

Course title: Molecular biology of mineralized tissues

Department: Center for Translational and Clinical Research, Department of Proteomics, School of Medicine, University of Zagreb, Zagreb, Croatia

Address : Salata 3, 10000 Zagreb

Total ECTS points: 5,0

Course leader : prof Lovorka Grgurevic, MD, PhD

Course associates : prof. Darko Bozic, Rudjer Novak PhD, prof Robert Likic, MD, PhD

Teaching plan

	No. classes
Lecture	10
Seminar	5
Practical	10
Total	25

1 class = 45 minutes

Course description:

The postgraduate course Molecular Biology of Mineralized Tissues brings the latest knowledge and new therapeutic approaches in the field of bone regeneration and metabolism. Participants will be informed with the basic structure of the skeletal system, in more detail with a review of recent research by lecturers as well as those in the world. They will be shown all the available technologies used in the discovery of new markers of both bone remodeling and regeneration. New insights into the molecular pathways involved in tooth growth and development and specific pathological processes will be covered in particular detail. Emphasis will be on new research leading to the regeneration of the bones of the upper and lower jaw and the analysis of saliva as a biological sample subject to numerous changes, including mechanical stimulation. We will introduce students with the procedure in drug development, especially relying on innovation and research of course leaders, conducting clinical studies and go through a whole series of steps that lead to the placement of the drug on the market. We will explain the concept of innovation through the design of new devices for bone regeneration.

Learning outcomes

1. Describe the structure of the skeletal system with emphasis on the difference of bone tissue types
2. Identify the main mechanisms of bone remodeling
3. Recall the key signaling molecules of bone metabolism and their role
4. Connect the acquired knowledge about the regeneration of periodontal tissues
5. State the basic principle of proteomic analysis
6. Sketch the events that take place during orthodontic dental displacement
7. Discuss problems and unknowns related to the analysis of biological fluids in the detection of markers of changes in bone metabolism

8. Explain the basic steps that are crucial in the development of a new drug related with the field of bone regeneration and placing it on the market

Course content

Lecture

	Lecture topics	Number of classes/hours
1.	- Anatomy of the skeletal system	2
2.	- Molecular basis of the structure of the skeletal system	2
3.	- The role of bone morphogenetic proteins in the process of cementogenesis. Implications for periodontal tissue regeneration	2
4.	- Molecular dilemmas in the identification of markers of bone metabolism disorders	2
5.	- Establishing a new drug on the market: from invention to application	2
6.	-	-
7.	-	-
8.	-	-
9.	-	-
10.	-	-

1 sat = 45 minuta

Seminari

	Seminar topics	Number of classes/hours
1.	-Examination of macroscopic and microscopic structure of the skeletal system	1
2.	- Bone remodeling	1
3.	- Proteomic methods in bone tissue analysis	1
4.	- Therapeutic use of bone morphogenetic proteins	1
5.	- Biological basis of orthodontic tooth displacement	1
6.	-	-
7.	-	-
8.	-	-
9.	-	-
10.	-	-

1 sat = 45 minuta

Vježbe

	practicals topics	Number of classes/hours
1.	-Differences in the type and structure of bone tissue	2
2.	- methods of preparation of bone tissue for analysis	2
3.	- isolation of biologically active molecules	2
4.	- basics of proteomic analysis related to the skeletal system	2
5.	- basic principles of in vivo testing of biologically active molecules	2
6.	-	-
7.	-	-
8.	-	-
9.	-	-
10.	-	-

