Depletion of SIRT6 enzymatic activity leads to DNA rapair mechanisms disruption, and genomic instability in Acute Myeloid Leukemia (AML) cells

SIRT6

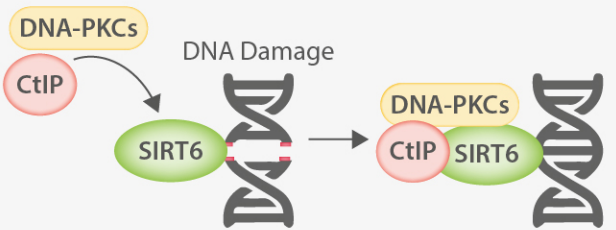
- NAD+-dependent nuclear deacetylase
- functions as genome-guardian by preserving DNA integrity in different tumor cells

SIRT6 overexpression

chromosomal instability and poor prognosis in a subgroup of AML patients

SIRT6-wt AML cells

DNA-damaging agents (DDAs)
DNR, Ara-C



- Promotion of DNA repair
- Genome integrity
- Reduced sensitivity to DDAs

SIRT6-depleted AML cells

DNA-damaging agents (DDAs)
DNR, Ara-C

In vitro

In vivo

- Reduced levels of PKCs and CtIP
  - Freezing of DNA repair mechanisms
  - Greater DNA damage
- Hypersensitivity to DDAs
- Reduction of blast-cell count and tumor growth

Cagnetta *et al.*, Haematologica, 2017