificity determining loop** (**SDL**) of the β6 (**HUM It-β6**) subunit.



Mutational ddG analysis through SDLs residues



Plot of interaction energy variation, as ddG average, sampling the 20 natural mutations per every SDL residue (orange curve). Green line, an ALA scan plot, ddG values by mutating for alanine. Purple line: conserved residues over different β subunits

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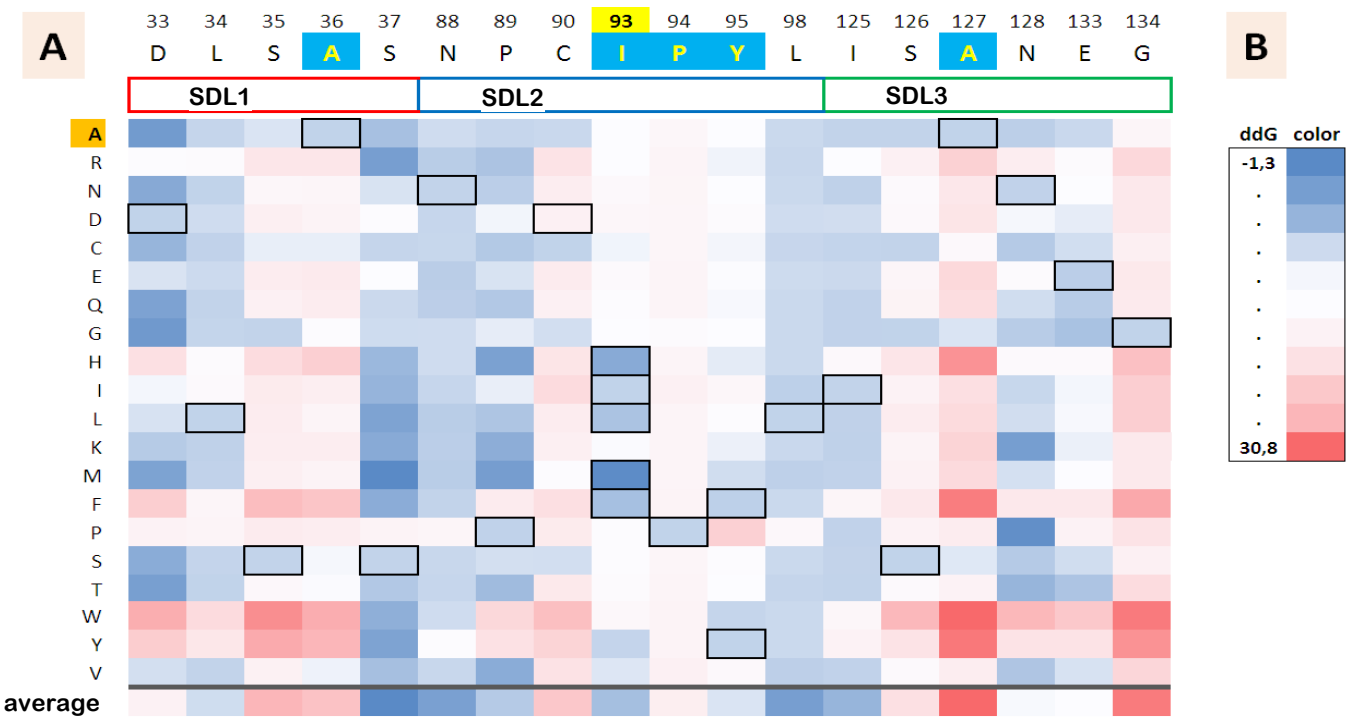

Those residues that are not conserved but has low tolerance to mutations are candidates to be an especificity determinanat between the integrin β6 and their ligand. From this analysis, we obtained 5 key residues

