THE EFFECTS OF MAGNETIC FIELDS (MFs) ON *IN VITRO* CULTURE OF hUMAN UMBILICAL CORD DERIVED MESENCHYMAL STEM CELLS (hUC-MSCs)

HASLINDA ABDUL HAMID

A thesis submitted in
fulfillment of the requirement for the award of the
Degree of Master of Science

Faculty of Applied Sciences and Technology
Universiti Tun Hussein Onn Malaysia

JULY 2018

This thesis is dedicated to Almighty "Allah " who gave me strength, knowledge, patience and wisdom). My " Parents " (For their unconditional love, devotion, cares and prays helps me to achieve this target). My " Brother & Nor Hafizah " (Their love, care, commitment and sincerity motivate me to finish this valuable work).

ACKNOWLEDGEMENT

Alhamdullilah, all praises be to Allah SWT. I am grateful to Almighty ALLAH who is the most congenital, most sympathetic and sustainers for the worlds for giving me the potency and the ability to do this research work.

I would like to express my deepest gratitude to Associate Prof. Dr Mohd Kamarulzaki Mustafa for his continuous guidance, encouragement, word of wisdom and motivation. His mentorship was paramount in providing a well-rounded experience consistent my long-term Bio-magnetic Research.

Millions of thanks to Associate Professor Dr Rajesh Ramasamy for his outstanding advisor in this project. He provided me creative ideas, thoughtful suggestions and guidance on projects planning which were very critical for me to finish my dissertation. His hardworking attitude and broad, insightful visions on the research set a distinguished example for me in my future research study.

Special thanks also go to Associate Professor Dr Azizi Miskon for his guidance through my study. Thank you introducing me to the fantastic world of stem cells research.

Finally, and most importantly, I would like thanking my family, Hazrie, Nor Hafizah, Qayyum, Iqram, Wafy and Naurah for their faith in me and allowing me to be as ambitious as I wanted. It was under their watchful eye that I gained so much drive and an ability to tackle challenges head on. Also, I thank to my friends Abdul Mutalib, Uzair, Younas, Auwal, Satar, Hamza, Malini, Nurul Afiqah, Rozita, Adila, Elson, Shamin Azwar and Khair for always give encouragement and support.

ABSTRACT

The potential hazardous effects of magnetic field (MF) exposures on individual have been extensively studied. However, a number of studies have surprisingly observed that response to optimal MF has significantly increased the proliferation rate of stem cells. Accordingly, this current study aims to investigate the potential impact of induced Static Magnetic Field (SMF) on human Umbilical Cord-Derived Mesenchymal Stem Cells (hUC-MSCs) using Samarium Cobalt ($SmCo_5$). $SmCo_5$ was selected for the study due to its known strong permanent moment magnetization, and stable against the influence of demagnetization. The 10,000 of hUC-MSCs at passage 3, seeding in 60 mm petri dish were grown in constant 'direct exposure' (DE) of 21.6 mT SMF, alongside with 'indirect exposure' (IE) and 'negative control' (NC) groups. The growth kinetic experiments in the current study exhibited exponential growth at day four in the DE group, compared to day six for both IE and NC groups. Population doubling time (PDT) was also performed and the results showed DE group contributed significantly to the change in PDT for a period of passage 3 with $p<0.05$. Cell cycle analysis after 18 hours revealed that DE group entered to the cell cycle at higher percentage where hUC-MSCs exposed with MF was committed into 55.18 % cells in S phase and 21.75 % cells at G2/M phase compared to IE. ($[^3H]$-TdR) revealed that DE group gave the highest proliferation capability at all points of seeding density, when compared to IE and NC groups. In addition, flow cytometer analysis discovered no significant difference in the expression of the surface markers of DE group compared to IE and NC. SMF also was observed to have the potential to induce higher expression of pluripotency-associated markers (*OCT4*, *SOX2*, *NANOG*, and *REX1*) in DE group than in the IE and NC groups as analyzed via RT-PCR. In conclusion, through MF exposure, small quantity of collected MSCs could be expanded rapidly in a short period of time. This finding may suggest MF as a new modality to expand MSC for various therapeutic applications.

ABSTRAK

Kesan MF yang berpotensi membawa kemudaratan kepada manusia telah dikaji secara meluas. Walau bagaimanapun, tindakbalas MF secara optimum telah meningkatkan kadar percambahan sel induk dengan begitu ketara. Oleh itu kajian yang sedang dijalankan adalah bertujuan untuk mengkaji kesan potensi ($SmCo_5$) kepada hUC-MSC yang berasal daripada tali pusat manusia. $SmCo_5$ telah digunakan dalam kajian ini kerana ia mempunyai momen magnetisasi yang berlaku secara berterusan, kukuh dan stabil terhadap pengaruh demagnetisasi. Di dalam kajian ini, 10,000 hUC-MSC daripada kumpulan 3 telah dikulturkan di dalam 60 mm petri dish dan didedahkan kepada (MF) DE 21.6 mT bersama-sama dengan kumpulan IE dan NC. Eksperimen kinetik pertumbuhan telah menunjukkan pertumbuhan eksponen berlaku pada hari keempat di dalam kumpulan DE, berbanding hari keenam untuk kedua-dua kumpulan IE dan NC. PDT juga dilakukan dan keputusan menunjukkan perubahan yang ketara berlaku pada kumpulan 3 dengan $p<0.05$. Analisis kitaran sel pada 18 jam, hUC-MSCs yang terdedah kepada MF memasuki kitaran sel jauh lebih tinggi berbanding pada kondisi normal dimana hUC-MSCs diawah MF berkomitmen pada 55.18 % sel di fasa S dan 21.75 % sel pada G2 / M. [^{3}H]-TdR) mendedahkan bahawa kumpulan DE memberi keupayaan pertumbuhan yang tinggi di semua titik pertumbuhan, berbanding dengan kumpulan IE dan NC. Di samping itu, analisis flow sitometer menunjukkan tidak terdapat perbezaan yang signifikan dalam penanda permukaan hUC-MSCs kepada kumpulan DE berbanding dengan IE dan NC. SMF juga dilihat berpotensi untuk mendorong ekspresi yang lebih tinggi transkripsi penanda pluripotent (*OCT4, SOX2, NANOG,* dan *REX1*) dalam kumpulan DE berbanding kumpulan IE dan NC seperti dianalisis melalui RT-PCR. Melalui pendedahan MF, jumlah kecil MSC yang dikumpul dapat dipertingkatkan dengan cepat dalam jangka waktu yang singkat. Penemuan ini mungkin mencadangkan MF sebagai modaliti baru untuk pengembangan MSC untuk pelbagai aplikasi terapeutik.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF SYMBOLS AND ABBREVIATIONS

±	-	Plus minus
μT	-	Microtesla
^{3}H- Tdr	-	Tritium thymidine
8-OhdG	-	*8*-Oxo-2'-deoxyguanosine
hAT-MSCs	-	human Adipose Tissue Derived Mesenchymal Stem Cells
A/m	-	Amperes per meter
AC	-	Alternate current
AP-1	-	Activator protein 1
APC	-	Antigen presenting cells
APC	-	Allophyceoerythrin
APK	-	Activated protein kinase
ATSCs	-	Adipose Tissue Stromal Cells
B	-	Magnetic field (Vector)
B7-1	-	CD80
B7-2	-	CD86
B cell	-	B lymphocyte
Bcl-2	-	B-cell lymphoma 2
BM	-	Bone marrow
BMMSCs	-	Bone Marrow Mesenchymal Stem Cells
BMP4	-	Bone morphogenetic protein 4
bp	-	Base pair
^{0}C	-	Degree celsius
Ca^{2+}	-	Calcium ion
CaM	-	Calmodulin
cAMP	-	cyclic Adenosine Monophosphate
CD	-	Cluster of differentiation

