Inhibition of ESCRT II-CHMP6 interactions impede cytokinetic abscission and leads to cell death

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Key words: Membrane fission / cell division / super resolution microscopy / macromolecular complexes / cellular filaments

Abstract

Recently the ESCRT-III filamentous complex has been designated as the driving force for mammalian cell abscission, i.e. fission of the intercellular membrane bridge connecting daughter cells at the end of cytokinesis. However, how ESCRT-III is activated to set on abscission has not been resolved. Here we revisited the role of the upstream canonical ESCRT players ESCRT-II and CHMP6 in abscission. Using high-resolution imaging we show that these proteins form high ordered structures at the intercellular bridge during abscission progression. Furthermore, we demonstrate that a truncated version of CHMP6, composed of its first 52 AA (CHMP6-N), arrives to the intercellular bridge, blocks abscission and subsequently leads to cell death. This phenotype is abolished in a mutated version of CHMP6-N, designed to prevent CHMP6-N binding to its ESCRT-II partner. Interestingly, deleting the first 10 AA from CHMP6-N does not interfere with its arrival to the intercellular bridge, but almost completely abolishes the abscission failure phenotype. Taken together, this data suggests an active role for ESCRT-II and CHMP6 in ESCRT-mediated abscission. Our work

advances the mechanistic understanding of ESCRT-mediated membrane fission in cells and introduces an easily applicable tool for upstream inhibition of the ESCRT pathway in live mammalian cells.