1 class = 45 minutes

Literature

1. Duale Reihe: Anatomija, (ur. hrv. izdanja: V. Katavić, Z. Petanjek, I. Vinter) Medicinska naklada Zagreb, 2018. – temeljni udžbenik po kojemu je koncipiran plan i program.
2. Platzer W. i sur.: Priručni anatomski atlas (3 dijela), (ur. hrv. izdanja: I. Vinter) Medicinska naklada Zagreb, 2011. – didaktički izvrsno organiziran udžbenik koji sadrži i osnovne sheme anatomskih struktura te predstavlja spoj udžbenika i anatomskeg atlasa. Može se dodatno koristiti uz temeljni udžbenik i atlas.
3. Bone Morphogenetic Proteins: System Biology Regulators (Editors: Vukicevic S, Sampath KT), Springer International Publishing AG, 2017.
4. Vukicevic S, Oppermann H, Verbanac D, Jankolija M, Popek I, Curak J, Brkljacic J, Pauk M, Erjavec I, Francetic I, Domic-Cule I, Jelic M, Durdevic D, Vlahovic T, Novak R, Kufner V, Bordukalo Niksic T, Kozlovic M, Banic Tomisic Z, Bubic-Spoljar J, Bastalic I, Vikic-Topic S, Peric M, Pecina M, Grgurevic L. The clinical use of bone morphogenetic proteins (BMPs) revisited: A novel BMP6 biocompatible carrier device OSTEOGROW for bone healing. *International Orthopaedics* 38:635-47, 2014.
5. Grgurević L, Christensen GL, Schulz T, Vukicevic S: Bone morphogenetic proteins in inflammation, glucose homeostasis and adipose tissue energy metabolism. *Cytokine and Growth Factor Reviews* 27:205-118, 2016
6. BMP3 Affects Cortical and Trabecular Long Bone Development in Mice. Ivan Banovac , Lovorka Grgurevic , Viktorija Rumenovic , Slobodan Vukicevic, Igor Erjavec. *Int. J. Mol. Sci.* 2022, 23, 785. <https://doi.org/10.3390/ijms23020785>
7. Bozic D, Grgurevic L, Erjavec I, Brkljacic J, Orlic I, Razdorov G, Grgurevic I, Vukicevic S, Plancak D. The proteome and gene expression profile of cementoblastic cells treated by bone morphogenetic protein-7 in vitro. *Journal of Clinical Periodontology* 39:80-90, 2012.

8.Vojka Zgombić Popović, Lovorka Grgurević, Vladimir Trkulja, Ruđer Novak, Dubravka Negovetić-Vranić. The Role of New Technologies in Defining Salivary Protein Composition Following Placement of Fixed Orthodontic Appliances – Breakthrough in the Development of Novel Diagnostic and Therapeutic Procedures. *Acta Clin Croat* 2020; 59:480-488. doi: 10.20471/acc.2020.59.03.12

CV (*curriculum vitae*) and bibliography of course leader

PERSONAL INFORMATION

Name and Family Name: Lovorka Grgurevic,

Scientific Personal Identification Number: 227434

WEBpages: <https://www.bib.irb.hr/pregled/znanstvenici/227434>

<https://scholar.google.hr/citations?user=804trCoAAAAJ&hl=hr>

h-index: 22, i10 index 34, total number of citations: 2585/January2022

URL for web site: <https://www.bib.irb.hr/pregled/znanstvenici/227434>

<https://scholar.google.hr/citations?user=804trCoAAAAJ&hl=hr>

Inventor on 12 patent applications

EDUCATION

2007 PhD at the University of Zagreb School of Medicine (UZSM)

2005 Msc at the UZSM

1997 MD, UZSM

CURRENT POSITION

2019 – Full Professor, Department of Anatomy, UZSM

2018 – Associate member, Department of Medical Sciences, **Croatian Academy of Sciences and Arts**

2016 – Head of the Department of Proteomics, Center for Translational and Clinical Research, UZSM

PREVIOUS POSITIONS

2013 – 2019 Associate Professor of Anatomy, UZSM

2013 – 2019 Head of the Department of Anatomy, UZSM

2010 Associate Professor at the University of Applied Health Sciences (UAHS), Zagreb

2008 – 2013 Assistant Professor of Anatomy at the UZSM

2007 Senior Instructor of Anatomy at the UZSM

2000 Teaching Assistant of Anatomy, UZSM

1998 Professional Associate of Anatomy UZSM

FELLOWSHIPS AND AWARDS

2018 “Let the Stars Shine” tribute awarded by nine Members of the European Parliament to the EU Project Osteogrow team and the presentation of the Project in the EU Parliament, Bruxelles, Belgium

