**Role of arrestins in CXCL12 induced migration in different cancer cell lines**

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***Background and aims:*** Arrestins are expressed ubiquitously in all cells and tissues, and they not only have a function in desensitization of most G-protein coupled receptors (GPCRs), but they also serve as multifunctional adaptors and scaffolds for GPCR signalling[1]. Extensive research demonstrates that arrestins have a function in development of cancer and tumour metastasis through chemotaxis, a directed cell migration. Over the years, various signalling molecules that are involved in CXCR4 triggered migration have been identified, however, there is still some uncertainty about which pathways are directly involved in cell migration. Our aim is to investigate the role of different arrestins' subtypes in CXCL12-induced migration and whether they are involved directly in cell migration, in cell polarization or act as scaffolds[2].

***Methods:*** MCF-7 cells were transfected chemically with Turbofect and 2 µg of different arrestins' DNA plasmids while Jurkat cells were transfected by electroporation transfection with 2 µg of different arrestins' DNA plasmids and pEGFP.C2 were transfected into these cells as control experiments. Chemotaxis and scratch assays were carried out after 24 hours of transfection.

***Summary of work and outcomes:*** Results shown that CXCL12 activation leads to a movement of arrestin-3 in adherent breast cancer cells, MCF-7 cells and that arrestin-3 is required for CXCL12- induced chemotaxis in suspension leukemic T-lymphocytes, Jurkat cells. Arrestin-3 seems to be the important arrestin subtype that is involved in migration of suspension and adherent cells. All results represent the mean ± SEM of at least 3 independent experiments.

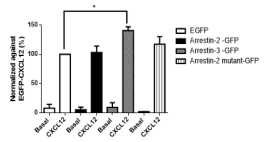


Fig 1. Overexpression of arrestin-3 caused an increase in number of migrating Jurkat cells towards 1 nM CXCL12. * denotes p<0.05 compared to EGFP CXCL12. One-way ANOVA, Bonferroni multiple comparison

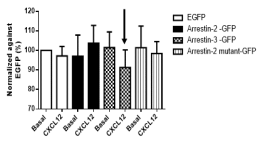


Fig 2. Quantification of migration of MCF-7 cells into the wound. Arrestin-3 overexpression seems to increase migration of MCF-7 cells slightly.

***Discussion:*** Arrestin-3 seems to play an important role in migration of both suspension leukemic T-lymphocytes, Jurkat and adherent breast cancer, MCF-7 cells. These experiments have been further confirmed by knockdown of arrestins using siRNA, which showed that loss of arrestin-3 led to a significant decrease in migration of Jurkat cells towards CXCL12.

***Conclusion:*** CXCL12 activation leads to movement of arrestin-3 in MCF-7 cells and arrestin-3 is required for CXCL12- induced chemotaxis in Jurkat cells. These studies suggested arrestin-3 may be involved directly in migration of cells but further experiments are needed to be done to show how arrestins were involved by investigating the role and activation of arrestins once CXCR4 receptors are activated by ligand CXCL12 through Bioluminescence Resonance Energy Transfer (BRET) studies.

***References:***

1. DeWire, SM *et al.* (2007). *Annu. Rev. Physiol.* **69,** 483-510.
2. DeFea, KA (2007). *Annu. Rev. Physiol.* **69,** 535-560