

# Histodinamika sel Natural Killer donor sehat yang dipaparkan eksosom dari darah pasien karsinoma Hepatoseluler = Histodynamics of Natural Killer cells from healthy donor exposed to exosomes from the blood of Hepatocellular carcinoma patients

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## Abstrak

Karsinoma hepatoseluler (KHS) adalah kanker primer liver dan penyebab kedua kematian akibat kanker. Eksosom pada lingkungan mikro KHS berfungsi untuk komunikasi antar sel dan bila endositoses ke sel NK dapat menyebabkan perubahan pada sel NK. Penelitian ini bertujuan menganalisis eksosom dari darah pasien KHS, perubahan fenotipe sel NK, dan uji pewarnaan histologi (peroksidase, toluidine blue) untuk mengamati perubahan granula azurofilik sel NK akibat endositoses eksosom. Metode penelitian meliputi isolasi sel NK dari donor sehat dan eksosom darah pasien KHS, karakterisasi eksosom dengan PSA, stimulasi sel NK dengan eksosom, flow cytometry reseptor pada sel NK dan CD81+ pada eksosom, imunofluoresens endositoses eksosom ke sel NK, pewarnaan toluidine blue dan peroksidase. Hasil menunjukkan eksosom berukuran 34,7 nm, bermuatan -4,33 mV dan positif CD81+. Perubahan reseptor sel NK sehat yang dipaparkan eksosom KHS tidak signifikan ( $P>0,05$ ). Imunofluoresens memperlihatkan endositoses eksosom ke sel NK. Pewarnaan sel NK toluidine blue menunjukkan metakromasia dan peroksidase negatif. Sel NK+eksosom mengalami perubahan hasil pewarnaan. Peneliti menyimpulkan bahwa eksosom dari darah pasien KHS sesuai kriteria MISEV 2018. Tidak terjadi perubahan fenotipe sel NK sehat yang dipaparkan eksosom dari darah pasien KHS. Pewarnaan peroksidase dan toluidine blue dapat digunakan sebagai metode pengamatan endositoses eksosom ke sel NK.

.....Hepatocellular carcinoma (HCC) is the primary liver cancer and the second leading cause of death from cancer. Exosomes in the HCC microenvironment function for communication between cells and when endocytosed to NK cells can cause changes in NK cells. This study aims to analyze exosomes from the blood of HCC patients, changes in NK cell phenotype, and histological staining tests (peroxidase, toluidine blue) to observe changes in NK cell azurophilic granules due to exosome endocytosis. NK cells from healthy donors and blood exosomes of KHS patients were isolated, exosomes characterized by PSA, stimulation of NK cells with exosomes, and flow cytometry of receptors on NK cells and CD81+ on exosomes were done. Endocytosis of exosomes onto NK cells were observed through immunofluorescence, then metachromasia and azurophilic granules of NK cells were observed after toluidine blue and peroxidase staining. Results showed The exosome is 34.7 nm in size, has a charge of -4.33 mV and is CD81+ positive. Changes in healthy NK cell receptors exposed to HCC exosomes were not significant ( $P>0.05$ ).

Immunofluorescence demonstrates exosome endocytosis in NK cells. Toluidine blue NK cell staining showed negative metachromasia and peroxidase. In NK cell+exosome there is a change in staining results. We concluded exosomes from the blood of HCC patients comply with MISEV 2018 criteria. There is no change in the phenotype of healthy NK cells exposed to exosomes from the blood of HCC patients. Peroxidase and toluidine blue staining can be used as a method of observing exosome endocytosis in NK cells.