2017 Award for the most noticed professional achievement in 2016th, Croatian Medical Chamber

2016 Highest scientific and art accomplishment award in the year 2015 in the medical research field for the scientific achievement of the great importance, Croatian Academy of Sciences and Arts

2014 Acknowledgement for the innovative and creative contribution in the research of bone morphogenetic proteins, Scientific Board of the 10th International Conference on Bone Morphogenetic Proteins, Berlin

2014 publication Domic-Cule I, Draca N, Tikvica Luetic A, Jezek D, Rogic D, Grgurevic L, Vukicevic S. TSH prevents bone resorption and with calcitriol synergistically stimulates bone formation in rats with low levels of calciotropic hormones. *Horm Metab Res*, 46: 305-312, 2014; was presented on the cover page.

2011 publication Grgurevic L, Macek B, Healy DR, Brault AL, Erjavec I, Cipic A, Grgurevic I, Rogic D, Galesic K, Brkljacic J, Stern-Padovan R, Paralkar VM, Vukicevic S. Circulating bone morphogenetic protein 1-3 isoform increases renal fibrosis. *Journal of the American Society of Nephrology* 22:681-9, 2011. Was introduced by the editor Hirokazu Okada: Tolloid-like Proteinases Orchestrate Extracellular Matrix Formation, Department of Nephrology, Faculty of Medicine, Saitama Medical University, Japan.

2010 European Science Foundation Travel Award (sponsored by Remedic Network Programme) for participation on 8th International Conference on Bone Morphogenetic Proteins. Leuven, Belgium.

2009 publication: Andriopoulos Jr B, Corradini E, Xia Y, Faasse SA, Chen S, Grgurevic L, Knutson MD, Pietrangelo A, Vukicevic S, Lin HY, Babitt JL. BMP-6 is a Key Endogenous Regulator of Hepcidin Expression and Iron Metabolism. *Nature Genetics* 41:482-487, 2009 was presented on the cover page.

2009 European Calcified Tissue Society Travel Award 36th European Symposium on Calcified Tissues. Vienna, Austria.

2008 UZSM Award for the best PhD Thesis in the School year 2007/2008

SUPERVISION OF DOCTORAL AND POSTDOCTORAL STUDENTS

2010 – 2022; Supervised 9 PhD students and currently supervising 5 PhD candidates. Currently supervising 4 postdocs. Organization: UZSM.

TEACHING ACTIVITIES

2019- Full professor of the graduate course “Anatomy and Clinical Anatomy” in Croatian and English language, UZSM

2017- Lecturer, postgraduate course “Structure 2”, UZSM

2014- Lecturer, postgraduate course “Basic and Applied Sciences in the Orthopaedics and Traumatology”, UZSM

2013- Lecturer, postgraduate course “Biochemical Methods in Biomedical Research, UZSM

2012- Coordinator of the graduate course “Molecular Biology of Mineralized Tissues”; University of Zagreb School of Dental Medicine

2012- Lecturer, postgrad. course “Physical Medicine and Rehabilitation”; UZSM

2011- Lecturer, postgrad. course “Bone Morphogenetic Proteins and Regeneration”, UZSM

2010- Lecturer, course “Functional Anatomy of the Locomotor System”, UAHS

2008- Coordinator of the postgrad. course “Proteomics in Biomedical Research” UZSM

2008- Lecturer, postgrad. course “Methods of Molecular Biology in Medicine”, UZSM

2003 - 2005 - Module “Rational drug application” and “Musculoskeletal diseases”, UZSM

