Targeting CD33 to Treat Alzheimer's Disease:

New insights into the role of CD33 in Alzheimer's Disease Progression

Current treatments for Alzheimer's Disease (AD) are focused on ameliorating the associated symptoms rather than addressing the cause. More population- and genetics-based evidence suggests that the immunomodulatory Siglec, CD33, could be a viable therapeutic target for AD. To understand CD33's pharmacological role in AD, GlycoNet researchers have developed a versatile scaffold technology that can rapidly profile and quantify weak affinities of protein-glycan interactions with high sensitivity and selectivity. The technology poses great potential to elucidate finer details about CD33 and its function in AD, as well as in applications that involve other lectin-glycan interactions.

Key Benefits

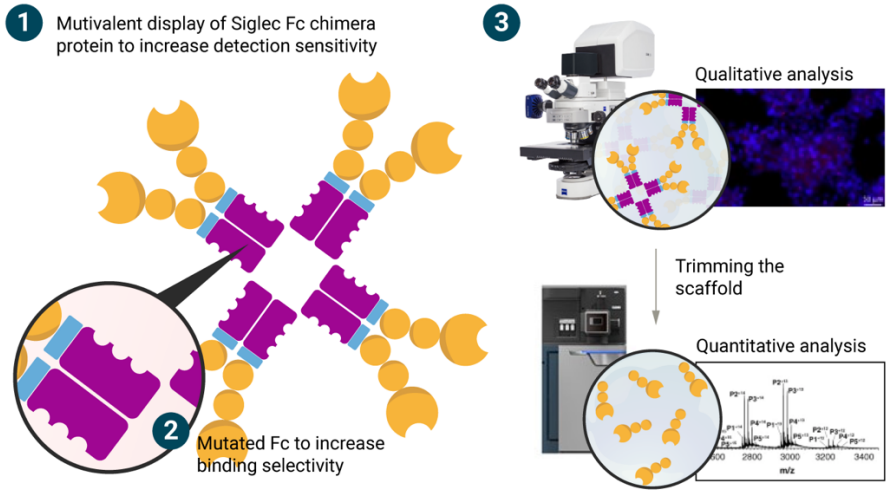
- Enhanced sensitivity for weak binding events
- High selectivity in whole cells without off-target binding
- Versatile scaffold compatible with different binding assays

Global Impact & Market

The prevalence of AD in Americans above 65 years old is ~10%, and it becomes 32% for those above 85 years old. The global market for AD treatment is estimated to reach over $6.3 billion by 2025. The steadily growing AD population represents one of the most underserved markets in terms of effective treatments. The need for enabling technologies to develop new treatments has become urgent, especially given the recurrent failure of several prominent disease-modifying agents such as benzodiazepines and anticholinergics.

The Immunomodulatory Siglec CD33

About 10% of global population are born with a truncated form of CD33, which makes these individuals less susceptible to AD. Research efforts aim to identify glycans that interact with CD33, and how the interactions contribute to neurodegeneration.



The Technology

① **Octameric presentation:** the multivalent display of the recombinant Siglec-Fc chimera protein increases binding avidity and makes binding events easier to detect.

② **Increased selectivity:** the scaffold is designed to abrogate off-target binding which causes false detection.

③ **Qualitative and quantitative measurements:** the modular scaffold can be used directly in qualitative assays (e.g. immunostaining), and can be trimmed to for quantitative assays (e.g. ESI-MS).

Application

The technology offers new insight into the biochemistry that underpins this Siglec and its relation to neurodegeneration, informing novel therapeutic design for the treatment of early onset AD. The versatility of the scaffold can also be adapted to probe protein-glycan interactions in other diseases. Given the similarity between brain and spinal fluid, there is a potential to expand identified therapeutic strategies to treat multiple sclerosis.

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