

## “Role of Natural Killer Cells in Cancer and Autoimmune Diseases: Colorectal Cancer and Rheumatoid Arthritis as Models”

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### Abstract:

Natural killer (NK) cells have been described to play a critical role in cancer and autoimmune diseases. However, these cells face multiple obstacles in performing their cytolytic functions, such as inability to migrate towards cancer sites. Besides, the role of NK cells in the pathogenesis of autoimmune diseases such as rheumatoid arthritis (RA) has not been clearly identified. Hence, this study aimed at increasing NK cell migration to colorectal cancer sites using dimethyl fumarate (DMF) or monomethyl fumarate (MMF) as well as investigating potential NK cell markers that may aid in understanding the state of NK cells in RA. Recombinant chemokines and supernatants collected from the cell line HCT-116 were used in chemotaxis and calcium mobilization of NK92 cell line. Upon pretreatment of NK92 with DMF or MMF, flow cytometry, western blot, qPCR and cytotoxicity assays were performed. In order to assess the role of NK cells in RA, in silico tools were used to identify genes that differentiate between various immune cells and NK cells, as well as NK cells of RA patients and healthy controls. This was validated on freshly isolated peripheral blood mononuclear cells and NK cells of healthy and RA individuals. CCL27, CCL28, CXCL16, and HCT-116 supernatants induced chemotaxis and mobilization of intracellular calcium in NK92 cells. Additionally, MMF or DMF pretreatment of NK92 cells upregulated the receptors CCR10 and CXCR6 and increased NK cytolytic activity. Besides, the identified genes were validated to be differentially expressed in NK cells compared to PBMCs as well as between NK cells of RA patients and healthy controls. In conclusion, this study aids in further understanding the potential role of NK cells in cancer and autoimmune diseases. Hence, our results suggest that NK cells could be harnessed as a tool for cancer immunotherapy and RA diagnosis.

### Supervisor & Co-Supervisor names:

- University of Sharjah:
  - Main Supervisor: Prof. Azzam A. Maghazachi
  - Co-Supervisor: Dr. Suad Hannawi

### Publications from the PhD thesis:

1. 1. Elemam NM, Hachim MY, Hannawi S, Maghazachi AA. differentially expressed genes of natural killer cells can distinguish rheumatoid arthritis patients from healthy controls. **Genes** 2020; 11:492.
2. 2. Elemam NM, Hannawi S, Maghazachi AA. Role of chemokines and chemokine receptors in rheumatoid arthritis. **Immunotargets and Therapy** 2020; 9: 43-56.

3. 3. Elemam NM, Al-Jaderi Z, Hachim MY, Maghazachi AA. HCT-116 colorectal cancer cells secrete chemokines which induce chemoattraction and intracellular calcium mobilization in NK92 cells. ***Cancer Immunology, Immunotherapy:CII*** 2019; 68: 883-895.
4. 4. Elemam NM, Hannawi S, Maghazachi AA. Innate lymphoid cells (ILCs) as mediators of inflammation, release of cytokines and lytic molecules. ***Toxins*** 2017;9.

#### Conferences from the PhD thesis:

1. Elemam NM, Hachim MY, Hannawi S, Maghazachi A. Natural killer cells gene expression can differentiate rheumatoid arthritis patients from healthy controls [abstract]. **8th Pan Arab Human Genetics Conference**; January 2020, Dubai, United Arab Emirates.
2. Elemam NM, Hachim MY, Hannawi S, Maghazachi A. Natural killer cells gene expression can differentiate rheumatoid arthritis patients from healthy controls [abstract]. **ACR/ARP Meeting, Atlanta, Georgia**, United States of America, Arthritis Rheumatology 2019; 71 (suppl 10). <https://acrabstracts.org/abstract/natural-killercells-gene-expression-can-differentiate-rheumatoid-arthritis-patients-fromhealthy-controls>.
3. Elemam NM, Hachim MY, Hannawi S, Maghazachi A. Natural killer cells gene expression can differentiate rheumatoid arthritis patients from healthy controls [abstract]. **The 7th Emirati-German Congress in Medicine and Dentistry**; November 2019, Sharjah, United Arab Emirates.
4. Maghazachi A, Elemam NM, Al-Jaderi Z. HCT116 colorectal cancer cells secrete chemokines which induce the chemotaxis and intracellular calcium mobilization of NK92 cells. Influence of dimethyl fumarate and monomethyl fumarate [abstract]. **Experimental Biology, San Diego, USA**, The FASEB Journal 2018; 32: 667.2-667.2.
5. Elemam NM, Al-Jaderi Z, Maghazachi AA. HCT-116 colorectal cancer cells release chemokines that induce the chemotaxis and intracellular calcium mobilization in NK92 cell lines. **UAE Graduate Student Research Conference**, American University of Sharjah, Sharjah, United Arab Emirates, 2018.