BI-LAYER BIOMIMETIC PROTEIN COATINGS ON HF-TREATED COMMERCIAL PURE MAGNESIUM FOR POTENTIAL BONE IMPLANT APPLICATIONS

NOOR JASMAWATI BINTI MAT NOOR

A thesis submitted in fulfilment of the
requirements for the award of the degree of
Doctor of Philosophy (Biomedical Engineering)

School of Biomedical Engineering and Health Sciences
Faculty of Engineering
Universiti Teknologi Malaysia

AUGUST 2020

DEDICATION

This thesis is dedicated to

My AMAZING:

ABAH; Mat Noor,

UMMI; Che Norma

My AWESOME:

four SISTERS and three BROTHERS

ACKNOWLEDGEMENT

In the name of Allah, The Most Gracious and The Most Merciful.
Salawat and Salam to prophet Nabi Muhammad S.A.W.

First and foremost, I would like to express my greatest gratitude to Allah S.W.T. for the wisdom that HE bestowed upon me, the strength, increase my belief only for ALLAH, peace of mind and good health in order to finish this research. Ya Rahman, Ya Rahim, Ya Hakiim, Ya Rashid, Ya Qawiy, Ya Waliy, Ya Hafiz, Ya Samii', Ya Mujib, Ya Aziz, Ya Allah, Ya Allah.

I would like to express my appreciation to my supervisor Prof. Dato' Ir. Dr. Mohammed Rafiq bin Dato' Abdul Kadir and PM. Dr. Ardiyansyah Syahrom for useful comments, remarks and engagement through the learning process of this research project.

ABSTRACT

Magnesium-based biomaterials have a great potential as biodegradable bone repair implants due to its mechanical properties which similar to natural bone, osteoconductive and osteogenic potential that promote the formation of new bones. The degradation of magnesium (Mg) has became the most crucial characteristic with regards to its success as bone implants. Additionally, good cellular response and attachment are desirable to allow the implant to be fully integrated with the human biological system. However, rapid degradation of Mg in the physiological environment hinders its clinical application. In order to improve Mg, as an ideal bone implant, a biocompatible protective surface coating that can reduce the biodegradation rate with better cell/surface interactions on pure Mg was developed. The present study aimed to develop bi-layer coatings to functionalise pure Mg surface, composed of non-toxic elements that decelerated the degradation rate in physiological solution while enhancing the cellular response of osteoblast cells (hFOB) on the treated surface of pure Mg. The hydrofluoride (HF) conversion surface treatment was applied as the first coating layer and acted as a protective film to decelerate the fast degradation rate. Then, biomimetic protein coatings from fetal bovine serum (FBS) and/or collagen type I were applied as the second coating layer to enhance cell/surface interactions of the implants. The *in-vitro* assessment was used to investigate the biodegradation performances of the developed bi-layered coatings. The treated surface and bi-layer coating were then subjected to FESEM, SEM, EDS measurement, XRD, ATR-FTIR, contact angle and protein release for surface characterisation analyses. The degradation rate was examined through *in-vitro* semi-static immersion, TAFEL extrapolation and EIS test in DMEM + 10% FBS solution. The bioactivity, biocompatibility and osteogenic differentiation measurements also have been conducted. Protein adsorption was detected with a complex chemical composition through the presence of amide, PO_4^{3-} and CO_3^{2-} groups incorporated fluoride ions on the treated surface. After 21 days immersion, both biomimetic protein coatings showed higher corrosion rate compared with the pure Mg but lower corrosion rate than the surface treated Mg. For long-term evaluation by the EIS test, the biomimetic collagen/apatite coating demonstrated a better protective corrosion product layer in the electrochemical corrosion by gradually increasing the charge transfer resistance value until 21 days immersion through a self-healing process. For the cytotoxicity test, after 28 days immersion, the collagen/apatite surface coated showed higher cell viability with 74.1% better cell adhesion and proliferation as well as forming 3D hFOB cells cellular network. Besides, both protein coatings can accelerate the osteogenic differentiation of hFOB cells. Collagen/apatite coating induced the highest ALP activity and gradually increased the Ca and collagen accumulation production in ECM. The 3D porous scaffold was also well accepted by hFOB cells for attachment, spreading, migrations and cell ingrowth. This research study concludes that the biomimetic collagen type I coating could be used to control implant degradation rate for long-term and enhance cell/surface interactions.

ABSTRAK

Biobahan berasaskan magnesium berpotensi tinggi sebagai implan pembaikan tulang terurai kerana sifat mekanikalnya yang sama dengan tulang semula jadi, potensi konduktif osteo dan genik osteo yang mendorong pembentukan tulang baru. Penguraian magnesium (Mg) telah menjadi ciri paling penting dalam kejayaannya sebagai implan tulang. Tambahan, tindak balas dan pelekatan selular yang baik diperlukan untuk implan bergabung sepenuhnya dengan sistem biologi manusia. Namun, penguraian pantas Mg dalam persekitaran fisiologi menghalang aplikasi klinikal. Justeru bagi menambah baik Mg sebagai implan tulang yang ideal, lapisan permukaan pelindung bioserasi yang dapat mengurangkan kadar penguraian dibangunkan beserta interaksi sel/permukaan yang lebih baik berbanding Mg tulen. Kajian ini bertujuan untuk membangunkan salutan dua lapisan pada permukaan Mg tulen, mengandungi unsur-unsur tidak toksik, yang melambatkan kadar penguraian dalam larutan fisiologi di samping meningkatkan tindak balas sel-sel osteoblas (hFOB) di atas permukaan Mg tulen terawat. Rawatan permukaan penukaran florik hidro (HF) digunakan sebagai lapisan pertama dan bertindak sebagai filem pelindung untuk melambatkan kadar penguraian. Kemudian, lapisan protein biomimetik dari *fetal bovine serum* (FBS) dan/atau kolagen jenis I digunakan sebagai lapisan kedua untuk meningkatkan interaksi sel/permukaan implan. Penilaian *in-vitro* telah digunakan untuk menyiasat prestasi penguraian salutan dua lapisan yang dibangunkan. Permukaan terawat dan salutan dua lapisan kemudiaannya dihantar ke FESEM, SEM, pengukuran EDS, XRD, ATR-FTIR, sudut sentuh dan pelepasan protein untuk analisis permukaan pencirian. Kadar penguraian dikenal pasti melalui kaedah rendaman semi-statik *in-vitro*, ekstrapolasi TAFEL dan ujian EIS dalam larutan DMEM + 10% FBS. Pengukuran bioaktiviti, bioserasi dan pengukuran pembezaan genik osteo juga telah dijalankan. Kehadiran protein dikesan dengan komposisi kimia yang kompleks, melalui kehadiran kumpulan amida, PO_4^{3-} dan CO_3^{2-} gabungan ion fluorida pada permukaan yang dirawat. Selepas rendaman 21 hari, kedua-dua lapisan protein biomimetik menunjukkan kadar karatan tinggi berbanding dengan Mg tulen, tetapi kadar karatan lebih rendah daripada permukaan Mg yang dirawat. Bagi penilaian jangka panjang melalui ujian EIS, lapisan kolagen biomimetik/apatit menghasilkan lapisan produk karatan pelindung yang lebih baik dalam elektrokimia karatan dengan peningkatan nilai rintangan pemindahan caj secara beransur sehingga 21 hari rendaman melalui proses penyembuhan diri. Untuk ujian toksik sel, setelah 28 hari rendaman, salutan permukaan kolagen/apatit menunjukkan daya maju sel yang tinggi dengan 74.1% lekatan dan percambahan sel yang lebih baik serta membentuk rangkaian 3D sel hFOB. Selain itu, kedua-dua lapisan protein dapat mempercepatkan pembezaan genik osteo sel hFOB. Salutan kolagen/apatit mendorong nilai aktiviti ALP yang tertinggi dan meningkatkan pengeluaran terkumpul Ca dan kolagen di ECM. Perancah berliang 3D juga diterima dengan baik oleh sel-sel hFOB untuk pelekatan, penyebaran, migrasi dan pertumbuhan sel. Kajian penyelidikan ini menyimpulkan bahawa lapisan kolagen biomimetik jenis I dapat digunakan untuk mengawal kadar penguraian implan pada jangka masa panjang dan meningkatkan interaksi sel/permukaan.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ALP	-	Alkaline phosphatase
ANOVA	-	One way analysis of variance
ARS	-	Alizarin red S
ASTM	-	American Society for Testing and Materials
ATR	-	Attenuated total reflectance
BSA	-	Bovine serum albumin
C	-	Carbon
Ca	-	Calcium
$CaCO_3$	-	Calcium carbonate
Cl	-	Chloride
CO_2	-	Carbon dioxide
CO_3^{2-}	-	Carbonate
-COOH	-	Carboxyl group
C=O	-	Carbonyl group
CH_2	-	Methylene group
Col-I	-	Collagen type I
DMEM	-	Dulbecco's modified eagle's medium
DMSO	-	Dimethylsulfoxide
ECM	-	Extracellular matrix
EDS	-	Energy dispersive spectroscopy
F	-	Fluorine ions
FBS	-	Fetal bovine serum
FESEM	-	Field emission scanning electron microscope

FTIR	-	Fourier transform infrared spectroscopy
HA	-	Hydroxyapatite
HBSS	-	Hank's balanced salt solution
HF	-	Hydrofluoride
HF	-	High frequency
MF	-	Middle frequency
LF	-	Low frequency
hFOB	-	Human foetal osteoblast cells
H_2O	-	Water
Mg	-	Magnesium
MgF_2	-	Magnesium fluoride
$Mg(OH)_2$	-	Magnesium hydroxide
$MgCO_3$	-	Magnesium carbonate
MSCs	-	Mesenchymal stem cell
MTT	-	3-(4,5-Dimethylthiazol-2-yl)-2,5 diphenyl tetrazolium bromide
N	-	Nitrogen
Na	-	Sodium
$NaHCO_3$	-	sodium bicarbonate
NaCl	-	Sodium chloride
N-H	-	Amide group
OD	-	Optical density
O^{2-}	-	Oxygen
OCP	-	Open circuit potential
OH	-	Hydroxide
P	-	Phosphate
PBS	-	Phosphate buffered saline

PO_4^{3-}	-	Phosphate
pH	-	Potential of hydrogen
R_S	-	Solution resistance
SBF	-	Simulated body fluid
SD	-	Standard deviation
SEM	-	Scanning electron microscopy
Ti	-	Titanium
TiO_2	-	Titania
UV	-	Ultraviolet-visible spectroscopy
XPS	-	X-ray photoelectron spectroscopy
XRD	-	The X-ray diffraction

LIST OF SYMBOLS

%	-	Percentage
At%	-	Atomic percentage
°	-	Degree
°C	-	Degree celcius
θ	-	Theta
Ω	-	Ohms
cm^2	-	Centimetre per square
g	-	Gram
g/L	-	Gram per litre
mg	-	Milligram
Hz	-	Hertz
kHz	-	Kilo hertz
μm	-	Micrometer
μg/ml	-	Microgram per millilitre
h	-	Hour
mmpy	-	Millimetre per year
mM/L	-	miliMolar per litre
mm	-	Millimetre
nm	-	Nanometre
rpm	-	Rotation per minute
V	-	Volt

LIST OF APPENDICES

CHAPTER 1

INTRODUCTION

1.1 Research Background

Magnesium (Mg) and its alloys are known as a suitable biodegradation implants in orthopaedic applications due to their degradation ability and similarity to human bone. Mg and its alloys present several advantages as compared with other metals such as titanium and stainless steel. The elastic modulus and density of Mg is as similar to the natural bone. Hence, the stress shielding effect could possibly be minimised. In addition, Mg is also an essential co-factor for about 700-800 enzyme systems that associated with the most important metabolic process in the human body [183]. The present of Mg^{2+} in the biological system could stimulate the new bone formation [9-11] by improving the osseointegration process. It also has a higher bone implant strength as compared to permanent Ti alloys implant [10, 117]. The most important is the release product from the degradation process would be converted into a soluble product. It is considered as a non-toxic oxide and could be safely excreted by kidneys [12, 13]. Hence, a subsequent surgery is not required to remove the Mg implant once the complete bone healing process was achieved at the surgery site.

Regardless of all advantages possessed by Mg and its alloys, the main drawback is a fast corrosion degradation of physiological environments [179, 182], which inhibited Mg from being as an ideal biodegradation implants and become feasible in the future. Fast degradation in human body will lead to a low mechanical strength of the implants at a rate that is faster than new bone formation and growth,

which might require a higher load strength [18, 161]. The largest achievement for Mg implants is the bioabsorbable Mg stents [2]. Mg is highly reactive under physiological environment. The corrosion reaction is mostly attributed from the composition of the exposure environment [186, 187], the impurity elements produced from the fabrication process [5, 6] and alloying composition [7, 8].

