Nasma Aqaqe-Tibi et al., J Med Oncl Ther 2019, Volume 4

ERG ENHANCER-BASED REPORTER IDENTIFIES LEUKEMIA CELLS WITH ELEVATED LEUKAEMOGENIC POTENTIAL DRIVEN BY ERG-USP9X FEED-FORWARD REGULATION

Nasma Aqaqe-Tibi, Muhammad Yassin, Abed Alkader Yassin, Eitan Kugler, Eric R Lechman, Olga I Gan, Amanda Mitchell, John E Dick, Shai Izraeli and **Michael Milyavsky**
Tel Aviv University, Israel

Acute leukaemia is a rapidly progressing blood cancer with low survival rates. Unfavorable prognosis is attributed to the insufficiently characterized subpopulation of leukemia stem cells (LSCs) that drive chemo resistance and leukemia relapse. Here authors utilized a genetic reporter which enables stemness assessment to enrich and functionally characterize LSCs. They revealed heterogeneous activity of the ERG+85 enhancer based fluorescent reporter in human leukemias. Cells with high reporter activity (tag BFP High) exhibited elevated expression of stemness and chemo-resistance genes, demonstrated increased clonogenicity and resistance to chemo and radio-therapy as compared to their tag BFP Neg counterparts. Moreover, tag BFP high enriched fraction was capable of regenerating the original cellular heterogeneity and demonstrated increased invasion ability. Most importantly, tag BFP High fraction was enriched for leukemia initiating cells in a xenograft assay. They also identified USP9X deubiquitinase enzyme as a novel ERG transcriptional target that sustains ERG+85 positive cells. Therapeutic targeting of USP9X led to the preferential inhibition of the ERG-dependent leukemias. In summary, they have developed a new strategy to characterize LSCs and propose ERG targeting via USP9X inhibition as a potential anti-leukaemia treatment.

BIOGRAPHY

Nasma Aqaqe-Tibi is a fourth year PhD student at Tel-Aviv University, currently working on characterization of gene regulatory networks responsible for human leukemia cells regeneration after genotoxic stress at Dr Milyavsky lab.

nasma.aqaqe@gmail.com