Interleukin-2 Acts Directly on Renal Cell Carcinoma Cells

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Background: Renal Cell Carcinoma (RCC) includes various subtypes, clear cell carcinoma representing the most frequent type (75%). Since many patients manifest the first symptoms at an advanced stage, immunotherapy is considered a possible treatment, such as application of interleukin-2 (IL-2). To date, it is known that IL-2 plays a role in the upregulation of the anti-tumor immune response. However, a direct influence of IL-2 on the kidney tumor cells has not yet been demonstrated.

Objectives: We aimed to investigate expression and functionality of the heterotrimeric IL-2 receptor (IL-2R) α (CD25), β (CD122), γ (CD132) complex on the RCC cells, as well as to reveal whether IL-2 acts directly on RCC cells.

Materials and Methods: For this in vitro project, 4 kidney cancer cell lines where used: ACHN (adenocarcinoma with papillary and clear cell characteristics), A-498 (clear cell carcinoma), Caki-1 (clear cell carcinoma), and Caki-2 (clear cell carcinoma) (from ATCC, USA). IL-2Rαβγ gene expression was detected by qPCR, Western Blot, and Flow Cytometry. IL-2R functionality was investigated by culturing the cells in the presence or absence of human recombinant IL-2 through MTT and BrdU-incorporation assays to measure proliferation and cell survival, and through Live-or-Dye™ Fixable Viability Staining to measure cell death.

Results: qPCR showed mRNA expression of β chain in 3 of 4 cancer cell lines, while at the protein level, Western Blot showed expression of the entire heterotrimeric IL-2Rαβγ complex and Flow Cytometry of the β and γ chain, in all cell lines. We also observed that IL-2 enhances cell proliferation or cell death, depending on cell line and IL-2 concentration.

Conclusion: We conclude that the IL-2R is functional, and that IL-2 could be used as a therapeutic option to act directly on the cancer cells. However, further investigation is required for better understanding the influence of IL-2 on the cancer cells.

Keywords: Renal cell carcinoma, Interleukin-2, IL-2Rαβγ