Cdks	-	Cyclin-dependent kinases
cDNA	-	Complementary DNA
CFU-F	-	Colony-forming unit fibroblastic
CO_2	-	Carbon dioxide
CPM	-	Count per minute
DC	-	Dendritic cells
DC	-	Direct current
DMEM	-	Dulbecco's Modified Eagle Medium
DMSO	-	Dimethyl sulfoxide
DNA	-	Deoxyribonucleic acid
E	-	Electric field
E2F	-	Transcription factor E2F
ECM	-	Extracellular matrix
ELF	-	Extremely low frequency
EMFs	-	Electromagnetic fields
ELF-EMF	-	Extremely low frequency electromagnetic fields
ER	-	Endoplasmic reticulum
ERK	-	Extracellular-regulated kinase
ESCs	-	Embryonic stem cells
F	-	Force
FACS	-	Fluorescent- activated sorting
FGF	-	Fibroblast growth factor
FITC	-	Fliorescein isothiocynate
G	-	Gauss
G_0	-	Quiescence phase
G1	-	Gap phase
G2	-	Second gap
GABAc	-	Gamma amino butyric acid rho
GADPH	-	Glyceraldehyde 3-phosphate dehydrogenase
G-CSF	-	Granulocyte colony stimulating factor
GHz	-	Gegahertz
Gy	-	Gray
H	-	*magnetic field* density

Hz	-	Hertz
hBMSCs	-	human Bone Marrow Stem Cells
HBS	-	Human Bovine Serum
hUCMSCs	-	human Umbilical Cord Mesenchymal Stem Cells
HSC	-	Haemotopoietic Stem Cells
hTERT	-	human Telomerase Reverse Transcription
IAIRC	-	International Agency for Research Cancer
ICAM-1	-	Intracellular Adhesion Molecule 1
ICM	-	Inner cell mass
ICNIRP	-	International Commission on Non Ionizing Radiation Protection
IF	-	Intermediate frequency
IF-EMF	-	Intermediate frequency electromagnetic field
IMP	-	Intramembrane proteins
iPSc	-	Induced pluripotent stem cells
kHz	-	Kilohertz
KV/m	-	Kilovolt meter
LF-EMF	-	Low frequency electromagnetic field
MAP	-	Mitogen activated protein
MAPK	-	Mitogen activated protein kinase
MFs	-	Magnetic fields
mG	-	Miligauss
mT	-	Militesla
MHz	-	Megahertz
MHC	-	Major histocompatible complex
MR	-	Magnetic resonance
MSCs	-	Mesenchymal stem cells
mW	-	Milliwatt
MW-EMF	-	Microwave electromagnetic field
OCT4	-	Octamer binding transcription factor-4
%	-	Percentage
PBS	-	Phosphate buffer saline
PCR	-	Polymerase chain reaction

PDT	-	Population doubling time
PE	-	Phycoerrythrin
PI	-	Propodium iodide
pRB	-	Retinoblastoma protein
q	-	Charged of particle
REAC TO-RGN	-	Radio Electric Asymmetric Conveyer Tissue Optimization Regenerative
RF	-	Radio frequency
RT-PCR	-	Reverse transcriptase polymerase reaction
S	-	Synthesis phase
SAR	-	Specific absorption rate
SAPK	-	Stretch- activated protein kinase
SCs	-	Stem cells
SCENIHR	-	Scientific Committee on Emerging and Newly Identified Health Risks
SF	-	Static field
SMF	-	Static magnetic field
$SmCo_5$	-	Samarium Cobalt Magnet
SH-SY5Y	-	Neuroblastoma cell line
T	-	Tesla
TGF-β	-	Transforming growth factor beta
TERT	-	Telomerase reverse transcriptase
N	-	Particle velocity (expressed of the vector)
VCAM-1	-	Vascullar cell adhesion molecule -1
W/Kg	-	Watts per kilogram
WLAN	-	Wireless local area network

LIST OF PUBLICATIONS

Haslinda Abdul Hamid, Mohd Kamarulzaki Mustafa, Azizi Miskon, Rajesh Ramasamy, Shalini Vellasamy (2013). " A Preliminary Study On The Effects Of Static Magnetic Field On Umbilical Cord Mesenchymal Stem Cells Proliferation. " Seminar Kebangsaan Aplikasi Sains dan Matematik 2013 (SKASM 2013) UTHM.

Haslinda Abdul Hamid, Mohd Kamarulzaki Mustafa, Rajesh Ramasamy " The Effects of Magnetic Field on human Umbilical Cord Mesenchymal Stem Cells (hUCMSCs) Proliferation." 21st Malaysian Society for Molecular Biology and Biotechnology (MSMBB) Scientific Meeting at Monash University, 3rd October 2014.

Haslinda Abdul Hamid, Mohd Kamarulzaki Mustafa, Rajesh Ramasamy, & Azizi Miskon." Fundamental Studies on the Effects of Magnetic Field on human Umbilcal Mesenchymal Stem Cells Proliferation." Research &Innovation Festival 3-4 November, 2014, UTHM.

Haslinda Abdul Hamid, Mohd Kamarulzaki Mustafa, Rajesh Ramasamy, Satar Jabbar Rahi, ZuraidahYusoff & Azizi Miskon." The Mitogenic Effects of Induced Magnetic Field on human Umbilical Cord derived Mesenchymal Stem Cells." 6th International Conference on Stem Cells and Cancers (ICSCC- 2015) Proliferation, Differentiation & Apoptosis 2-5 October, Punei, India

CHAPTER 1

INTRODUCTION

1.1 Background of study

Magnetic field (MF) is a physical quantity that is nearly as old as the earth. The Earth's MF also known as geomagnetic field plays an important role in sustaining life on earth since it shields the earth from the solar wind that could destroy the ozone layer, which absorbs most of the harmful ultraviolet radiation. Humans and other living things are naturally exposed to Earth's MF, which is not harmful. Apart from Earth's MF, there are other sources of MF such as magnetized materials known as permanent magnets.

MFs are of two types namely, the endogenous and exogenous fields. Endogenous fields are those MFs that are produced within the body. This type of MF occurs at various electrically excitable organs such as heart (electrocardiogram), brain (electroencephalogram) and eye (electrooculogram). It is also formed from the actions of the musculoskeletal system (Hastings & Mahmud, 1988; Levin, 2003). On the other hand, exogenous fields are MFs produced by sources outside the body and can be classified as natural exogenous fields such as the Earth's geomagnetic field (e.g., Samarium Cobalt ($SmCo_5$) or Neodymium Ferum Boron (NdFeB)) or artificial exogenous (man-made MF) fields like power lines, transformers, appliances, radio transmitters, and medical devices. Artificial exogenous fields MFs can be generated and manipulated to mimic the day-to-day exposure levels obtained at work places, public places and homes as shown in Table 1.1.

Other than MFs, electrical field (EF) is also associated with biological effects that can modulate neural growth and orientation *in vitro*, and has been successful modulate neural growth and orientation *in vitro*, and has been successfully applied in

therapeutic alternatives for spinal cord injuries (Patel & Poo,1984; Duffell *et al.*, 2008). Cells response towards EF was initially described as passive, and had been determined through physical properties of cells, however, it has been reported that cells can also actively respond towards EF stimulations (Markx, 2008).

Electromagnetic fields (EMFs) on the other hands are produced when electrical current flows through an electrical conductor; such as in power lines (Goodman *et al.*, 1993). Like MF and EF, EMF can also significantly exhibit biological effects towards cells, such as altered growth rate, RNA quantities, proteins, cell surface characteristics, and in overall development (Liboff *et al.*, 1984; Takahashi *et al.*, 1986; Marron *et al.*, 1988; Delgado *et al.*, 1982). However EMF-based technologies have not progressed to clinical translation and the reason for this is the scepticism due to differences in experimental exposure protocols.

Frequent human exposure to MFs has raised serious health concerns as MF has been associated with some medical complications. Several types of cancer (Ahlbom *et al.*, 2000), tumours (Feychting *et al.*, 1997), Glioblastoma (Kheifets *et al.*, 1995), (Repacholi & Greenebaum, 1999) and leukemia (Greenland *et al.*, 2000) have been associated with MF exposure. Although many hypotheses were put forward to explain serious health effects of MF, no scientific explanation for the health effects of these fields has been established. Interestingly, a study had concluded that optimal MF exposure for a definite short period of time could surprisingly and significantly promotes cell growth. Many researchers have proven the good effects of MF exposure such as MF exposure will accelerate the healing of bone fractures and halt the osteoporosis process (Sun *et al.*, 2009; Chalidis *et al.*, 2011; Massari *et al.*, 2009). Accordingly, current study aims to investigate the potential impact of induced static magnetic field (SMF) on human Umbilical Cord-Derived Mesenchymal Stem Cells (hUC-MSCs) using Samarium Cobalt (SmC_{O5}).

