

# LYTAC Platform for Targeted Extracellular Protein Degradation

A fully genetically encodable lysosome-targeting chimera (LYTAC) platform for targeted degradation of extracellular proteins. This system enables programmable, cell-directed clearance of disease-associated proteins.

# The state of the s

# **Technology ID**

**BDP 8886** 

# **Category**

Therapeutics/Platform
Technology
Selection of Available
Technologies

### **Authors**

David Baker

## View online page



### What is the Problem?

Many diseases, including cancer, autoimmune disorders, and neurodegenerative conditions, are driven by the presence of harmful proteins outside cells. Current therapies often struggle to eliminate these extracellular proteins effectively, especially when they are not enzymes or receptors that can be easily targeted. Additionally, these extracellular proteins are often not amenable to small molecule inhibition or intracellular degradation technologies like proteolysis targeting chimeras (PROTACs). The lysosome-targeting chimera (LYTAC) approach addresses this by linking a target-binding domain to a lysosome-targeting motif, enabling the internalization and degradation of extracellular proteins via the lysosomal pathway. However, existing LYTACs often rely on synthetic conjugates or complex manufacturing processes, limiting their therapeutic flexibility and delivery options.

# What is the Solution?

This technology introduces a de novo protein-based LYTAC platform that is entirely genetically encodable. The system uses computationally designed proteins that bind to both a target extracellular protein and a lysosome-trafficking receptor, such as M6PR. These proteins are engineered to induce receptor-mediated endocytosis, directing the bound target to the lysosome for degradation. This approach allows for the selective removal of proteins that were previously considered "undruggable," including secreted factors, membrane receptors, and other extracellular proteins. The platform is adaptable to a wide range of targets and can be delivered using protein, mRNA, or gene therapy formats.

# What is the Competitive Advantage?

- -Fully Genetically Encodable: Unlike chemically synthesized LYTACs, this platform can be delivered via gene or mRNA therapy for sustained expression.
- -Modular and Customizable: Proteins are built from scratch for high specificity, stability, and modularity to direct degradation of different proteins.
- -Broad Target Range: Capable of degrading secreted proteins, membrane receptors, and other extracellular targets.
- -Simplified Manufacturing: Eliminates the need for chemical conjugation or complex bioconjugate synthesis.

### **Patent Information:**

### WO2025038596A1

### References

1. Huang, B., Abedi, M., Ahn, G., Coventry, B., Sappington, I., Tang, C., Wang, R., Schlichthaerle, T., Zhang, J. Z., Wang, Y., Goreshnik, I., Chiu, C. W., Chazin-Gray, A., Chan, S., Gerben, S., Murray, A., Wang, S., O'Neill, J., Yi, L., Yeh, R., Misquith, A., Wolf, A., Tomasovic, L. M., Piraner, D. I., Duran Gonzalez, M. J., Bennett, N. R., Venkatesh, P., Ahlrichs, M., Dobbins, C., Yang, W., Wang, X., Sahtoe, D. D., Vafeados, D., Mout, R., Shivaei, S., Cao, L., Carter, L., Stewart, L., Spangler, J. B., Roybal, K. T., Greisen, P. J., Li, X., Bernardes, G. J. L., Bertozzi, C. R., Baker, D.(2025), https://www.nature.com/articles/s41586-024-07948-2, https://www.nature.com/, 638, 796-804