Surface modification and coating methods on Mg are efficient to reduce the fast degradation rate and increase the biocompatibility of the surface. The degradation rate must be in a slower mode to give a sufficient time to the body to deal with the degradation product, as well as allow the regeneration process for the new bone tissue formation around the Mg implant. Wang et al. [14] classified these two coating methods as chemical and physical surface modifications which are also known as physico-chemical method. The initial layer produced from the surface chemical modification is purposely to enhance the adhesion of second layer coating and become as a protective layer from the corrosive environment [15]. The outer coating layer produced from the physical coating could potentially increase the bioactivity and biocompatibility of the coated implant surface.

Surface modification from chemical reaction would form a new phase layer that covers the entire outer surface of Mg implant. This dense and compact layer become as a protective layer for Mg, hence, reduce the degradation rate. This type of method is capable to coat complex shape with ordered or non-ordered structure. The new phase of coating layer is not in passive conditions, and by time, it will gradually dissolve. The release ions from the treated surface are non-toxic to the surrounding tissue around the implantation site. Fluoride conversion coating would form MgF_2 phase on the pure Mg surface. MgF_2 has higher chemical stability and more stable in water compared to MgO, $Mg(OH)_2$ and $MgCl_2$ [124, 202], high adhesive strength and forming in a good compactness [181]. Therefore, MgF_2 coating layer possesses a high corrosion resistance in physiological environment [116].

The second coating layer is formed to enhance the bioactivity and biocompatibility of the surface using organics agent in the coating solution. Biomimetic protein coating can stimulate the osteoconduction and osseointegration of the Mg implants surface. Collagen type I (Col-I) and fetal bovine serum (FBS) are two types of protein that have been used for biomimetic coating. They are used to develop protein coating layer on the MgF_2 layer. Both proteins are biodegradable and biocompatible to the surrounding tissue and can be used in soft and hard tissue for regeneration process. It was reported that the adsorption of protein (FBS) on the pure Mg surface could effectively increase the corrosion resistance [162]. Previous findings also reported that collagen-based materials could be beneficial in multiple functions such as to produce porous matrices [156], hydrogels [194], scaffolds [154] and surface coatings [157, 158, 185].

Therefore, pure Mg was used in this study for the chemical surface modification by applying the fluoride conversion coating to develop MgF_2 layer. Subsequently, biomimetic protein coating was performed as the second coating layer using collagen type I and fetal bovine serum as the protein agent in the medium cell coating solution. The study was aimed to develop a functionalize biocompatible protective bi-layer coating that can possibly reduce the degradation rate of Mg in the early stages of bone healing. Hence, it would simultaneously enhance the cell/surface interaction to produce better osteconductive and osseointegration.

1.2 Problem Statement

Magnesium has a limitation as a Mg-based biomaterial implant in orthopaedic application. After implantation, Mg surface reacts with the surrounding tissue and degrade rapidly *in vivo* effect from low corrosion resistance. Large volume of hydrogen evolution produces on the implant surface and accumulates around the implantation site [46, 47]. This leads to lower the mechanical integrity of the implant

and may delay the healing process of the fracture bone [52, 60]. Many researches examine the degradation of Mg in SBF, mSBF, HBSS and now interest on using cell culture medium such as EMEM and DMEM as the immersion solution. To mimic the in vivo environment, a lot of factors have to be considered not only the immersion itself.

A few studies regarding the collagen type I coating [157, 185] or MgF_2 coating on pure Mg [116, 127]. Nevertheless, all the studies only focus on single coating, individually. The study on the protein coating with MgF_2 as the inner layer has not performed yet. Furthermore, no details study related with the osseointegration and promotes the cellular response to the Mg surface together with the acceptable analysis in *in-vitro* degradation using TAFEL and EIS analysis.

1.3 Research Objectives

This thesis presents a study on *in-vitro* assessment of biomimetic protein coatings on treated surface of pure Mg with the following objectives:

i. To synthesis the bi-layer functionalise coating on pure Mg.
ii. To evaluate the biomimetic protein coatings and treated surface of pure Mg in terms of its surface morphology, chemical composition, crystalline structure, chemical functionality, wettability and protein release.
iii. To analyse the effects of bi-layer coatings and treated surface on *in-vitro* degradation of magnesium.
iv. To evaluate the bioactivity, biocompatibility and osteogenic differentiation of the bi-layer coatings and treated surface.

1.4 Scopes of Research

The scopes of the study are as follows:

1. Hydrofluoric acid with concentration of 49% was used for surface modification of pure Mg.
2. Biomimetic coating was applied as coating technique for two types of protein solution; in which collagen type I and fetal bovine serum were dissolved in cell culture medium to produce outer coating layer on the treated surface.
3. The pure Mg, treated surface and bi-layer protein coatings were subjected to microstructural characterization using field emission scanning microscope (FESEM), scanning emission scanning microscope (SEM), energy dispersive spectroscopy (EDS) measurement, X-Ray diffraction (XRD), fourier transform infrared spectroscopy (ATR-FTIR), contact angle measurement and protein release using Bradford Assay.
4. The *in-vitro* degradation behaviour of all samples was examined through semi-static immersion test, potentiodynamic polarisation (TAFEL) and electrochemical impedance spectroscopy (EIS) using cell culture medium (DMEM + FBS) as immersion solution.
5. Application of indirect MTT assay using different concentration of extract solution at various immersion days in DMEM + FBS solution, cell adhesion and proliferation, and cell morphology for the purpose of biocompatibility analysis using human fetal osteoblast (hFOB) cells.
6. Osteogenic differentiation analysis on each surface was performed through filamentous actin (F-actin) staining, alkaline phosphatise (ALP) activity, Alizarin Red S for ECM mineralization and collagen secretion using Picro Sirius Red staining.
7. Application of biomimetic protein coating on the ordered structure porous Mg scaffold and analysis of the cell morphology behaviour between 2D and 3D structure.

1.5 Significance of Research

This study was focused in the bone implant applications. It includes a specific study area on the development of a better biodegradation resistance, bioactive and biocompatibility coating. It is expected that the incorporation of fluorine ions in the protein matrices and apatite deposition will improve the functionality and slow down the degradation rate of the surface coating. This alternative could possibly reduce the corrosion cost due to the damage of equipment and/or loss of product efficiency. The removal of damage tissue is necessary to avoid the possibility of long-term complications along the implantation process.

1.6 Thesis Structure and Organization

This thesis is divided into five chapters:

Chapter one covers the overview of the research background, problem statement, objectives and scopes of research, as well as the significance of the research study.

Chapter two discuss about the literature review that emphasizes on bone and bone morphology. The introduction of biomaterials and biocompatibility in clinical applications with the emphasis on Mg as a biomaterial were reviewed. The possibility of troubleshooting that might occur related to the function of Mg as a biomaterial was also discussed, as well as the various types of surface modification and coating techniques on Mg to improve the materials performance as an implant. Moreover, the influence of surface modification of Mg on host respond and the reaction of osteoblast cells attached on the Mg implant surface were also discussed. The *in-vitro* corrosion

measurement of Mg was critically discussed, with a slight additional introduction on the introduction of porous scaffold on bone tissue engineering.

Chapter three presents about the materials and methodology used in the experiments. The flow of the study started with the synthesis of bi-layer protein coating. Then, the characterisation, *in-vitro* degradation test, biocompatibility and osteogenic differentiation until application of 2D biomimetic coating technique on ordered porous structure of Mg scaffold were the following steps.

Chapter four explains the details of results and discussion on the performance of bi-layer protein coatings on pure Mg surface in *in-vitro* degradation behaviour, bioactivity, biocompatibility and osteogenic differentiation. Furthermore, the application of biomimetic protein coating protocol on 2D surface to the ordered porous structure was also investigated through cell morphology behaviour.

Chapter five is the summary and conclusion of the findings from this study, as well as the suggestions for the future research.

REFERENCES

1. Li, L., Gao, J., and Wang, Y. (2004). Evaluation of cyto-toxicity and corrosion behavior of alkali-heat-treated magnesium in simulated Body fluid. *Surface and Coatings Technology, 185,* 92-98.
2. Zhang, E., Xu, L., and Yang, K. (2005). Formation by ion plating of Ti-coating on pure Mg for biomedical applications. *Scripta Materialia, 53,* 523-527.
3. Kannan, M.B. (2010). Influence of microstructure on the in-vitro degradation behaviour of magnesium alloys. *Materials Letters, 64,*739-742.
4. Lee, J., Han, G., Kim, Y., Byun, J., Jang, J., Seok, H., and Yang, S. (2009). Effects of impurities on the biodegradation behavior of pure magnesium. *Metals and Materials International, 5*(6), 955-961.
5. Brar, H.S., Platt, M.O., Sarntinoranont, M., Martin, P.I., and Manuel, M.V. (2009). Magnesium as a biodegradable and bioabsorbable material for medical implants. *JOM, 61,* 31-34.
6. Yun, Y., Dong, Z., Yang, D., Schulz, M.J., Shanov, V.N., Yarmolenko, S., Xu, Z., Kumta, P., and Sfeir, C. (2009). Biodegradable Mg corrosion and osteoblast cell culture studies. *Materials Science and Engineering: C, 29,* 1814-1821.
7. Inoue, H., Sugahara, K., Yamamoto, A., and Tsubakino, H. (2002). Corrosion rate of magnesium and its alloys in buffered chloride solutions. *Corrosion Science, 44,* 603-610.
8. Lopez, H.Y., Cortes, D.A., Escobedo, S., and Mantovani, D. (2006). In vitro bioactivity assessment of metallic magnesium. *Key Engineering Materials, 309-311,* 453-456.
9. Ng, W.F., Chiu, K.Y., and Cheng, F.T. (2010). Effect of pH on the in vitro corrosion rate of magnesium degradable implant material. *Materials Science and Engineering: C, 30,* 898-903.
10. Castellani, C., Lindtner, R A., Hausbrandt, P., Tschegg, E., Stanzl-Tschegg, S. E., Zanoni, G., Beck, S., and Weinberg, A. –M. (2011). Bone-implant interface strength and osseointegration: Biodegradable magnesium alloy versus standard titanium control. *Acta Biomaterialia, 7*(1), 432-440.

11. Ng, W.F., Wong, M.H., and Cheng, F.T. (2010). Stearic acid coating on magnesium for enhancing corrosion resistance in Hanks' Solution. *Surface and Coatings Technology, 204,* 1823-1830.
12. Shi, P., Ng, W.F., Wong, M.H., and Cheng, F.T. (2007). Improvement of corrosion resistance of pure magnesium in Hank's Solution by microarc oxidation with sol-gel TiO_2 sealing. *Journal of Alloys and Compounds, 469,* 286-292.
13. Song, G., and Song, S. (2007). A possible biodegradable magnesium implant material. *Advanced Engineering Materials, 9*(4), 298-302.
14. Wang, Y., Xiong, G., Luo, H., He, F., Huang, Y., and Zhou, X. (2008). Preparation and characterization of a new biomedical magnesium-calcium alloy. *Materials & Design, 29*(10), 2034-2037.
15. Wen, Z., Wu, C., Dai, C., and Yang, F. (2009). Corrosion behaviors of Mg and its alloys with different Al contents in a modified simulated body fluid. *Journal of Alloys and Compounds, 488*(1), 392-399.
16. Mueller, W.D., de Mele, M.F.L., Nascimento, M.L., and Zeddies, M. (2009). Degradation of magnesium and its alloys: Dependence on the composition of the synthetic biological media. *Journal of Biomedical Materials Research Part A, 90A*(2), 487-495.
17. Mueller, W.D., Nascimento, M.L., Zeddies, M., Córsico, M., Gassa, L.M., and de Mele, M.A.F.L. (2007). Magnesium and its alloys as degradable biomaterials: Corrosion studies using potentiodynamic and EIS electrochemical techniques. *Materials Research, 10*(1), 5-10.
18. Song, G. (2007). Control of biodegradation of biocompatable magnesium alloys. *Corrosion Science, 49*(4), 1696-1701.
19. Feser, K., Kietzmann, M., Baumer, W., Krause, C., and Bach, F.W. (2010). Effects of degradable Mg-Ca alloys on dendritic cell function. *Journal Biomaterials Applications, 25*(7), 685-697.
20. Wang, H., Shi, Z.M., and Yang, K. (2008). Magnesium and magnesium alloys as degradable metallic biomaterials. *Advanced Materials Research, 32,* 207-210.
21. Hassel, T., Bach, F.W., and Krause, C. (2007). Influence of the alloy composition on the mechanical and electrochemical properties of binary Mg-Ca alloys and its corrosion behaviour in solutions at different chloride concentrations. *In: Kainer,*

K.U., editor. Magnesium : Proceedings of the 7th International Conference on Magnesium Alloys and Their Applications: Wiley, VCH, 789.