The rationale of using of MSCs (specifically hUC-MSCs) is that MSCs are capable of differentiating into several cell types namely adipocyte, chondrocyte, osteocytes, neural cells, cardiomyocytes, kidney tissue and hepatocytes. In addition hUC-MSCs are hypoimmunogenic as such they are incapable of inducing an immune response because they do not possess co-stimulatory factors that are indispensable in the course of any immune response. These characteristics make MSCs suitable for the treatment of various diseases that require allogenic cell transplantation without the need to use immunosuppressive drugs. Therefore, the therapeutic potential of hUC-MSCs

can harnessed by determining the optimal conditions as well as the MF magnitude required to readily stimulate propagation of hUC-MSCs following exposure to MF.

Depending on the magnitude of the MF, cells respond differently when they are exposed to MFs. In fact, MF could alter cells' plasma membrane, change their surface and cytoskeleton, influence their proliferation, and as well as other biological processes. The plasma membrane is a primary biological receiver of magnetic signals, and it responds to MF by changes of its membrane potential, and modulates the distribution and activity of integral membrane proteins and ion channels (e.g., Ca^{2+} channels) (Francisco *et al.*, 2013; Ross *et al.*, 2015).

For the purpose of this study, we designed a controllable model that employs $SmCo_5$ as the source of MF, and provides simulation of those long-term effects within a relatively short time. Samarium cobalt was chosen as a magnetic source in this experiment because it possesses a strong permanent moment magnetization and stable against the influence of demagnetization. It is also suitable for relatively high temperature experiment and rust resistant so no surface treatment is needed.

Table 1.1 and Table 1.2 show the MF range that is not harmful to human cells and therefore, in line with the experimental propose of this work, through MF exposure small quantity of collected MSCs can be expanded rapidly in a short period of time which can provide a ready-to-use source of mesenchymal stem cells (MSCs) for various clinical applications.

Table 1.1: The Exogenous magnetic field associated with different sources in homes, workplaces and public areas

Field Source (Exogenous)	Magnetic Level/Electric	(Magnetic Field Range)	References
Natural fields (Earth's magnetic field)	200 V/m	70 μT	(Zanella, 1998)
Household Appliances	Extremely Low Frequency 50/60 Hz	0.01-0.5 μT at 1 m 0.1-30 μT at 0.3 m	(Zanella, 1998)
Microwave and oven	2.45 GHz		(Zanella, 1998)
Office Appliances: -Video Display Terminals (VDT)	30-3,000 Hz	0.02-0.65 μT at 0.3 m	(Breysse *et al.*, 1994)
Research Facilities : a) Linear accelerator b) Nuclear Magnetic Resonance c) Bubble chamber d) Magnetohydronamic (MHD) generator and fusion plants	 0 0 0 0	 0.1-5 mT 1-60 mT > 50 mT 1–50 mT	(Zanella, 1998)
Power System: a) 380 KV transmission Line b) 15 KV distribution Line c) MWh S/C Magnetic Energy Storage (SMES)	ExtremelyLow Frequency 50/60 Hz	1-20 μT 0.05-0.4 μT 0.5 T (maximum accessible field)10 mT at 300 m	(Zanella, 1998)
Transportation: a) Magnetically-levitated trains b) Subway	0 Extremely Low Frequency 50/60 Hz	 2-6 mT (head level) 20-50 mT (floor level) 0.7-1 mT	(Zanella, 1998)

Table 1.1 (continued)

Industries: a) Welding Machines b) Aluminium Production c) Security Systems d) Electric and Induction Furnaces e) Average Exposure of workers	 0, Extremely Low Frequency 50/60 Hz 0 0.1-10,000 Hz 1-10,000 Hz 0, Extremely Low Frequency 50/60 Hz	 0.2-10 mT 1-10 mT/60 mT up to 1 mT 5 mT 1 μT, electrical 0.17 μT, non electrical	(Zanella, 1998)
Medicine: a) Magnetic resonance imaging (MRI) b) Therapeutic devices	 0 12-75 Hz	 0.5-2 mT (operator) 2 T (patient) 1-10 mT	(Zanella, 1998)
The current limits for magnetic field strengths approved by U.S. Food and drug Administration (FDA)		3 T	(Schafer *et al.*, 2010)

REFERENCES

Abdallah, B. M., & Kassem, M. (2008). Human mesenchymal stem cells: from basic biology to clinical applications. *Gene Therapy*, *15*(2), 109–16.

Aggarwal, S., & Pittenger, M. F. (2005). Human mesenchymal stem cells modulate allogeneic immune cell responses. *Transplantation*, *105*(4),1815–1822.

Ahlbom, A., Day, N., Feychting, M., Roman, E., Skinner, J., Dockerty, J., Verkasalo, P. K. (2000). A pooled analysis of magnetic fields and childhood leukaemia. *British Journal of Cancer*, *83*(5), 692–698.

Arnhold, S. J., Goletz, I., Klein, H., Stumpf, G., Beluche, L. A., Rohde, C., Lutz, F. (2007). Isolation and characterization of bone marrow–derived equine mesenchymal stem cells. *American journal of veterinary research, 68*(10), 1095-1105.

Anjos-Afonso, F., & Bonnet, D. (2007). Nonhematopoietic/endothelial SSEA-1cells define the most primitive progenitors in the adult murine bone marrow mesenchymal compartment. . *Blood, 109*(3), 1298–306.

Baksh, D., Yao, R., & Tuan, R. S. (2007). Comparison of Proliferative and Multilineage Differentiation Potential of Human Mesenchymal Stem Cells Derived from Umbilical Cord and Bone Marrow. *Stem Cells*, *25*(6),1384–1392.

Baal, N., Reisinger, K., Jahr, H., Bohle, R.M., Liang, O., Munstedt, K., Rao, C.V., Preissner, K.T., and Zygmunt, M.T. (2004). Expression of transcription factor Oct-4 and other embryonic genes in CD133 positive cells from human umbilical cord blood. *Thromb. Haemost. 92,* 767–775.

Ballif, B. A, & Blenis, J. (2001). Molecular mechanisms mediating mammalian mitogen-activated protein kinase (MAPK) kinase (MEK)-MAPK cell survival signals. *Cell Growth & Differentiation : The Molecular Biology Journal of the American Association for Cancer Research*, *12*(8), 397–408.

Barlow, S., Brooke, G., Chatterjee, K., Price, G., Pelekanos, R., Rossetti, T., Atkinson, K. (2008). Comparison of human placenta- and bone marrow-derived multipotent mesenchymal stem cells. *Stem Cells and Development*, *17*(6), 1095–1107.

Batsali AK, Kastrinaki MC, Papadaki HA, Pontikoglou C. (2013). Mesenchymal Stem Cells Derived from Wharton's Jelly of the Umbilical Cord: Biological Properties and Emerging Clinical Applications. *Current Stem Cell Research & Therapy, 8,* 144-155.

Beltrami, A. P., Cesselli, D., Bergamin, N., Marcon, P., Rigo, S., Aurizio, F. D., Puppato, E. (2009). Multipotent cells can be generated in vitro from several adult human Multipotent cells can be generated in vitro from several adult human organs (heart , liver , and bone marrow).*Blood*,*110*(9), 3438–3446.

Bianco,P, Robey, P. G. Simmons, P. J. (2008). NIH Public Access. *Cell*, *2*(4), 313–319.

Blanc, K. Le, Rasmusson, I., Sundberg, B., Hassan, M., & Uzunel, M. (2004). Treatment of severe acute graft-versus-host disease with third party haploidentical mesenchymal stem cells. *The Lancet*,*363*, 1439–1441.

Bosch, P., Pratt, S. L., & Stice, S. L. (2006). Isolation, Characterization, Gene Modification, and Nuclear Reprogramming of Porcine Mesenchymal Stem Cells. *Biol Reprod*, *74*(1), 46–57.

Bosnakovski, D., Mizuno, M., Kim, G., Takagi, S., Okumura, M., Fujinaga, T. (2005). Isolation and multilineage differentiation of bovine bone marrow mesenchymal stem cells. *Cell Tissue Res*,*319*(2), 243-53.

Boyer L.A, Lee T.I, Cole M.F, Johnstone S.E, Levine S.S, Zucker J.P, Guenther M.G, Kumar R.M, Murray H.L, Jenner R.G, Gifford D.K, Melton D.A, Jaenisch R, Youg R.A. (2005). Core transcriptional regulatory circuitry in human embryonic stem cells. *Cell*,*122*, 947–956.

