Cell Cycle 14:20, 3219; October 15, 2015; © 2015 Taylor & Francis Group, LLC

Cut or NoCut: the role of JADE1S in regulating abscission checkpoint

Comment on: Siriwardana NS, et al. The novel function of JADE1S in cytokinesis of epithelial cells. Cell Cycle 2015; 14(17):2821-34; PMID:26151225; http://dx.doi.org/10.1080/15384101.2015.1068476.

Rytis Prekeris*; Department of Cell and Developmental Biology; School of Medicine; Anschutz Medical Campus; University of Colorado Denver; Aurora, CO USA; Email: Rytis.Prekeris@ucdenver.edu; http://dx.doi.org/10.1080/15384101.2015.1089074

The last step of cell division is the separation of 2 daughter cells via a process known as cytokinesis. After replication of the genetic material, the mother cell divides by the formation of the cleavage furrow, leaving 2 daughter cells connected by a thin intracellular bridge (ICB). The resolution of this bridge (abscission) results in the separation of the 2 daughter cells. Recent work from many laboratories has established abscission as a complex event that involves coordinated changes in cytoskeleton organization and membrane transport.[1]

While the machinery governing abscission during cytokinesis remains to be fully understood, recycling endosomes and ESCRT protein complexes have emerged as key regulators of abscission.[2] ESCRT complexes (complexes 0, I, II and III) were originally described as regulators of multi-vesicular body formation. Since then, several ESCRT subunits, namely Tsg101, Alix, and ESCRT-III complex proteins were demonstrated to be required for cytokinesis.[2] The model of ESCRT recruitment to the ICB is as follows: Alix and/or Tsg101 are recruited to the midbody (MB) by binding to the midbody protein CEP55. These components then recruit various ESCRT-III members, such as CHMP4, to the MB. CHMP4 has the ability to form ~5 nm filaments that are proposed to mediate abscission.[2] The key to the recruitment of the ESCRTs from the MB to the abscission site remains somewhat unclear, but it was shown to involve targeted delivery of Rab11/FIP3-containing endosomes, eventually leading to severing of central spindle microtubules and localized actin depolymerization at the abscission site.[3]

The abscission event involves the severing of the ICB on one (asymmetric abscission) or on both sides of the MB. In the case of asymmetric abscission, one of the daughter cells retains the MB.[1] These post-mitotic MB derivatives (MB^d) were shown to be present in less differentiated, stem cell-like populations *in vitro* and *in vivo*.[4] Similarly, MB^d accumulation in cancer cells leads to elevated aggressiveness and increased proliferation.[4] Thus, it is clear that the timing and location of the abscission site is not a stochastic event, but is tightly regulated by the dividing cell. Consistent with that hypothesis, recent studies identified an abscission checkpoint (NoCut), which is dependent on Aurora B and ANCHR (Abscission/NoCut Checkpoint Regulator) proteins.[5] What remains essentially unknown is the molecular machinery governing the activity of the NoCut checkpoint. In this paper Maria Panachenko and colleagues identified JADE1S as novel regulator of the NoCut checkpoint.[6] Just like ANCHR, JADE1S appears to be a negative regulator of abscission. Consistent with this hypothesis, JADE1S overexpression arrests cells in cytokinesis, while JADE1S depletion leads to a decrease in cytokinesis frequency, presumably due to faster cytokinesis. Finally, the authors show that Aurora B activity is also required for JADE1S repression of abscission.[6] All data are consistent with JADE1S playing a role in mediating NoCut checkpoint function.

JADE1S has emerged as a surprising component of the NoCut checkpoint. Originally, JADE1 was identified as a member of a family of PHD zinc finger proteins that regulate histone H4 acetylation by binding to histone acetylase HBO1.[7] Surprisingly, HBO1 is not required for JADE1S function as a component of the NoCut checkpoint.[6] Indeed, HBO1 does not localize to the abscission site and HBO depletion does not appear to affect abscission. Thus, regulation of the NoCut checkpoint appears to be a completely novel function of JADE1. Intriguingly, JADE1 comes in 2 different splice isoforms, and only one of them, JADE1S, plays a role in regulating abscission.

Despite the emergence of JADE1S as an important mediator of the NoCut checkpoint, many questions remain. It is unclear how JADE1S actually functions. If it does not require HBO1 for its cytokinetic function, does it also bind to other acetylases that function outside the nucleus? Or perhaps its NoCut activity does not require acetylation? How does Aurora B regulate JADE1S? Finally, what is the connection between JADE1S and known abscission regulators, such as microtubules, the ESCRT complex and Rab11/FIP3-endosomes? Additional research will needed to understand the NoCut mechanism in general and JADE1S function in particular.

References

1. Schiel JA, et al. Trends Cell Biol 2013; 23(7):319-27; PMID:23522622; http://dx.doi.org/10.1016/j.tcb.2013.02.003
2. Hurley JH. Crit Rev Biochem Mol Biol 2010; 45(6):463-87; PMID:20653365; http://dx.doi.org/10.3109/10409238.2010.502516
3. Schiel JA, et al. Nat Cell Biol 2012; 14(10):1068-78; PMID:23000966; http://dx.doi.org/10.1038/ncb2577
4. Kuo TC, et al. Nat Cell Biol 2011; 13(10):1214-23; PMID:21909099; http://dx.doi.org/10.1038/ncb2332
5. Mendoza M, et al. Nat Cell Biol 2009; 11(4):477-83; PMID:19270692; http://dx.doi.org/10.1038/ncb1855
6. Siriwardana NS, et al. Cell Cycle 2015; 14(17):2821-34; PMID:26151225; http://dx.doi.org/10.1080/15384101.2015.1068476
7. Panchenko MV, et al. J Biol Chem 2004; 279(53):56032-41; PMID:15502158; http://dx.doi.org/10.1074/jbc.M410487200