22. Hassel, T., Bach, F.W., Golovko, A.N., and Krause, A. (2006). Investigation of the mechanical properties and the corrosion behaviour of low alloyed magnesium-calcium-alloys for use as absorbable biomaterial in the implant technique. *In: Pekguleryuz, M., editor. Conference of Metallurgists : Magnesium Technology in the Global Age. Montreal, Quebec, Canada*, 359.
23. Denkena, B., Podolsky, C., Lucas, A., Hassel, T., Witte, F., Palm, O., and Hurschler, C. (2005). Degradable implants made of magnesium alloys. *5th Euspen International Conference,* vol. 6.
24. Kannan, M.B., and Raman, R.K.S. (2008). In vitro degradation and mechanical integrity of calcium-containing magnesium alloys in modified-simulated body fluid. *Biomaterials, 29*(15), 2306-2314.
25. Liu, C., Xin, Y., Tang, G., and Chu, P.K. (2007). Influence of heat treatment on degradation behavior of bio-degradable die-cast AZ63 magnesium alloy in simulated body fluid. *Materials Science and Engineering: A, 456*(1-2), 350-357.
26. Song, Y.W., Shan, D.Y., and Han, E.H. (2008). Electrodeposition of hydroxyapatite coating on AZ91D magnesium alloy for biomaterial application. *Materials Letters, 62*(17-18), 3276-3279.
27. Zhou, W., Shen, T., and Aung, N. (2010). Effect of heat treatment on corrosion behaviour of magnesium alloy AZ91D in simulated body fluid. *Corrosion Science, 52*(3), 1035-1041.
28. Liu, C., Xin, Y., Tian, X., and Chu, P.K. (2007). Degradation susceptibility of surgical magnesium alloy in artificial biological fluid containing albumin. *Journal of Materials Research, 22,* 1806-1814.
29. Levesque, J., Hermawan, H., Dube, D., and Mantovani, D. (2008). Design of a pseudo-physiological test bench specific to the development of biodegradable metallic biomaterials. *Acta Biomaterialia,* 4(2), 284-295.
30. Kannan, M.B., and Raman, R.K.S. (2008). Evaluating the stress corrosion cracking susceptibility of Mg-Al-Zn alloy in modified-simulated body fluid for orthopaedic implant application. *Scripta Materialia, 59*(2), 175-178.
31. Fekry, A.M., and El-Sherif, R.M. (2009). Electrochemical corrosion behavior of magnesium and titanium alloys in simulated body fluid. *Electrochimica Acta, 54*(28), 7280-7285.

32. Eliezer, A., and Witte, F. (2010). Corrosion behaviour of magnesium alloys in biomedical environments. *Advanced Materials Research, 95,* 17-20.
33. Xin, Y., Liu, C., Huo, K., Tang, G., Tian, X., and Chu, P.K. (2009). Corrosion behavior of ZrN/Zr coated biomedical AZ91 magnesium alloy. *Surface and Coatings Technology, 203*(17-18), 2554-2557.
34. Xin, Y., Liu, C., Zhang, W., Jiang, J., Tang, G., Tian, X., and Chu, P.K. (2008). Electrochemical behavior Al_2O_3/Al coated surgical AZ91 magnesium alloy in simulated body fluids. *Journal of the Electrochemical Society, 155*(15), 178.
35. Wang, Y., Wei, M., Gao, J., Hu, J., and Zhang, Y. (2008). Corrosion process of pure magnesium in simulated body fluid. *Materials Letters, 62*(14), 2181-2184.
36. Xin, Y., Liu, C., Zhang, X., Tang, G., Tian, X., and Chu, P.K. (2007). Corrosion behavior of biomedical AZ91 magnesium alloy in simulated body fluids. *Journal of Materials Research, 22*(7), 2004-2011.
37. Witte, F., Feyerabend, F., Maier, P., Fischer, J., Stormer, M., Blawert, C., Dietzel, W., and Hort, N. (2007). Biodegradable magnesium-hydroxyapatite metal matrix composites. *Biomaterials, 28*(13), 2163-2174.
38. Rettig, R., and Virtanen, S. (2008). Time-dependent electrochemical characterization of the corrosion of a magnesium rare in Si-Earth alloy simulated body fluids. *Journal of Biomedical Materials Research Part A, 85A*(1), 167-175.
39. Rettig, R., and Virtanen, S. (2009). Composition of corrosion layers on a magnesium rare-earth alloy in simulated body fluids. *Journal of Biomedical Materials Research Part A, 88A*(2), 359-369.
40. Yan, T., Tan, L., Xiong, D., Liu, X., Zhang, B., and Yang, K. (2010). Fluoride treatment and in vitro corrosion behavior of an AZ31D magnesium alloy. *Materials Science and Engineering: C, 30*(5), 740-748.
41. Yang, J.X., Cui, F.Z., Yin, Q.S., Zhang, T., and Wang, X.M. (2009). Characterization and degradation study of calcium phosphate coating on magnesium alloy bone implant in vitro. *IEEE Transactions on Plasma Science, 37*(7), 1161-1168.
42. Cui, F.Z., Yang, J.X., Jiao, Y.P., Yin, Q.S., and Zhang, Y. (2008). Calcium phosphate coating on magnesium alloy for modification of degradation behavior. *Frontiers of Material Science in China, 2*(2), 143-148.
43. Alvarez-Lopez, M., Pereda, M.D., del Valle, J.A., Fernandez-Lorenzo, M., Garcia-Alonso, M.C., Ruano, O.A., and Escudero, M.L. (2009). Corrosion

behaviour of AZ31 magnesium alloy with different grain sizes in simulated biological fluids. *Acta Biomaterialia, 6*(5), 1763-1771.

44. Mueller, W.D., Lucia Nascimento, M., and Lorenzo de Mele, M.F. (2010). Critical discussion of the results from different corrosion studies of Mg and Mg alloys for biomaterial applications. *Acta Biomaterialia, 6*(5), 1749-1755.
45. Feyerabend, F., Fischer, J., Holtz, J., Witte, F., Willumeit, R., Drücker, H., Vogt, C., and Hort, N. (2010). Evaluation of short-term effects of rare earth and other elements used in magnesium alloys on primary cells and cell lines. *Acta Biomaterialia, 6*(5), 1834-1842.
46. Zheng, Y.F., Gu, X.N., Xi, Y.L., and Chai, D.L. (2010). In vitro degradation and cytotoxicity of Mg/Ca composites produced by powder metallurgy. *Acta Biomaterialia, 6*(5), 1783-1791.
47. Gu, X., Zheng, Y., Cheng, Y., Zhong, S., and Xi, T. (2009). In vitro corrosion and biocompatibility of binary magnesium alloys. *Biomaterials, 30*(4), 484-498.
48. Gunde, P., Angela, F., Anja, C.H., Patrik, S., and Peter, J.U. (2010). The influence of heat treatment and plastic deformation on the bio-degradation of a Mg-Y-Re alloy. *Materials Science Forum*, *618-619,* 71-74.
49. Walker, J., Shadanbaz, S., Kirkland, N. T., Stace, E., Woodfied, T., Staiger, M. P., and Dias, G. J. (2012). Magnesium alloys: Predicting in vivo corrosion with in vitro immersion testing. *Journal of Biomedical Materials Research Part B: Applied Biomaterials, 100B*(4), 1134-1141.
50. Wang, J., Zeng, R., Chen, J., and Chen, R. (2009). Corrosion behaviour of magnesium alloy AZ53 in simulated body fluids. *Material Science Forum*, 610, 1174.
51. Quach, N.-C., Uggowitzer, P.J., and Schmutz, P. (2008). Corrosion behaviour of an Mg-Y-Re alloy used in biomedical applications studied by electrochemical techniques. *Comptes Rendus Chimie, 11*(9), 1043-1054.
52. Wang, H.X., Guan, S.K., Wang, X., Ren, C.X., and Wang, L.G. (2010). In vitro degradation and mechanical integrity of Mg-Zn-Ca alloy coated with Ca-deficient hydroxyapatite by the pulse electrodeposition process. *Acta Biomaterialia, 6*(5), 1743-1748.
53. Zhang, S., Li, J., Song, Y., Zhao, C., Zhang, X., Xie, C., Zhang, Y., Tao, H., He, Y., Jiang, Y., and Bian, Y. (2009). In vitro degradation, hemolysis and MC3T3-

E1 cell adhesion of biodegradable Mg-Zn alloy. *Materials Science and Engineering: C, 29*(6), 1907-1912.

54. He, W., Zhang, E., and Yang, K. (2010). Effect of Y on the bio-corrosion behavior of extruded Mg-Zn-Mn alloy in Hank's solution. *Materials Science and Engineering: C, 30*(1), 167-174.
55. Zhang, Y., Song, X., Yang, C., Gao, S., Klausen, L. H., Zhang, Y., Dong, M., and Kjems, J. (2015). Chitosan/siRNA functionalized titanium surface via a layer-by-layer approach for in vitro sustained gene silencing and osteogenic promotion. *International Journal of Nanomedicine, 10*(1), 2335-2346.
56. Xu, L., Zhang, E., and Yang, K. (2009). Phosphating treatment and corrosion properties of Mg–Mn–Zn alloy for biomedical application. *Journal of Materials Science: Materials in Medicine, 20*(4), 859-867.
57. Long Li, Ming Zhang, Ye Li, Jie Zhao, Ling Qin and Yuxiao Lai. (2017). Corrosion and biocompatibility improvement of magnesium-based alloys as bone implant materials: a review. *Regenerative Biomaterials, 4*(2), 129-137.
58. Kraus, T., Fischerauer, S.F., Hanz, A.C., Uggowitzer, P.J., Loffler, J.F., and Weinber, A.M. (2012). Magnesium alloys for temporary implants in osteosynthesis: in vivo studies of their degradation and interaction with bone. *Acta Biomaterialia, 8*(3), 1230.
59. Kuwahara, H., Al-Abdullat, Y., Mazaki, N., Tsutsumi, S., and Aizawa, T. (2001). Precipitation of magnesium apatite on pure magnesium surface during immersing in Hank's solution. *Materials Transactions, 42*(7), 1317.
60. Witte, F., Kaese, V., Haferkamp, H., Switzer, E., Meyer-Lindenberg, A., Wirth, C.J., and Windhagen, H. (2005). In vivo corrosion of four magnesium alloys and the associated bone response. *Biomaterials, 26* (17), 3557.
61. Staiger, M.P., Pietak, A.M., and Huadmai, J. (2006). Magnesium and its alloys as orthopaedic biomaterials: a review. *Biomaterials, 27,* 1728.
62. Suchanek, W., and Yoshimura, M. (1997). Processing and properties of hydroxyapatite-based biomaterials for use as hard tissue replacement implants. *J Mater Res Innov, 13,* 94.
63. Agarwal, S., Curtin, J., and Duffy, B. (2016). Biodegradable magnesium alloys for orthopaedic applications: a review on corrosion, biocompatibility and surface modifications. *Mater. Sci. Eng. C Mater. Biol. Appl., 68,* 948–963.

64. Chen, Y., Xu, Z., Smith, C., and Sankar, J. (2014). Recent advances on the development of magnesium alloys for biodegradable implants. *Acta Biomaterialia, 10,* 4561.

65. Zhang, S., Zhang, X., and Zhao, C. (2010). Research on an Mg-Zn alloy as a degradable biomaterial. *Acta Biomaterialia, 6,* 626–640.

66. Zhang, B., Hou, Y., and Wang, X. (2011). Mechanical properties, degradation performance and cytotoxicity of Mg–ZN–Ca biomedical alloys with different compositions. *Mater Sci Eng C, 31,* 1667–1673.

67. Ding, WJ. (2016). Opportunities and challenges for the biodegradable magnesium alloys as next-generation biomaterial. *Regener Biomater, 3,* 79–86.

68. Affatato, S., Ruggiero, A., and Merola, M. (2015). Advanced biomaterials in hip joint arthroplasty. A review on polymer and ceramics composites as alternative bearings. *Composites Part B: Engin, 83,* 276–83.

69. Zhang, N., Wang, Y., and Xu, W. (2016). Poly(lactide-co glycolide)/hydroxyapatite porous scaffold with microchannels for bone regeneration. *Polymers, 8,* 218.

70. Willliams, D. (2006). New Interests in Magnesium. *Medical Device Technology, 17*(3), 9-10.

71. Yang, J.X., Jiao, Y.P., Cui, F.Z., Lee, I.S., Yin, Q.S., and Zhang, Y. (2008). Modification of degradation behavior of magnesium alloy by IBAD coating of calcium phosphate. *Surface and Coatings Technology, 202*(22-23), 5733-5736.

72. Hiromoto, S., and Tomozawa, M. (2011). Hydroxyapatite coating of AZ31 magnesium alloy by a solution treatment and its corrosion behavior in NaCl solution. *Surface and Coatings Technology, 205*(19), 4711-4719.

73. Li-li, T., Qiang, W., Fang, G., Xiao-song, X., Jian-hong, Q., and Ke, Y. (2010). Preparation and characterization of Ca-P coating on AZ31 magnesium alloy. *Transactions of Nonferrous Metals Society of China, 20*(Suppl. 2), 648-654.

74. Gray-Munro, J.E., and Strong, M. (2009). The mechanism of deposition of calcium phosphate coatings from solution onto magnesium alloy AZ31. *Journal of Biomedical Materials Research Part A, 90A*(2), 339-350.

75. Wang, Q., Tan, L., Xu, W., Zhang, B., and Yang, K. (2011). Dynamic behaviors of a CaP coated AZ31B magnesium alloy during in vitro and in vivo degradations. *Materials Science and Engineering: B, 176*(20), 1718-1726.

