Washington University in St. Louis
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LRP1 AND THE BLOOD BRAIN BARRIER

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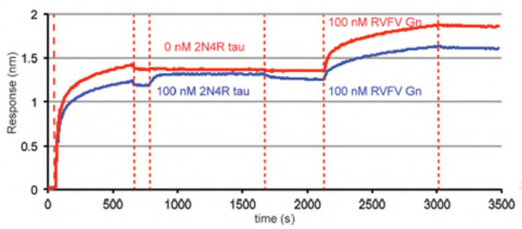
T-019577 - Lrp1 and the blood brain barrier

Technology Description

Researchers in Gaya Amarasinghe's laboratory at Washington University have engineered new protein fragments (RVFV Gn) to target LRP1, which was recently identified as an essential entry factor for Rift Valley Fever Virus (RVFV). The fragments target either CL_{II} or CL_{IV} of LRP1 with high affinity.

Stage of Research



Data from BLI-based sequential binding assays. Immobilized LRP1 CL_{IV} is sequentially dipped into RVFV Gn and 2N4R tau with competition experiments (blue) and non-blocked controls (red). Pre-association of RVFV Gn with LRP1 CL_{IV} almost completely prevented binding of tau to LRP1 CL_{IV}.

Dose-response curve of fragments has been established *in vitro.* LRP1 can be effectively targeted *in vitro* in cell culture and *in vivo* in a murine model. Targeting LRP1 is highly effective at preventing RVFV lethality *in vivo* in C57BL/6 mice & can block RVFV infection in liver and brain.

LRP1 was recently identified as a key regulator of neurodegenerative ligands such as tau[1] and α-Synuclein[2]. In combination with a viral glycoprotein, preliminary data shows near-total prevention of tau binding to LRP1 *in vitro*. Cell to cell spread of pathogenic tau binding occurs by disrupting tau's ability to bind to host protein.

Publications

Ganaie et al. Lrp1 is a host entry factor for Rift Valley fever virus. Cell (2021).

Applications

- Rift Valley fever virus, but in particular diseases involving LRP1 (e.g. tauopathies such as Alzheimer's).

Key Advantages

- **LRP1 is expressed ubiquitously and conserved across cell types.**

- **Mechanism of action of RVFV directly interacts with LRP1.**

Patents

- Patent pending.

Related Web Links – Gaya Amarasinghe

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[1]Rauch et al. (2020). LRP1 is a master regulator of tau uptake and spread. Nature 580, 381–385. 10.1038/s41586-020-2156-5.

[2]Chen et al. (2022). LRP1 is a neuronal receptor for α-synuclein uptake and spread. Mol Neurodegeneration 17, 57. 10.1186/s13024-022-00560-w.