

# Dimitrios Agas

## Brief Curriculum vitae

### *Education:*

- **Degree** in Biological Sciences - University of Camerino (2002)
- **PhD** in Biology - University of Camerino (2006)
- **PhD** in Industrial and Environmental Hygiene – University of Rome “La Sapienza” (2009)

### *Actual Position:*

- Contract Professor of Physiology - University of Camerino, School of Biosciences and Veterinary Medicine
- Research Associate - University of Camerino, School of Biosciences and Veterinary Medicine

### *Work experience:*

- Research Associate - University of Camerino, School of Biosciences and Veterinary Medicine. Project: “Immuno-modulating activity of the plasmid coding p62: avant-garde perspective for the treatment of inflammatory bone disease.” (May 2016 - April 2019)
- Research Fellowship – University of Camerino, School of Biosciences and Biotechnology/CureLab Oncology US Project: “DNA plasmid coding p62-SQSTM1 as an antiosteoporotic vaccine.” (2013- 2016)
- Research Associate - University of Rome “La Sapienza”/University Camerino, School of Biosciences and Biotechnology Project: “Novel functional pirols with anti-inflammatory activity for the realization of bioactive nanoparticles for bone diseases (2011- 2012)
- Research Fellowship - Consortium IMPAT (Bologna, Italy). School of Biosciences and Biotechnology - University of Camerino (2010 - 2011)
- FELASA C Course on “Laboratory Animal Science IV” in the Biomedical Sciences Research Center Alexander Fleming, Vari (Greece), 2010
- Fellowship - University of Camerino, - Department of Comparative Morphology and Biochemistry - (2005-2006)
- Fellowship - University of Connecticut Health Center, Department of Medicine (Farmington CT, USA) (December, 2004 – September, 2005)
- Fellowship - University of Connecticut Health Center, Department of Medicine (Farmington CT, USA) (September 2004)
- Fellowship Global Italia Srl “Development of Methodologies related to the two-dimensional electrophoresis technology” University of Camerino - Department of Comparative Morphology and Biochemistry (April 2003)
- Fellowship - University of Camerino, Department of Comparative Morphology and Biochemistry for the (March 2003)

### *Main research activities:*

- Regulation of bone remodeling and bone marrow physiology: molecular mediators and signaling pathways involved in osteoblast precursors and bone marrow stromal/mesenchymal stem cell homeostasis.
- Stromal/mesenchymal stem cells growth and differentiation by functionalized polymers micro and nanostructured for tissue repair

### *Technology Transfer Activity and Grants:*

- Member of the selected FAR project 2014: "A p62 /SQSTM 1-coding DNA Plasmid as a Bone Effective Anabolic Agent "
- Member of Research Collaboration Agreement CureLab Oncology – University of Camerino (2013-2016)
- Member of the selected FAR project 2012: "At the Crossroad of Autophagy and Cancer: A Signaling Hub Protein p62 / SQSTM1 as Target for Breast Cancer Immunotherapy" 2011-2012
- Selected Business Plan Spin-off Dental Bioengineering Start-up – Consorzio IMPAT – Bologna 2009
- Start Cup Umbria-Marche competition 2009 (1° prize)
- IMPAT Valorization Grant: Progetto Impresa – Consorzio IMPAT – Bologna (MEIaBIO Group).
- IMPAT Valorization Grant: Progetto Impresa – Consorzio IMPAT – Bologna (O.I.D. Group).
- Project PRIN/Cofin Year 2005 protocol 2005037175-002 (Operative Unit Component).

### *Patents:*

- Agas D, Marchetti L, Panero S, Sabbieti MG, Serra Moreno J "Electroactive materials for biomedical applications" Patent Number(s): IT1408988-B Published July 16, 2014.
- Shneider A, Venanzi F, Agas D, Concetti A, Sabbieti MG, Gabai V, Sherman M, Shifrin V. "Methods and compositions relating to p62 for the treatment and prevention of inflammation-associated diseases" U.S. Patent Application No. 61/921, 504 filed on December 29, 2013.