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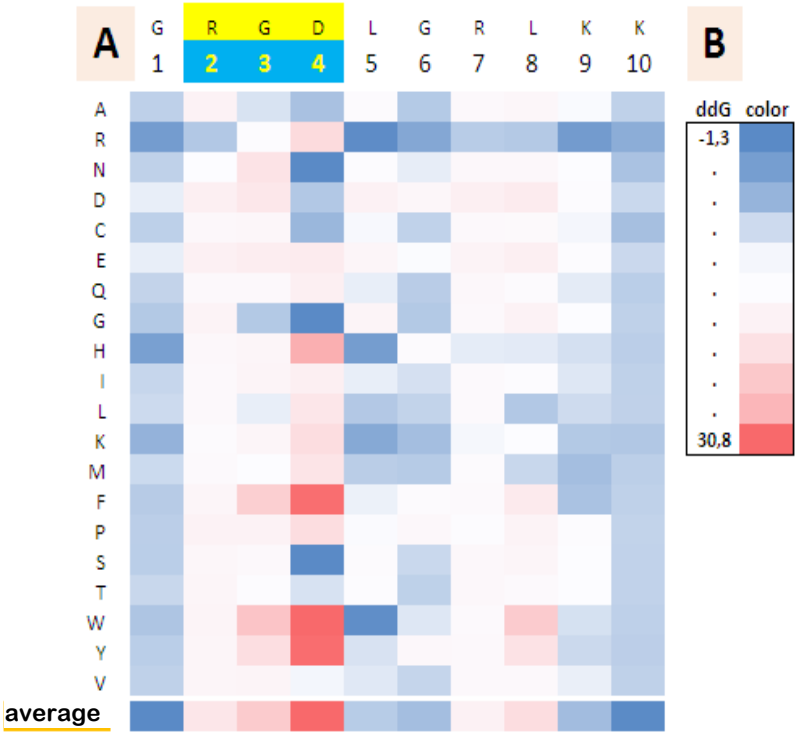
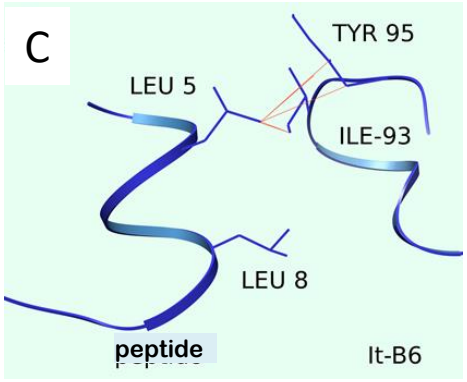
RGD peptide|| Detailed Mutational ddG Heatmap