76. Bakkar, A., and Neuber, V. (2007). Electrodeposition onto magnesium in air and water stable ionic liquids: From corrosion to successful plating. *Electrochemistry Communications, 9*(9), 2428-2435.

77. Peixoto Barbosa, D., and Knornschild, G. (2009). Anodization of Mg-alloy AZ91 in NaOH solutions. *Surface and Coatings Technology, 203*(12), 1629-1636.

78. Jianrui, L., Yina, G., and Weidong, H. (2006). Study on the corrosion resistance of phytic acid conversion coating for magnesium alloys. *Surface and Coatings Technology*, 20:1536-1541.

79. Li, J.-Z., Huang, J.-G., Tian, Y.-W., and Liu, C.-S. (2009). Corrosion action and passivity mechanism of magnesium alloy in fluoride solution. *Transactions of Nonferrous Metals Society of China, 19*(1), 50-54.

80. Wu, C., Wen, Z., Dai, C., Lu, Y., and Yang, F. (2010). Fabrication of calcium phosphate/chitosan coatings on AZ91D magnesium alloy with a novel method. *Surface and Coatings Technology, 204*(20), 3336-3347.

81. Shi, Y., Qi, M., Chen, Y., and Shi, P. (2011). MAO-DCPD composite coating on Mg alloy for degradable implant applications. *Materials Letters, 65*(14), 2201-2204.

82. Ping, L., Yin, L., Meiqing, G., Haidong, F., and Xinhua, X. (2011). Corrosion and drug release properties of EN-plating/PLGA composite coating on MAO film. *Materials Science & Engineering: C (Materials for Biological Applications), 31*(7), 1285-1289.

83. Shengxue, Y., Qiaoyan, L., Jing, H., Zhanwei, Z., and Qianyun, Z. (2006). Preparation and performance of rare earths chemical conversion film on magnesium alloy. *Journal of Rare Earths, 24*(1, Supplement 1), 397-400.

84. Ferreira, P.C., Piai, K.d.A., Takayanagui, A.M.M. and Segura-Munoz, S.I. (2008). Aluminum as a risk factor for Alzheimer's disease. *Revista Latino-Americana De Enfermagem, 16*(1), 151-157.

85. Flaten, T.P. (2001). Aluminium as a risk factor in Alzheimer's disease, with emphasis on drinking water. *Brain Research Bulletin, 55*(2), 187-196.

86. Yuen, C.K., and Ip, W.Y. (2010). Theoretical risk assessment of magnesium alloys as degradable biomedical implants. *Acta Biomaterialia, 6*(5), 1808-1812.

87. Waksman, R., Pakala, R., Kuchulakanti, P.K., Baffour, R., Hellinga, D., and Seabron, R. (2006). Safety and efficacy of bioabsorbable magnesium alloy stents

in porcine coronary arteries. *Catheterization and Cardiovascular Interventions, 68,* 607–617.

88. Waksman, R., Pakala, R., Hellinga, D., Baffour, R., Kuchulakanti, P., and Seabron, R. (2005). Effect of bioabsorbable magnesium alloy stent on neointimal formation in a porcine coronary model. *European Heart Journal, 26,* 417.
89. Erbel, R., Mario, C.D., Bartunek, J., Bonnier, J., Bruyne, B.d., and Eberli, F.R. (2007). Temporary scaffolding of coronary arteries with bioabsorbable magnesium stents: a prospective, nonrandomised multicentre trial. *The Lancet, 369,* 1869–1875.
90. Waksman, R., Erbel, R., Mario, C.D., Bartunek, J., Bruyne, B.D., and Eberli, F.R. (2009). Early- and long-term intravascular ultrasound and angiographic findings after bioabsorbable magnesium stent implantation in human coronary arteries. *JACC: Cardiovascular Interventions, 2,* 312–320.
91. Gray-Munro, J.E., Seguin, C., and Strong, M. (2009). Influence of surface modification on the in vitro corrosion rate of magnesium alloy AZ31. *Journal of Biomedical Materials Research Part A, 91A,* 221–230.
92. Wong, H.M., Yeung, K.W.K., Lam, K.O., Tam, V., Chu, P.K., and Luk, K.D.K. (2010). A biodegradable polymer-based coating to control the performance of magnesium alloy orthopaedic implants. *Biomaterials, 31*(8), 2084-2096.
93. Keim, S., Brunner, J.G., Fabry, B., and Virtanen, S. (2011). Control of magnesium corrosion and biocompatibility with biomimetic coatings. *Journal of Biomedical Materials Research Part B: Applied Biomaterials, 96*(1), 84–90.
94. Dearnly, P.A. (2005). A brief review of test methodologies for surface-engineered biomedical implant alloys. *Surface and Coatings Technology, 198,* 483-490.
95. Rucdi, W.M., and Murphy, A.O. (2002). Principle of fracture management. *AO Publishing, Dübendorf Switzerland,* 13–14.
96. Zhang, Y., and Zhang, G., and Wei, M. (2009). Controlling the biodegradation rate of magnesium using biomimetic apatite coating. *Journal of Biomedical Materials Research Part B: Applied Biomaterials, 89*(2), 408–414.
97. Li, J., Cao, P., Zhang, X., Zhang, S., and He, Y. (2010). In vitro degradation and cell attachment of a PLGA coated biodegradable Mg-6Zn based alloy. *Journal of Materials Science, 45,* 6038-6045.

98. Sealy, M.P., and Guo, Y. (2010). Surface integrity and process mechanics of laser shock peening of novel biodegradable magnesium–calcium (Mg–Ca) alloy. *Journal of the Mechanical Behavior of Biomedical Materials, 3,* 488–496.

99. Wang, J., Tang, J., and Zhang, P. (2012). Surfacemodification of magnesium alloys developed for bioabsorbable orthopedic implants: a general review. *Journal of BiomedicalMaterials Research Part B: Applied Biomaterials,* vol. 100, no. 6, pp. 1691–1701.

100. Sankara Narayan,T.S. N., Park, I.S., and Min, H. L. (2015). Surface modification of magnesium and its alloys for biomedical applications: opportunities and challenges. *Surface Modification of Magnesium and its Alloys for Biomedical Applications, 1,* 29–87.

101. Sankara Narayan,T.S. N., Seshadri, T., Kwon, Y., and Kim, K. H. (2007). Calcium phosphate-based coatings on titanium and its alloys. *Journal of Biomedical Materials Research Part B: Applied Biomaterials, 85*(1), 279–299.

102. Ducheyne, P., Hench, L.L., Kagan, A., Martens, M.A., Bursens, A., and Mulier, J.C. (1980). Effect of hydroxyapatite impregnation on skeletal bonding of porous coated implants. *Journal of Biomedical Materials Research, 14,* 225-237.

103. Geng, F., Tan, L., Jin, X.X., Yang, J., and Yang, K. (2009). The preparation, cytocompatibility, and in vitro biodegradation study of pure β-TCP on magnesium. *Journal of Materials Science: Materials in Medicine, 20,* 1149-1157.

104. Wang, H., Guan, S., Wang, X., Ren, C., and Wang, L.G. (2010). In vitro degradation and mechanical integrity of Mg-Zn-Ca alloy coated with Ca-deficient hydroxyapatite by the pulse electrodeposition process. *Acta Biomaterialia, 6,* 1743-1748.

105. Tapsir, Z., Jamaludin, F.H., Pingguan-Murphy, B., and Saidin, S. (2017). Immobilisation of hydroxyapatite-collagen on polydopamine grafted stainless steel 316L: Coating adhesion and in vitro cells evaluation. *Journal of Biomaterials Applications, 32*(7), 987-995.

106. Leon, B., and Jansen, J.A. (2009). Thin calcium phosphate coatings for medical implants. *Springer*. Doi:10.1007/978-0-387-77718-4.

107. Zhang, C., Zeng, R., Chen, R., Liu, C., and Gao, J. (2010). Preparation of calcium phosphate coatings on Mg-1.0Ca alloy. *Transactions of Nonferrous Metals Society of China, 20,* 655-659.

108. Zhou, F. Y., Wang, B. L., Qiu, K. J., Lin, W. J., Li, L., Wang, Y. B., Nie, F. L., and Zheng, Y. F. (2012). Microstructure, corrosion behaviour and cytotoxicity of Zr-Nb alloys for biomedical application. *Materials Science and Engineering: C, 32,* 851-857.

109. Keim, S., Brunner, J.G., Fabry, B., and Virtanen, S. (2011). Control of magnesium corrosion and biocompatibility with biomimetic coatings. *Journal of Biomedical Materials Research - Part B Applied Biomaterials, 96 B*(1), 84-90.

110. Song, Y., Zhang, S., Li, J., Zhao, C., and Zhang, X. (2010). Electrodeposition of Ca-P coatings on biodegradable Mg alloy: In vitro biomineralization behaviour. *Acta Biomaterialia, 6*(5), 1736-1742.

111. Meng, E.C., Guan, S.K., Wang, H.X., Wang, L.G., Zhu, S.J., Hu, J.H., Ren, C.X., Gao, J.H., and Feng, Y.S. (2011). Effect of electrodeposition modes on surface characteristics and corrosion properties of fluorine-doped hydroxyapatite coatings on Mg-Zn-Ca alloy. *Applied Surface Science, 257*(11), 4811-4816.

112. Wei, Z., Du, H., and Zhang, E. (2011). The formation mechanism and biocorrosion property of $CaSiO_3/CaHPO_4 \cdot 2H_2O$ composite conversion coating on the extruded Mg-Zn-Ca alloy for bone implant application. *Surface and Interface Analysis, 43,*791-794.

113. Xu, L., Pan, F., Yu, G., Yang, L., Zhang, E., and Yang, K. (2009). In vitro and in vivo evaluation of the surface bioactivity of a calcium phosphate coated magnesium alloy. *Biomaterials, 30*(8), 1512-1523.

114. Hara, N., Kobayashi, Y., Kagayab, D., and Akao, N. (2007). Formation and breakdown of surface films on magnesium and its alloys in aqueous solutions. *Corrosion Science, 49*(1), 166–175.

115. Gray, J.E., and Luan, B. (2002). Protective coatings on magnesium and its alloys — a critical review. *Journal of Alloys and Compounds, 336,* 88–113.

116. Chen, X.B., Birbilis, N., and Abbot, T.B. (2011). Review of Corrosion-Resistant Conversion Coatings for Magnesium and Its Alloys. *Corrosion (Houston), 67*(3), 035005-1-035005-16.

117. Li, Z., Gu, X., Lou, S., and Zheng, Y. (2008). The development of binary Mg-Ca alloys for use biodegradable materials within bone. *Biomaterials, 29*(10), 1329-1344.

118. Turhan, M.C., Lynch, R., Killian, M.S., and Virtanen, S. (2009). Effect of acidic etching and fluoride treatment on corrosion performance in Mg alloy AZ91D (MgAlZn). *Electrochimica Acta, 55,* 250–257.

119. Lorenz, C., Brunner, J.G., Kollmannsberger, P., Jaafar, L., Fabry, B., and Virtanen, S. (2009). Effect of surface pre-treatments on biocompatibility of magnesium. *Acta Biomaterialia, 5,* 2783–2789.

120. Gu, X., Zheng, W., Cheng, Y., and Zheng, Y. (2009). A study on alkaline heat treated Mg-Ca alloy for the control of the biocorrosion rate. *Acta Biomaterialia, 5,* 2790-2799.

121. Friedrich, H.E., and Mordike, B.L. (2006). Magnesium technology : metallurgy, design data, applications. *Berlin ; New York: Springer*, xxii, 677.

122. Hiromoto, S., Shishido, T., Yamamoto, A., Maruyama, N., Somekawa, H., and Mukai, T. (2008). Precipitation control of calcium phosphate on pure magnesium anodization. *Corrosion Science, 50*(10), 2906-2913.

123. Carboneras, M., GarcÃa- Alonso, M.C., and Escudero, M.L. (2011). Biodegradation kinetics of modified magnesium-based materials in cell culture medium. *Corrosion Science, 53*(4), 1433-1439.

124. Chiu, K.Y., Wong, M.H., Cheng, F.T., and Man, H.C. (2007). Characterization and corrosion studies of fluoride conversion coating on degradable Mg implants. *Surface & Coatings Technology, 202*(3), 590-598.

125. Zhang, C.Y., Gao, J.C., and Liu, C.L. (2011). Effect of fluoride treatment on corrosion property of AZ31 magnesium alloy in Hank's solution. *Changsha, China: Trans Tech Publications, 239-242,*186-190.

126. da Conceicao, T.F., Scharnagl, N., Blawert, C., Dietzel, W., and Kainer, K.U. (2010). Surface modification of magnesium alloy AZ31 by hydrofluoric acid treatment and its effect on the corrosion behaviour. *Thin Solid Films, 518*(18), 5209-5218.

127. Li, J., Huang, J., Tian, Y., and Liu, C. (2009). Corrosion action and passivation mechanism of magnesium alloy in fluoride solution. *Transactions of Nonferrous Metals Society of China, 19*(1), 50-54.