### **Teaching activity**

#### **- Main Teaching Activity:**

#### **University of Camerino**

- 2014/2015 **Physiology** module (6 CFU) L-BB - BIOSCIENCES AND
- 2015/2016 BIOTECHNOLOGY L-13 (Integrate with Anatomy and Physiology)
- 2016/2017 -School of Bioscience and Veterinary Medicine - University of Camerino
- 2017/2018 **Physiology** (6 CFU) L-BB - BIOSCIENCES AND
- 2018/2019 BIOTECHNOLOGY L-2 - School of Bioscience and Veterinary Medicine - University of Camerino

#### **University of Genova**

- 2017/2018 **Cellular Aspects of Biomodulation** - Master in Laser dentistry (1 CFU)
- 2018/2019

- Other Teaching Activity:

- 2013 - 2014 **General Biology Laboratory I** in the Laboratory I course [ST0009]
- 2010 - 2012 Theoretical and practical laboratories in the course **Laboratory I & II** (Mod.Cell Biotechnology) (School of Bioscience and Biotechnology)
- 2007 - 2009 Theoretical and practical laboratories in the course **Structure and Functions of Cells and Tissues** (Faculty of Bioscience and Biotechnology)
- 2007 - 2009 Theoretical and practical laboratories in the course **Genetics and molecular techniques in the alimentary field** (Faculty of Bioscience and Biotechnology)

Expert in the field and exam committee member:

- From 2011 – **Stem cells technologies and Animal models** - School of Bioscience and Veterinary Medicine - [ST0539] [LM-BS] 12CFU University of Camerino
- 2005-2008 - **Animal Biology** - Faculty of Pharmacy, University of Camerino
- 2008 **Structure and Functions of Cells and Tissues** - Faculty of Bioscience and Biotechnology, University of Camerino

*Co-Supervisor of Master Degree Thesis in Biological Sciences (LM-6) - Molecular Diagnostics and Biotechnology:*

2011 - 2018

- “Sequestosome 1/p62 regulates differentiation of bone marrow-derived mesenchymal stem cells” Candidate: Ali Dawood
- “P(HPMAm-lac)-PEG hydrogels hybridized with hyaluronan improves cartilage repair in a mouse model of collagen-induced arthritis” Candidate: Jiadila Hairula
- “Aggregating protein domains affect immunity and bone homeostasis in mice” Candidate: Elisabetta Polimanti
- “Plasmid DNA-coding p62: a new therapeutic approach in osteoporosis” Candidate: Giovanna Lacava
- “Ectopic trabecular bone formation in Poly-Q disease”. Candidate: Luca Vagni
- “Complexity and perplexity of proteotoxicity of adjuvants, used for DNA vaccination, in bone metabolism”. Candidate: Simone Compagnoni
- BMP2 differentially modulates FGF-2 isoform effects in osteoblasts”. Candidate: Luca Di Blasio

*Supervisor of Bachelor Degree (Final elaboration) in Biosciences and Biotechnology (classe L2-L13) Curriculum: Biotechnology/Biology*

2014 - 2018

- “Effects of Plasmid Encoding INF- $\gamma$  on Bone and Bone Marrow Niches” Candidate: Francesca Basha
- “Hydrogels hybridized with hyaluronans as promising anti-inflammatory compounds” Candidate: Abir Hussein
- Approaches for analysis of Bone Marrow Adiposity in a mouse model of osteoporosis” Candidate: Cristina Fracassi
- “Effect of low-level laser therapy on stromal stem cell growth and differentiation” Candidate: Simona Renzi
- “The effects of photobiomodulation of 980nm diode laser therapy on osteoblast maturation” Candidate: Dimitra Kesis
- “p62 deficiency shifts mesenchymal stem cell commitment toward adipogenesis and disrupts bone marrow homeostasis in aged mice” Candidate: Anita Mehrdadian
- “Prevalence of different genotypes of HPV between the province of Chieti and Europe” Candidate: Nicolle Zandaly Nieto Rodriguez
- “Morphological characteristics of bone marrow in FGF2 isoforms null mice” Candidate: Moming Aizimaiti
- “Importance of p62 in mesenchymal/stromal stem cell maintenance and differentiation” Candidate: Anxhela Braho
- “p62 Deficiency Enhances Inflammatory Response in Bone Marrow” Candidate: Casey Mitchell

