

## HVEM Muteins for Cancer and Other Uses

Researchers at the La Jolla Institute for Immunology and the Albert Einstein College of Medicine together have generated HVEM mutants that selectively recognize either the TNF ligand LIGHT or the Ig ligands BTLA and CD160 *in vitro*. Knock-in mice expressing these muteins maintain expression of all the proteins in the HVEM network yet demonstrate selective functions for LIGHT or BTLA/CD160.

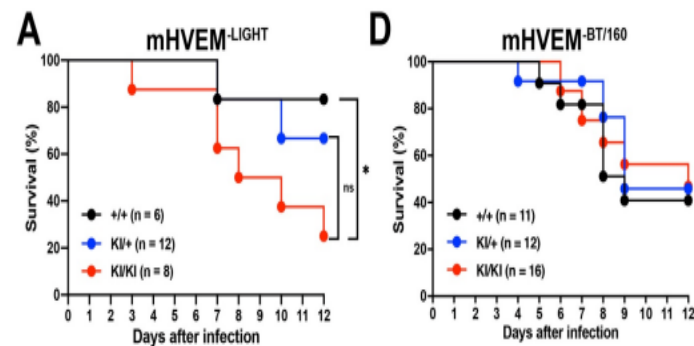
Herpes virus entry mediator (HVEM) is a tumor necrosis factor (TNF) receptor contributing to a broad range of immune functions involving diverse cell types. It interacts with both a TNF ligand, LIGHT, as well as the immunoglobulin (Ig) superfamily members BTLA and CD160. Assessing the functional impact of HVEM binding to specific ligands in different settings has been complicated by the multiple interactions of HVEM and HVEM binding partners. Additionally, HVEM's failure to properly interact with BTLA has been implicated in B cell lymphomas and autoimmune disorders, while HVEM's failure to properly interact with LIGHT has been implicated in viral diseases. As such, it would be beneficial to find a way to restore proper HVEM-BTLA or HVEM-LIGHT binding without affecting HVEM binding to its other partners to prevent off-target effects.

Researchers at LJI and AECOM have found a way to do just that by creating HVEM muteins that are only able to bind one HVEM partner. Mouse data have shown that HVEM muteins able to bind only LIGHT cause mice to be less susceptible to *Yersinia* infection while HVEM muteins able to bind only BTLA cause mice to be less susceptible to liver inflammation.

### ADVANTAGES:

- Bind only one of HVEM's binding partners, reducing off-target effects
- Can be used for the treatment of cancer, autoimmune, or bacterial diseases
- Humanized versions of HVEM muteins are ready to be tested *in vitro* and *in vivo*

*HVEM muteins that selectively bind only one binding partner for the treatment of cancer, autoimmune, and bacterial diseases*



*Survival curves of mice challenged with Yersinia infection & treated with LIGHT-binding-deficient or BTLA-binding deficient HVEM muteins*