

INTISARI

PROFIL EKSPRESI MIKRO RNA BERKAITAN DENGAN SEL T REGULATOR SEBAGAI RESPON PAPAN MEDAN LISTRIK STATIS FREKUENSI MENENGAH PADA SUKARELAWAN SEHAT

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Latar Belakang. *Electro-Capacitive Cancer Therapy* (ECCT) merupakan sebuah alat terapi medan listrik non kontak frekuensi menengah berbentuk rompi yang dikembangkan di Indonesia yang telah lolos uji secara klinis fase 1. Perubahan miRNA dapat menunjukkan aktivitas Treg, khususnya dalam terapi kanker. Berdasarkan hal tersebut maka perlu dikaji secara molekuler efek dari paparan medan listrik ECCT dengan melihat perubahan profil miRNA yang berkaitan dengan Treg.

Tujuan Penelitian. Mengetahui perubahan ekspresi miRNA yang berkaitan dengan aktivitas Treg (miR-15a/16, miR-17, miR-126, miR-146a, dan miR-150) pada paparan ECCT pada sukarelawan sehat. Dari hasil tersebut dianalisis pengaruh perubahan miRNA terhadap aktivitas Treg secara *in silico*.

Metode Penelitian. Penelitian ini dilakukan di Laboratorium Terpadu FKKMK UGM. Plasma yang digunakan berjumlah empat sampel *pre* dan empat sampel *post* pemakaian rompi ECCT dengan medan listrik frekuensi 100 kHz dan intensitas 18 Vpp selama 21 hari. Kedelapan sampel plasma tersebut diperoleh dari penelitian sebelumnya (uji klinis 1 ECCT). Plasma tersebut kemudian dilakukan isolasi total RNA, kemudian dilakukan sintesis cDNA. Hasil cDNA RNA dilakukan *profiling* menggunakan primer miRNA target. Metode pengujian profil ekspresi miRNA yang digunakan adalah qRT-PCR. Hasil pembacaan qRT-PCR berupa *delta cycle of threshold* (C_T) antara *pre* dan *post* kemudian dianalisis secara statistik menggunakan SPSS dengan melakukan uji normalitas dengan uji Shapiro-Wilk, jika terdistribusi normal maka dilanjutkan dengan uji *paired T-test* dan dihitung perubahan kelipatan ekspresi dengan metode Livak. Analisis *in silico* menggunakan DIANA miRPath untuk mengetahui miRNA fungsional dalam regulasi Treg.

Hasil. Hasil dari penelitian ini tidak terdapat perubahan dari ekspresi miRNA secara signifikan setelah paparan ECCT. Secara *in silico* didapatkan pengaruh miRNA terhadap Treg berkaitan dengan *TGF-beta signaling pathway* yang berperan terhadap faktor transkripsi, ko-aktivator serta ko-represor yang berperan dalam angiogenesis, apoptosis dan sistem imun. Perubahan ekspresi miRNA dimungkinkan dapat meningkatkan respon imun yang berperan terhadap anti tumor.

Kata Kunci : ECCT, miRNA, Respon Imun, Treg, Sukarelawan Sehat

ABSTRACT

MICRO RNA EXPRESSION PROFILE RELATED TO THE REGULATORY T CELLS AS A RESPONSE TO THE EXPOSURE OF THE STATIC ELECTRIC FIELD WITH INTERMEDIATE FREQUENCY ON THE HEALTHY VOLUNTEERS

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Background. Electro-Capacitive Cancer Therapy (ECCT) is a medium-frequency non-contact electric field therapy device in the form of a vest developed in Indonesia that has been clinically trial phase 1. Changes of miRNA indicate changes in Treg activity, particularly in cancer therapy. Based on this, it is still necessary to study molecularly effects of exposure to the ECCT electric field by looking at changes in the miRNA profile associated with Tregs.

Objectives. This research is to determine changes in miRNA expression related to Treg activity (miR-15a / 16, miR-17, miR-126, miR-146a, and miR-150) on ECCT exposure in healthy volunteers. In silico analyzed will be perform to understand the effect of changes in miRNA on Treg activity .

Methods. This research was conducted in laboratory of FKMK UGM. The plasma used was four samples pre and post exposure ECCT with an electric field of 100 kHz frequency and 18 Vpp intensity for 21 days. The eight plasma samples were obtained from previous studies (clinical trial phase 1). The plasma was then isolated for total RNA using miRNeasy Serum / Plasma Advanced Kit, then synthesized cDNA. The results of cDNA RNA were profiled containing the target miRNA primers. The miRNA expression profile testing method used was qRT-PCR. The results of the qRT-PCR readings in the form of delta cycle of threshold (CT) between pre and post were analyzed statistically with SPSS, normality test with the Shapiro-Wilk test then continued with the paired T-test and calculated the change of expression using the Livak method. In silico analysis was performed using DIANA miRPath to determine miRNAs associated with mechanism of Treg.

Result. The result of this study showed no significant change in miRNA expression after ECCT exposure. In silico study was found that the miRNA effect on Tregs related TGF-beta signaling pathway that plays a role in transcription factors, co-activators and co-repressors that play a role in angiogenesis, apoptosis and suppression of the immune system. It is possible that changes in miRNA expression can increase the immune response that plays a role in anti-tumor.

Keywords: ECCT, miRNA, Immune Response, Treg, Healthy Volunteers