## Articles in Peer-Reviewed International Journals

1. Lacava G, Laus F, Amaroli A, Marchegiani A, Censi R, Di Martino P, ...Agas D. (2019) P62 deficiency shifts mesenchymal/stromal stem cell commitment toward adipogenesis and disrupts bone marrow homeostasis in aged mice. *J. Cell. Physiol.* [e-pub ahead of print]
2. Hanna R, Agas D, Benedicenti S, Ferrando S, Laus F, Cuteri V, Lacava G, ... (2019) A comparative study between the effectiveness of 980nm photobiomodulation delivered by hand-piece with Gaussian versus flat-top profiles on osteoblasts maturation. *Front Endocrinol.* 10:92
3. Agas D, Lacava G, Sabbieti MG. (2019) Bone and bone marrow disruption by endocrine-active substances. *J. Cell. Physiol* 234:192-213
4. Amaroli A, Agas D, Laus F, Cuteri V, Hanna R, Sabbieti MG, Benedicenti S. (2018) The Effects of Photobiomodulation of 808 nm Diode Laser Therapy at Higher Fluence on the in Vitro Osteogenic Differentiation of Bone Marrow Stromal Cells. *Front Physiol.* 2018 Feb 23;9:123. doi: 10.3389/fphys.2018.00123. eCollection
5. Sabbieti MG, Lacava G, Amaroli A, Marchetti L, Censi R, Di Martino P, Agas D. (2018) Molecular Adjuvants Based On Plasmids Encoding Protein Aggregation Domains Affect Bone Marrow Niche Homeostasis. *Curr Gene Ther.* 17:391-397
6. Sabbieti MG, Marchetti L, Censi R, Lacava G, Agas D. (2017) Role of PTH in Bone Marrow Niche and HSC Regulation. *Current Stem Cell Reports* 3: 210-217
7. Agas D, Gusmão Silva G, Laus F, Marchegiani A, Capitani M, Vullo C, Catone G, Lacava G, Concetti A, Marchetti L, Sabbieti MG. (2017) INF- $\gamma$  encoding plasmid administration triggers bone loss and disrupts bone marrow microenvironment. *J Endocrinol.* 232:309-321
8. Di Martino P, Censi R, Gigliobianco MR, Zerrillo L, Magnoni F, Agas D, Quaglia W, Lupidi G. (2017) Nano-medicine improving the bioavailability of small molecules for the prevention of neurodegenerative diseases. *Curr Pharm Des.* 23(13):1897-1908
9. Sabbieti MG, Dubbini A, Laus F, Paggi E, Marchegiani A, Capitani M, Marchetti L, Dini F, Vermonden T, Di Martino P, Agas D, Censi R. (2016) In vivo biocompatibility of p(HPMAm-lac)-PEG hydrogels hybridized with hyaluronan. *J Tissue Eng Regen Med.* Oct 24. doi: 10.1002/term.2207
10. Agas D, Concetti F, Capitani M, Lacava G, Concetti A, Marchetti L, Laus F, Marchegiani A, Azevedo V, Sabbieti MG, Venanzi FM (2016) Administration of DNA Plasmid Coding Protein Aggregating Domain Induces Inflammatory Bone Loss, *Curr Gene Ther.* 16:144-52
11. Dubbini A, Censi R, Butini ME, Sabbieti MG, Agas D, Vermonden T, Di Martino P (2015) Injectable hyaluronic acid/PEG-p(HPMAm-lac)-based hydrogels dually cross-linked by thermal gelling and Michael addition. *Eur Pol J,* 72: 423-437.
12. Sabbieti MG, Agas D, Capitani M, Marchetti L, Concetti A, Vullo C, Catone G, Gabai V, Shifrin V, Sherman MY, Shneider A, Venanzi FM (2015) Plasmid DNA-coding p62 as a bone effective anti-inflammatory/anabolic agent. *Oncotarget,* 6: 3590-3599.
13. Agas D, Marchetti L, Douni E, Sabbieti MG. (2015) The unbearable lightness of bone marrow homeostasis. *Cytokine Growth Factor Rev,* 26:347-59.
14. Capitani M, Saade F, Havas KM, Angeletti M, Concetti F, Agas D, Sabbieti MG, Concetti A, Venanzi FM, Petrovsky N. (2014) Plasmids encoding protein aggregation domains act as molecular adjuvants for DNA vaccines. *Curr Gene Ther.* 3:161-169.
15. Serra Moreno J, Sabbieti MG, Agas D, Marchetti L, Panero S. (2014) Polysaccharides immobilized in polypyrrole matrices are able to induce osteogenic differentiation in mouse mesenchymal stem cells. *J Tissue Eng Regen Med.* 8:989-99.
16. Agas D, Marchetti L, Capitani M, Sabbieti MG. (2013) The dual face of parathyroid hormone and prostaglandins in the osteoimmune system. *Am J Physiol Endocrinol Metab.* 10:E1185-94.
17. Sabbieti MG, Agas D, Marchetti L, Coffin DJ, Xiao L, Hurley MM (2013) BMP-2 differentially modulates FGF-2 isoform effects in osteoblasts from newborn transgenic mice. *Endocrinology* 154:2723-2733.
18. Agas D, Sabbieti MG, Marchetti L, Xiao L, Hurley MM. (2013) FGF-2 enhances Runx-2/Smads nuclear localization in BMP-2 canonical signaling in osteoblasts. *J Cell Physiol.* 228:2149-2158.
19. Agas D, Sabbieti MG, Marchetti L. (2013) Endocrine disruptors and bone metabolism. *Arch Toxicol.* 87:735-751.

