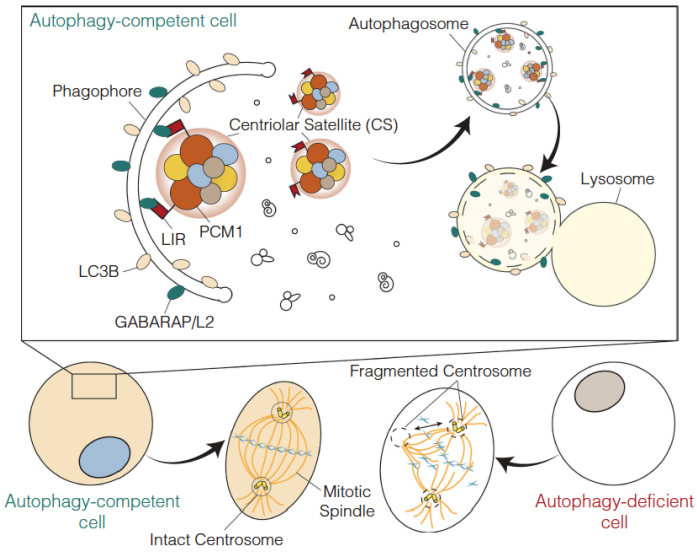
Annual highlight

Selective autophagy maintains centrosome integrity and accurate mitosis by turnover of centriolar satellites.

-Holdgaard SG et al, Nat Commun. 2019 Sep 13;10(1):4176.

Doryphagy is a novel selective autophagy by which centriolar satellites are removed from the centrosome.

The centrosome is the major microtubule-organizing center and is responsible for the equal distribution of DNA during cell division, by orchestrating the formation of the mitotic spindle. In addition to cell division, centrosome functions include a large number of cellular processes, such as cell migration, ciliogensis, cell polarity and cell adhesion, all of them playing a critical role in cancer biology. Centrosome composition is regulated by centriolar satellites (CS), large protein complexes whose assembly depends on the protein PCM1 that acts as a scaffold factor. By using pharmacological and genetic inhibition of macroautophagy, we observed that autophagy-deficient cells displayed a mitotic delay, followed by unbalanced chromosome segregation and formation of micronuclei, eventually leading to post-mitotic cell death. Since the analysis of centrosome composition revealed an accumulation of specific centrosome proteins in the CS in autophagy-deficient cells, we speculated that this could be the reason of CS dysfunction and accumulation, and thus hypothesized a role for macroautophagy in their degradation. By means of proteomic and biochemical approaches, besides genetic and computational models, we demonstrated that CS are indeed a true substrate of autophagy. We were thus able to identify at the aminoacidic level the interaction between PCM1 and the autophagy receptor GABARAP as responsible for CS selective autophagy, that we named *doryphagy* (from the Greek work for satellite, "doryphóros"). In sum, we described a novel selective autophagy process responsible for the mantainance of functional CS and centrosome. Although our study is focused on cell division, we expect that doryphagy may affect all centrosome-related functions, and to be particularly interesting from a cancer perspective. Indeed, our findings open a large number of questions, currently topic of further studies, and could represent a first step towards innovative approches in cancer medicine.



Schematic model illustrating the degradation of centriolar satellites by selective autophagy. The centriolar satellite protein PCM1 directly binds GABARAP/L2 through a LIR motif. This interaction mediates the selective engulfment of the CSs targeted for degradation into phagophores. Notably, macroautophagy inhibition results in loss of pericentriolar material integrity, which has an impact on centrosome stability and causes aberrant mitoses.