

A TREM2 VARIANT PROTEIN LIBRARY FOR MAPPING INTERACTIONS WITH LIGANDS

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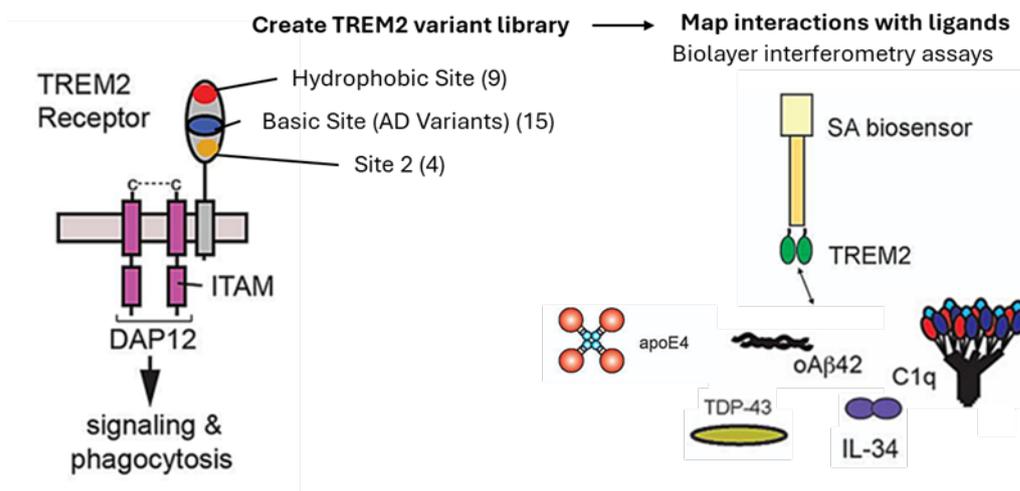
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Value Proposition: Variant protein library that can map ligand binding.

Technology Description

Researchers at Washington University in St. Louis have developed a TREM2 variant protein library that can be used to map interactions with ligands to guide development of therapies to target TREM2 function in diseases. TREM2 is an extracellular receptor expressed on macrophages and microglia. Ligand binding to TREM2 can elicit signals that control macrophage and microglia activation and function. Recently, TREM2 has become an important drug target for multiple diseases where macrophage and microglia function are important, including some cancers, Alzheimer's and other neurodegenerative diseases, and atherosclerosis and stroke.

This library allows for more variants to be studied to gain a better understanding of the binding mechanisms with ligands.



Stage of Research

- Developed an extensive protein array of 28 TREM2 variants that could be used to map binding to ligands
- Utilized structurally designed TREM2 variants to map binding to ligands
- Investigated the major TREM2 AD risk variants R47H, R62H, D87N, and T96K
- Identified major binding sites on TREM2 for apoE4, TDP-43, oAβ42

Publications

Greven JA, Wydra JR, Greer RA, Zhi C, Camitta C, Song Y, Alexander-Brett JM, Brett TJ. Biophysical mapping of TREM2-

ligand interactions reveals shared surfaces for engagement of multiple Alzheimer's disease ligands. Res Sq [Preprint]. 2024 Sep 12;rs.3.rs-4850141. doi: 10.21203/rs.3.rs-4850141/v1. Update in: Mol Neurodegener. 2025 Jan 9;20(1):3. doi: 10.1186/s13024-024-00795-9. PMID: 39315272; PMCID: PMC11419269.

Applications

- Map interactions with ligands to guide development of therapies to target TREM2 function

Key Advantages

- High-throughput way to map what surfaces on TREM2 engagement with various ligands
- Allows for more variants to be studied to gain a better understanding of the binding mechanisms with ligands

Related Web Links – [Thomas Brett Profile](#); [Brett Lab](#)