Nalidixic acid blocks division, but not growth, in *Chlamydomonas reinhardtii*

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Chlamydomonas reinhardtii is a green microalga that divides by multiple fission. During a long G1 phase, a cell can grow to many times its original size and pass several commitment points (CPs), the points of no return after which a cell is irreversibly committed to divide. A cell that passes *n* CPs then completes *n* rounds of DNA replication, mitosis and cytokinesis in quick succession, releasing up to 2^n daughters. How the chloroplast, with its own genome and division machinery, is linked to this cycle is still poorly understood. We treated synchronised cultures with nalidixic acid, a DNA gyrase inhibitor that targets the chloroplast, and followed their physiological, transcript and protein changes for 48 h. Treated cells commit later than controls but at the same size, yet they never divide. Instead, they keep growing, reaching 16× their starting volume by 36 h and 16× their DNA per cell by 48 h, while their nucleoids (the DNA–protein complexes of the chloroplast) become fewer and larger. Chloroplast stress proteins such as HSP22E/F, VIPP2, CLPB3 and DEG1C rise, while chloroplast-encoded and chloroplast ribosomal proteins fall, followed by photosystem I and then the photosystem II core. Mitochondrial and carbon metabolism are upregulated later. Proteins of mitosis (S/M phase) and chloroplast division are first delayed and then accumulate without division taking place. Together, these results suggest that chloroplast genome integrity is a checkpoint for cell division in multiple fission, but not for growth.