PRESENTATION TITLE: *Validation of a Therapeutic Target and Development of a High-Throughput Screen to Identify CUT Domain Inhibitors*

ABSTRACT: It is well established that defects in DNA repair contribute to the development of cancer. Paradoxically, increased DNA repair efficiency, in particular of the base excision repair (BER) pathway, is essential for many cancer cells, not only to resist genotoxic treatments but also to proliferate in the presence of elevated reactive oxygen species (ROS) produced by cancer-associated metabolic changes. We have now identified DNA repair accessory proteins that are acutely needed in cancer cells in which the RAS pathway is activated. In contrast to BER enzymes, accessory proteins are not essential to normal cells under physiological conditions. These proteins are required only in situation of excessive DNA damage, as that caused by altered metabolism in RAS-driven cancer cells or by genotoxic cancer treatments. This provides an opportunity to develop new drugs targeting accessory proteins to which cancer cells have become addicted. We will present the validation of DNA repair accessory proteins as therapeutic targets and the biochemical assays that led to the development of a high-throughput screen.