A Genome-Wide CRISPR Screen Identifies SORT1 as a Mediator of Galectin-1 Intracellular Trafficking

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Despite their clear importance regulating critical cellular functions such as cell migration, a detailed understanding of the mechanistic biology of the galectin family of glycan-binding proteins remains elusive. Along with the biochemical challenges inherent to the study of lectin-glycan interactions, investigations into the mechanisms of galectin function are complicated by the fact that several members of this family do not exclusively function via glycan-binding activity. Galectin-1, for example, is secreted and internalized via unconventional and poorly-understood mechanisms, and is known to exhibit both extracellular activity, dominated by its interaction with cell-surface glycans, and intracellular activity, where it is believed to be involved in RNA processing and maturation.

Here, we present a genome-wide CRISPR screen that investigates the mechanism of galectin-1 internalization and demonstrate that its internalization is mediated in part by the trafficking receptor sortilin. We identify a point mutant deficient in sortilin-binding to facilitate separate study of galectin-1's glycan-dependent and glycan-independent activity and highlight the potential applicability of this endogenous protein-internalization machinery to the intracellular delivery of large biomolecules.

Bibliographic references:

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