20. Agas D, Marchetti L, Hurley MM, Sabbieti MG. (2013) Prostaglandin F2 $\alpha$ : a bone remodeling mediator. *J Cell Physiol.* 228:25-9.
21. Serra Moreno J, Agas D, Sabbieti MG, Di Magno M, Migliorini A, Loreto MA. (2012) Synthesis of novel pyrrolyl-indomethacin derivatives. *Eur J Med Chem.* 57:391-7.
22. Sabbieti MG, Agas D, Palermo F, Mosconi G, Santoni G, Amantini C, Farfariello V, Marchetti L. (2011) 4-nonylphenol triggers apoptosis and affects 17- $\beta$ -estradiol receptors in calvarial osteoblasts. *Toxicology* 290:334-341.
23. Sabbieti MG, Agas D, Maggi F, Vittori S, Marchetti L. (2011) Molecular mediators involved in *Ferulago campestris* essential oil on osteoblast metabolism. *J. Cell. Biochem.* 112:3742-54.
24. Sabbieti MG, Agas D, Marchetti L., Santoni G, Amantini C, Xiao L, Menghi G, Hurley MM (2010) Signaling pathways implicated in PGF2 $\alpha$  effects on Fgf2 $^{+/+}$  and Fgf2 $^{-/-}$  osteoblasts. *J. Cell. Physiol.* 224:465-474.
25. Capacchietti M, Sabbieti MG, Agas D, Materazzi G, Menghi G, Marchetti L (2009) Ultrastructure and lectin cytochemistry of secretory cells in lingual glands of the Japanese quail. *Histol. & Histopathol.* 24:1087-96.
26. Sabbieti MG, Agas D, Santoni G, Menghi G, Materazzi S, Marchetti L. (2009) Involvement of p53 in phthalate effects on mouse and rat osteoblasts. *J. Cell. Biochem.* 107:316-27.
27. Sabbieti MG, Agas D, Xiao L, Marchetti L, Coffin JD, Doetschman T, Hurley MM (2009) Endogenous FGF-2 is critically important in PTH anabolic effects on bone. *J. Cell. Physiol.* 219:143-51.
28. Serra Moreno J, Panero S, Materazzi S, Martinelli A, Sabbieti MG, Agas D, Materazzi G. (2009) Polypyrrole-polysaccharide thin films characteristics: Electrosynthesis and biological properties *J. Biomed. Mater. Res. A* 88:832-40.
29. Sabbieti MG, Agas D, Materazzi S, Capacchietti M, Materazzi G, Hurley MM, Menghi G, Marchetti L. (2008) Prostaglandin F2 $\alpha$  involves heparan sulphate sugar chains and FGFRs to modulate osteoblast growth and differentiation. *J. Cell. Physiol.* 217:48-59.
30. Naganawa T, Xiao L, Coffin JD, Doetschman T, Sabbieti MG, Agas D, Hurley MM. (2008) Reduced expression and function of bone morphogenetic protein-2 in bones of Fgf2 null mice. *J. Cell. Biochem.* 103:1975-88.
31. Agas D, Marchetti L, Menghi G, Materazzi S, Materazzi G, Capacchietti M, Hurley MM, Sabbieti MG (2008) Anti-apoptotic Bcl-2 enhancing requires FGF-2/FGF receptor 1 binding in mouse osteoblasts *J. Cell. Physiol.* 214:145-52.
32. Agas D, Sabbieti MG, Capacchietti M, Materazzi S, Menghi G, Materazzi G, Hurley MM, Marchetti L. (2007) Benzyl butyl phthalate influences actin distribution and cell proliferation in rat Py1a osteoblasts *J. Cell. Biochem.* 101:543-551.
33. Naganawa T, Xiao L, Abogunde E, Sobue T, Kalajzic I, Sabbieti MG, Agas D, Hurley MM. (2006): In vivo and in vitro comparison of the effects of FGF-2 null and haplo-insufficiency on bone formation in mice. *Biochem. Biophys. Res. Commun.* 339: 490-498.
34. Marchetti L, Sabbieti MG, Agas D, Menghi M, Materazzi G, Menghi G, Hurley MM. (2006) PGF2 $\alpha$  increases FGF-2 and FGFR2 trafficking in Py1a rat osteoblasts via clathrin independent and importin  $\beta$  dependent pathway. *J. Cell. Biochem.* 97:1379-1392.

