Efek Stimulasi Eksosom dari Serum Sehat pada Sel NK Subyek Karsinoma Hepatoselular In Vitro = Stimulation Effect Of Exosome From Healthy Sera To Nk Cells Of Hepatocellular Carcinoma Subject In Vitro

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Abstrak

Karsinoma hepatoselular memiliki prognosis yang buruk akibat keterbatasan terapi seperti terlambat diagnosis, kurangnya biomarker spesifik, dan ketidakpekaan terhadap agen tumor ini. Imunoterapi berbasis sel NK autologus dengan stimulasi eksosom menjadi modalitas pengembangan imunoterapi berbasis sel NK untuk pasien karsinoma hepatoseluler. Sel NK pasien karsinoma hepatoseluler diisolasi dari darah vena perifer dan eksosom diisolasi dari serum darah donor sehat. Karakterisasi eksosom dengan particle size analyzer dan flow cytometry. Stimulasi eksosom ke sel NK selama 24 jam kemudian evaluasi ekspresi reseptor NKp44, NKp46, NKp30, NKG2D, KIR2D, dan NKG2A serta ekspresi perforin dan granzyme B. Visualisasi interaksi sel NK dengan fraksi sel mononuklear lainnya (CD4, CD8, CD11c, dan CD19) dengan imunofluorens. Ukuran partikel < 100 nm, muatan listrik negatif dan CD63+CD81+ (positif ganda) hasil isolasi eksosom. Terjadi peningkatan ekspresi reseptor NKp44, NKp46, NKp30, NKG2D, penurunan ekspresi NKG2A, serta peningkatan ekspresi perforin dan granzyme B pada sel NK terinduksi eksosom. Tidak ada interaksi sel berupa sinapsis imun antara sel NK terstimulasi eksosom dengan fraksi sel mononuklear lain pasien karsinoma hepatoseluler. Stimulasi eksosom ke sel NK pasien karsinoma hepatoseluler memulihkan kemampuan sitotoksik sel NK.

.....Hepatocellular carcinoma has a poor prognosis due to limitations of therapy such as late diagnosis, lack of specific biomarkers, and insensitivity to this tumor agent. Autologous NK cell-based immunotherapy with exosome stimulation is a modality for developing NK cell-based immunotherapy for hepatocellular carcinoma patients. NK cells from hepatocellular carcinoma patients were isolated from peripheral venous blood, and exosomes were isolated from the blood serum of healthy donors. Exosome characterization with a particle size analyzer and flow cytometry. Stimulation of exosomes on NK cells for 24 hours, then evaluation of expression of NKp44, NKp46, NKp30, NKG2D, KIR2D, and NKG2A receptors, as well as perforin and granzyme B expression. Visualization of interactions of NK cells with other mononuclear cell fractions (CD4, CD8, CD11c, and CD19) by immunofluorescence. Particle size < 100 nm, negative electric charge, and CD63+CD81+ (double positive) exosome isolated results. There was increased expression of receptors NKp44, NKp46, NKp30, NKG2D, decreased expression of NKG2A, and increased expression of perforin and granzyme B in exosome-induced NK cells. There was no cell interaction in the form of immune synapses between exosome-stimulated NK cells and other mononuclear cell fractions in hepatocellular carcinoma patients. Stimulation of exosomes into NK cells of hepatocellular carcinoma patients restores the cytotoxic ability of NK cells.