Docket #: S20-197

Therapeutic Anti-CD22 Antibody for Treating Lysosomal Storage Disorders and Neurodegenerative Diseases

Researchers in the Wyss-Coray Lab are investigating a potential therapeutic antibody to treat lysosomal storage disorders and other related neurodegenerative diseases.

Lysosome dysfunction is a shared feature of rare genetic lysosomal storage diseases (LSDs) and common age-related neurodegenerative diseases. Microglia, the brain-resident macrophages, are particularly vulnerable to lysosome dysfunction due to the stress of clearing dying neurons and debris. One LSD that shares many features with Alzheimer's disease (AD), including microglial dysfunction, is Niemann Pick Type C disease (NPC). There are currently no FDA-approved treatments for NPC, and no previous investigational drugs have directly targeted microglial dysfunction.

Researchers in the Wyss-Coray lab previously found that CD22, a cell-surface molecule, is upregulated on microglia in the aging mouse brain where it inhibits clearance of protein aggregates and debris. CD22 blockade improved cognitive function in aged mice. Notably, soluble CD22 (sCD22) is increased in the cerebrospinal fluid (CSF) of patients with NPC and AD. Motivated by these findings, they set out to understand the role of sCD22 in the human brain. Combining genome wide screens with antibody engineering, they developed a therapeutic monoclonal antibody specifically designed to target CD22 in the human brain and improve microglial lysosome function, with therapeutic implications for both NPC and AD.

Related technology: Stanford Docket 17-443: "Methods to Improve Phagocytosis for Treatment of Age-Related Diseases"

Applications

- Lysosomal Storage Disorders: Niemann-Pick Disease Type C, Niemann-Pick Disease, Fabry Disease, Gaucher Disease, Tay-Sachs Disease
- Age-Related Neurodegenerative Diseases: Dementia, Parkinson's Disease, Alzheimer's Disease

Advantages

- Novel target for lysosomal storage disorders
- Rare disease area (potential for special FDA status)
- Potentially useful across several indications

Publications

- J. V. Pluvinage, J. Sun, C. Claes, R. A. Flynn, M. S. Haney, T. Iram, X. Meng, R. Lindemann, N. M. Riley, E. Danhash, J. P. Chadarevian, E. Tapp, D. Gate, S. Kondapavulur, I. Cobos, S. Chetty, A. M. Pa?ca, S. P. Pa?ca, E. Berry-Kravis, C. R. Bertozzi, M. Blurton-Jones, T. Wyss-Coray, The CD22-IGF2R interaction is a therapeutic target for microglial lysosome dysfunction in Niemann-Pick type C. Sci. Transl. Med. 13, eabg2919 (2021).
- J. V. Pluvinage, M. S. Haney, B. A. H. Smith, J. Sun, T. Iram, L. Bonanno, L. Li, D. P. Lee, D. W. Morgens, A. C. Yang, S. R. Shuken, D. Gate, M. Scott, P. Khatri, J. Luo, C. R. Bertozzi, M. C. Bassik, T. Wyss-Coray, CD22 blockade restores homeostatic microglial phagocytosis in ageing brains. Nature 568, 187–192 (2019).
- Bu, Xian-Le, Pu-Yang Sun, Dong-Yu Fan, Jun Wang, Hao-Lun Sun, Yuan Cheng, Gui-Hua Zeng et al. "Associations of plasma soluble CD22 levels with brain amyloid burden and cognitive decline in Alzheimer's disease." Science Advances 8, no. 13 (2022): eabm5667. ,

Patents

- Published Application: WO2021236577

- Published Application: 20230174668

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