Brandau, S., Jakob, M., Hemeda, H., Bruderek, K., Janeschik, S., Bootz, F., & Lang, S. (2010). Tissue-resident mesenchymal stem cells attract peripheral blood neutrophils and enhance their inflammatory activity in response to microbial challenge. *Journal of Leukocyte Biology*, *88*(5),1005–1015.

Breysse PN, Matanoski GM, Elliott EA, Francis M, Kaune W, Thomas K. (1994). 60 Hz magnetic field exposure assessment for an investigation of leukemia in telephone line workers. *Am J Ind Med; 26*, 681- 691.

Burns, C. E., & Zon, L. I. (2002). Portrait of a stem cell. *Developmental Cell*, *3*(5), 612–614.

Buttiglione, M., Roca, L., Montemurno, E., Vitiello, F., Capozzi, V., & Cibelli, G. (2007). Radiofrequency radiation (900 MHz) induces Egr-1 gene expression and affects cell-cycle control in human neuroblastoma cells. *Journal of Cellular Physiology*, *213*(3), 759–767.

Campagnoli, C., Roberts, I. A. G., Kumar, S., Bennett, P. R., Bellantuono, I., & Fisk, N. M. (2016). Identification of mesenchymal stem / progenitor cells in human first-trimester fetal blood , liver , and bone marrow. *Blood 98*(8), 2396–2403.

Campisi, J. (2005). Senescent cells, tumor suppression, and organismal aging: Good citizens, bad neighbors. *Cell*, *120*(4), 513–522.

Caplan, A. I. (2007). Adult mesenchymal stem cells for tissue engineering versus regenerative medicine. *Journal of Cellular Physiology*, *213*(2),341–347.

Ceccarelli, G., Bloise, N., Mantelli, M., Gastaldi, G., Fassina, L., Cusella De Angelis, M. G., Visai, L. (2013). A Comparative Analysis of the *In Vitro* Effects of Pulsed Electromagnetic Field Treatment on Osteogenic Differentiation of Two Different Mesenchymal Cell Lineages. *BioResearch Open Access*, *2*(4), 283–294.

Chalidis, B., Sachinis, N., Assiotis, A., & Maccauro, G. (2011). Stimulation of bone formation and fracture healing with pulsed electromagnetic fields: biologic responses and clinical implications. *International Journal of Immunopathology and Pharmacology*, *24*(1 Suppl 2), 17–20.

Chambers, I., Colby, D., Robertson, M., Nichols, J., Lee, S., Tweedie, S., & Smith, a. (2003). Functional expression cloning on *nanog*, a pluripotency sustaining factor in embryonic stem cells. *Cell*, *113*, 643–655.

da Silva Meirelles, L., Caplan, A. I., & Nardi, N. B. (2008). In Search of the *In Vivo* Identity of Mesenchymal Stem Cells. *Stem Cells*, *26*(9), 2287–2299.

Delgado, J. M., Leal, J., Monteagudo, J. L., & Gracia, M. G. (1982). Embryological changes induced by weak, extremely low frequency electromagnetic fields. *J. Anat.*, *134*(3), 533–51.

Dent P., Yacoub A., Fisher P.B., Hagan M.P., Grant S. (2003). MAPK pathways in radiation responses. *Oncogene 22*, 5885–5896.

Dezawa, M., Ishikawa, H., & Itokazu, Y. (2005). Bone Marrow Stromal Cells Generate Muscle Cells and Repair Muscle Degeneration. *Science (New York,*

N.Y.), *30*,314–318.

Ding D-C, Chang Y.H, Shyu W.C, Lin SZ, (2015). Human umbilical cord mesenchymal stem cells: a new era for stem cell therapy. *Cell Transplantation*, *24*, 339–347.

Do, J. T., & Scholer, H. R. (2009). Regulatory circuits underlying pluripotency and reprogramming. *Trends in Pharmacological Sciences*, *30*(6), 296–302.

Dobson J, (2007). *Magnetic Properties of Biological Materials.* In Frank S, Barnes & Ben Greenebaum. Bioengineering and biophysical Aspects of Electromagnet Fields. Broken Sound Parkway New York. Taylor & Francais Group. 101-113.

Dolmetsch RE, Pajvani U, Fife K, Spotts JM, Greenberg ME. (2001). Signaling to the nucleus by an L-type calcium channel-calmodulin complex through the MAP kinase pathway. S*cience 294*, 333–339.

Dominici M, Le Blanc K, Mueller I, Slaper-Cortenbach I, Marini F, Krause D, Deans R, Keating A, Prockop Dj, Horwitz E.(2006). Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement. *Cytotherapy, 8*(4), 315-7.

Du, L., Fan, H., Miao, H., Zhao, G., & Hou, Y. (2014). Extremely low frequency magnetic fields inhibit adipogenesis of human mesenchymal stem cells. *Bioelectromagnetics*, *35*(7), 519–530.

Duffell, L. D., Donaldson, N. D. N., Perkins, T. A., Rushton, D. N., Hunt, K. J., Kakebeeke, T. H., & Newham, D. J. (2008). Long-term intensive electrically stimulated cycling by spinal cord-injured people: Effect on muscle properties and their relation to power output. *Muscle and Nerve*, *38*(4), 1304–1311.

Fanelli C1, Coppola S, Barone R, Colussi C, Gualandi G, Volpe P, Ghibelli L.(1999). Magnetic fields increase cell survival by inhibiting apoptosis via modulation of Ca^{2+} influx. *The FASEB journal: official publication of the Federation of American Societies for Experimental Biology*, *13*, 95-102.

Feychting, M., Forssen, U., Floderus, B. (1997). Occupational and residential magnetic field exposure and leukemia and central nervous system tumors. Epidemiology, *8*(4), 384–389.

Francisco, A. C., del Mar, S. A. M., Irene, C., Sandra, R. A., Josefa, L., Elisa, R. M., Isabel, N. M. (2013). Could radiotherapy effectiveness be enhanced by electromagnetic field treatment. *International Journal of Molecular Sciences*,

14(7), 14974–14995.

Freberg, C. T., Dahl, J. A., Timoskainen, S. and Collas, P. (2007). Epigenetic reprogramming of *OCT4* and *NANOG* regulatory regions by embryonal carcinoma cell extract. *Mol. Biol. Cell 18,* 1543-1553.

Friedenstein A.J., Chailakhjan R.K., Lalykina K.S. (1970). The development of fibroblast colonies in monolayer cultures of guinea-pig bone marrow and spleen cells. *Cell Tissue Kinet. 3*(4), 393–403.

Friedenstein, A.J., Chailakhyan, R.K., Latsinik, N.V., Panasyuk, A.F., Keiliss-Borok IV. (1974a). Stromal cells responsible for transferring the microenvironment of the hemopoietic tissues. Cloning in vitro and retransplantation *in vivo*. *Transplantation, 17*,331-40.

Friedenstein, A.J., Deriglasova, U.F, Kulagina, N.N., Panasuk, A.F., Rudakowa S.F., Luriá E.A., Rudakow I.A. (1974b). Precursors for fibroblasts in different populations of hematopoietic cells as detected by the *in vitro* colony assay method. *Exp Hematol.,2,* 83-92.

Funk, R. H. W., Monsees, T., & Ozkucur, N. (2009). Electromagnetic effects - From cell biology to medicine. *Progress in Histochemistry and Cytochemistry*, *43(4),* Gang, E., Bosnakovski, D., & Figueiredo, C. (2007). SSEA-4 identifies mesenchymal stem cells from bone marrow. *Blood*, *109*(4), 1743–1751.

Gang, E., Bosnakovski, D., & Figueiredo, C. (2007). SSEA-4 identifies mesenchymal stem cells from bone marrow. *Blood*, *109*(4), 1743–1751.

Gargett, C. E., Schwab, K. E., Zillwood, R. M., Nguyen, H. P. T., & Wu, D. (2009). Isolation and Culture of Epithelial Progenitors and Mesenchymal Stem Cells from Human Endometrium. *Biology of Reproduction*, *80*(6), 1136–1145.

Go, M. J., Takenaka, C., & Ohgushi, H. (2008). Forced expression of *Sox2* or *Nanog* in human bone marrow derived mesenchymal stem cells maintains their expansion and differentiation capabilities. *Experimental Cell Research*, *314*(5), 1147–1154.

Goodman, R., Chizmadzhev, Y., & Shirley-Henderson, A. (1993). Electromagnetic fields and cells. *Journal of Cellular Biochemistry*, *51*(4),436–441.

