

P039 Apoptosis following cytokinesis failure in a model of X-linked neutropenia does not require p53

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Cytokinesis failure is the cause of the inherited immune disorder X-linked neutropenia (XLN). Activating mutations in the gene encoding the Wiskott-Aldrich Syndrome protein (WASp) are found in all XLN patients. U937 and HT1080 cells were used to model XLN by lentiviral transduction of eGFP-WASp1294T. The active mutant WASp1294T promoted actin polymerisation, resulting in excessive filamentous actin accumulating throughout the cell. During mitosis, delocalised filamentous actin surrounded chromosomes and the mitotic spindle and filled the cytoplasm within the cleavage furrow. Anaphase onset was delayed in 50% of divisions and cytokinesis failed in 10% of divisions. Apoptosis was triggered in the resulting binucleated cells. U937 cells do not express p53, so apoptosis induction was independent of p53. Experiments with HCT116 cell lines with an intact p53 response and a derivative cell line with knock out of p53 confirmed this p53 independent removal of cells expressing eGFP-WASp1294T. Ongoing studies aim to further define the mechanisms underlying apoptosis in this system.