

## 48. **A novel treatment strategy targeting shugoshin 1 in hematological malignancies**

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### Abstract

The shugoshin 1 (sgo 1) belongs to the family of mitotic kinase and plays an important role in mitosis. For example, sgo 1 is involved in maintenance of centromeric cohesion from prophase to the metaphase-anaphase transition, regulating kinetochore microtubule stability, sensing interkinetochore tension and ensuring bipolar attachment of kinetochores. Aberrant expression of the mitotic kinase is associated with chromosomal instability, a common feature of hematological malignancies. The present study found that sgo 1 was aberrantly expressed in a variety of types of human leukemia cell lines (n=10, e.g., HL-60, NB4, MOLM-13, K562, EOL-1, etc.), as well as freshly isolated leukemia cells from individuals with acute myelogenous leukemia (AML, n=43) compared with bone marrow mononuclear cells from healthy volunteers (n=9), as measured by real-time PCR. In addition, we found that depletion of sgo 1 by a small interfering RNA (siRNA) slowed the proliferation of NB-4 and EOL-1 cells compared to the control siRNA transfected cells, in parallel with induction of precocious dissociation of centromeric cohesion and separation of sister chromatids in these cells. Furthermore, we found that sgo 1 silencing by siRNA accumulated EOL-1 cells in the M phase of the cell cycle, followed by apoptosis, as measured by cell cycle analysis and detection of the cleaved forms of caspase 3 and PARP by immunocytochemistry, respectively. Taken together, sgo 1 may be a promising molecular target for individuals with AML.