Gotherström, C., Ringdén, O., Westgren, M., Tammik, C., & Le Blanc, K. (2003). Immunomodulatory effects of human foetal liver-derived mesenchymal stem cells. *Bone Marrow Transplantation*, *32*(3), 265–272.

Goto Y, Taniura H, Yamada K, Hirai T, Sanada N, nakamichi N, Yoneda T (2006).

The Magnetism Responsive Gene NTAN1 in Mouse brain. *Neurochem Int. 49*(4), 334-341.

Grassi, C., D'Ascenzo, M., Torsello, A., Martinotti, G., Wolf, F., Cittadini, A., & Azzena, G. B. (2004). Effects of 50 Hz electromagnetic fields on voltage-gated Ca^{2+} channels and their role in modulation of neuroendocrine cell proliferation and death. *Cell Calcium*, *35*(4), 307–315.

Greber, B., Lehrach, H., & Adjaye, J. (2007). Silencing of core transcription factors in human EC cells highlights the importance of autocrine FGF signaling for self-renewal. *BMC Developmental Biology*, *7*, 1–15.

Greco, S. J., Liu, K., & Rameshwar, P. (2007). Functional Similarities Among Genes Regulated by *Oct4* in Human Mesenchymal and Embryonic Stem Cells. *Stem Cells*, *25*(12), 3143–3154.

Greenland S, Sheppard AR, K. W. (2000). A pooled analysis of magnetic fields, wire codes, and childhood leukemia. *Epidemiology*, *11*(6), 624–34.

Gurkan, U. A., & Akkus, O. (2008). The mechanical environment of bone marrow: A review. *Annals of Biomedical Engineering*, *3*6(12),1978–1991.

Hacia, J. G., Lee, C. C. I., Jimenez, D. F., Karaman, M. W., Ho, V. V., Siegmund, K. D., & Tarantal, A. F. (2008). Age-related gene expression profiles of rhesus monkey bone marrow-derived mesenchymal stem cells. *Journal of Cellular Biochemistry*, *103*(4), 1198–1210.

Han, S. M., Han, S. H., Coh, Y. R., Jang, G., Ra, J. C., Kang, S. K., Youn, H. Y. (2014). Enhanced proliferation and differentiation of Oct4- And Sox2-overexpressing human adipose tissue mesenchymal stem cells. *Experimental and Molecular Medicine*, *46*(6), 1-9.

Han, S. M., Coh, Y. R., Ahn, J. O., Jang, G., Yum, S. Y., Kang, S. K., Youn, H. Y. (2015). Enhanced hepatogenic transdifferentiation of human adipose tissue mesenchymal stem cells by gene engineering with *Oct4* and *Sox2*. *PLoS ONE*, *10*(3), 1–15.

Hartwell, L., & Weinert, T. (1989). Checkpoints: controls that ensure the order of cell cycle events. *Science*, *246*(4930),629–634.

Hartwig, V., Giovannetti, G., Vanello, N., Lombardi, M., Landini, L., & Simi, S. (2009). Biological effects and safety in magnetic resonance imaging: A review. *International Journal of Environmental Research and Public Health*, *6*(6),1778–1798.

Hastings, G.W., Mahmud F.A. (1988.). Electrical effects in bone. *Scientific American, 213*(2),18–25.

Hida, N., Nishiyama, N., Miyoshi, S., Kira, S., Segawa, K., Uyama, T.,Umezawa, A. (2008). Novel Cardiac Precursor-Like Cells from Human Menstrual Blood-Derived Mesenchymal Cells. *Stem Cells*, *26*(7), 1695–1704.

Hogg, R. C., Buisson, B., & Bertrand, D. (2005). Allosteric modulation of ligand-gated ion channels. *Biochemical pharmacology*, *70*(9), 1267-1276.

Hui, C. K., Safwani, W. K. Z. W., Chin, S. S., Malek, A. A. S. A., Hassan, N., Fazil, M. S., Sathappan, S. (2012). Human serum promotes the proliferation but not the stemness genes expression of human adipose-derived stem cells. *Biotechnology and Bioprocess Engineering*, *17*(6), 1306–1313.

International Commission on Non-ionizing Radiation Protection (ICNIRP) (1998): Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300GHz). *Health Phys. 74*, 494-522.

Izadpanah, R., Kaushal, D., Kriedt, C., Tsien, F., Patel, B., Dufour, J., & Bunnell, B. A. (2008). Long-term in vitro expansion alters the biology of adult mesenchymal stem cells. *Cancer Research*, *68*(11), 4229–4238.

Jain, A., Mathur, N., Jeevashankar, M., Mukhopadhyay, A., Agarwal, R., Deorari, A. K., & Paul, V. K. (2013). Does mesenchymal stem cell population in umbilical cord blood vary at different gestational periods. *Indian Journal of Pediatrics*, *80*(5), 375–379.

Javani Jouni, F., Abdolmaleki, P., & Movahedin, M. (2013). Investigation on the effect of static magnetic field up to 15 mT on the viability and proliferation rate of rat bone marrow stem cells. *In Vitro Cellular & Developmental Biology - Animal*, *49*(3), 212–219.

Jin, M., Blank, M., & Goodman, R. (2000). ERK1/2 phosphorylation, induced by electromagnetic fields, diminishes during neoplastic transformation. *Journal of Cellular Biochemistry*, *78*(3), 371–379.

Jordan, A., Wust, P., Scholz, R., Tesche, B., Fähling, H., Mitrovics, T., Felix, R. (1996). Cellular uptake of magnetic fluid particles and their effects on human adenocarcinoma cells exposed to AC magnetic fields *in vitro*. *International Journal of Hyperthermia*, *12*(6), 705–22.

Kassis, I., Zangi, L., Rivkin, R., Levdansky, L., Samuel, S., Marx, G., & Gorodetsky, R. (2006). Isolation of mesenchymal stem cells from G-CSF-mobilized

human peripheral blood using fibrin microbeads. *Bone Marrow Transplantation*, *37*(10), 967–76.

Kazemnejad, S., Allameh, A., Soleimani, M., Gharehbaghian, A., Mohammadi, Y., Amirizadeh, N., & Jazayery, M. (2009). Biochemical and molecular characterization of hepatocyte-like cells derived from human bone marrow mesenchymal stem cells on a novel three-dimensional biocompatible nanofibrous scaffold. *Journal of Gastroenterology and Hepatology*, *24*(2), 278–87.

Kerkis, I., Kerkis, A., Dozortsev, D., Stukart-Parsons, G. C., Gomes Massironi, S. M., Pereira, L. V., Cerruti, H. F. (2006). Isolation and Characterization of a Population of Immature Dental Pulp Stem Cells Expressing OCT-4 and Other Embryonic Stem Cell Markers. *Cells Tissues Organs*, *184*(3–4), 105–116.

Kheifets, L., Afifi, A., Buffler, P., Zhang, Z. (1995). Occupational electric and magnetic field exposure and brain cancer: A meta-analysis. *J. Occup. Environ. Med.*,*37*,1327–1341.

Kim, E.-C., Leesungbok, R., Lee, S.-W., Lee, H.-W., Park, S. H., Mah, S.-J., & Ahn, S.-J. (2015). Effects of moderate intensity static magnetic fields on human bone marrow-derived mesenchymal stem cells. *Bioelectromagnetics*, *36*(4),267–276.

Kim, J. H., Jee, M. K., Lee, S. Y., Han, T. H., Kim, B. S. B. S., Kang, K. S., & Kang, S. K. (2009). Regulation of adipose tissue stromal cells behaviors by endogenic Oct4 expression control. *PLoS ONE*, *4*(9),1-11

Klyushnenkova, E., Mosca, J. D., Zernetkina, V., Majumdar, M. K., Beggs, K. J., Simonetti, D. W., McIntosh, K. R. (2005). T cell responses to allogeneic human mesenchymal stem cells: Immunogenicity, tolerance, and suppression. *Journal of Biomedical Science*, *12*(1), 47–57.

Kocaoemer, A., Kern, S., Klüter, H., & Bieback, K. (2007). Human AB Serum and Thrombin-Activated Platelet-Rich Plasma Are Suitable Alternatives to Fetal Calf Serum for the Expansion of Mesenchymal Stem Cells from Adipose Tissue. *Stem Cells*, *25*(5), 1270–1278.

Kochupurakkal, B. S., Sarig, R., Fuchs, O., Piestun, D., Rechavi, G., & Givol, D. (2008). Nanog inhibits the switch of myogenic cells towards the osteogenic lineage. *Biochemical and Biophysical Research Communications*, *365*(4),846–850.

