Inhibitors of poly(ADP-ribose) polymerase (PARP) have recently entered the clinic for the treatment of homologous recombination–deficient cancers. Despite the success of this approach, resistance to PARP inhibitors (PARPis) is a clinical hurdle, and it is poorly understood how cancer cells escape the deadly effects of PARPis without restoring BRCA1/2 function. By synergizing the advantages of next-generation sequencing with functional genetic screens in tractable model systems, novel mechanisms providing useful insights into DNA damage response (DDR) have been identified. BRCA1/2 models not only are tools to explore therapy escape mechanisms but also yield basic knowledge about DDR pathways and PARPis’ mechanism of action. Moreover, alterations that render cells resistant to targeted therapies may cause new synthetic dependencies that can be exploited to combat resistant disease.

**Venue:** Lecture Hall Container, Institute of Cancer Research (ICR), Borschkegasse 8a, 1090 Vienna

**Time:** November 15th, 2019, 13.00

**Host:** Gergely Szakács