128. Sankara Narayanan, T. S. N., Park, I. S., and Lee, M. H. (2014). Tailoring the composition of fluoride conversion coatings to achieve better corrosion protection of magnesium for biomedical applications. *Journal of Materials Chemistry B, 2*(21), 3365-3382.

129. Bakhsheshi-Rad, H. R., Idris, M. H., Kadir, M. R. A., and Daroonparvar, M. (2013). Effect of fluoride treatment on corrosion behavior of Mg−Ca binary alloy for implant application. *Transactions of Nonferrous Metals Society of China, 23*(3), 699−710.

130. Lin, D. J., Hung, F. Y., Yeh, M. L., Lee, H. P., and Lui, T. S. (2017). Correlation between Anti-Corrosion Performance and Optical Reflectance of Nano Fluoride Film on Biodegradable Mg-Zn-Zr Alloy: a Non-Destructive Evaluation Approach. *Int. J. Electrochem. Sci., 12* (5), 3614 – 3634.

131. Mao, L.,Yuan, G., Niu, J., Zong, Y., and Ding, W. (2013). In vitro degradation behavior and biocompatibility of Mg–Nd–Zn–Zr alloy by hydrofluoric acid treatment. *Materials Science and Engineering: C, 33* (1), 242-250.

132. Pereda, M.D., Alonso, C., Gamero, M., del Valle, J.A., and Fernandez Lorenzo de Mele, M. (2011). Comparative study of fluoride conversion coatings formed on biodegradable powder metallurgy Mg: the effect of chlorides at physiological level. *Materials Science & Engineering: C (Materials for Biological Applications), 31*(5), 858-65.

133. Verdierc, S., van der Laaka, N., Delalandea, S., Metsonb, J., and Dalard, F. (2004). The surface reactivity of a magnesium–aluminium alloy in acidic fluoride solutions studied by electrochemical techniques and XPS. *Applied Surface Science, 235*(4), 513–524.

134. Witte, F., Fischer, J., Nellesen, J., Vogt, C., Vogt, J., Donath, T., and Beckmann, F. (2010). In vivo corrosion and corrosion protection of magnesium alloy LAE442. *Acta Biomaterialia, 6*(5), 1792-1799.

135. Zheng, Y., Wu, J., Ng, J.C., Wang, G., and Lian, W. (2002). The absorption and excretion of fluoride and arsenic in humans. *Toxicology Letters, 133,* 77–82.

136. Tingting, Y., Lili, T., Dangsheng, X., Xinjie L., Bingchun Z., and Ke Y. (2010). Fluoride treatment and in vitro corrosion behavior of an AZ31B magnesium alloy. *Materials Science and Engineering C, 30* (5) 740–748.

137. Berglundh, T., Abrahamsson, I., Albouy, J., and Lindhe, J. (2007). Bone healing at implants with a fluoride-modified surface: an experimental study in dogs. *Clin. Oral Impl. Res., 18,* 147–152.

138. Grillo, C.A., Alvarez, F., and Fernandez Lorenzo de Mele, M.A. (2011). Biological effects of magnesium particles degradation on UMR-106 cell line:

Influence of fluoride treatments. *Colloids and Surfaces. B, Biointerfaces, 88*(1), 471-476.

139. He, F., Yang, G., Wang, X., and Zhao, S. (2009). Bone responses to rough titanium implants coated with biomimetic Ca-P in rabbit tibia. *Journal of Biomedical Materials Research Part B: Applied Biomaterials, 90B*(2), 857–863.
140. De Groot, K., Wolke J. G. C., and Jansen, J. A. (1998). Calcium phosphate coatings for medical implants. *Proceedings of the Institution of Mechanical Engineers Part H, Journal of engineering in medicine, 212*(2), 137-147.
141. Liu, Y., Huse, R. O., De Groot, K., Buser, D., and Hunziker, E. B. (2007). Delivery mode and efficacy of BMP-2 in association with implants. *Journal of Dental Research, 86,* 84-89.
142. Shah, A.K., Lazatin, J., Sinha, R. K., Lennox, T., Hickok, N. J., and Tuan, R. S. (1999). Mechanism of BMP-2 stimulated adhesion of osteoblastic cells to titanium alloy. *Biology of the Cell, 91*(12), 131-142.
143. Geibler, U., Hempel, U., Wolf, C., Scharnweber, D., Worch, H., and Wenzel, K.W. (2000). Collagen type I-coating of Ti6A14V promotes adhesion of osteoblasts. *Journal of Biomedical Materials Research, 51*(4), 752-760.
144. Bierbaum, S., Beutner, R., Hanke, T., Scharnweber, D., Hempei, U., and Worch, H. (2003). Modification of Ti6Al4V surfaces using collagen I, III, and fibronectin. I. Biochemical and morphological characteristics of the adsorbed matrix. *Journal of Biomedical Materials Research Part A, 67*(2), 421–430.
145. Gobeaux, F., Mosser, G., Anglo, A., Panine, P., Davidson, P., Giraud-Guille, M.-M., and Belamie, E. (2008). Fibrillogenesis in Dense Collagen Solutions: A Physicochemical Study. *Journal of Molecular Biology, 376*(5), 1509-1522.
146. Mouw, J.K., Ou, G., and Weaver, V.M. (2014).Extracellular matrix assembly: a multiscale deconstruction. *Nat. Rev. Mol. Cell Biol., 15,* 771–785.
147. Chen, F.-M., and Liu, X. (2016). Advancing biomaterials of human origin for tissue engineering. *Progress in Polymer Science, 53,* 86-168.
148. NA, Biologie, in: É. Du, R.P. Inc. (Eds.), Biologie, Première é, Saint-Laurent, 1995.
149. Matton, G., Anseeuw, A., and De Keyser, F. (1985). The history of injectable biomaterials and the biology of collagen. *Aesthetic Plast. Surg, 9,* 133–140.

150. Trelstad, R.L., Hayashi, K., and Gross, J. (1976). Collagen fibrillogenesis: intermediate aggregates and suprafibrillar order. *Proc. Natl. Acad. Sci. U. S. A, 73*(11), 4027–4031.

151. Birk, D.E., Fitch, J.M., Babiarz, J.P., Doane, K.J., and Linsenmayer, T.F. (1990). Collagen fibrillogenesis in vitro: interaction of types I and V collagen regulates fibril diameter. *Journal of Cell Science,* 95, 649–657.

152. Thomas E. Kruger, Andrew, H., Miller and Wang, J. (2013). Collagen Scaffolds in Bone Sialoprotein-Mediated Bone Regeneration. *The Scientific World Journal, 2013*(2), 812718.

153. Kadler, K.E., Hill, A., and Canty-Laird, E.G. (2008). Collagen fibrillogenesis: fibronectin, integrins, and minor collagens as organizers and nucleators. *Curr. Opin Cell Biol., 20*(5-24) 495–501.

154. Chen, F.M., Sun, H.H., Lu, H., and Yu, Q. (2012). Stem cell-delivery therapeutics for periodontal tissue regeneration. *Biomaterials,.33*(27), 6320-6344.

155. Mushahary, D., Wen, C., Kumar, J.M., Lin, J., Harishankar, N., and Hodgson, P. (2014). Collagen type-I leads to in vivo matrix mineralization and secondary stabilization of Mg–Zr–Ca alloy implants. *Colloids Surfaces B Biointerfaces, 122,* 719–728.

156. Chen, F.-M., and Liu, X. (2016). Advancing biomaterials of human origin for tissue engineering. *Progress in Polymer Science, 53,* 86-168.

157. Zhao, N., and Zhu, D. (2014). Collagen Self-Assembly on Orthopedic Magnesium Biomaterials Surface and Subsequent Bone Cell Attachment. *PLOS ONE, 9*(10), e110420.

158. Park, H.C., Pant, H.R., and Kim, C.S. (2013). Effect on corrosion behavior of collagen film/fiber coated AZ31 magnesium alloy. *Dig. J. of Nanomaterials and Biostructures. 8*(3), 1227–1234.

159. Honn, K. V., Singley, J. A., and Chavin, W. (1975). Fetal bovine serum: A multivariate standard. *Experimental Biology and Medicine, 149*(2), 344-347.

160. Catledge, S.A., Vohra, Y.K., Bellis, S.L., and Sawyer, A.A. (2004). Mesenchymal stem cell adhesion and spreading on nanostructured biomaterials. *J. Nanosci. Nanotechnol, 4*(8), 986–989.

161. Witte, F. (2009). The History of Biodegradable Magnesium Implants: A Review. *Acta Biomaterialia, 6*(5), 1680-1692.

162. Yamamoto, A., and Hiromoto, S. (2009). Effect of inorganic salts, amino acids and proteins on the degradation of pure magnesium in vitro. *Materials Science and Engineering C, 29*(5), 1559–1568.

163. Yang, L., Hort, N., Willumeit, R., and Feyerabend, F. (2012). Effects of corrosion environment and proteins on magnesium corrosion. *Corrosion Engineering, Science and Technology, 47*(5), 335-339.

164. Barrere, F. (2002). *Biomimetic calcium phosphate coatings: Physicochemistry and biological activity*. Enschede: University of Twente.

165. Baker, K.C., Anderson, M.A., Oehlke, S.A., Astashkina, A.I., Haikio, D.C., Drelich, J., and Donahue, S.W. (2006). Growth, characterization and biocompatibility of bone-like calcium phosphate layers biomimetically deposited on metallic substrata. *Materials Science and Engineering: C, 26*(8), 1351-1360.

166. Barrere, F. (2003). Osteogenecity of octacalcium phosphate coatings applied on porous metal implants. *Journal of Biomedical Materials Research Part A, 66A*(4), 779-788.

167. Landi, E., Tampieri, A., Mattioli-Belmonte, M., Celotti, G., Sandri, M., Gigante, A., Fava, P., and Biagini, G. (2006). Biomimetic Mg- and Mg.CO_3-substituted hydroxyapatites: synthesis characterization and in vitro behaviour. *Journal of the European Ceramic Society, 26*(13), 2593-2601.

168. Habibovic, P., Barrere, F., van Blitterswijk, C.A., de Groot, K., and Layrolle, P. (2002). Biomimetic hydroxyapatite coating on metal implants. *Journal of the American Ceramic Society, 85*(3), 517-522.

169. Cheng, M., Wahafu, T., Jiang, G., Liu, W., Qiao, Y., Peng, X., Cheng, T., Zhang, X., He, G., and Liu, X. (2016). A novel open-porous magnesium scaffold with controllable microstructure and properties for bone regeneration. *Scientific Reports, 6*(1), doi:10.1038/srep24134.

170. Bigi, A., Falini, G., Foresti, E., Ripamonti, A., Gazzano, M., and Roveri, N. (1993). Magnesium influence on hydroxyapatite crystallization. *Journal of Inorganic Biochemistry, 49*(1), 69-78.

171. Bowen, P. K., Drelich, J., and Goldman, J. (2013). A new in vitro-in vivo correlation for bioabsorbable magnesium stents from mechanical behaviour. Materials Science and Engineering: C, 33(8), 5064-5070.

172. Zhu, L., Ye, X., Tang, G., Zhao, N., Gong, Y., Zhao, Y., Zhao, J., and Zhang, X. (2007). Biomimetic coating of compound titania and hydroxyapatite on titanium. *Journal of Biomedical Materials Research Part A, 83*(4), 1165-1175.

173. Kokubo, T. (1996). Formation of biologically active bone-like apatite on metals and polymers by a biomimetic process. *Thermochimica Acta, 280-281,* 479- 490.

174. Lin, C.-M., and Yen, S.-K. (2006). Biomimetic growth of apatite on electrolytic TiO_2 coatings in simulated body fluid. *Materials Science and Engineering: C, 26*(1), 54-64.

175. Hu, J., Wang, C., Ren, W.C., Zhang, S., and Liu, F. (2010). Microstructure evolution and corrosion mechanism of dicalcium phosphate dihydrate coating on magnesium alloy in simulated body fluid. *Materials Chemistry and Physics, 119*(1-2), 294-298.

176. Barrere, F., van der Valk, C. M., Meijer, G., Dalmeijer, R. A. J., de Groot, K., and Layrolle, P. (2003). Osteointegration of biomimetic apatite coating applied onto dense and porous metal implants in femurs of goats. *Journal of Biomedical Materials Research Part B: Applied Biomaterials, 67*(1), 655-665.

177. Wen, H.B., Wolke, J.G.C., de Wijn, J.R., Liu, Q., Cui, F.Z., and de Groot, K. (1997). Fast precipitation of calcium phosphate layers on titanium induced by simple chemical treatments. *Biomaterials, 18*(22), 1471-1478.

178. Hou, R., Willumeit-Romer, R., Garamus, V. M., Frant, M., Koll, J., and Feyerabend, F. (2018). The adsorption of protein on degradable magnesium – Which factors are relevant?. *ACS Applied Materians and Interfaces.* Doi:10.1021/acsami.8b17507.