Kolbabová, T., Malkemper, E. P., Bartoš, L., Vanderstraeten, J., Turčáni, M., & Burda, H. (2015). Effect of exposure to extremely low frequency magnetic fields on melatonin levels in calves is seasonally dependent. *Scientific Reports*, *5*, 1–9.

Kolf, C. M., Cho, E., & Tuan, R. S. (2007). Mesenchymal stromal cells. Biology of adult mesenchymal stem cells: regulation of niche, self-renewal and differentiation. *Arthritis Research & Therapy*, *9*(1), 204.

Kratchmarova, I., Blagoev, B., Haack-Sorensen, M, Kassem, M., Mann, M. (2005). Mechanism of Divergent Growth Factor Effects in Mesenchymal Stem Cell Differentiation. *Science*, *308*(5727), 1472–1477.

Kuroda, T., Tada, M., Kubota, H., Kimura, H., Hatano, S., Suemori, H., Tada, T. (2005). Octamer and Sox elements are required for transcriptional cis regulation of Nanog gene expression. *Molecular and Cellular Biology*, *25*(6), 2475–85.

Le Blanc K, Tammik C, Rosendahl K, Zetterberg E, Ringden O. (2003). HLA expression and immunologic properties of differentiated and undifferentiated mesenchymal stem cells. *Exp Hematol.*,*31*,890-896.

Lengler, J., Bittner, T., Münster, D., Gawad, A. E. D. A., & Graw, J. (2005). Agonistic and antagonistic action of AP2, Msx2, Pax6, Prox1 and Six3 in the regulation of Sox2 expression. *Ophthalmic Research*, *37*(6),301–309.

Levin, M. (2003). Bioelectromagnetics in Morphogenesis. *Bioelectromagnetics*, *24*(5), 295–315.

Liboff, A. R. (1984). Geomagnetic cyclotron resonance in living cells. *Journal of Biological Physics*, *13*(4), 99–102.

Li, C., Wu, X., Tong, J., Yang, X., Zhao, J., Zheng, Q., Ma, Z. (2015). Comparative analysis of human mesenchymal stem cells from bone marrow and adipose tissue under xeno-free conditions for cell therapy. *Stem Cell Research & Therapy*, *6*(1),55.

Limana, F., Zacheo, A., Mocini, D., Mangoni, A., Borsellino, G., Diamantini, A., Capogrossi, M. C. (2007). Identification of myocardial and vascular precursor cells in human and mouse epicardium. *Circulation Research*, *101*(12),1255–1265.

Lin, C.-S., Xin, Z.-C., Deng, C.-H., Ning, H., Lin, G., & Lue, T. F. (2010). Defining adipose tissue-derived stem cells in tissue and in culture. *Histology and*

Histopathology, *25*(6), 807–815.

Lindstrom, E., Lindstrom, P., Berglund, A., Lundgren, E., & Mild, K. H. (1995). Intracellular calcium oscillations in a T-cell line after exposure to extremely-low-frequency magnetic fields with variable frequencies and flux densities. *Bioelectromagnetics*, *16*(1), 41–47.

Lodish, H., Berk, A., Zipursky S L, Matsudaira, P, Baltimore D, & Darnell J. (2000). *Molecular Cell Biology*, 4th ed. New York: W. H. Freeman.

Loebel, D. A.,Watson, C. M., De Young, R. A., & Tam, P. P. (2003). Lineage choice and differentiation in mouse embryos and embryonic stem cells. *Developmental Biology*, *264*(1),1–14.

Low, C. B., Liou, Y.-C., & Tang, B. L. (2008). Neural differentiation and potential use of stem cells from the human umbilical cord for central nervous system transplantation therapy. *Journal of Neuroscience Research*, *86*(8), 1670–1679.

Majumdar, M. K., Thiede, M. a, Haynesworth, S. E., Bruder, S. P., & Gerson, S. L. (2000). and Osteogenic Lineages. *Cell Biochemistry and Function*, *848*, 841–848.

Marędziak, M., Marycz, K., Śmieszek, A., Lewandowski, D., & Toker, N. Y. (2014). The influence of static magnetic fields on canine and equine mesenchymal stem cells derived from adipose tissue. *In Vitro Cellular & Developmental Biology - Animal*, *50*(6), 562–571.

Marędziak, M., Tomaszewski, K., Polinceusz, P., Lewandowski, D., & Marycz, K. (2017). Static magnetic field enhances the viability and proliferation rate of adipose tissue-derived mesenchymal stem cells potentially through activation of the phosphoinositide 3-kinase/Akt (PI3K/Akt) pathway. *Electromagnetic Biology and Medicine*, *36*(1),45–54.

Marinelli, F., La Sala, D., Cicciotti, G., Cattini, L., Trimarchi, C., Putti, S., Cinti, C. (2004). Exposure to 900 MHz Electromagnetic Field Induces an Unbalance between Pro-Apoptotic and Pro-Survival Signals in T-Lymphoblastoid Leukemia CCRF-CEM Cells. *Journal of Cellular Physiology*, *198*(2), 324–332.

Markx, G. H. (2008). The use of electric fields in tissue engineering: A review. *Organogenesis*, *4*(1),11–7.

Marron, M. T., Goodman, E. M., Sharpe, P. T., & Greenebaum, B. (1988). Low

frequency electric and magnetic fields have different effects on the cell surface. *FEBS Letters*, *230*(1–2),13–16.

Massari, L., Caruso, G., Sollazzo, V., & Setti, S. (2009). Pulsed electromagnetic fields and low intensity pulsed ultrasound in bone tissue. *Clinical Cases in Mineral and Bone Metabolism : The Official Journal of the Italian Society of Osteoporosis, Mineral Metabolism, and Skeletal Diseases*,*6*(2), 149–54.

Matic, I., Antunovic, M., Brkic, S., Josipovic, P., Mihalic, K. C., Karlak, I., Marijanovic, I. (2016). Expression of *OCT-4* and *SOX-2* in bone marrow-derived human mesenchymal stem cells during osteogenic differentiation. *Macedonian Journal of Medical Sciences*, *4*(1),9–16.

McRobbie, D. W., Moore, E. A., Graves, M. J., & Prince, M. R. (2006). *MRI from picture to proton*. *MRI from Picture to Proton*. 1st ed: Cambridge University Press: Cambridge, New York, USA,

Mellstrom, B.; Savignac, M.; Gomez-Villafuertes, R.; Naranjo, J.R. (2008). $Ca2^{+}$-operated transcriptional networks: molecular mechanisms and in vivo models. *Physiol. Rev., 88,* 421- 449

Miao, Y., Lv, D., Wang, P., Wang, X.-C., Chen, J., Miao, C., & Song, C.-P. (2006). An Arabidopsis glutathione peroxidase functions as both a redox transducer and a scavenger in abscisic acid and drought stress responses. *The Plant Cell*, *18*(10),2749–2766.

Miskon, A., Uslama, J. (2010). A Numerical Study on Magnetic Fields Effects on Stem Cell Differentiation. *International Journal of Integrated Engineering*,*2* (3),7–16.

Miura, Y., Miura, M., Gronthos, S., Allen, M. R., Cao, C., Uveges, T. E., Zhang, L. (2005). Defective osteogenesis of the stromal stem cells predisposes CD18-null mice to osteoporosis. *Proceedings of the National Academy of Sciences of the United States of America*, *102*(39), 14022–7.

Miyakoshi, J. (2005). Effects of static magnetic fields at the cellular level. *Progress in Biophysics and Molecular Biology*, *87*, 213–223.

Miyakoshi, J. (2006). The review of cellular effects of a static magnetic field. *Science and Technology of Advanced Materials*, *7*(4),305–307.

Mueller SM, Glowacki J. Age-related decline in the osteogenic potential of human bone marrow cells cultured in threedimensional collagen sponges. *J Cell Biochem, 82*(4),583–590.

Nadri, S., Soleimani, M., Hosseni, R. H., Massumi, M., Atashi, A., & Izadpanah, R. (2007). An efficient method for isolation of murine bone marrow mesenchymal stem cells. *International Journal of Developmental Biology*, *51*(8),723–729.

Nathan, S., De, S. Das, Thambyah, A., Fen, C., Goh, J., & Lee, E. H. (2003). Cell-Based Therapy in the Repair of Osteochondral Defects: A Novel Use for Adipose Tissue. *Tissue Engineering*, *9*(4), 733–744.