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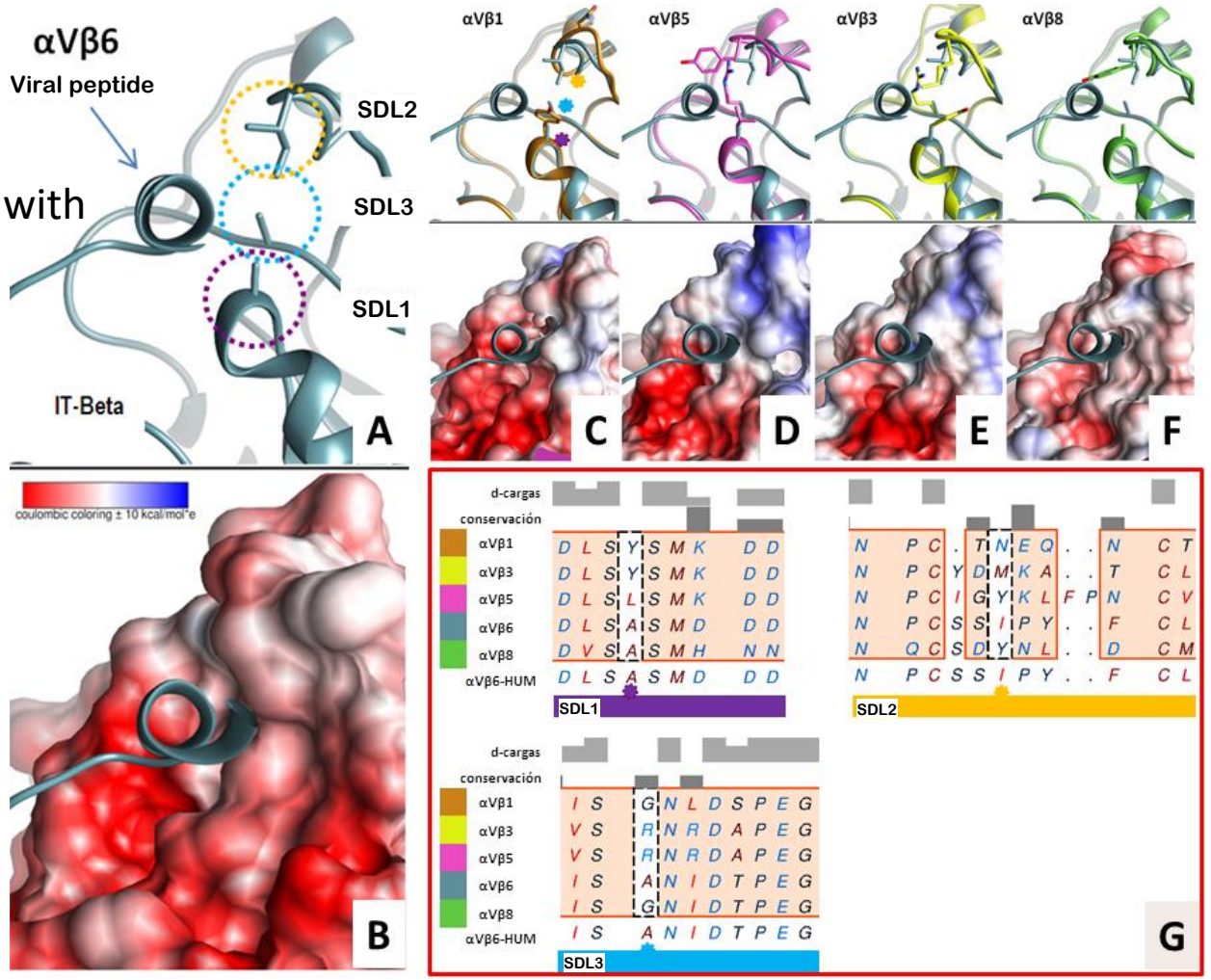
BOVINE || Molecular analysis of βx-It/site A FMDV interaction

i-Tasser

β6 interaction with the peptide

aa sequence of every β subunit β1, β3, β5, β8



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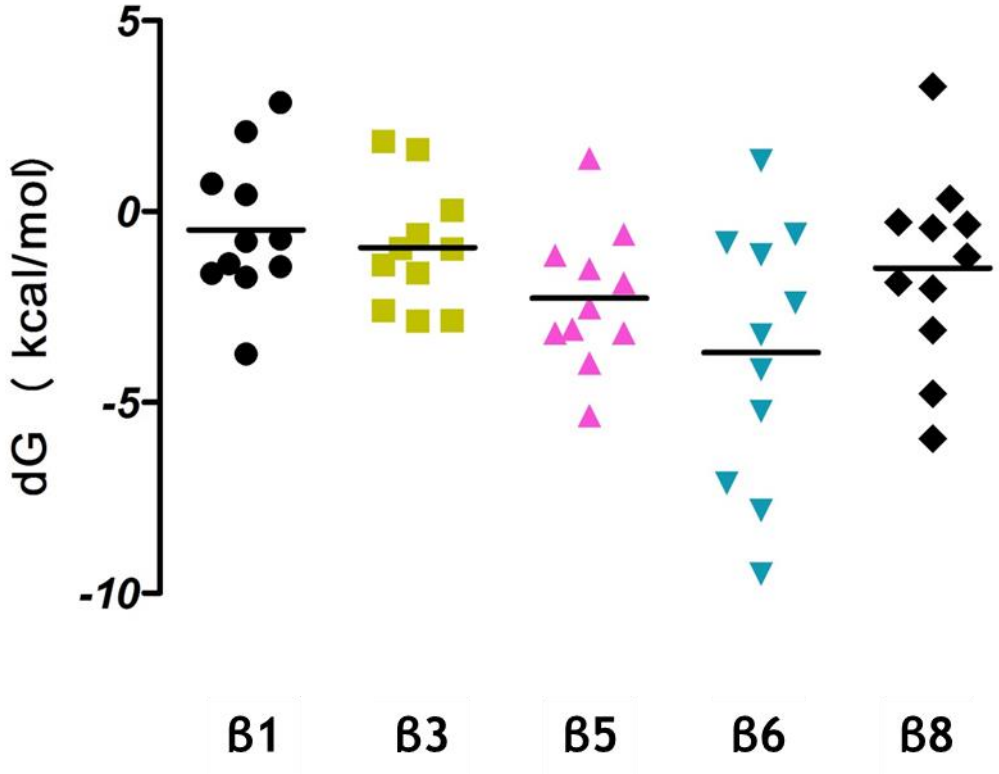