179. Tian, P., and Liu, X. (2015). Surface modification of biodegradable magnesium and its alloys for biomedical applications. *Regen. Biomater,* 135–151.

180. Yang, J., Jiao, Y., Yin, Q., Zhang, Y., and Zhang, T. (2008). Calcium phosphate coating on magnesium alloy by biomimetic method: Investigation of morphology, composition and formation process. *Front. Mater. Sci. China, 2*(2), 149–155.

181. Makkar, P., Kang, H. J., Padalhin, A. R., Park, I., Moon, B. –G., and Lee, B. T. (2018). Development and properties of duplex MgF_2/PCL coatings on biodegradable magnesium alloy for biomedical applications. *PLOS ONE, 13*(4), e0193927.

182. Nguyen, T., Waterman, J., Staiger, M., and Woodfield, T. (2012). Controlling in vitro corrosion rate of pure Mg with rough surface texture via biomimetic coating systems. *Corrosion Engineering, Science and Technology, 47*(5), 358-364.

183. Lu, W., Chen, Z., Huang, P., and Yan, B. (2012). Microstructure, Corrosion Resistance and Biocompatibility of Biomimetic HA-Based Ca-P Coatings on ZK60 Magnesium Alloy. *Int. J. Electrochem. Sci.,* 7-12668 – 12679.

184. Cui, W., Beniash, E., Gawalt, E., Xu, Z., and Sfeir, C. (2013). Biomimetic coating of magnesium alloy for enhanced corrosion resistance and calcium phosphate deposition. *Acta Biomater, 9*(10), 8650-8659.

185. Zhao, N., Workman, B., and Zhu, D. (2014). Endothelialization of novel magnesium-rare earth alloys with fluoride and collagen coating. *Int. J. Mol. Sci., 15,* 5263-5276.

186. Zhen, Z., Xi, T.F., and Zheng, Y.F. (2013). A review on in vitro corrosion performance test of biodegradable metallic materials. *Trans. Nonferrous Met. Soc. China, 23,* 2283–2293.

187. Witte, F., Fischer, J., Nellesen, J., Crostack, H.-A., Kaese, V., Pisch, A. (2006). In vitro and in vivo corrosion measurements of magnesium alloys. *Biomaterials, 27,* 1013– 1018.

188. Erbel, R., Di Mario, C., Bartunek, J., Bonnier, J., de Bruyne, B., and Eberli, F.R. (2007). Temporary scaffolding of coronary arteries with bioabsorbable magnesium stents: a prospective, non-randomised multicentre trial. *Lancet, 369,* 1869–1875.

189. Bosiers, M. (2009). Absorbable metal stent implantation for treatment of below-the-knee critical limb Ischemia: 6-Month Analysis. *Cardiovasc. Intervent. Radiol, 32,* 424–435.

190. Mordike, B.L., and Ebert, T. (2001). Magnesium properties - applications – potential. *Mater. Sci.Eng. A, 302,* 37–45.

191. Xin, Y., Hu, T., and Chu, P.K. (2011). In vitro studies of biomedical magnesium alloys in a simulated physiological environment: A review. *Acta Biomater., 7,* 1452-1459.

192. Walker, J., Shadanbaz, S., Woodfield, T. B. F., Staiger, M. P., and Dias, G. J. (2014). The in vitro and in vivo evaluation of the biocompatibility of Mg alloys. *Biomedical Materials, 9*(1), 015006. doi:10.1088/1748-6041/9/1/015006.

193. Pinto, R., Ferreira, M.G.S., Carmezim, M.J., and Montemor, M.F. (2011). The corrosion behavior of rare-earth containing magnesium alloys in borate buffer solution. *Electrochim. Acta, 56,* 1535–1545.

194. Giraud Guille, M. M., Helary, C., Vigier, S., and Nassif, N. (2010). Dense fibrillar collagen matrices for tissue repair. Soft Matter, 6(20), 4963.

195. Witte, F., N. Hort, C. Vogt, S. Cohen, K.U. Kainer, R. Willumeit, and F. Feyerabend. (2008) 'Degradable biomaterials based on magnesium corrosion', *Current Opinion in Solid State and Materials Science,* 12(5-6): p. 63-72.

196. Li, L., Gao, J. and Wang, Y. (2004). Evaluation of cyto-toxicity and corrosion behavior of alkali-heat-treated magnesium in simulated body fluid. *Surface and Coatings Technology, 185*(1), 92-98.

197. Lee, S., Choi, J., Shin, S., Im, Y. –M., Song, J., Kang, S. S., Nam, T. –H., Webster, T. J., Kim, S. –H., and Khang, D. (2011). Analysis on migration and activation of live macrophages on transparent flat and nanostructured titanium. *Acta Biomaterialia, 7,* 2337-2344.

198. M.D. Pereda, C. Alonso, L. Burgos-Asperilla, J.A. del Valle, O.A. Ruano, P. Perez, M.A. Fernández Lorenzo de Mele. (2010) 'Corrosion inhibition of powder metallurgy Mg by fluoride treatments', *Acta Biomaterialia* 6 (2010) 1772–1782.

199. Zhao, L., Mei, S., Wang, W., Chu, P. K., Wu, Z., and Zhang, Y. (2010). The role of sterilization in the cytocompatibility of titania nanotubes. *Biomaterials, 31,* 2055-2063.

200. Anawati, Asoh, H., and Ono, S. (2015). Enhanced uniformity of apatite coating on a PEO film formed on AZ31 Mg alloy by an alkali pretreatment. *Surface and Coatings Technology, 272,* 182-189.

201. Drynda, A., Hassel, T., Hoehn, R., Perz, A., Bach, F. –W., and Peuster, M. (2009). Development and biocompatibility of a novel corrodible fluoride-coated magnesium-calcium alloy with improved degradation kinetics and adequate mechanical properties for cardiovascular applications. *Journal of Biomedical Materials Research Part A, 93*(2), 763-775.

202. Ono, S., Asami, K., and Masuko, N. (2001). Mechanism of chemical conversion coating film growth on magnesium and magnesium alloys. *Materials Transactions, 42*(7), 1225-1231.

203. Lin, D. –J., Hung, F. –Y., Yeh, M. –L., Lee, H. –P., and Lui, T. –S. (2017). Development of a novel micro-textured surface using duplex surface modification for biomedical Mg alloy applications. *Materials Letters, 206,* 9-12.

204. Tomozawa, M., Hiromoto, S., and Harada, Y. (2010). Microstructure of hydroxyapatite-coated magnesium prepared in aqueous solution. *Surface and Coatings Technology, 204*(20), 3243-3247.

205. Da Conceicao, T. F., and Scharnagl, N. (2015). Fluoride conversion coatings for magnesium and its alloys for the biological environment. *Surface Modification of Magnesium and its Alloys for Biomedical Applications, 2,* 1-22.

206. Prescott, H. A., Li, Z. –J., Kemnitz, E., Deutsch, J., and Lieske, H. (2005). New magnesium oxide fluorides with hydroxy groups as catalysts for Michael additions. *J. Mater. Chem., 15*(43), 4616–4628.

207. Rodríguez-Lorenzo, L. M., Hart, J. N., and Gross, K. A. (2003). Influence of fluorine in the synthesis of apatites. Synthesis of solid solutions of hydroxy-fluorapatite. *Biomaterials, 24*(21), 3777-3785.

208. Van Muylder, J. (1963). M. Pourbaix. Atlas D'equilibres E´lectrochimiques. *Ed. Gauthier-Villars et Cie, Paris,*139.

209. Crichton, W. A., Parise, J. B., Muller, H., Breger, J., Marshall, W. G., and Welch, M. D. (2012). *Mineralogical Magazine, 76,* 25–36.

210. V. S. Vaiss, R. A. Berg, A. R. Ferreira, I. Borges, Jr and A. A. Leitao, (2009). The Journal of Physical Chemistry A, 113(23), 6494–6499.

211. Wang, Y., Zhang, S., Zeng, X., Cheng, K., Qian, M., and Weng, W. (2007). In vitro behavior of fluoridated hydroxyapatite coatings in organic-containing simulated body fluid. *Materials Science and Engineering C, 27,* 244–250.

212. Yang, P., Liu, Q., Liu, J., Zhang, H., Li, Z., Li, R., Liu, L., and Wang, J. (2017). Bovine serum albumin-coated graphene oxide (GO) for effective adsorption of uranium(VI) from aqueous solutions. *Ind. and Eng. Chem. Res., 56*(13), 3588-3598.

213. Yang, L., and Zhang, E. (2009). Biocorrosion behavior of magnesium alloy in different simulated fluids for biomedical application. *Materials Science and Engineering: C, 29*(5), 1691-1696.

214. Hu, Y., Zhu, Y., Zhou, X., Ruan, C., Pana, H., and Catchmark, J. M. (2016). Bioabsorbable cellulose composites prepared by an improved mineral-binding process for bone defect repair. *J. Mater. Chem. B, 4,* 1235.

215. Mavropoulos, E., Costa, A. M., Costa, L. T., Achete, C. A., Mello, A., Granjeiro, J. M., and Rossi, A. M. (2011). Adsorption and bioactivity studies of albumin onto hydroxyapatite surface. *Colloids and Surfaces B: Biointerfaces, 83,* 1–9.

216. Peng, J., Zhang, X., Li, Z., Liu, Y., and Yang, X. (2015). Titania nanotube delivery fetal bovine serum for enhancing MC3T3-E1activity and osteogenic gene expression. *Materials Science and Engineering C, 56,* 438–443.

217. Rodio, M., and Intartaglia, R. (2018). Serum Albumin Protein-Mediated Ultra-Fast Laser Synthesis of Calcium Phosphate Nanoceramic in Aqueous Solution. *Nanoscience and Nanotechnology, 8*(2), 25-30.

218. Marques, P.A.A.P., Cachinho, S. C. P., Magalhaes, M. C. F., Correia, R. N., and Fernandes, M. H. V. (2004). Mineralisation of bioceramics in simulated plasma with physiological CO_2/HCO_3^- buffer and albumin. *Journal of Materials Chemistry, 14*(12), 1861-1866.

219. Lee, C. –S., and Belfort, G. (1989). Changing activity of ribonuclease A during adsorption: A molecular explanation. *Proc. Natl. Acad. Sci., 86,* 8392-8396.

220. Xia, Z., Yu, X., and Wei, M. (2011). Biomimetic collagen/apatite coating formation on Ti6Al4V substrates. *Journal of Biomedical Materials Research Part B: Applied Biomaterials, 100B*(3), 871-881.

221. Chen, Y., Mak, A. F. T., Wang, M., and Li, J. (2006). Composite coating of bonelike apatite particles and collagen fibers on poly L-lactic acid formed through an accelerated biomimetic coprecipitation process. *Journal of Biomedical Materials Research Part B: Applied Biomaterials, 77B*(2), 315-322.

222. Iafisco, M., Foltran, I., Sabbatini, S., Tosi, G., and Roveri, N. (2012). Electrospun nanostructured fibers of collagen-biomimetic apatite on titanium alloy. *Bioinorganic Chemistry and Applications,* 1-8.

223. Hu, C. (2018). Fabrication and characterization of collagen-apatite composites for bone tissue engineering. University of Connecticut.

224. Bu, H., and Li, G. (2018). Comparative investigation of hydroxyapatite/collagen composites prepared by $CaCl_2$ addition at different time points in collagen self-assembly process. *J Mater Sci., 53,* 6313.

225. Cui, F. Z., Wang, Y., Cai, Q., and Zhang, W. (2008). Conformation change of collagen during the initial stage of biomineralization of calcium phosphate. *J. Mater. Chem., 18,* 3835–3840.

226. Pang, X., Lin, L., and Tang, B. (2017). Unraveling the role of calcium ions in the mechanical properties of individual collagen fibrils. *Scientific Reports, 7,* 46042.
227. Kikuchi, M., Ikoma, T., Itoh, S., Matsumoto, H. N., Koyama, Y., Takakuda, K., Shinomiya, K., and Tanaka, J. (2004). Biomimetic synthesis of bone-like nanocomposites using the self-organization mechanism of hydroxyapatite and collagen. *Composites Science and Technology, 64,* 819–825.
228. Iafisco, M., Morales, J. G., Hernandez-Hernandez, M. A., Garcia-Ruiz, J. M., and Roveri, N. (2010). Biomimetic carbonate–hydroxyapatite nanocrystals prepared by vapor diffusion. *Advanced Engineering Materials, 12*(7), B218-B223.
229. Venugopal, J., Low, S., Choon, A. T., Sampath Kumar, T. S., and Ramakrishna, S. (2007). Mineralization of osteoblasts with electrospun collagen/hydroxyapatite nanofibers. *Journal of Materials Science: Materials in Medicine, 19*(5), 2039–2046.
230. Nudelman, F., Lausch, A. J., Sommerdijk, N. A. J. M., and Sone, E. D. (2013). In vitro models of collagen biomineralization. *Journal of Structural Biology, 183*(2), 258-269.
231. Shen, D., Horiuchi, N., Nozaki, S., Miyashin, M., Yamashita, K., and Nagai, A. (2017). Synthesis and enhanced bone regeneration of carbonate substituted octacalcium phosphate. *Bio-Medical Materials and Engineering, 28,* 9–21.
232. Tampieri, A., Celotti, G., Landi, E., Sandri, M., Roveri, N., and Falini, G. (2003). Biologically inspired synthesis of bone-like composite: Self-assembled collagen fibers/hydroxyapatite nanocrystals. *Journal of Biomedical Materials Research, 67A*(2), 618-625.
233. Gadaleta, S. J., Paschalis, E. P., Betts, F., Mendelsohn, R., and Boskey, A. L. (1996). Fourier transform infrared spectroscopy of the solution-mediated conversion of amorphous calcium phosphate to hydroxyapatite: New correlations between X-Ray diffraction and infrared data. *Calcif Tissue Int., 58,* 9–16.
234. Combes, C., and Rey, C. (2010). Amorphous calcium phosphates: Synthesis, properties and uses in biomaterials. *Acta Biomaterialia, 6,* 3362–3378.
235. Yamasaki, Y., Yoshida, Y., Okazaki, M., Shimazu, A., Uchida, T., Kubo, T., Akagawa, Y., Hamada, Y., Takahashi, J., and Matsuura, N. (2002). Synthesis of

functionally graded $MgCO_3$ apatite accelerating osteoblast adhesion. *Journal of Biomedical Materials Research, 62*(1), 99-105.

