## Circulating Endothelial Progenitor Cells and Aortic Wall Changes in Male Wistar Rat Exposed to Chronic Mild Stress and High Fat Diet with the Possible Role of Pentoxifylline. Histological, Immunohistochemical and Flowcytometric Study

#### **Thesis**

Submitted for Partial Fulfillment of M.Sc. Degree in Histology

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#### List of Abbreviations

AGE Advanced glycation end products

BBB Blood brain barrier

bFGF Basic fibroblast growth factor

BWG Body weight gain

CCT diet 4% cholesterol, 0.5% cholic acid, and 0.2%

thiouracil

CD133 Cluster of differentiation 133 CD31 Cluster of differentiation 31 CD34 Cluster of differentiation 34

CEPCs Circulating endothelial progenitor cells

CHF Congestive heart failure
CMS Chronic mild stress
CVD Cardiovascular diseases

DSM-IV Diagnostic and statistical manual of mental

disorders 4<sup>th</sup> edition

DSM-IV Diagnostic and statistical manual of mental

disorders, 4th ed.

FITC Fluorescein isothiocyanate

FST Forced swim test

G-CSF Granulocyte-Colony Stimulating Factor

HGF Hepatocyte growth factor

ICAM-1 Intercellular adhesion molecule 1

IEL Internal elastic lamina

IFN-α Interferon alpha IFN-γ interferon gamma

IGF-1 Insulin-like Growth Factor 1

IL-1 Interleukin-1
IL-10 Interleukin-10
IL-12 Interleukin-12
IL-13 Interleukin-13
IL-2 Interleukin-2
IL-4 Interleukin-4
IL-6 Interleukin-6

IL-8 Interleukin-8 IMI Imipramine

IMR Intima-media ratio

iNOS inducible Nitric Oxide Synthase

LDL Low Density Lipoproteins
MAOI Monoamine oxidase inhibitor
MDD Major depressive Disorder
MMPs Matrix metalloproteinases

NK cells Natural killer cells

NO Nitric Oxide OFT Open field test

oxLDL Oxidized Low Density Lipoproteins

PBS Phosphate buffered saline PDGF Platelet-derived growth factor

PE Phycoerythrin

PECAM Platelet endothelial cell adhesion molecule

PTX Pentoxifylline

RAGE Receptor of advanced glycation end products

ROS Reactive oxygen species

SDF-1α Stromal-derived factor 1 alpha

SEM Standard Error of Mean SIT Social interaction test SP Sucrose preference SPT Sucrose preference test

SSRIs Selective serotonin reuptake inhibitors

Tie-1 Tyrosine kinase receptor 1
Tie-2 Tyrosine kinase receptor 2

TIMP Tissue inhibitors of metalloproteinases

 $\begin{array}{ll} TNF\text{-}\alpha & Tumour \ necrosis \ factor \ alpha \\ TNF\text{-}\beta & Tumour \ necrosis \ factor \ beta } \\ VCAM\text{-}1 & Vascular \ adhesion \ molecule \ 1 \\ VE\text{-}cadherin & Vascular \ endothelial \ cadherin \\ \end{array}$ 

VEGF Vascular endothelial growth factor

VEGFR-2 Vascular endothelial cell growth-factor receptor 2

VLA-4 Very-late-antigen 4 vWF von Willebrand factor

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#### Introduction

Both neuropsychiatric disorders and cardiovascular diseases (CVD) constituted a huge burden on our society. According to World Health Organization (WHO) statistics, the three leading causes of mortality by the year 2030 were predicted to be acquired immunodeficiency syndrome, depressive disorders and ischemic heart disease (*Mathers and Loncar*, 2005).

A substantial body of literature provided strong evidence that a bidirectional association between mood disorders and cardiovascular diseases existed in humans, though the precise neurobiological mechanisms that underlie this association were not fully understood (*Grippo*, 2009; *Joynt et al.*, 2003).

Joynt et al. (2003) reported that coronary artery disease, myocardial infarction and congestive heart failure (CHF) were associated with altered mood states and depressive syndromes and were considered to be risk factors for cardiac morbidity and mortality.

On the other hand, seasonal mood changes have been correlated with seasonal variation in coronary heart disease, as *Sher* (2001) found that winter depression contributed to winter increase in incidence and mortality of cardiovascular disease. Patients with depression had more than two folds higher risk of developing heart failure and repeated hospital admissions as reported by *Pasic et al.* (2003). *Penninx et al.* (2001) showed that major depressive disorder (MDD) was associated with increased risk of cardiac mortality and the more severe the depression the greater the risk for subsequent cardiac mortality. Whereas, *Zellweger et al.* (2004) considered depression as a risk factor for cardiac events in patients with

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