DESCRIPTION FOR THE GENERAL PUBLIC

MYC is a proto-oncogene with a well-documented essential role in the pathogenesis and maintenance of several types of cancer. Elevated MYC levels have been found in up to 70% of human cancers and growth of these cancers depends on MYC. Although research in the past decades has shed light on many aspects of MYC functions, full understanding of its role in normal and malignant cells still remains a major challenge. Currently, despite relentless efforts, no MYC-targeting therapies are clinically available. As an alternative approach research focuses on determining crucial targets of MYC. MYC is a transcription factor that binds to specific E-box sequences in the genome to regulate expression of adjacent genes. MYC targets are amongst others involved in cell growth, metabolism, apoptosis and differentiation. It is estimated that approximately 15% of all genes are directly regulated by MYC. However, there is no universal set of MYC targets as many of them are cell type- and development stage-specific. Despite efforts to determine the MYC targetome, a comprehensive analysis of direct MYC targets essential for different types of cancer is missing. The aim of this project is to identify on a genome-wide scale functional MYC binding sites and target genes relevant for growth of cancer cells. In our project we propose an innovative approach employing the CRISPR/Cas9 technology to disrupt MYC binding sites. Our strategy will allow us to pinpoint the MYC binding sites and target genes essential for cancer cell growth in a comprehensive and unbiased way. The results will help to understand the mechanisms underlying cancer cell addiction to MYC and may the pave way for potential targeted therapies. It will also provide a unique tool for a genome-wide interrogation of the MYC targetome generally applicable to a variety of cell types and conditions.