236. Bosh, N., Deggelmann, L., Blattert, C., Mozaffar, H., and Muller, C. (2018). Synthesis and characterization of Halar® polymer coating deposited on titanium substrate by electrophoretic deposition process. *Surface & Coatings Technology, 347,* 369–378.
237. Mushahary, D., Wen, C., Kumar, J. M., Lin, J., Harishankar, N., Hodgson, P., Pande, G., and Li, Y. (2014). Collagen type-I leads to in vivo matrix mineralization and secondary stabilization of Mg–Zr–Ca alloy implants. *Colloids and Surfaces B: Biointerfaces, 122,* 719–728.
238. Teng, S. –H., Lee, E. –J., Park, C. –S., Choi, W. –Y., Shin, D. –S., and Kim, H. -E. (2008). Bioactive nanocomposite coatings of collagen/hydroxyapatite on titanium substrates. *J Mater Sci: Mater Med, 19,* 2453–2461.
239. Hum, J., and Boccaccini, A. R. (2018). Collagen as Coating Material for 45S5 Bioactive Glass-Based Scaffolds for Bone Tissue Engineering. *Int. J. Mol. Sci., 19,* 1807.
240. Pace, C. N., Fu, H., Fryar, K. L., Landua, J., Trevino, S. R., Shirley, B. A., Hendricks, M. M., Iimura, S., Gajiwala, K., Scholtz, J. M., and Grimsley, G. R. (2011). Contribution of hydrophobic interactions to protein stability. *J Mol Biol, 6, 408*(3), 514–528.
241. Camilloni, C., Bonetti, D., Morrone, A., Giri, R., Dobson, C. M., Brunori, M., Gianni, S., and Vendruscolo, M. (2016). Towards a structural biology of the hydrophobic effect in protein folding. *Scientific Reports, 6,* 28285.
242. Zeng, R. C., Li, X. T., Liu, L. J., Li, S. Q., and Zhang, F. (2016). In vitro degradation of pure Mg for esophageal stent in artificial saliva. *Journal of Materials Science & Technology, 32,* 437–444.
243. Johnson, I., Jiang, W., and Liu, H. (2017). The effects of serum proteins on magnesium alloy degradation in vitro. *Scientific Reports, 7,* 14335.
244. Gu, X. N., Zheng, Y. F., and Chen, L. J. (2009). Influence of artificial biological fluid composition on the biocorrosion of potential orthopedic Mg–Ca, AZ31, AZ91 alloys. *Biomed. Mater., 4,* 065011.
245. Wagener, V., and Virtanen, S. (2016). Protective layer formation on magnesium in cell culture medium. *Materials Science and Engineering: C, 63,* 341–351.

246. Marco, I., Feyerabend, F., Willumeit-Romer, R., and Van der Biest, O. (2016). Degradation testing of Mg alloys in Dulbecco's modified eagle medium: Influence of medium sterilization. *Materials Science and Engineering: C, 62,* 68–78.

247. Naddaf Dezfuli, S., Huan, Z., Mol, J.M.C., Leeflang, M.A., Chang, J., and Zhou, J. (2014). Influence of HEPES buffer on the local pH and formation of surface layer during in vitro degradation tests of magnesium in DMEM. *Progress in Natural Science: Materials International, 24*(5), 531–538.

248. Waterman, J., Pietakb, A., Birbilis, N., Woodfielda, T., Diasb, G., and Staiger, M.P. (2011). Corrosion resistance of biomimetic calcium phosphate coatings on magnesium due to varying pretreatment time. *Materials Science and Engineering: B, 176,* 1756– 1760.

249. Xin, Y., Huo, K., Tao, H., Tang, G., and Chu, P. K. (2008). Influence of aggressive ions on the degradation behavior of biomedical magnesium alloy in physiological environment. *Acta Biomaterialia, 4,* 2008–2015.

250. Meiheng, L., Qian, C., Wenjin, Z., Wangyu, H., and Yong, S. (2011). Corrosion behaviour in SBF from titania coatings on Mg-Ca alloy. Journal of Mg-Ca alloy. Journal of Materials Science, 46(7), 2365-2369.

251. Wan, P., Lin, X., Tan, L., Li, L., Li, W., and Yang, K. (2013). Influence of albumin and inorganic ions on electrochemical corrosion behavior of plasma electrolytic oxidation coated magnesium for surgical implants. *Applied Surface Science, 282,*186– 194.

252. Tie, D., Feyerabend, F., Hort, N., Willumeit, R., and Hoeche, D. (2010). XPS studies of magnesium surfaces after exposure to Dulbecco's Modified Eagle Medium, Hank's Buffered Salt Solution, and Simulated Body Fluid. *Advanced Engineering Materials, 12*(12), B699-B704.

253. Gorgieva, S., and Kokol, V. (2011). Collagen- vs. gelatine-based biomaterials and their biocompatibility: Review and perspectives. *Biomaterials Applications for Nanomedicine.* doi:10.5772/24118.

254. Kim, J., Mousa, H. M., Park, C. H., and Kim, C. S. (2017). Enhanced corrosion resistance and biocompatibility of AZ31 Mg alloy using PCL/ZnO NPs via electrospinning. *Applied Surface Science, 396,* 249-258.

255. Ji, X. –J., Cheng, Q., Wang, J., Zhao, Y. –B., Han, Z. –Z., Zhang, F., Li, S. –Q., Zeng, R. –C., and Wang, Z. -L. (2019). Corrosion resistance and antibacterial

effects of hydroxyapatite coating induced by polyacrylic acid and gentamicin sulfate on magnesium alloy. *Frontiers of Materials Science.* Doi:10.1007/s11706-019-0448-1.

256. Feliu, Jr., S., Samaniego, A., Bermudez, E., El-Hadad, A., Llorente, I., and Galván, J. (2014). Effect of native oxide film on commercial magnesium alloys substrates and carbonate conversion coating growth and corrosion resistance. *Materials, 7*(4), 2534-2560.
257. Pan, Y., He, S., Wang, D., Huang, D., Zheng, T., Wang, S., Dong, P., and Chen, C. (2015). In vitro degradation and electrochemical corrosion evaluations of microarc oxidized pure Mg, Mg–Ca and Mg–Ca–Zn alloys for biomedical applications. *Materials Science and Engineering: C, 47,* 85–96.
258. Wang, Y., Cui, L. –Y., Zeng, R. –C., Li, S. –Q., Zou, Y. –H., and Han, E. -H. (2017). In vitro degradation of pure magnesium—The effects of glucose and/or amino acid. *Materials, 10,* 725.
259. Lindahl, C., Engqvist, H., and Xia, W. (2013). Influence of surface treatments on the bioactivity of Ti. *Biomaterials*, 2013, Article ID 205601, 13 pages.
260. Wen, Z., Wu, C., Dai, C., and Yang, F. (2009). Corrosion behaviors of Mg and its alloys with different Al contents in a modified simulated body fluid. *Journal of Alloys and Compounds, 488,* 392–399.
261. Zeng, R. –C., Qi, W. –C., Zhang, F., and Li, S. -Q. (2016). In vitro corrosion of pure magnesium and AZ91 alloy—the influence of thin electrolyte layer thickness. *Regenerative Biomaterials, 2016,* 49–56.
262. Srinivasan, A., Blawert, C., Huang, Y., Mendis, C. L., Kainer, K. U., and Hort, N. (2014). Corrosion behavior of Mg–Gd–Zn based alloys in aqueous NaCl solution. *Journal of Magnesium and Alloys, 2,* 245-256.
263. Chelliah, N. M., Padaikathan, P., and Kumar, R. (2019). Evaluation of electrochemical impedance and biocorrosion characteristics of as-cast and T4 heat treated AZ91 Mg-alloys in Ringer's solution. *Journal of Magnesium and Alloys, 7,* 134–143.
264. El-Moneim, A. A., Ismail, K. M., and Badawy, W. A. (2014). Sputter-deposited Mg-Zr Alloys – Surface characteristics and electrochemical behavior in borate solutions. *Z. Phys. Chem., 228*(9). doi:10.1515/zpch-2014-0550.
265. Hou, R. –Q., Scharnagl, N., Willumeit-Römer, R., and Feyerabend, F. (2018). Different effects of single protein vs. protein mixtures on magnesium

degradation under cell culture conditions. *Acta Biomaterialia.* Doi:1.1016/j.actbio.2019.02.013.

266. Cordoba, L. C., Marques, A., Taryba, M., Coradin, T., and Montemor, F. (2018). Hybrid coatings with collagen and chitosan for improved bioactivity of Mg alloys. *Surface & Coatings Technology, 341,* 103–113.
267. Thomas, S., Medhekar, N. V., Frankel, G. S, and Birbilis, N. (2015). Corrosion mechanism and hydrogen evolution on Mg. *Current Opinion in Solid State and Materials Science, 19,* 85–94.
268. Zeng, R. –C., Sun, L., Zheng, Y. –F., Cui, H. –Z., and Han, E. H. (2014). Corrosion and characterisation of dual phase Mg–Li–Ca alloy in Hank's solution: The influence of microstructural features. *Corrosion Science, 79,* 69–82.
269. GururajAcharya, M., and Nityanansda Shetty, A. (2019). The corrosion behavior of AZ31 alloy in chloride and sulfate media – A comparative study through electrochemical investigations. *Journal of Magnesium and Alloys, 7,* 98–112.
270. Zheng, T., Hu, Y., and Yang, S. (2017). Effect of grain size on the electrochemical behavior of pure magnesium Anode. *Journal of Magnesium and Alloys, 5,* 404–411.
271. Srinivasan, A., Shin, K. S., and Rajendran, N. (2016). Influence of bicarbonate concentration on the conversion layer formation onto AZ31 Magnesium alloy and its electrochemical corrosion behaviour in simulated body fluid. *RSC Adv*ances, 6(55), 49910-49922.
272. Cordoba, L. C., Helary, C., Montemor, F., and Coradin, T. (2018). Bi-layered silane-TiO_2/collagen coating to control biodegradation and biointegration of Mg alloys. *Materials Science & Engineering C,* doi:10.1016/j.msec.2018.09.032.
273. Waterman, J., Birbilis, N., Dias, G. J., Woodfieldl, T. B. F., and Staiger, M. P. (2012). Improving in vitro corrosion resistance of biomimetic calcium phosphate coatings for Mg substrates using calcium hydroxide layer. *Corrosion Engineering, Science and Technology, 47*(5), 340-345.
274. Zeng, R. –C., Hu, Y., Guan, S. –K., Cui, H. –Z., and Han, E. -H. (2014). Corrosion of magnesium alloy AZ31: The influence of bicarbonate, sulphate, hydrogen phosphate and dihydrogen phosphate ions in saline solution. *Corrosion Science, 86,* 171-182.

275. Kieke, M., Feyerabend, F., Lemaitre, J., Behrens, P., and Willumeit Romer, R. (2016). Degradation rates and products of pure magnesium exposed to different aqueous media under physiological conditions. *BioNanoMaterials, 17*(3-4).

276. Williams, G., McMurray, H.N., and Grace, R. (2010). Inhibition of magnesium localised corrosion in chloride containing electrolyte. *Electrochimica Acta, 55,* 7824–7833.

277. Williams, G., and Grace, R. (2011). Chloride-induced filiform corrosion of organic coated magnesium. *Electrochimica Acta, 56,* 1894–1903.

278. Bakhsheshi-Rad, H.R., Hamzah, E., Daroonparvar, M., Ebrahimi-Kahrizsangi, R. and Medraj, M. (2014). In-vitro corrosion inhibition mechanism of fluorine-doped hydroxyapatite and brushite coated Mg–Ca alloys for biomedical applications. *Ceramics International, 40*(6), 7971–7982.