#### **Book chapter:**

Marchetti L., Sabbieti M.G., Agas D. (2012) Phthalate esters: bioaccumulation and intracellular signal modifications in in vivo and in vitro models. Book title - Phthalates: Chemical Properties, Impacts on Health and the Environment - In: Nova Science Publishers, Inc. (2012) ISBN: 978-1-62081-994-4

## Proceedings:

- I. Agas D., Sabbieti M.G., Xiao L., Naganawa T., Hurley M.M. (2005): Endogenous FGF2 is critically important in PTH induction of Bcl2, phosphorylation of CREB and Runx2 nuclear accumulation in osteoblasts. *J. Bone Miner. Res.* 20-9 Suppl. 1, S71
- II. Agas D. Sabbieti M.G. Marchetti L. (2011) PGF2 $\alpha$  activates DNA damage check-point molecules on osteoblasts. *Eur. J. Histochem.* 55, Suppl.1, 14
- III. Sabbieti M.G., Agas D., Hurley M.M., Xiao L., Marchetti L. (2011) Runx/Smads interaction is impaired in osteoblasts from Fgf2 $^{-/-}$  mice. *Eur. J. Histochem.* 55, Suppl.1, 20
- IV. Marchetti L., Agas D., Sabbieti M.G. (2011) Heparan sulphate sugar chains are involved in PGF2 $\alpha$  - induced osteoblast growth and differentiation mice. *Eur. J. Histochem.* 55 Suppl.1, 21
- V. V. Censi R., Dubbini A., Gigliobianco M.R., Magnoni F., Sabbieti M.G., Agas D., Laus F., Paggi E., Marchegiani A., Di Martino P. (2015) In-situ Dually Cross-linked Hybrid Hyaluronan/p(HPMAm-lac)-PEG Hydrogels for Protein Release and Tissue Engineering. Proceeding of 10th Anniversary Conference of the Hellenic Society for Biomaterials 10th Anniversary Conference of the Hellenic Society for Biomaterials Athens Greece November 26-28 pp 1-1
- VI. Censi R., Dubbini A., Hennink WE., Vermonden T., Sabbieti MG., Agas D., Laus F., Paggi E., Marchegiani A., Di Martino P. (2015) Novel Injectable Hybrid Hydrogels As Biocompatible And Biodegradable Matrices For Pharmaceutical And Biomedical Applications. SIB Società Italiana Biomateriali. Atti SIB, Conferenza Società Italiana Biomateriali, Portonovo, Ancona June 03-05 Società Italiana Biomateriali pp1-1
- VII. Censi R., Sabbieti M.G., Dubbini A., Laus F., Paggi E., Marchegiani A., Agas D., Di Martino P. (2016) In-vivo biocompatibility of p(HPMA-lac)-PEG hydrogels hybridized with hyaluronan.
- VIII. 4th Congress on Innovation in Drug Delivery, Site-Specific Drug Delivery. Antibes-Juan-les Pins France September 25-28 pp1-1