UNIVERSITI PUTRA MALAYSIA

METALLOTHIONEIN GENE EXPRESSION IN PERIPHERAL BLOOD LYMPHOCYTES AS BIOMARKERS OF CADMIUM EXPOSURE AMONG MALE DIE CASTING WORKERS IN BANGI, MALAYSIA

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By

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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Master of Science

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Oktober 2010

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Introduction: Die casting is the process of forcing and shaping molten metal usually non ferrous under high pressure into mold cavities which probably emits cadmium (Cd). Cd causes Metallothionein (MT) gene expression. Quantitative reverse transcriptase polymerase chain reaction (RT-PCR) is applicable as a biomarker of Cd exposure. **Objective:** Objective of this study is to determine the relationship between urinary and blood concentrations of Cd with MT gene expression in peripheral blood lymphocytes among die casting male workers in a non ferrous metal industry in Bangi, Selangor. **Methodology:** A cross sectional study was carry out on 61 respondents. 33 respondents who performed task in die casting process was chosen as exposed group while 28 workers who performed task in the administrative division considered as comparative group. Questionnaires were administered to obtain the sociodemography information of respondents. Early shift of minimum 15 ml urine sample was taken from respondents to determine urine cadmium (UCd) concentration using Graphite Furnace Atomic

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Absorption Spectrometry (GFAAS). 10ml of blood sample was taken to determine the blood cadmium (BCd) concentration using GFAAS and MT gene expression level using RT-PCR. **Results:** The mean±SD of UCd level was 0.037±0.047µg/g creatinine for exposed group and 0.025±0.031 µg/g creatinine for comparative group and the difference was not statistically significant (Z=1.369, p=0.863). The mean±SD for BCd concentration was 0.729±0.11 µg/dL for exposed group and 0.323±0.156 µg/dL for comparative group and the difference were statistically significant (t=9.95, p=0.001).The mean±SD MT basal expression was 1.91±0.28 for exposed group and 1.69±0.28 for comparative group and the difference were statistical significant (t=2.391, p=0.02). The mean±SD MT induction expression was 2.62±0.54 for exposed group and 2.11±0.36 for comparative group and the difference was statistically significant (t=3.56, p=0.001). The relationship between MT basal expression and BCd in exposed group showed a significant moderate positive correlation between the two variables(r = 0.487, p=0.004) and the relationship between MT induction expression and BCd in exposed group showed a significant weak positive correlation between two variables (r=0.167, p=0.035). Both MT basal expression and MT induction expression showed no significant relationship with UCd in exposed group with r=0.09, p=0.067and r=-0.199, p=0.763 respectively. **Conclusion:** There was a significant correlation between BCd level and MT gene expression. BCd and MT basal expression in appears to be a strong biomarkers for Cd recent exposure.

(Keywords: Die Casting, Male Workers, UCd, BCd, MT Gene Expression)

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Abstract tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Sarjana Sains

EKSPRESI GEN METALLOTHIONEIN DALAM LIMFOSIT PERIFERI DI KALANGAN PEKERJA LELAKI TUANGAN ACUAN LOGAM DI BANGI, MALAYSIA

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Pendahuluan: Tuangan acuan logam merupakan satu proses paksaan cairan logam di bawah tekanan tinggi ke dalam satu rongga acuan. Cd menyebabkan ekspresi gen metallothionein (MT). Pengukuran kuantitatif transkriptase terbalik reaksi polimerase berantai (RT-PCR) boleh digunakan sebagai salah satu penanda biologi bagi pendedahan Cd. **Objektif:** Objektif kajian ini adalah untuk menentukan hubungan antara kepekatan Cd dalam urin dan darah dengan ekspresi gen MT dalam limfosit periferi dikalangan pekerja lelaki tuangan acuan logam di Selangor. **Metodologi:** Satu kajian keratan lintang dijalankan dengan 61 responden. 33 responden terdiri daripada kumpulan kajian yang bekerja di bahagian tuangan acuan dan 28 responden terdiri daripada kumpulan bandingan yang bekerja di bahagian pentadbiran. Kajian soal selidik dilakukan untuk mendapatkan maklumat sosiodemografi responden. Sampel urin awal syif diambil dari responden untuk mengukur kepekatan urin kadmium (UCd) dengan menggunakan Grafit Furnace Spektrometri Serapan Atom (GFAAS). Sampel darah

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diambil dari responden untuk mengukur kepekatan darah kadmium (BCd) menggunakan GFAAS dan tahap ekspresi gen MT menggunakan RT-PCR. **Keputusan:** Min±Sisihan piawai kepekatan UCd adalah 0.037±0.047µg/g kreatinin untuk kumpulan kajian dan 0.025±0.031 µg/g kreatinin untuk kumpulan bandingan dan perbezaannya tidak mempunyai hubungan yang signifikan (Z=1.369, p=0.863). Min±Sisihan piawai untuk konsentrasi BCd adalah 0.729 ± 0.11 µg/dL untuk kumpulan kajian dan 0.323 ± 0.156 µg/dL bagi kumpulan bandingan dan perbezaanya mempunyai hubungan yang signifikan (t = 9.95, p 0.001). Min±Sisihan piawai ekspresi MT basal adalah 1.91±0.28 untuk kumpulan kajian dan 1.69±0.28 untuk kumpulan bandingan dan perbezaannya mempunyai hubungan yang signifikan (t=2.391, p =0.02). Min±Sisihan piawai ekspresi MT induksi adalah 2.62 ±0.54 untuk kumpulan kajian dan 2.11±0.36 untuk kumpulan bandingan dan perbezaannya mempunyai hubungan yang sifnifikan (t=3.56, p=0.001). Hubungan antara ekspresi MT basal dan BCd memperolehi hubungan moderat dan positif yang signifikan antara kedua-dua pembolehubah untuk kumpulan kajian (r=0.487, p=0.004) dan hubungan antara ekspresi MT induksi dan BCd diperolehi korelasi lemah dan positif yang signifikan antara kedua-dua pembolehubah (r = 0.167, p=0.035). Kedua-dua ekspresi MT basal dan MT induksi tidak mempunyai hubungan yang signifikan dengan UCd dan r = 0.09, p=0.067 dan r = -0.199, p=0.763. **Kesimpulan:** Kajian ini membuktikan kepekatan BCd mempunyai hubungan yang signifikan dengan ekspresi gen MT basal. Ekspresi gen MT basal merupakan penanda kuat biologi khusus untuk pendedahan baru Cd.

(Kata kunci: Tuangan Acuan Logam, Pekerja Lelaki, UCd, BCd, Ekspresi Gen MT)

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I certify that a Thesis Examination Committee has met on date of viva voce to conduct the final examination of **OOI KEOK LOO** on her **Master of Science** thesis entitled **"Metallothionein gene expression in peripheral blood lymphocytes as biomarkers among male die casting workers in Bangi, Malaysia"** in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998.The Committee recommends that the student be awarded degree of Master of Science.

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DECLARATION

I declare that the thesis is my original work except for the synthesis of tested compounds, docking experiment, quotations and citations which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or at any other institution.

OOI KEOK LOO

Date: 12 Oktober 2010

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