279. Lopez, A. J., Otero, E., and Rams, J. (2010). Sol-gel silica coatings on ZE41 magnesium alloy for corrosion protection. *Surface and Coatings Technology, 205*(7), 2375-2385.

280. Kheradmandfard, M., Fathi, M. H., Ahangarian, M., Mohammadi Zahrani, E. (2012). In vitro bioactivity evaluation of magnesium-substituted fluorapatite nanopowders. *Ceramics International, 38,* 169–175.

281. Pan, C. –J., Hou, Y., Wang, Y. –N., Gao, F., Liu, T., Hou, Y. –H., Zhu, Y. –F., Ye, W., and Wang, L. -R. (2016). Effects of self-assembly of 3-phosphonopropionic acid, 3-aminopropyltrimethoxysilane and dopamine on the corrosion behaviors and biocompatibility of a magnesium alloy. *Materials Science and Engineering: C, 67,* 132–143.

282. Kunjukunju, S., Roy, A., Ramanathan, M., Lee, B., Candiello, J. E., and Kumta, P. N. (2013). A layer-by-layer approach to natural polymer-derived bioactive coatings on magnesium alloys. *Acta Biomaterialia, 9,* 8690–8703.

283. Wang, H., Song, Y., Yu, J., Shan, D., and Han, H. (2017). Characterization of filiform corrosion of Mg–3Zn Mg Alloy. *Journal of the Electrochemical Society, 164*(9), C574-C580.

284. Liu, X., Zhen, Z., Liu, J., Xi, T., Zheng, Y., Guan, S., Zheng, Y., and Cheng, Y. (2015). Multifunctional MgF_2/Polydopamine Coating on Mg Alloy for Vascular Stent Application. *Journal of Materials Science & Technology, 31,* 733-743.

285. Hong, D., Chen, H. –X., Yu, H. –Q., Liang, Y., Wang, C., Lian, Q. –Q., Deng, H. –T., and Ge, R. -S. (2015). Morphological and proteomic analysis of early

stage of osteoblast differentiation in osteoblastic progenitor cells. *Exp Cell Res, 316*(14), 2291–2300.

286. Kwon, Y. –D., Lee, D. –W., and Hong, S. -O. (2014). Magnesium vs. machined surfaced titanium - osteoblast and osteoclast differentiation. *Journal of Advanced Prosthodont, 6,* 157-164.
287. Balaji Raghavendran, H. R., Puvaneswary, S., Talebian, S., Raman Murali, M., Vasudevaraj Naveen, S., Krishnamurithy, G., McKean, R., and Kamarul, T. (2014). A comparative study on in vitro osteogenic priming potential of electron spun scaffold PLLA/HA/Col, PLLA/HA, and PLLA/Col for tissue engineering application. *PLoS ONE, 9*(8), e104389.
288. Venter, C., and Niesler, C. U. (2019). Rapid quantification of cellular proliferation and migration using ImageJ. *BioTechniques, 66,* 99-102.
289. Li, Z., Huang, B., Mai, S., Wu, X., Zhang, H., Qiao, W., Luo, X., and Chen, Z. (2015). Effects of fluoridation of porcine hydroxyapatite on osteoblastic activity of human MG63 cells. *Science and Technology of Advanced Materials, 16*(3), 035006.
290. Park, J. –W., Hanawa, T., and Chung, J. -H. (2019). The relative effects of Ca and Mg ions on MSC osteogenesis in the surface modification of microrough Ti implants. *International Journal of Nanomedicine,14,* 5697–5711.
291. Anselme, K. (2000). Osteoblast adhesion on biomaterials. *Biomaterials, 21*(7), 667-681.
292. Lourenc, B. N., Marchioli, G., Song, W., Reis, R. L., Van Blitterswijk, C. A., Karperien, M., van Apeldoorn, A., and Mano, J. F. (2012). Wettability influences cell behavior on superhydrophobic surfaces with different topographies. *Biointerphases, 7*(1), 46.
293. Yen, M., Chien, C. –C., Chiu, I., Huang, H. –I., Chen, Y. –C., Hu, H. –I., and Yen, B. L. (2007). Multilineage differentiation and characterization of the human fetal osteoblastic 1.19 cell line: A possible in vitro model of human mesenchymal progenitors. *STEM CELLS, 25*(1), 125–131.
294. Subramaniam, M., Jalal, S. M., Rickard, D. J., Harris, S. A., Bolander, M. E., and Spelsberg, T. C. (2002). Further characterization of human fetal osteoblastic hFOB 1.19 and hFOB/ERa Cells: Bone formation in vivo and karyotype analysis using multicolor fluorescent in situ hybridization. *Journal of Cellular Biochemistry, 87*(1), 9–15.

295. Zouani, O. F., Rami, L., Lei, Y., and Durrieu, M. C. (2013). Insights into the osteoblast precursor differentiation towards mature osteoblasts induced by continuous BMP-2 signaling. *Biology Open, 2,* 872–881.

296. DeMali, K. A., Wennerberg, K., and Burridge, K. (2003). Integrin signaling to the actin cytoskeleton. *Current Opinion in Cell Biology, 15,* 572–582.

297. Hoffmann, B., and Schafer, C. (2010). Filopodial focal complexes direct adhesion and force generation towards filopodia outgrowth. *Cell Adhesion & Migration, 4,* 190-193.

298. Mattila, P. K., and Lappalainen, P. (2008). Filopodia: molecular architecture and cellular functions. *Nature Reviews Molecular Cell Biology, 9*(6), 446-454.

299. LEE, J. –W., LEE, K. –B., JEON, H. –S., and PARK, H. -K. (2011). Effects of surface nano-topography on human osteoblast filopodia. *Analytical Sciences, 27*(4), 369.

300. Gough, J. E., Notingher, I., and Hench, L.L. (2003). Osteoblast attachment and mineralized nodule formation on rough and smooth 45S5 bioactive glass monoliths. *Journal of Biomedical Materials Research, 68A*(4), 640-650.

301. Chen, L., Shi, K., Frary, C. E., Ditzel, N., Hu, H., Qiu, W., and Kassem, M. (2015). Inhibiting actin depolymerization enhances osteoblast differentiation and bone formation in human stromal stem cells', Stem Cell Research, 15(2), 281-289.

302. Zheng, Y., Xiong, C., Wang, Z., and Zhang, L. (2015). Enhanced osteoblast cells adhesion, spreading, and proliferation to surface-carboxylated poly(etheretherketone). *Journal of Bioactive and Compatible Polymers, 30*(3), 302-318.

303. Nagai, H., Kobayashi-Fujioka, M., Fujisawa, K., Ohe, G., Takamaru, N., Hara, K., Uchida, D., Tamatani, T., Ishikawa, K., and Miyamoto, Y. (2015). Effects of low crystalline carbonate apatite on proliferation and osteoblastic differentiation of human bone marrow cells. *Journal of Materials Science: Materials in Medicine, 26*(2), 99.

304. Harris, S. A., Enger, R. J., Riggs, L. B., and Spelsberg, T. C. (2009). Development and Characterization of a Conditionally Immortalized Human Fetal Osteoblastic Cell Line. *Journal of Bone and Mineral Research, 10*(2), 178-186.

305. Product catalog of osteoblast cell. hFOB 1.19 (ATCC® CRL11372 ™)

306. Wang, Y., Zhang, S., Zeng, X., Ma, L. L., Weng, W., Yan, W., and Qian, M. (2007). Osteoblastic cell response on fluoridated hydroxyapatite coatings. *Acta Biomaterialia, 3,* 191–197.

307. Huo, W. T., Zhao, L. Z., Yu, S., Yu, Z. T., Zhang, P. X. and Zhang, Y. S. (2017). Significantly enhanced osteoblast response to nano-grained pure tantalum. *Scientific Reports, 7*(1). doi:10.1038/srep40868.

308. Quarles, L. D., Yohay, D. A., Lever, L. W., Caton, R., and Wenstrup, R. J. (2009). Distinct proliferative and differentiated stages of murine MC3T3-El cells in culture: An in vitro model of osteoblast development. *Journal of Bone and Mineral Research, 7*(6), 683-692.

309. Liu, X., Lim, J. Y., Donahue, H. J., Dhurjati, R., Mastro, A. M., and Vogler, E. A. (2007). Influence of substratum surface chemistry/energy and topography on the human fetal osteoblastic cell line hFOB 1.19: Phenotypic and genotypic responses observed in vitro. *Biomaterials, 28*(31), 4535–4550.

310. Zhang, Z., Sun, J., Hu, H., Wang, Q., and Liu, X. (2011). Osteoblast-like cell adhesion on porous silicon-incorporated TiO_2 coating prepared by micro-arc oxidation. *Journal of Biomedical Materials Research Part B: Applied Biomaterials, 97B*(2), 224-234.

311. Jeon, H., and Kim, G. H. (2012). Effects of a Cell-Imprinted Poly(dimethylsiloxane) Surface on the Cellular Activities of MG63 Osteoblast-like Cells: Preparation of a Patterned Surface, Surface Characterization, and Bone Mineralization. *American Chemical Society, Langmuir, 28,* 13423−13430.

312. Wagener, V., Schilling, A., Mainka, A., Hennig, D., Gerum, R., Kelch, M.-L., and Virtanen, S. (2016). Cell adhesion on surface-functionalized magnesium. *ACS Applied Materials & Interfaces, 8*(19), 11998-12006.

313. Ahmad Agha, N., Willumeit-Romer, R., Laipple, D., Luthringer, B., and Feyerabend, F. (2016). The degradation interface of magnesium based alloys in direct contact with human primary osteoblast cells. *PLOS ONE, 11*(6), E0157874.

314. Jia, G., Chen, C., Zhang, J., Wang, Y., Yue, R., Luthringer - Feyerabend, B. J. C., Willumeit-Roemer, R., Zhang, H., Xiong, M., Huang, H., G., Frank Feyerabend, Y. (2018). In vitro degradation behavior of Mg scaffolds with three-dimensional interconnected porous structures for bone tissue engineering. *Corrosion Science, 144,* 301-312.

315. Xie, C., Gao, Q., Wang, P., Shao, L., Yuan, H., Fu, J., Chen, W., and He, Y. (2019). Structure-induced cell growth by 3D printing of heterogeneous scaffolds with ultrafine fibers. *Materials and Design,* 108092.
316. Keselowsky, B. G., Collard, D. M., and Garcia, A. J. (2005). Integrin binding specificity regulates biomaterial surface chemistry effects on cell differentiation. *Proceedings of the National Academy of Sciences, 102*(17), 5953-597.
317. Zeng, R. -C., Yin, Z. -Z., Chen, X. -B., and Xu, D. -K. Corrosion types of magnesium alloys. *Magnesium Alloys – Selected Issue.* doi:10.5772/intechopen.80083.
318. Tomozawa, M., and Hiromoto, S. (2011). Microstructure of hydroxyapatite- and octacalcium phosphate-coatings formed on magnesium by a hydrothermal treatment at various pH values. *Acta Materialia, 59*(1), 355-363.
319. Viti, F., Scaglione, S., Orro, A., and Milanesi, L. (2014). Guidelines for managing data and processes in bone and cartilage tissue engineering. *BMC Bioinformatics, 15*(Suppl 1), S14.
320. Bonassar, L. J., and Vacanti, C. A. (1998). Tissue engineering: the first decade and beyond. *J. Cell Biochem Suppl, 30-31,* 297-303.
321. Sikavitsas, V. I., Temenoff, J. S., and Mikos, A. G. (2001). Biomaterials and bone mechanotransduction. *Biomaterials, 22*(19) 2581–2593.
322. Petite, H., Vandamme, K., Monfoulet, L., and LogeartAvramoglou, D. (2011). Strategies for improving the efficacy of bioengineered bone constructs: A perspective. *Osteoporosis International, 22*(6) 2017–2021.
323. Shepherd, J., and Best, S. (2011). Calcium phosphate scaffolds for bone repair. *Journal of the Minerals, Metals and Materials Society, 63,* 83-92.
324. Levi, B., and Longaker M. T. (2011). Concise review: Adipose-derived stromal cells for skeletal regenerative medicine. *Stem Cells, 29,* 576-582.
325. Dhandayuthapani, B., Yoshida, Y., Maekawa, T., and Kumar, D. S. (2011). Polymeric scaffolds in tissue engineering application: a review. *International Journal of Polymer Science, 2011,* 1-19.
326. Biga, L. M. *Anatomy & Physiology, Bone Structure.* https://open.oregonstate.education/aandp/chapter/6-3-bone-structure/

LIST OF PUBLICATIONS

1. Jasmawati, N., Fatihhi, S. J., Putra, A.M.S, Ardiyansyah Syahrom, Harun, M.M., Ochsner, A., and Abdul Kadir, M.R. (2015). Mg-based porous metals as cancellous bone analogous material: A review. *J Materials: Design and Applications, 231,* 544-556.

2. Jasmawati, N., Joy, R.P., Djuansjah, Kadir, M.R.A., and Sukmana, I. (2015). Porous Magnesium Scaffolds for Bone Implant Applications: A Review. *Advanced Materials Research, 1125,* 437-440.