Neupane, M., Chang, C., Kiupel, M., & Yuzbasiyan-Gurkan, V. (2008). Isolation and Characterization of Canine Adipose–Derived Mesenchymal Stem Cells. *Tissue Engineering Part A*, *14*(6), 1007–1015.

Nuccitelli, R., Nuccitelli, P., Li, C., Narsing, S., Pariser, D. M., & Lui, K. (2011). The electric field near human skin wounds declines with age and provides a noninvasive indicator of wound healing. *Wound Repair and Regeneration*, *19*(5),645–655.

Orford, K. W., & Scadden, D. T. (2008). Deconstructing stem cell self-renewal: Genetic insights into cell-cycle regulation. *Nature Reviews Genetics*, *9*(2), 115–128.

Oshima, J., & Campisi, J. (1991). Fundamentals of cell proliferation: control of the cell cycle. *Journal of Dairy Science*, *74*(8), 2778–87.

Palmieri, S. L., Peter, W., Hess, H., & Schöler, H. R. (1994). *OCT4*transcription factor is differentially expressed in the mouse embryo during establishment of the first two extraembryonic cell lineages involved in implantation. *Developmental Biology*, *166*(1),259-267

Pandita, T. K., Lieberman, H. B., Lim, D. S., Dhar, S., Zheng, W., Taya, Y., & Kastan, M. B. (2000). Ionizing radiation activates the ATM kinase throughout the cell cycle. *Oncogene*, *19*(11),1386–1391.

Park, S. B., Seo, K. W., So, A. Y., Seo, M. S., Yu, K. R., Kang, S. K., & Kang, K. S. (2012). *SOX2* has a crucial role in the lineage determination and proliferation of mesenchymal stem cells through Dickkopf-1 and c-MYC. *Cell Death and Differentiation*, *19*(3), 534–545.

Patel, N. B., & Poo, M. M. (1984). Perturbation of the direction of neurite growth by pulsed and focal electric fields. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *4*(12), 2939–2947.

Pesce M, Schollar. H. (2004). *Oct-4*: Gatekeeper in the Beginnings of Mammalian

Development. *Stem Cells, 19*, 271-278.

Pierantozzi, E., Gava, B., Manini, I., Roviello, F., Marotta, G., Chiavarelli, M., & Sorrentino, V. (2011). Pluripotency regulators in human mesenchymal stem cells: expression of *NANOG* but not of *OCT-4* and *SOX-2*. *Stem Cells and Development*, *20*(5), 915–923.

Pittenger, M. F., Pittenger, M. F., Mackay, A. M., Beck, S. C., Jaiswal, R. K., Douglas, R., Marshak, D. R. (1999). Multilineage Potential of Adult Human Mesenchymal Stem Cells. *Science*, *284*, 143-147.

Potenza L, Ubaldi L, De Sanctis R, De Bellis R, Chuciarrini L, Dacha M (2011). Effects of Static Magnetic Field on Cell Growth and Genen Expression on *Escherichia Coli*. *Mutat Res. 561*(1-2), 53-62.

Preston, S. L., Alison, M., Forbes, S. J., Direkze, N. C., Poulsom, R., & Wright, N. A. (2003). The new stem cell biology: something for everyone. *Mol Pathol.*, *56*, 86–96.

Prockop, D. J. (2003). Further proof of the plasticity of adult stem cells and their role in tissue repair. *The Journal of Cell Biology*, *160*(6), 807–809.

Quirici, N., Soligo, D., Bossolasco, P., Servida, F., Lumini, C., & Deliliers, G. L. (2002). Isolation of bone marrow mesenchymal stem cells by anti-nerve growth factor receptor antibodies. *Exp Hematol*, *30*(7), 783–791.

Rando, T. A. (2006). Stem cells, ageing and the quest for immortality. *Nature*, *441*(7097), 1080–1086.

Rastegar, F., Shenaq, D., Huang, J., Zhang, W., Zhang, B.-Q., He, B.-C., He, T.-C. (2010). Mesenchymal stem cells: Molecular characteristics and clinical applications. *World Journal of Stem Cells*, *2*(4), 67–80.

Repacholi, M. H., & Greenebaum, B. (1999). Interaction of static and extremely low frequency electric and magnetic fields with living systems: health effects and research needs. *Bioelectromagnetics*, *20*(3), 133–160.

Reyes, M., & Verfaillie, C. M. (2001). Characterization of multipotent adult progenitor cells, a subpopulation of mesenchymal stem cells. *Annals of the New York Academy of Sciences*, *938*, 231–233.

Ridzuan, R. (2014). *Generation and Characterization of Rat Bone Marrow Mesenchymal Stem Cells.* University Putra Malaysia; Master' Thesis.

Riekstina, U., Cakstina, I., Parfejevs, V., Hoogduijn, M., Jankovskis, G., Muiznieks, I., Ancans, J. (2009). Embryonic stem cell marker expression pattern in

human mesenchymal stem cells derived from bone marrow, adipose tissue, heart and dermis. *Stem Cell Reviews and Reports*, *5(4),* 378–386.

Rinaldi, S., Maioli, M., Pigliaru, G., Castagna, A., Santaniello, S., Basoli, V., Ventura, C. (2014). Stem cell senescence. Effects of REAC technology on telomerase-independent and telomerase-dependent pathways. *Scientific Reports*, *3*, 4–11.

Rodda, D. J., Chew, J. L., Lim, L. H., Loh, Y. H., Wang, B., Ng, H. H., & Robson, P. (2005). Transcriptional regulation of Nanog by *OCT4* and *SOX2*.*Journal of Biological Chemistry*, *280*(26),24731–24737.

Ross, C. L., Siriwardane, M., Almeida-porada, G., Porada, C. D., Brink, P., Christ, G. J., & Harrison, B. S. (2015). The effect of low-frequency electromagnetic field on human bone marrow stem / progenitor cell differentiation. *Stem Cell Research*, *15*(1), 96–108.

Rufer, N., Brümmendorf, T. H., Kolvraa, S., Bischoff, C., Christensen, K., Wadsworth, L., Lansdorp, P. M. (1999). Telomere Fluorescence Measurements in Granulocytes and T Lymphocyte Subsets Point to a High Turnover of Hematopoietic Stem Cells and Memory T Cells in Early Childhood. *J. Exp. Med*, *190*(2), 157–167.

Rzhaninova A.A, Gornostaeva S.N, Goldshtein D.V. (2005). Isolation and phenotypical characterization of mesenchymal stem cells from human fetal thymus. *Bull Exp Biol Med139,* 134–140.

Sadri, M., Abdolmaleki, P., Abrun, S., Beiki, B., & Samani, F. S. (2017). Static Magnetic Field Effect on Cell Alignment, Growth, and Differentiation in Human Cord-Derived Mesenchymal Stem Cells. *Cellular and Molecular Bioengineering*, *10*(3), 249–262.

Seshi, B., Kumar, S., & Sellers, D. (2000). Human bone marrow stromal cell: coexpression of markers specific for multiple mesenchymal cell lineages. *Blood Cells, Molecules & Diseases*, *26*, 234–246.

Seo, E., Basu-Roy, U., Zavadil, J., Basilico, C., & Mansukhani, A. (2011). Distinct Functions of Sox2 Control Self-Renewal and Differentiation in the Osteoblast Lineage. *Molecular and Cellular Biology*, *31*(22), 4593–4608.

Scientific Committee on Emerging and Newly Identified Health Risks(SCENIHR) (2007). Possible effects of Electromagnetic Fields (EMF) on Human Health. European Commission: *Brussels, Belgium*,1-64.

Schafer, R., Bantleon, R., Kehlbach, R., Siegel, G., Wiskirchen, J., Wolburg, H., Schlemmer, H. P. (2010). Functional investigations on human mesenchymal stem cells exposed to magnetic fields and labeled with clinically approved iron nanoparticles. *BMC Cell Biology*, *11*(22),1-17.

Schallmoser, K., Bartmann, C., Rohde, E., Bork, S., Guelly, C., Obenauf, A. C., Wagner, W. (2010). Replicative senescence-associated gene expression changes in mesenchymal stromal cells are similar under different culture conditions. *Haematologica*, *95*(6),867–874.

Schonitzer, V., Wirtz, R., Ulrich, V., Berger, T., Karl, A., Mutschler, W., Böcker, W. (2014). *SOX2* is a potent inhibitor of osteogenic and adipogenic differentiation in human mesenchymal stem cells. *Cellular Reprogramming*, *16*(5), 355–65.

