We are currently working on the relationship between genetic instability and carcinogenesis through the model of Bloom syndrome (BS), which displays one of the strongest known correlations between chromosomal instability and a high risk of cancer at an early age.

This suggests that early initial events occurring in BS cells lead to genetic instability, which probably underlies the diversity of independent cancers developed by BS patients. Such early events may also be involved in the initiation of carcinogenesis in the general population and may be common to several kinds of cancers. BS is caused by mutations in the BLM gene, which encodes BLM, a RecQ 3’-5’ DNA helicase. The specific functions of BLM remain unclear, but it is widely thought that it is involved in restarting blocked replication forks. In the absence of BLM, cells display a high rate of sister chromatid exchanges (SCEs) (Fig. 1), pathognomonic for BS, mitotic abnormalities and high levels of oxidative stress.
Our research activities also focus on the specific role of BLM during G2 phase and mitosis. We showed that BLM is recruited at centromeres from G2 to mitosis, where it cooperates with PICH to recruit topoisomerase IIa, likely to facilitate correct centromere disjunction and to prevent the formation of supernumerary ultrafine anaphase bridges. We recently showed that a CDA defect in BS cells was fully responsible for the increase in ultrafine anaphase bridges frequency (Gemble et al., submitted).

Our projects aim to improve our understanding of (a) how cells tolerate endogenous replication stress and the DNA damage associated with BLM and/or CDA deficiencies, (b) the consequences of CDA deficiency for DNA damage responses in BS and non-BS conditions, (c) the link between CDA deficiency and carcinogenesis in the general population.