2003 – 2008 - Lecturer, elective course „Bone“, UZSM

1998– Lecturer graduate course “Anatomy and Clinical Anatomy” for Croatian and English medical study at UZSM and students of School of Dental Medicine University of Zagreb

List of projects (19 projects in total)

2018-2022 EU funded HORIZON 2020 project: „OSTEOproSPINE - Novel Bone Regeneration Drug Osteogrow: Therapeutic Solution for Lumbar Back Pain“, PI: S. Vukicevic, funds: 6 million EUR, team member (TM) and principal investigator (PI) of the Work Package 5 (WP5). <https://osteoprospline.eu/>

2017-2022 EU and Croatian Ministry of Science, Education and Sports funded project “Reproductive and Regenerative Medicine- research of new platforms and potentials”, Scientific Centre of Excellence, funds: 37,999 million HRK, TM and PI of the antifibrotic program. <http://cermm.hr/>

2018 and 2019 University of Zagreb Research Support, funds: 25.000,00 HRK and 37.000,00 HRK, PI.

2017-2019 Donation of the Adris Foundation for the project: New markers for the detection and monitoring of breast tumors - BIOBREAST, funds: 90.000,00 HRK, PI. <https://www.adris.hr/odnosi-s-javnosc/zaklada-adris/istaknuti-projekti/novi-markeri-za-otkrivanje-i-pracenje-tumora-dojke-biobreast/>

Participation on the Croatian Science Foundation funded projects (state your role in the project (Principal Investigator/team member), most important publications and most important results)

2016-2018 “Newly discovered BMP1 circulating isoforms as biomarkers and therapeutic targets for human diseases BMP1-IsoFor”, funds: 0,999 million HRK, PI. <https://mef.unizg.hr/znanost/istrazivanje/web-stranice-projekata/projekt-hrzz-bmp1-isofor;>

Publication: Grgurevic L et al. Growth Factors. 2017 Dec;35(6):201-215.

Most important result: in-house produced monoclonal anti-BMP1 antibody treats experimental fibrosis.

2011-2014 “A novel anabolic targeted therapy for osteoporosis: BONE6-BIS consortium, PI: S. Vukicevic, funds: 1,4398 million HRK, TM. <http://stariweb.mef.hr/druga.php?grupa=051104010100>

Publication: Dumic-Cule, I. et al. International Orthopaedics (2015) 39: 1005.

Most important result: BMP6 showed great potential for the repair of segmental bone defects. We continued to develop the BMP6 based bone-healing device, which is currently in phase II clinical trial

INSTITUTIONAL RESPONSIBILITIES

2015- Member of the Intellectual Property Management Committee, UZSM

2015- Vice President of the Student’s Research Evaluation Committee, UZSM

2013- Member of the Committee for the recruitment of officers and employees, UZSM

2013- Member of the Animal Welfare Working Group, UZSM

2010 – 2015 President of the Student’s Research Evaluation Committee, UZSM

2010 – 2011 Member of the Committee for the selection of students for the Graduate Studies in English, UZSM

MEMBERSHIPS:

2019- Foundation “Mila For All” Council, member

2015 – 2018 Vice president of the Croatian Calcified Tissues Society

2014- Croatian society for the study of laboratory animals, member

2002- Croatian Calcified Tissues Society, member

2001- European Calcified Tissue Society, member

2000- Croatian Association of Anatomy, Embryology and Histology, member

1998- Croatian Medical Association, member

Editorial Board Member: South European Journal of Orthodontic and Dentofacial research; EC orthopedics editorial panel E (cronicon); Acta pharmaceutica; Surgical and radiological anatomy; Clinical Case Reports

CAREER BREAKS: Maternity leaves: April 1st 1999–May 18th 2000 // May 30th 2006 – July 12th 2007 // October 15th 2011–April 12th 2012.

Bibliography

URL for web site: <https://www.bib.irb.hr/pregled/znanstvenici/227434>

<https://scholar.google.hr/citations?user=804trCoAAAAJ&hl=hr>