Pharmacological interventions of phosphatidylinositol 3-kinase on nuclear events during conjugation of *Tetrahymena thermophila*

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SUMMARY

Phosphatidylinositol 3-kinase (PI3K) has been linked to diverse signal transduction processes in eukaryotes. Here we focus on the role of the PI3K and performed pharmacological treatment with potent PI3K inhibitors in order to identify the central regulator(s) of the nuclear events during conjugation in *Tetrahymena thermophila*. Treatment at early stages of conjugation causes a block of the irreversible pairing-reaction, and subsequent phosphorylation at histone H3S10 in the micronucleus, results in failure of meiosis. The treatment after commitment to meiosis, on the other hand, causes abnormal new macronuclear differentiation and degradation of the parental macronucleus. Live-cell imaging with autophagosome/lysosome indicators shows that the parental macronucleus, in the presence of the inhibitors, shows imperfection of autophagic events on the nucleus. Indeed, the immunofluorescence observations reveal that the signals against Twi1 and RNApol-II initially present in the parental macronucleus are replaced by the new macronucleus even in the presence of the inhibitors, whereas the signal against dimethylation at histone H3K4 is stacked up in the parental macronucleus or it is often overlapped with the new macronucleus. These results suggest that PI3K-signaling is activated at different stages, which are involved in various kinds of the nuclear events that are essential for proper conjugation.