# Article information:

LAG3 associates with TCR-CD3 complexes and suppresses signaling by driving co-receptor-Lck dissociation - PMC  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9106921/>

# Article summary:

1. LAG3 is an inhibitory receptor that is highly expressed on exhausted T cells and is now a major immunotherapeutic target for the treatment of cancer and other diseases.

2. LAG3 associates with the T cell receptor (TCR)-CD3 complex in CD4+ and CD8+ T cells, even in the absence of binding to MHC class II, its canonical ligand.

3. A phylogenetically conserved, acidic, tandem glutamic acid–proline repeat in the LAG3 cytoplasmic tail lowers the pH at the immune synapse and causes the dissociation of the tyrosine kinase Lck from the CD4 or CD8 co-receptor, which results in a loss of co-receptor-TCR signaling and limited T cell activation.

# Article rating:

May be slightly imbalanced: The article presents the information in a generally reliable way, but there are minor points of consideration that could be explored further or claims that are not fully backed by appropriate evidence. Some perspectives may also be omitted, and you are encouraged to use the research topics section to explore the topic further.

# Article analysis:

The article “LAG3 associates with TCR-CD3 complexes and suppresses signaling by driving co-receptor-Lck dissociation” provides an interesting insight into how LAG3 inhibits T cell function. The authors provide evidence that LAG3 can associate with the TCR-CD3 complex even in the absence of binding to MHC class II, its canonical ligand. They also demonstrate that a phylogenetically conserved, acidic, tandem glutamic acid–proline repeat in the LAG3 cytoplasmic tail lowers the pH at the immune synapse and causes the dissociation of tyrosine kinase Lck from CD4 or CD8 co-receptors, resulting in a loss of co-receptor-TCR signaling and limited T cell activation.

The article appears to be well researched and reliable as it provides evidence for its claims through experiments conducted on wild type (Lag3+/+) or Lag3−/− CD8+ and CD4+ T cells stimulated with CD3ε and CD28 Abs in both presence and absence of MHC class II antigen presenting cells. The authors also provide detailed descriptions of their methods used to conduct these experiments as well as clear explanations for their results.

However, there are some potential biases present within this article that should be noted. For example, while it is mentioned that LAG3 is now a major immunotherapeutic target for treating cancer and other diseases, there is no mention of any potential risks associated with targeting this receptor or any discussion about alternative treatments available for these conditions. Additionally, while it is stated that LAG3 has an unusual cytoplasmic tail lacking any tyrosine based motifs but containing two phylogenetically conserved regions with no known function - a six amino acid ‘KIEELE’ motif and a glutamic acid–proline rich tandem repeat (‘EP’) motif - there is no exploration into what other functions these regions may have or how they may affect other aspects of cellular biology beyond inhibiting T cell function.

# Topics for further research:

* Immunotherapeutic risks associated with targeting LAG3
* Alternative treatments for cancer and other diseases
* Functions of the KIEELE motif in LAG3
* Functions of the EP motif in LAG3
* Effects of LAG3 on other aspects of cellular biology
* Role of LAG3 in immune synapse formation

# Report location:

<https://www.fullpicture.app/item/adf855c4003616125bfd66cb6e3da653>