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## **Blocking LINGO-1 for CNS remyelination and repair: From discovery to clinical trials**

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**L**INGO-1 is a Leucine rich repeat, Ig domain containing, Nogo receptor interactive protein that is selectively expressed in CNS oligodendrocytes and neurons. Its expression is developmentally regulated, as well as up-regulated in CNS diseases and spinal cord injury. LINGO-1 negatively regulates oligodendrocyte differentiation and myelination, neuronal survival and axonal regeneration by activating RhoA and inhibiting ATK phosphorylation. Across diverse animal CNS disease models, targeted LINGO-1 inhibition promotes neuron and oligodendrocyte survival, axon regeneration, oligodendrocyte differentiation, remyelination and functional recovery. The targeted inhibition of LINGO-1 therefore represents a novel approach for the treatment of neurological diseases. BIIB033 is the first anti-LINGO-1 anti-body to enter clinical development for CNS repair. The Phase I study found anti-LINGO-1 to be safe and well tolerated up to the maximum planned dose of 100 mg/kg. BIIB033 is currently being evaluated in Phase II clinical study for the treatment of RRMS and SPMS.

### **Biography**

Sha Mi obtained her PhD in Molecular and Cellular Biology from Rutgers University and her Postdoctoral training in the laboratory of Richard Roberts (Nobel Laureate) at the Cold Spring Harbor Laboratory. Her major interests include the identification of novel CNS specific proteins involved in the regulation of neuronal cell survival, axonal regeneration, neuronal damage repair and remyelination. Her current focus is to identify therapeutics for the treatment of demyelination diseases such as MS. Her group is the first to identify proteins, LINGO-1 and DR6, that block remyelination repair in laboratory tissue culture and in animal disease models, and whose inhibition will allow for remyelination and repair of damaged axons.

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