Stillman, B. (1996). Cell cycle control of DNA replication. *Science, 74*(5293),1659-64.

Schreier, N., Huss, A., Roosli, M.(2006). The prevalence of symptoms attributed to electromagnetic field exposure: A cross-sectional representative survey in Switzerland. *Soc. Prev. Med. 51*, 202–209

Shahbazi-gahrouei, D., Razavi, S., & Salimi, M. (2014). Effect of extremely low-frequency (50 Hz) field on proliferation rate of human adipose-derived mesenchymal stem cells. Journal of Radiobiologi, *1*(2), 31-37

Shih, D. T., Lee, D.-C., Chen, S.-C., Tsai, R.-Y., Huang, C.-T., Tsai, C.-C., Chiu, W.-T. (2005). Isolation and characterization of neurogenic mesenchymal stem cells in human scalp tissue. *Stem Cells*, *23*(7), 1012–20.

Stewart, M. C., & Stewart, A. A. (2011). Mesenchymal Stem Cells: Characteristics, Sources, and Mechanisms of Action. *Veterinary Clinics of North America: Equine Practice*, *27*(2), 243–261.

Sun, L.-Y., Hsieh, D.-K., Yu, T.-C., Chiu, H.-T., Lu, S.-F., Luo, G.-H., Chiou, T.-W. (2009). Effect of pulsed electromagnetic field on the proliferation and differentiation potential of human bone marrow mesenchymal stem cells. *Bioelectromagnetics, 30(4),* 251–260.

Sun, T, & Ma, Q. (2013). Repairing neural injuries using human umbilical cord blood. Mol Neurobiol. *47*(3),938-45.

Takahashi, K., Heine, U. I., Junkr, J. L., Colburn, N. H., & Rice, J. M. (1986). Role of cytoskeleton changes and expression of the h-ras oncogene during

promotion of neoplastic transformation in mouse epidermal jb6 cells. *Cancer Research*, *46*(11), 5923–5932.

Takahashi, K., & Yamanaka, S. (2006). Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors. *Cell*, *126*(4), 663–676.

Tateishi, K., Ashihara, E., Honsho, S., Takehara, N., Nomura, T., Takahashi, T., Oh, H. (2007). Human cardiac stem cells exhibit mesenchymal features and are maintained through Akt/GSK-3β signaling. *Biochemical and Biophysical Research Communications*, *352*(3), 635–641.

Tong, C. K., Vellasamy, S., Chong Tan, B., Abdullah, M., Vidyadaran, S., Fong Seow, H., & Ramasamy, R. (2011). Generation of mesenchymal stem cell from human umbilical cord tissue using a combination enzymatic and mechanical disassociation method. *Cell Biology International*, *35*(3),221–226.

Tracey, D., Klareskog, L., Sasso, E. H., Salfeld, J. G., & Tak, P. P. (2008). Tumor necrosis factor antagonist mechanisms of action: A comprehensive review. *Pharmacology and Therapeutics*, *117*(2), 244–279.

Trohatou, O., Zagoura, D., Bitsika, V., Pappa, K. I., Antsaklis, A., Anagnou, N. P., & Roubelakis, M. G. (2014). Sox2 Suppression by miR-21 Governs Human Mesenchymal Stem Cell Properties. *StemnCells Translational Medicine*, *3*(1), 54–68.

Tse W.T., Pendleton J.D., Beyer W.M., Egalka M.C., G. E. (2003). Suppression of allogeneic T-cell proliferation by human marrow stromal cells: implications in transplantation. *Transplantation*, 75(3), 389-397

Tyson, J. J., Csikasz-Nagy, A., & Novak, B. (2002). The dynamics of cell cycle regulation. *BioEssays*, *24*(12), 1095–1109.

Vellasamy, S. (2011). *Generation and Characterization of mesenchymal stem cells derived from Umbilical cord, Placenta and Placental membrane*. University Putera Malaysia. Ph.D.Thesis

Vellasamy, S. (2012). Isolation and characterisation of mesenchymal stem cells derived from human placenta tissue. *World Journal of Stem Cells*, *4(6)*, 53-61

Vermeulen,K.,Van Bockstaele,D.R.,Berneman, Z. N., (2003). The cell cycle:a review of regulation,deregulation and therapeutic targets in cancer. *Cell Proliferation*, *36*(3), 131–149.

Wan Safwani, W. K. Z., Makpol, S., Sathapan, S., & Chua, K. (2012). 5-Azacytidine Is Insufficient for Cardiogenesis in Human Adipose-Derived Stem Cells. *Journal of Negative Results in BioMedicine*, *11*(1), 1-9

Wagner, W., Horn, P., Castoldi, M., Diehlmann, A., Bork, S., Saffrich, R., Ho, A. D. (2008). Replicative senescence of mesenchymal stem cells: A continuous and organized process. *PLoS ONE*, *3*(5), 1-12

Wagner, W., Bork, S., Horn, P., Krunic, D., Walenda, T., Diehlmann, A., Ho, A. D. (2009). Aging and replicative senescence have related effects on human stem and progenitor cells. *PLoS ONE, 4*(6), 1-13.

Wang, Z., Sarje, A., Che, P. L., & Yarema, K. J. (2009). Moderate strength (0.23-0.28 T) static magnetic fields (SMF) modulate signaling and differentiation in human embryonic cells. *BMC Genomics, 10*, 1–23.

Watson N, Divers R, Kedar R, Mehindru A, Mehindru A, Borlongan M.C, Borlongan C.V. (2015). Discarded Wharton jelly of the human umbilical cord: a viable source for mesenchymal stromal cells. *Cytotherap,17,*18–24.

Wei, X., Yang, X., Han, Z., Qu, F., Shao, L., & Shi, Y. (2013). Mesenchymal stem cells: a new trend for cell.*Acta Pharmacologica Sinica 34*(6),747-754.

Wiskirchen, J. (2000). Human fetal lung fibroblasts: in vitro study of repetitive magnetic field exposure at 0.2, 1.0 and 1.5 T. *Radiology. 215*(3), 858-862.

Wolf, F. I., Torsello, A., Tedesco, B., Fasanella, S., Boninsegna, A., D'Ascenzo, M., Cittadini, A. (2005). 50-Hz extremely low frequency electromagnetic fields enhance cell proliferation and DNA damage: Possible involvement of a redox mechanism. *Biochimica et Biophysica Acta - Molecular Cell Research*, *1743*(1-2), 120–129.

Woodbury, D., Schwarz, E. J., Prockop, D. J., & Black, I. B. (2000). Adult rat and human bone marrow stromal cells differentiate into neurons. *Journal of Neuroscience Research*, *61*(4),364–370.

Wu, Y.-L., Ma, S.-R., Peng, T., Teng, Z.-H., Liang, X.-Y., Guo, G.-Z., Li, K.-C. (2014). Effects of pulsed electromagnetic field on differentiation of HUES-17 human embryonic stem cell line. *International Journal of Molecular Sciences*, *15*(8), 14180–90.

Xu, R., Barron, T. L., Gu, F., Root, S., Peck, R. M., Yu, J., Thomson, J. A. (2008). *NANOG* is a Direct Target of TGFβ/Activin Mediated SMAD Signaling in Human ES Cells. *Cell Stem Cell*, *3*(2), 196–206.

Yan, J., Dong, L., Zhang, B., & Qi, N. (2010). Effects of extremely low-frequency magnetic field on growth and differentiation of human mesenchymal stem cells. *Electromagnetic Biology and Medicine, 29*, 165–176

Yoon DS, Choi Y, Jang Y, Lee M, Choi WJ, Kim SH, Lee JW.(2014). SIRT1 directly regulates *SOX2* to maintain self-renewal and multipotency in bone marrow-derived mesenchymal stem cells. *Stem Cells,32*,3219–3231.

Zhang Y, Li C, Jiang X, Zhang S, Wu Y, Liu B, Tang P, Mao N (2013). Human placenta-derived mesenchymal progenitor cells support culture expansion of long-term culture-initiating cells from cord blood CD34+ cells. *Exp Hematol,32*(7), 657-64.

Zimmermann, S., Voss, M., Kaiser, S., Kapp, U., Waller, C. F., & Martens, U. M. (2003). Lack of telomerase activity in human mesenchymal stem cells. *Leukemia : Official Journal of the Leukemia Society of America, Leukemia Research Fund, U.K*, *17*(6), 1146–9.