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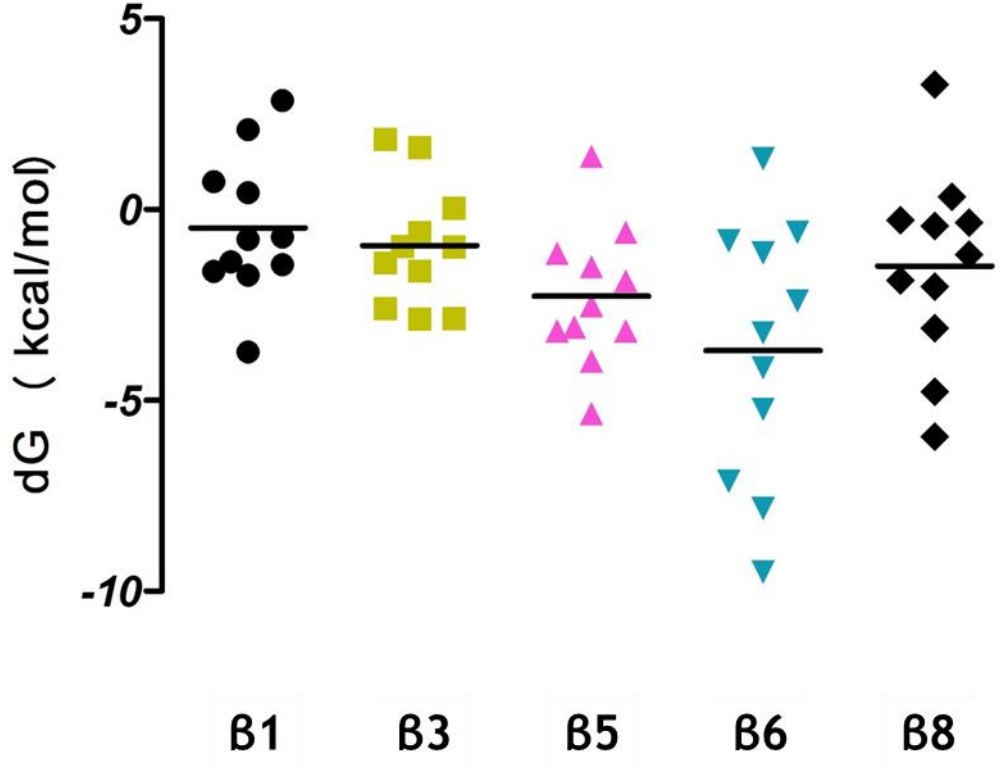

- the bovine integrin αVβ6 preferentially presents a unique hydrophobic interface which supports their specificity for the alfa helix presented at the end of the RGD peptide. IT subunits (β3 and β5) at the same interaction interface residues, present more polar or bulky amino acids which result in a less compatible interaction

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CONCLUSIONS

- By computational means is possible to detect those relevant residues at β6 integrin and RGD peptide interaction in human and bovine model.
- The higher affinity of the β6 integrin for the antigenic site A of FMDV originates in the hydrophobic nature and volume of three aa keys of the SDLs.
- This is compatible with the aa of the nonpolar face of the amphipathic helix downstream of the viral RGD motif.

Thank you!

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