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## Regulation of cell-trafficking in hematologic malignancies: Translating cellular mechanisms to therapeutic applications

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The progression of most of the hematologic malignancies (HMs) involves a continuous egress of tumor cells from the bone marrow (BM) into the peripheral blood and re-entrance into the BM. The interaction of tumor cells with extracellular matrix proteins and BM cells, as well as factors in the BM milieu (cytokines, chemokines, angiogenesis) plays a crucial role in the pathogenesis and drug resistance of HMs.

We showed that by blocking CXCR4/SDF1 we were able to disrupt the interaction of tumor cells with the BM microenvironment, which in turn enhanced the efficacy of cytotoxic agents against multiple myeloma, lymphoma and chronic myeloid leukemia. Based on these results a Phase I/II clinical trial is being conducted. Mechanistically, we have also shown the inhibition of either the receptor-ligand interaction or inhibition of proteins downstream of CXCR4, such as Rho GTPases, interrupted the interaction of tumor cells with the BM microenvironment. Similarly, we found that inhibition of interaction of P-Selectin ligand in the tumor cells and the P-selectin in endothelial cells and stromal cells in the BM sensitized the tumor cells to therapy. Moreover, we found that tumor progression induces hypoxia in the BM microenvironment, which in turn, induces egress of tumor cells from the BM and enhances homing of circulating cells to new BM niches.

Targeting cell trafficking-regulating proteins (chemokines receptors, adhesion molecules and downstream signaling) and/ or the hypoxic response is a novel approach for prevention of tumor spread in HMs, and opens a window to develop new tumor targeted therapies.

## Biography

Abdel Kareem Azab is an Assistant Professor at Washington University of St. Louis School of Medicine. He completed his pharmacy studies, M.Sc. in medicinal chemistry and Ph.D. in pharmaceutical sciences focusing on targeted drug delivery to cancer at the Hebrew University of Jerusalem, and a post doctoral training focusing on cancer cell biology at Harvard Medical School. Dr. Azab achieved several national and international awards, and published more than 40 peer reviewed articles, a book chapter and 4 patents. He serves as a senior editor of the American Journal of Cancer Biology, and a reviewer for many other journals.

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